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Eman N AlBastaki, Aysha E AlMadani, Jamil Ahmed

**IN THE NAME OF ALLAH,  
THE MOST GRACIOUS,  
THE MOST MERCIFUL**



Kingdom of Saudi Arabia  
Ministry of Education  
Majmaah University



# MJHS

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# Majmaah Journal of Health Sciences

### Vision

The Majmaah Journal of Health Sciences shall be an international peer reviewed journal, which intends to serve researchers through prompt publication of significant advances, and to provide a forum for the reporting and discussion of news and issues concerning health sciences.

### Mission

To lead the debate on health and to engage, inform, and stimulate the academicians, researchers, and other health professionals in ways that will improve outcomes for patients.

### Objectives

- To promote research & evidence based practice in health sciences, so that a firm scientific knowledge base is developed, from which more effective practice may be evolved.
- To ensure that the results of the research are rapidly disseminated to the practicing clinicians and educators, in a fashion that conveys their significance for knowledge, culture and daily life.

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**Majmaah University, Post Box 66, AlMajmaah 11952, KSA**

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## Editorial

From Editor's Desk.....



At the outset let me express my gratitude to our beloved Rector Dr. Khalid Bin Saad Al Meqrin and Vice Rector for Graduate Studies and Scientific Research Prof. Dr. Mohammad Bin Abdullah Al-Shaaya for the trust endowed upon me.

MJHS is proud to bring forth its second issue of Vol 8:2020. The editorial team strives hard to publish the issues on time; I express my sincere thanks to the international panel of experts and team of Associate Editors for their efforts to improve the publication process of MJHS office.

MJHS in middle of this Global pandemic outbreak of COVID 19 take this opportunity to assist health workers and researchers working under challenging conditions to bring this outbreak to a close by considering the researches related to COVID 19 with prime importance and publishing it as soon as possible without any delay.

As you know the saying “An investment in knowledge always pays the best interest”, this journal is meant for disseminating the knowledge, ideas and experiences through scientific articles. Authors who are submitting their research in MJHS are encouraged to enrich their scientific contributions by plagiarism checking and get their manuscripts professionally edited prior to submission; especially the authors for whom English is a second language. However, the language editing does not guarantee publication and any costs incurred are the sole responsibility of the author.

The editorial team would like to thank all authors, reviewers, readers for your continuous support for the success of MJHS.

**Dr.Khalid Mohammed Alabdulwahhab**

**Editor in Chief**



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## Original article

# Correlates of psychiatric morbidity among Pakistani medical students: A cross sectional survey

Rafia Zubair,<sup>1</sup> Umar Farooq Dar<sup>2</sup>.

1. MBBS Student, Gujranwala medical college, Gujranwala, Pakistan

2. Assistant professor, Department of family and community medicine, College of medicine, Jouf University, KSA

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Corresponding author: Dr. Umar Farooq Dar, FCPS (Community medicine)

Assistant professor (Department of family and community medicine,  
College of medicine, Jouf University, KSA)

Email:ufdar@ju.edu.sa

## ABSTRACT

### Aim & Background:

Cultural variations among medical students is one of the factors causing stress and psychological morbidity. This study was carried out to determine presence of psychological morbidity and its association with different sociodemographic characteristics among medical students of a public sector college.

### Methods:

This cross-sectional study was carried out in Gujranwala Medical College, Gujranwala. Eighty-six students out of one hundred selected students by simple random sampling completed the self-administered proforma. It contained socio demographic profile, 12-item General Health Questionnaire (GHQ-12) and standardized sources of academic stress. Psychological morbidity or stress was labelled if student scored GHQ score  $\geq 21$ .

### Results:

Twenty-three students (26.7%) were GHQ-12 cases (i.e., scored  $\geq 21$ ) i.e. suffering from severe stress. Among these students, majority were female (73.91%), in their clinical years (73.91%) and living in hostel (56.52%). Academic concerns and psychosocial factors like feeling of being lonely, mood swings and being worried about expectations of parents were major stressors among all the students. Hostelers were worried about the quality of food in mess and feeling of homesickness.

### Conclusion:

It is noteworthy, that in our study population, academic demands were additional sources of psychological morbidity besides other personal and psychosocial issues. It is the need of the hour to intervene at the psychological, social and academic level to improve the quality of life for medical students. This will help in avoiding many psychological problems in the future.

**Keywords:** Academic stress, psychiatric morbidity, medical students, medical education, GHQ 12,

## الملخص

### خلفية البحث و الهدف:

الاختلافات الثقافية بين طلاب الطب هي واحدة من العوامل التي تسبب التوتر والاعتلال النفسي. لقد أجريت هذه الدراسة لتحديد وجود اعتلال نفسي و مدى ارتباطه مع الخصائص الاجتماعية والديموغرافية المختلفة لطلاب الطب في الكلية الحكومية.

طريقه: أجريت هذه الدراسة المقطعية في كلية الطب بمدينة جوجرانوالا، والتي كانت في صورة استبيان ذاتي الإداره، عدد ستة وثمانون طالباً من بين مائة طالب تم اختيارهم عن طريقأخذ عينات عشوائية بسيطة. احتوى الاستبيان على المعلومات الديموغرافية والاجتماعية، ١٢ بندًا الخاصة باستبيان الصحة العامة (GHQ-12) والمصادر القياسية للتوتر الأكاديمي. تم حديد التوتر والاعتلال النفسي إذا سجل الطالب درجة أعلى من أو تساوي ٢١ على مقياس GHQ.

### النتائج:

ثلاثة وعشرون طالباً (٢٦,٧٪) كانوا من حالات GHQ-12، أي يعانون من توتر شديد. سجلوا درجة أعلى من أو تساوي ٢١ من بين هؤلاء الطلاب ، كانت الغالبية من الإناث (٩١٪)، في سنوات الدراسة السريرية (٩١٪) أو الذين يعيشون في نزل (٥٢٪). الاعترافات الأكademie والعامول النفسي والاجتماعية مثل الشعور بالوحدة وتقلبات المزاج والقلق بشأن توقعات أولياء الأمور كانت الضغوطات الرئيسية لجميع الطلاب. ساكنوا النزل كانوا أيضاً قلقين بشأن نوعية الطعام المقدم لهم بالإضافة إلى الشعور بالوحدة.

### الخلاصة:

تجدر الإشارة إلى أنه في المجتمع قيد الدراسة ، كانت المطالب الأكademie مصادر إضافية للاعتلال النفسي بالإضافة إلى القضايا الشخصية والنفسيّة الاجتماعية الأخرى. إننا بحاجة إلى التدخل على المستوى النفسي والاجتماعي والأكاديمي لتحسين جودة الحياة لطلاب الطب حيث أن هذا سوف يساعد على تجنب العديد من المشاكل النفسية في المستقبل.

## INTRODUCTION

In a medical or biological context stress is explained as a physical, mental, social, environmental or emotional element that causes bodily or mental strain and unease [1]. It is an unavoidable part of medical college experience that can affect students at any time and place [2,3].

Medical students are burdened under high expectations from the society. They are expected to be the master of their skills and learn a large amount of information [4]. They have to make personal and social sacrifices to do well in a competitive environment which places them under a lot of stress [5, 6]. Moreover, in recent years due to rising awareness about quality of life issues and increased demand of quality thereof, medical students feel stressed. This phenomenon of being constantly under strain may be due to awareness of the fact that they are carrying a huge responsibility.

The process of learning and cognitive functioning in medical students can be adversely affected by high levels of stress [7]. Previous studies suggest that in the beginning, some medical students develop mental health problems that are worse in the beginning but regresses with passage of time[7, 8]. One article stated that "they experience multiple fears in metamorphosis from insecure student to an expert physician" [9]. As a matter of fact, change of environment has a great negative influence on a person's psychological condition [10-12]. Distress experienced during medical school can not only cause immediate morbidity but

can also foretell later problems in a doctor's life. It may possibly lead to personal suffering and may effect quality of health care provided to the patient. Due to awareness of this issue amongst the medical community, there have been many studies worldwide on psychosocial problems of the medical students but local data is scarce.[14-17] Most of them have focused on psychosocial problems e.g. stress, burnout and depression.[15-17] However, the current study aims to find out the prevalence and causes of stress focusing on stressors like academic as well as psychosocial and other factors in relation to psychiatric morbidity. We are experiencing a revolutionary change in medical education in Pakistan. The emphasis on mental health issues among medical students have been very less so far. A search of local studies on the subject did not yield any data which could be used as a baseline for comparison purpose.

## Methodology :

This cross-sectional observational survey was carried out among the male and female undergraduate students of Gujranwala Medical College, Gujranwala from 1st May 2015 to 30th January 2016. The college has an enrollment of one hundred students each year (500 total students) and an annual system of examination, which is structured into 5 years i.e. first two foundation years and three clinical course years. Required sample size was 93 rounded off to one hundred, taking expected prevalence of severe stress 20.9% [13] at 7.5% mar-

gin of error and total population of 500. Taking sampling frame of all enrolled students in medical college, 100 male and female students were selected from all five years using simple random probability sampling. These students were approached for voluntary participation in the study after ethical approval. Eighty-six students (86%) responded to the self-administered data collection tool which included the sociodemographic profile, 12 item General Health Questionnaire (GHQ-12) and 28-item source of stress questionnaire.

General Health Questionnaire (GHQ-12) is a standard screening instrument to detect current, diagnosable psychiatric disorders and is intended for use in general practice and community settings.<sup>[18-21]</sup> The GHQ scoring method (0-1-2-3-4) was adopted, and a cut-off point of 21 was used in accordance with previous studies (and is noted as “psychiatric morbidity” in the result section).<sup>[14, 15]</sup> The 28-item source of stress questionnaire previously used by Sreeramareddy et al was adapted with subtle adjustments to the contents.<sup>[13]</sup> In majority of the questions the frequency of occurrence of each potential stressor was rated as ‘never’, ‘rarely’, ‘sometimes’, ‘frequently’ and ‘always’ and scored using Likert scale as 0,1,2,3 and 4. To allow for inferential statistical calculation, the 5-way Likert responses were reduced to binomial responses of ‘less’ (i.e. ‘never’/‘rarely’/‘sometimes’) and ‘more’ (i.e. ‘frequently’/‘always’).

Data was entered and analyzed using the statistical package for social sciences version 21 (SPSS 21, IBM, Illinois). Categorical varia-

bles like sex, psychological morbidity, source of stress was presented as frequencies and percentages. The continuous variable like score on GHQ-12 was presented as mean  $\pm$  standard deviation. Data was stratified to determine the effect of different characteristics on psychological morbidity using Chi-square test of significance (Fischer exact test in case of any cell expected count less than five). A p value of  $\leq 0.05$  was considered as significant.

## Results

The total sample size of this study was 100 out of which 86 (86%) responded. There were 65 (75.6%) females and 21 (24.4%) males, 23 (26.7%) were in their foundation years and 63 (73.3%) were in their clinical years. In our study, 30 (34.9%) were day scholars and 56 (65.1%) were living in hostels, 5 (5.8%) of them were living with single parent and 81 (94.2%) were having both of their parents alive and living together. All of them were Muslims. According to GHQ-12 categorization, 17.4% of the students fall in the category of low distress, 55.8% in typical distress, 20.9% in psychosocial distress and 5.8%, in severe distress. Among sampled population, twenty-three students scored  $\geq 21$  on the general health questionnaire (GHQ-12) and were considered as having psychological morbidity i.e. cases. The mean score on GHQ-12 was  $17.56 \pm 5.112$ . Academic concerns (e.g. dissatisfaction with teaching methodology (55.8%) and pre-exam tension (41.9%)) and psychosocial factors (e.g. experiencing high

expectations from parents (53.5%), mood swings (40.7%) and headache (29.1%)) were major stressors among all the students and being worried about the quality of food in mess

(52.3%) and feeling of homesickness (17.4%) were major stressors in the students living in hostel. (Table I).

Table I: 12-Item General Health Questionnaire (GHQ-12) and Sources of stress in students

Categorization of Psychological morbidity	Low distress	15(17.4%)
	Typical distress	48(55.8%)
	Evidence of psychosocial distress	18(20.9%)
	Severe distress	5(5.8%)
Possible Causes of stress	Response	n (%)
Any sibling doctor or a medical student	Yes	20 (23.3%)
Family setup of living	Joint	18(20.9%)
	Nuclear	68(79.1%)
Headache	Frequently, always	25(29.2%)
Social circle	Limited	58(67.4%)
Reason of studying medicine	Forced by parents	8(9.3%)
	Influenced by siblings	9(10.5%)
Can your parents afford your studies/fulfill all requirements?	Not easily Not at all	8(9.3%) 1(1.2%)
Being satisfied with academic score	Somehow	56(65.1%)
	Not at all	8(9.3%)
Being worried about expectations of parents and family	Yes	46(53.5%)
Satisfied with hostel life	Somehow	39(45.3%)
	Not at all	13(15.1%)
Difficulty in adjusting with roommates	Somehow	20(23.3%)
	Yes	9(10.5%)
Satisfied with quality of food in mess	Somehow	15(17.4%)
	Not at all	45(52.3%)
How often do you visit your home?	Every weekend	40(46.5%)
	Twice a month	12(14%)
	Once a month	6(7%)
	After 3-4 months	2(2.3%)
Feeling of homesickness	Frequently, always	15(17.4%)
How often do you fall sick?	Once a week	5(5.8%)
	Twice a month	17(19.8%)
Difficulty in study	Frequently, always	24(27.9%)

Satisfied with teaching methodology	No	48(55.8%)
Feeling of being lonely in gathering	Frequently, always	12(14%)
Feeling of nausea, vomiting, diarrhea, palpitations etc. during exams	Frequently, always	36(41.9%)
Feeling of being dumb	Frequently, always	12(14%)
Suicidal thoughts	Frequently, always	2(2.3%)
Any voices in mind/hallucinations	Frequently, always	3(3.5%)
Mood swings	Frequently, always	35(40.7%)
Difficulty in sleeping	Frequently, always	15(17.4%)

Table II: Effects of sociodemographic data on General Health Questionnaire (GHQ-12) categories

Variables	Categories	Psychological morbidity n (%)	No psychological morbidity n (%)	P Value using chi square test
Gender	Male Female	6(26.08%) 17(73.91%)	15(23.8%) 48(76.19%)	0.828
Class	Foundation years Clinical years	6(26.08%) 17(73.91%)	17(27%) 46(73%)	0.934
Living status	Day scholar Living in hostel	10(43.47%) 13(56.52%)	20(31.74%) 43(68.25%)	0.312
Current status of parents	Both alive and living Single parent	20(86.95%) 3(13.04%)	61(96.82%) 2(3.17%)	0.116

Among the students who had psychological morbidity, 73.91% were females and 26.08% males ( $p=0.828$ ). 73.9% were in their clinical years and 26.08% were in their foundation years ( $p=0.934$ ). Among 23 students with psychological morbidity, 56.52% were living in hostel and 43.47% were day scholars ( $p=0.312$ ). Among GHQ cases, 86.95% had both their parents alive and living together and

13.04% had single parents ( $p=0.116$ ). All of the results were non-significant.

Students with morbidity compared to those with no morbidity demonstrated significant differences as assessed on the GHQ-12 scores.

Values which led to psychiatric morbidity was significantly associated with feeling of being lonely (83.3%,  $p=0.000$ ), mood swings (45.7%,  $p=0.001$ ), feeling of being dumb

(66.7%, p=0.002), being sick (p=0.002), being worried about expectations of parents (37%, p=0.022), family setup of living (p=0.033), difficulty in adjusting with roommates (22.2%, p=0.035) and being satisfied with academic score (50%, p=0.041). In addition there were non-significant differences related to any voices in mind/hallucinations (33.3%, p=1.000), suicidal thoughts (50%, p=0.466).

## Discussions

In our study, twenty-three students (26.7%) scored  $\geq 21$  on the GHQ-12 and were considered as having psychological morbidity. 17.4% of the students fall in the category of low distress, 55.8% in typical distress, 20.9% in psychosocial distress and 5.8%, in severe distress. GHQ cases came out to be 26.6% and so the rest of them i.e. 73.3% were GHQ non-cases. The mean score on GHQ-12 was  $17.56 \pm 5.112$ . Based on the results analysis, we may suggest that the stress level is high among our sampled population. In previous studies, similar results were reported. In a study by Yussuf et al., researchers found overall prevalence of stress about 25.9% among Nigerian medical students. They utilized GHQ-12, and 40 item stressor questionnaires. From the various factors involved to cause stress the students perceived academic requirements to be the most stressful (among 58.2% of the participants). In their cross sectional study, Yussuf et al reported that students who had morbidity increased the risk four times if the learning materials were not adequate and competition

with their peers raised the risk to nine times as compared to others.<sup>[16]</sup> Sreeramareddy et al reported psychological morbidity prevalence about 20.9%. The commonly reported causative factors were ethnicity (Indian origin), medicine as family profession and preclinical years..<sup>[13]</sup>

The observed similar psychological morbidity in male and female medical students in our study was inconsistent with previous findings which reported higher stress in female medical students<sup>[26-28]</sup>. In a study by Shaikh et al [29] stress level in male students came out to be higher as compared to female students. The reason behind this could possibly be due to the fact that in our study we collected data for a smaller sample. Consistent with our finding, one study has reported equal levels of stress in both the sexes.<sup>[24]</sup> The high morbidity level among the students living in hostels as compared to the day scholars is consistent with the findings of previous studies which have also reported the same<sup>[24,30]</sup>. It is also a possibility that students feel more stressed because they face homesickness as they are away from their localities.

Another variable which we took into account was the current status of parents of these children. We wanted to find out whether the students living with single parent feel more stressed as compared to those living with both of their parents. However, we observed that the students living with both of their parents were more stressed as compared to those having single parent. Miller & Surtees<sup>[31]</sup> used the GHQ-30, Dahlin et al<sup>[10]</sup> used a Higher Ed-

ucation Stress Inventory (HESI). In addition, Sreeramareddy et al [13] and Ko et al [30] used a cut off 4/5 for GHQ-12 and AD Yousaf, BA Issa used a cut off value of 3 for GHQ-12. While present study used a cut off value of 21 for GHQ-12. Contrary to previous studies that identified academic issues as more common sources of stress to medical students [13, 26, 30, 32-34]. The current study observed that both academic (e.g., ‘dissatisfaction with teaching methodology’, and ‘pre-exam tension’) and psychosocial issues (e.g., ‘experiencing high expectations from parents’, ‘mood swings’ and ‘headache’) were common to the cohort. According to other studies, academic issues (i.e., ‘being disturbed about competing with peers’ and ‘being worried about lack of special guidance from the college’) were particularly of concern among students who had morbidity [13, 26, 30, 32-34]. In contrast with earlier findings, psychosocial issues (‘feeling of being lonely’, ‘mood swings’, ‘feeling of being dumb’, ‘being sick’, ‘being worried about expectations of parents’, ‘difficulty in adjusting with roommates’ and ‘being satisfied with academic score’) were particularly of concern among students who had morbidity. In our study, among sources of stress, the worry of high expectations from parents carried a great weightage corresponding to the results obtained by previous studies. This could possibly be due to the facts that parents want their children to share their burden, they want their children to stand on their feet or there could be another possible explanation that to have medical gradates in one’s household is a so-

cietal glamour in itself. These could overburden the students with undue pressures that could possibly result in negative psychological consequences, thus explaining why ‘expectations from parents’ could be perceived as a highlighted source of stress. Similarly, a large number of students showed difficulty in adjusting with roommates which is manifested in a way that they feel lonely. Being away from home adds to the stress. A large number of students have reported that they are not satisfied with their academic score so they have a feeling of being dumb. Being sick and having mood swings are also among significant causes. Surprisingly though, our cohorts (and those who had morbidity) expressed no financial difficulties despite previous reports of association of financial concerns and debts with psychological morbidity.

## Conclusion

We may conclude that psychological morbidity is noteworthy among medical students. Besides the psychosocial/personal issues, academic demands were additional sources of psychological problems in our cohort. It is the need of the hour to make interventions regarding social and psychological support and academic excellence to improve the quality of life in these medical students. The proposed interventions include stress relieving exercises, workshops to cope with academic stress, time management workshops for students in the start of medical school and mentorship program. With the help of promotion of prin-

ciples of mental health education, the effect of these sources can be reduced and psychological problems arising in the future can be avoided. These students would be able to offer their services more efficiently and effectively in their practical lives. Limitations:

Limitations of current study include single center study with a small sample size. Smaller sample size lead to unequal distribution of sociodemographic characteristics (gender, living with family or in hostel).

#### **Conflict of interest:**

We declare no conflict of interest. The study was not funded.

#### **Acknowledgement:**

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## Original Article

# A novel in vitro cell culture model of human foreskin to study the immunogenicity of live attenuated influenza vaccine

Waleed Mahallawi<sup>1,2</sup> and Hamdi H. Almaramhy<sup>3</sup>

1. Department of Clinical Laboratory Sciences, Taibah University, Madinah 42362, Saudi Arabia

2. Department of Clinical Infection, Microbiology and Immunology,  
University of Liverpool, United Kingdom

3 .Pediatric surgery division, Department of surgery, college of medicine, Taibah  
University, Madinah 42362, Saudi Arabia

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Corresponding author :Waleed Mahallawi , Department of Clinical Laboratory Sciences,  
Taibah University, Madinah 42362, Saudi Arabia

### Abstract

#### Background:

The foreskin of the penis is a part of the mucosal immune system, an important first line of defense against antigens and infection. We tested cell culture derived from human foreskin tissues to observe the immunogenicity of live attenuated influenza vaccine (LAIV). The aims of this study is to use a novel in vitro cell culture model of human foreskin to assess LAIV in priming humoral as well as cellular immune responses. Also, to provide a new model that could be used to investigate the immunogenicity of the intranasal vaccines in foreskin tissue.

#### Methods:

Foreskin samples (n=21) were obtained from infant boys who had undergone circumcision at Pediatric urology department in Madinah Children and Maternity Hospital, Saudi Arabia. The samples were collected within for weeks of time. No clinical conditions were found during the time of surgery for those who gave foreskin samples i.e., all were healthy. We isolated a single cell suspension from fresh foreskin tissues and measured the frequency of total T cell subsets (CD4 and CD8) using multiparameter flow cytometry. ELISA was also used to measure the antibody titrations in cell culture supernatants following stimulation.

#### Results:

Significant higher antibody levels were detected ( $p < 0.05$ ) by ELISA following stimulation of foreskin mononuclear cells (MNCs) with LAIV when compared with unstimulated negative controls. Furthermore, there was a significant increase in total CD4+ and CD8+ T-cell responses ( $p < 0.05$ ) after stimulation with LAIV. Additionally, Interferon gamma (IFN $\gamma$ ) was also detected in a significant manner after LAIV stimulation.

#### Conclusions:

Understanding mucosal immunity to respiratory tract infections such as influenza viruses may provide important support to the improvement of effective intranasal vaccines against other respiratory infections. LAIV is found to be immunogenic to trigger cellular and humoral immune response in MNCs derived from human foreskin.

#### Keyword:

Foreskin, Humoral Immunity, Cellular Immunity, Cell culture model LAIV.

### الملخص

#### مقدمة:

يعتبر الجلد الذي يزال خلال عملية ختان الذكور(القف) أحد أهم مكونات جهاز المناعة. قمنا في هذه الدراسة باستخدام الخلايا المناعية الموجودة في هذا الجلد كنموذج لدراسة مدى مقدرة تطعيم الانفلونزا على استحثاث الخلايا المناعية.

#### طريقة البحث:

تم عزل الخلايا الليمفاوية من القلف لعدد عشرين طفلاً بعد خضوعهم لعملية الختان في مستشفى الأطفال في المدينة وذلك بعدأخذ موافقة الوالدين. تم اختيار الأطفال الأصحاء الذين ليس لديهم أي أعراض ظاهرية أثناء الختان وتم فصل خلاياهم واستحثاثها بعد إضافة تراكيز محددة من تطعيم الانفلونزا وتم استخدام تقنية التدفق الخلوي لقياس استجابة الخلايا الثانية بتوسيعها ٤ و ٨. كما تمت دراسة مقدرة التطعيم على افراز الخلايا البائية للأجسام المضادة وقياس ذلك بتقنية الأليزير.

#### النتائج:

أظهرت النتائج نجاح استخدام هذا النموذج كنظام مناعي متكامل لديه المقدرة على التعامل مع فيروس الانفلونزا الموجود في التطعيم. فكان هناك استجابة مناعية قوية للخلايا الثانية والبائية بعد الاستحثاث مقارنة بالخلايا التي لم يتم استحثاثها.

#### الخلاصة:

إن فهم خصائص الجهاز المناعي الموجود في خلايا الجلد بعد الختان يلعب دوراً هاماً في الدراسات المستقبلية لمثل هذا النوع من الأبحاث حيث يمكن أن يستخدم مستقبلاً لدراسة ميكروبات أكثر لاسيما الفيروسات التي تصيب الجهاز التنفسى. أيضاً نجاح هذا النموذج يفتح مجالاً واسعاً لنطوير النموذج واستخدامه على نطاق أوسع.

## Introduction

Circumcision is a cultural, medical, and religious process in which the human foreskin (HFS) is either partially or entirely removed by surgery. Cells segregated from the circumcised tissues are called foreskin cells. These cells can serve as feeder cell lines for embryonic stem cells used in research.<sup>[1]</sup> Circumcision is beneficial in decreasing the risk of infection<sup>[2-4]</sup>. For example, a recent study confirmed that circumcision lowers HIV infection rate in heterosexual men by 50-60%.<sup>[5]</sup> Therefore, WHO and UNAIDS have recommended male circumcision as a vital measure of a broad HIV prevention bundle for males.<sup>[6]</sup> In addition, it has been proven that among infants <1 year of age with urinary tract infections (UTIs), about 86% were uncircumcised boys.<sup>[7]</sup> Based on this evidence, the American Academy of Pediatrics (AAP) and the CDC strongly recommend male circumcision.<sup>[8]</sup> In the USA, the CDC estimates that 81% of males aged 14 to 59 years are circumcised.<sup>[9]</sup> In Saudi Arabia, circumcision for boys is obligatory according to Sharia Law<sup>[10]</sup>, which ensures a supply of foreskin for scientific use. Both humoral and cellular immune responses in the genital mucosa have a vital role in the prevention of sexually transmitted infections (STIs), including infection with HIV-1.<sup>[11]</sup> Mucosal immunity is an important compartment of the immune system and the foreskin is an important component of the mucosal immune system. However, its role in mucosal immunity has not been fully characterized.<sup>[12]</sup> Cell cul-

tures initiated from HFS tissues have been used for isolation of viruses from diagnostic specimens because the tissues are readily available, and preparation is not difficult. Investigators have recommended greater use in diagnosis and research.<sup>[13]</sup> In this study, we investigated the potential use of foreskin-derived cell culture as a novel human model to study immune response to live attenuated influenza vaccine (LAIV) as an alternative to currently used animal models.<sup>[2, 14, 15]</sup> Foreskin-derived cell culture has been shown to be useful in characterizing the levels of CD4+ and CD8+ T cells, memory T cells, and the production of pro-inflammatory cytokines in HIV infection.<sup>[16]</sup> In this study, we developed an HFS cell culture model to observe the immunogenicity of LAIV. We isolated a single cell suspension from fresh foreskin tissues and measured the frequency of foreskin T cell subsets using multiparameter flow cytometry and ELISA for antibody detection. By studying immune cells from HFS, we aimed to determine if HFS could serve as an *in vitro* human model to assess immune response to different influenza viruses.

## Methods

### *Foreskin samples*

A total of twenty-one foreskin tissues were obtained from male infants (6 -30 months of age) undergoing circumcision at local hospitals in the Madinah region after signed consent obtained from parents. Foreskins were immediately placed in HANKS transport medium,

containing glutamine (2mM), penicillin (50 U/mL), and streptomycin (50 $\mu$ g/mL) (Sigma-Aldrich) and transferred to the laboratory for processing and isolation of MNCs.

Ethical statement: the study has been approved by Taibah University Ethical Committee (Ref No. MLT 2018050).

#### *Isolation of foreskin mononuclear cells*

Cell suspensions were prepared using a modified cell suspensions protocol from a previously described method that was used to isolate MNCs from the nose-associated lymphoid tissues (NALT). [17, 18] Foreskin samples were processed within one hour of surgery. The tissues were cut into small pieces, then transferred to an 8 cm-diameter sterile Petri dish and checked grossly. Each sample was mechanically disrupted and minced using a single sterile scalpel. The samples were then enzymatically digested with dispase II (Sigma-Aldrich) to release cells into the medium. The tissue-dispase II mixture was then kept in a water bath shaker for 2 hours at 37°C at 100 rpm. The remaining tissues were then cut, minced and incubated in cell release medium (RPMI 1640 medium with HEPES supplemented with 10% fetal bovine serum [FBS], glutamine [2mM], penicillin [50U/mL], and streptomycin [50 $\mu$ g/mL], Sigma-Aldrich). The cell suspension was then passed through a 70- $\mu$ m sterile nylon mesh to eliminate debris and then centrifuged at 400 g for 10 min. The cells were washed twice in sterile phosphate-buffered saline (PBS) and divided into two portions. One was cultured in 3 mL of

RPMI complete medium for antibody production and the second was processed for T cell proliferation assay Carboxyfluorescein succinimidyl ester (CFSE) staining.

#### *Intranasal vaccine FluMist (LAIV)*

FluMist vaccine LAIV Formula (2010-11) includes the following influenza strains; A/H1N1/2009; A/H3N2 and B influenza strains (BEI Resources, American Type Culture Collection (ATCC)).

#### *Cell culture and foreskin MNCs stimulation for antibody production*

Following foreskin MNCs isolation, each cell suspension was adjusted to contain 4 x10<sup>5</sup> cells/mL. Foreskin MNCs were co-cultured in RPMI complete medium in the presence and absence of LAIV. Unstimulated cells were used as a negative control. After preparation, a volume of 250  $\mu$ L of cell suspension were cultured in a sterile 96 well cell culture plate (Costar) and placed in the incubator in a humidified, 5% CO<sub>2</sub> atmosphere at 37°C. Cell culture supernatants were then collected at different time points and assayed by ELISA for measuring antibodies induced in response to LAIV stimulation.

#### *Carboxyfluorescein succinimidyl ester (CFSE) staining*

Foreskin MNCs were prepared and resuspended in sterile PBS in 45 ml sterile tube. CFSE was prepared at 5mM just before use by adding 5  $\mu$ L of neat to 10 ml sterile PBS. After that, 3 ml of the preparation were added to the

cells then kept into the incubator in 5% CO<sub>2</sub> at 37°C for 8 min. Adding of 10 ml ice cooled RPMI 1640 complete medium to block the reaction and then centrifuged at 400 x g for 10 min and then the supernatant discarded. The pellet was resuspended into 2 ml RPMI complete and then cells number was calculated via a haemocytometer. After adjusting cells concentration to 4 x10<sup>5</sup> cells/ml, cells were stimulated with LAIV and then incubated with 5% CO<sub>2</sub> at 37°C for four days. After incubation, cell culture supernatants were collected for cytokines analysis and cells collected for T cell proliferation assay by flow cytometer.

#### *Measurement of LAIV induced antibody levels by ELISA*

Antibodies induced by LAIV stimulation were analyzed following the ELISA procedure as previously described [18]. In brief, ELISA plates were coated with 100 µL of LAIV (2 µg/mL) and incubated overnight at 4°C. After 5 washings, plates were blocked with 200-µL of 10% FBS followed by incubation of cell culture supernatants at different dilutions for 1.5 hour and then discarded and blotted on dry tissues. Then 50 µL of alkaline phosphatase conjugate of anti-human IgG, IgM and IgA (Sigma) were added and incubated for 1.5 hour. Afterward 5 washings, 50 µL of p-nitrophenyl phosphate (PNPP) substrate was added. Optical density (OD) was measured at 405 nm.

#### T cells proliferation assay

Following foreskin MNCs stimulation with LAIV and incubation, percentage of prolifera-

tive T cell subpopulations including CD4+ and CD8+ T cells subsets was analyzed by CFSE (FITC) and T cell marker staining followed by flow cytometry (BD FACScalibur (BD Biosciences)). CellQuest software was used for flow cytometer data acquisition. Data analysis was performed using WinMDI 2.9 software. Subsequent stimulation, cells were harvested in 0.02% BSA-PBS buffer (Sigma-Aldrich). Cells were washed and centrifuged at 400xg for 8 min. The supernatants were thrown away then the cell pellet was resuspended in 50 µl 0.02% BSA for surface staining. A volume of 5 µl of mouse anti-human CD4-PE-Cy5 and 5 µl of mouse anti-human CD8-PE (BD) were added to stain CD4+ as well as CD8+ T cells. The cells with the antibodies were incubated at 4°C for 30 min. Then the cells were washed two times with 500 µl 0.02% BSA and then centrifuged for 8 min at 400g at 4°C. The cells were then resuspended in 300 µl 0.02% BSA and transported to FACS tube (Falcon) for analysing flow cytometer.

#### Statistical analysis

All the calculations and statistical analysis were performed using GraphPad Prism statistical software (version 5, USA). Data were expressed as mean ± standard deviation (SD). Two-group comparisons were performed using paired two test. A P < 0.05 was considered significant for all tests.

#### Results

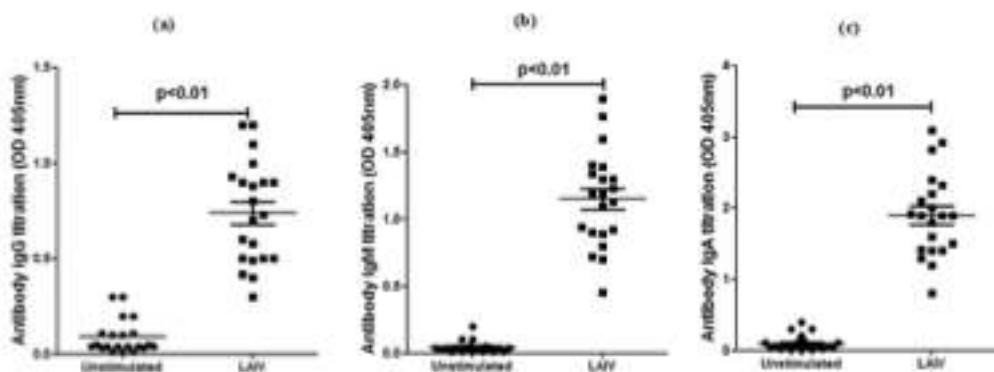
### LAIv elicits for stronger humoral immune t response

LAIv primes for stronger humoral immune response in the foreskin cell culture model. ELISA was used to measure the antibody levels in cell culture supernatants at different time points. Significant antibody levels were detected at day 10 following stimulation of MNCs with LAIV when compared with unstimulated negative control. Interestingly, all antibody classes were detected. Antibody class IgA was dominant over the other two classes whereas IgM was higher than IgG class antibody; (Fig. 1, p <0.05, n=21 (a) IgG, (b) IgM and (c) IgA).

### LAIv induces cellular immune response

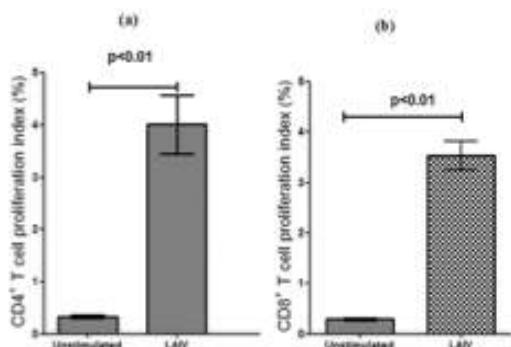
The percentage of total T cell proliferation index using CFSE staining shows significant increase in total T cell responses following LAIV stimulation in CD4+ (Fig. (2 a), p <0.05, n=21) and CD8+(Fig. (2 b), p <0.05, n=21) when compared with unstimulated negative control. CD4+ T cell proliferation index

was used to quantify the CD4+ T cell response following LAIV stimulation. Gating strategy illustrated in figure 3. Lymphocyte and CD4+ and CD8+ T cell gates were used in this analysis during flow cytometry. Lymphocytes were gated on the basis of their forward scatter and side scatter properties. As shown in figure (3 a) the lymphocytes were gated on region 1 (R1). CD4+ T cell gate was then set as region 2 (R2) as in (figure 3 b). Finally, R2-gated CD4+ T cells were shown in a new window as in (figure 3 c) with CD4-PE on y axis against CFSE (FITC) on x axis. The CD4+ T cell proliferative index was defined as the percentage of proliferating CD4+ T cell of total CD4 T cells = A/A+B, A= upper left quadrant, B=upper right quadrant). Representative proliferative index of CD4+ T cell following stimulation with LAIV (figure 3 d) was shown as compared to unstimulated negative control (3 c). Moreover, stimulation with LAIV induced also significant increases in IFN $\gamma$  in the foreskin-derived MNCs (p<0.01, n=21) (data not shown).

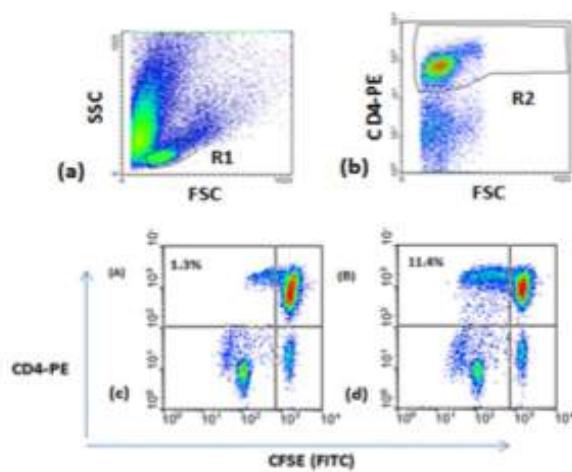


**Figure 1:** Significant antibody levels were detected (p <0.05, n=21) following stimulation of MNCs with LAIV when compared with unstimulated negative controls. Interestingly, all antibody classes were detected (IgG (a), IgM (b) and IgA(c)).

## Discussion



**Figure 2:** Significant increase in total T-cell responses after stimulation ( $p < 0.05$ ,  $n=21$ ). Stimulation with LAIV induced significantly increases in total CD4+ (a) and CD8+ (b) T cells when compared with unstimulated negative control.



**Figure 3:** Representative CD4<sup>+</sup> T cell proliferation index following stimulation with LAIV (c) was shown as compared to unstimulated negative control (d)). Representative CD4<sup>+</sup> T cells and gating strategy used in quantifying CD4<sup>+</sup> and CD8<sup>+</sup> proliferation index using CFSE staining.

To the best of our knowledge, the present study is the first to report immune cell densities in the HFS using LAIV as immunogen for stimulation. We also provided the first evidence that foreskin-derived MNCs can be used as a model for an in vitro human cell culture model for studying mucosal immune response to res-

piratory pathogens such as influenza viruses. Influenza is a very transmissible acute respiratory illness initiated by influenza virus. The virus infects the mucosa of the host respiratory tract. Intranasal immunization with activated vaccine is more potent than intravenous inactivated vaccine and is a more biologically appropriate means of vaccination against respiratory infections such as influenza since it imitates natural infection.<sup>[19]</sup> Our results show a significant antibody production following stimulation with LAIV. As presented, IgA class antibody shows to be dominant over the other two classes, which is consistence with other study, which showed higher antibody levels in mucosal system.<sup>[19]</sup> IgG class antibody level appears to be the lowest among all classes which is expected as all subjects are infants less than three years. Therefore, they were expectedly less exposed to influenza viruses during their lives compared with adult. LAIV provokes secretory IgA, the major antibody secreted at mucosal surfaces, which plays an essential role in protecting against influenza and is a critical part of the immune system, being the second line of defense against pathogens.<sup>[20-22]</sup> LAIV seems to be superior in eliciting nasal IgA and CD4 T cells when compared with natural infection and inactivated influenza vaccine. However, LAIV is about as strong as natural infection in providing cross-protective immunity.<sup>[19]</sup>

The local mucosal immune tissue critically influence intranasal vaccination.<sup>[23]</sup> Human adenoids and tonsils are the main mucosal immune organs, specifically the NALT in hu-

mans and are recognized as essential points of induction of mucosal (and systemic) immunity against upper respiratory tract pathogens.<sup>[24, 25]</sup> Natural influenza infection elicits a wide-range of immune responses, which include humoral and cellular components.<sup>[26, 27]</sup> Mucosal antibodies are potent defenders of the upper respiratory airways and points of viral access. Serum antibodies mostly defend the lower respiratory tract Existing inactivated influenza vaccines induce strain-specific antibodies and not CD8+ T cells.<sup>[28]</sup> Our results also show significant increase in cellular immune responses after LAIV stimulation namely, CD4+ and CD8+ T cells. This result is in accordance with another study showed that LAIV mimics natural infection through viral replication in the upper respiratory tract and provokes many immune responses, comprising antibodies and CD4+ and CD8+ T cells.<sup>[29]</sup>

Several models have been used to study and evaluate infections caused by several influenza viruses. In a previous study, we showed that NALT from human adenoids and tonsils is one of the most successful models for that purpose.<sup>[18]</sup> Now we show that an HFS model is an alternative and novel in vitro cell human model. The present study demonstrates the ability of MNC-derived from human foreskin to be used as a model for studying humoral and cellular immune response. An advantage of HFS is that all immune cells are present in these tissues, which is well documented.

<sup>[1, 30]</sup> Additionally, a previous study investigated mucosal response of tissues from

the penises of transformed males following penile removal and found that the penis is a site of efficient mucosal response<sup>[31]</sup>. Studies in animal models have found that the presence of CD4 T cells in the foreskin of infected monkeys played a crucial role in fighting the HIV virus.<sup>[2]</sup> The role of IFN $\gamma$  is very essential in fighting viral infection as influenza virus. IFN $\gamma$  is released in large quantities in several immune compartments such as, macrophages, activated CD8 T cells, NK T cells, and Th1 CD4 T cells.<sup>[32, 33]</sup> Our data shows the ability of HFS model to produce IFN $\gamma$ , which mimics the natural viral infection, and this is consistency with several studies that demonstrated the ability of LAIV to induce the secretion of IFN $\gamma$ .<sup>[34-36]</sup>

Our data can be added to the accumulation of evidences to verify the appropriateness of foreskin to study the interactions between influenza virus and the immune system. This result is consistent with a study in children when T cells were produced abundantly, which might offer clinical protection.<sup>[26]</sup> In addition, another study reported similar results after intranasal LAIV.<sup>[28]</sup> The finding of significant antibody levels following stimulation of MNCs with LAIV means the model is valid for other studies to assess the immune responses to different pathogens that cause infection in humans such as MERS-CoV, pneumonia and many others. This result is also consistent with several studies of the NALT model.<sup>[37-40]</sup>

## Conclusion

This study using an in vitro cell culture model of HFS to measure humoral as well as cellular immune responses to LAIV provides a new model to attest and study of intranasal vaccines. Use of human-derived cells is a more realistic model for investigation of the immune response against pathogens that cause human infection such as influenza viruses. Understanding mucosal immunity to respiratory tract infections such as influenza viruses may lead to meaningful improvements in effective intranasal vaccines against other respiratory infections.

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## Author Contributions

All authors having contributed equally to the work.

## Disclosure of potential conflicts of interest

The authors claim no conflict of interest.

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## Original Article

# Prevalence and risk factors of diabetic neuropathy in Qassim, Saudi Arabia

Amal A Almohisen<sup>1</sup>, Lama M Almuhsen<sup>2</sup>, Khawlah K Alhatlany<sup>2</sup>, Reham H Alghalth<sup>3</sup>, Ashwaq M Almutairi<sup>2</sup>, Fatmah A Almarzog y<sup>3</sup>, Haneen A Alghasham<sup>2</sup>, Ghaida M Almohsen<sup>3</sup>

1. Assistant professor, Department of Statistics and OR, King Saud University

2. Medical intern, Unaizah College of Medicine, Qassim University

3. Medical student, Unizah College of Medicine, Qassim university

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Corresponding author : Lama M Almuhsen<sup>2</sup>, Unaizah College of Medicine,

Qassim University, Qassim, Saudi Arabia, 19519. Email: dr.lama.mmm@hotmail.com

### Abstract

#### Background:

Diabetic neuropathy is the commonest early and long-term complication of diabetes. Saudi Arabia has a high prevalence of diabetic neuropathy reaching (65%), which necessitate the establishment of a preventive program. The aim of the study was to measure the prevalence of diabetic neuropathy and its associated risk factors in Qassim, Saudi Arabia.

#### Methods:

A cross-sectional study that utilized an adopted a translated version of Michigan neuropathy screening instrument. An electronic questionnaire was filled by each participant after obtaining informed consent. The questionnaire included questions about neuropathy in addition to added questions about demography of participants. After data collection, SPSS version 21.00 was used for data analysis.

#### Results:

A total of 374 patients have been included in the analysis. Of which (54%) were females, and (97.1%) were Saudis with a mean age of (53.6±11.9). The prevalence of diabetic neuropathy was (38.2%). Significant associations with abnormal total scores included; low education ( $p=0.007$ ), hypertension ( $p = 0.017$ ), high body mass index ( $p < 0.001$ ), use of insulin and/or multidrug for diabetes ( $p < 0.001$ ). Further analysis of sex, age, and smoking did not show any significance with diabetic neuropathy.

#### Conclusion:

Our study concluded that more than one third of diabetics in Qassim region are having diabetic neuropathy. Paying attention to risk factors is an important factor for early detection of the condition.

#### Key words:

Diabetic neuropathy - risk factors - Qassim - Saudi Arabia.

### الملخص

#### الخلفية :

المرض العصبي السكري يعتبر أكثر المضاعفات الأولية التي تدوم مع مريض السكري ومعدل انتشارها في السعودية يصل إلى (٦٥٪)، مما يبرز أهمية تنظيم برامج وقائية. هدف الدراسة الحالية يتمثل في تحديد معدل انتشار مرض العصبي السكري والعوامل المساعدة على المرض في منطقة القصيم بالمملكة العربية السعودية.

#### طريقة البحث :

دراسة مستعرضة استخدمت نسخة مترجمة من استبيان ميشigan الكشف عن العصبي السكري. تم جمع البيانات عن طريق تعريف الاستبيان الإلكتروني عن طريق المرضى. تم تحليل البيانات باستخدام البرنامج الإلكتروني (SPSS).

#### النتائج :

تم تحليل (٣٧٤) استبيان. الإناث مثلن (٥٤٪) من العينة والجنسية السعودية (٩٧,١٪) ومتوسط الأعمار (٥٣,٦ سنة). تم اكتشاف علاقة بين مرض العصبي السكري وعدة عوامل هي: مستوى التعليم المنخفض ( $P > 0,001$ ), ارتفاع ضغط الدم ( $P > 0,001$ ), ارتفاع معدل كثافة الجسم ( $P > 0,001$ ), استخدام الأنسولين أو تعدد الأدوية ( $P > 0,001$ ). غير أن التحليل لم يجد أي علاقة مؤثرة مع الجنس أو العمر أو التدخين.

#### الخلاصة :

نستخلص من النتائج أن ما يقارب ثلث العينة من مرضى السكري في منطقة القصيم يعانون من مرض العصبي السكري. يجب مراعاة العوامل المساعدة على المرض للوصول للتشخيص المبكر.

## Introduction

Diabetes and its complications have become a huge burden. Its prevalence is increasing year after year. Globally, it is affecting around (382) million people. Prevalence rates are variable from one country to another, and Saudi Arabia is considered as one of the top ten countries with a prevalence reaching (23.9%)<sup>[1]</sup>.

One complication is diabetic neuropathy. The commonest and earliest long-term complication [2]. The prevalence of diabetic neuropathy among diabetics has been reported as high as (50%)<sup>[3]</sup>. Diabetic neuropathy is defined as sensorimotor polyneuropathy that is diagnosed in a diabetic patient when other causes are excluded [4]. While the association of pain is not necessary for diagnosis, it can accompany the condition in some cases<sup>[5]</sup>. The pathogenesis of diabetic neuropathy is believed to be multifactorial. Which develops in the presence of risk factors through multiple pathways, including; oxidative stress, glycation end products and proinflammatory processes [6]. Usually the diabetic patients who have developed neuropathy present with different clinical manifestations such as; numbness, loss of sensation, foot ulcers, and even amputation. With progression of complications, even mortality can result from such conditions<sup>[7]</sup>. Which makes the early recognition and management of diabetic neuropathy crucial for a better prognosis. Risk factors represent an important hint to the caring physician to screen and diagnose diabetic neuropathy. The risk factors can be easily identi-

fied. Hyperglycemia, high blood pressure, hyperlipidemia and smoking are well known risk factors<sup>[8]</sup>. Prevention is a key in diabetic neuropathy. Tight glycaemic control and lifestyle modification to reduce the cardiovascular risk are the mainstay of prevention. Other options represent symptomatic treatment by foot care, antidepressants and anticonvulsants [9]. As we recognized the necessity of early diagnosis of diabetic neuropathy, and as no such topic has been studied in Qassim region, we conducted this study concerning the prevalence and associated risk factors of diabetic neuropathy.

## Methods

### *Study design*

This was cross-sectional study.

### *The population*

All the attendants primary care centers if Al-Qassim region were invited to participate in the questionnaire as long as they are eligible according to the criteria.

Inclusion criteria included patients diagnosed with type II diabetes mellitus, Age (25-90) of Both genders and all nationalities.

We excluded patients with neurological abnormalities (Epilepsy, Stroke, Parkinson, Cerebral Palsy, etc.) and patients whom age is less than 25 or more than 90.

### *Sample size*

According to the General authority for statistical reports in Saudi Arabia, the general population of Al-Qasim is around (980,000)<sup>[10]</sup>. Which make the diabetic patients around (234220), considering that diabetes preva-

lence is (23.9%) [1].

Using an online sample calculator (Raosoft.com), with a margin error of (5%), confidence level (95%), and response distribution of (50%). The required sample size was calculated to be (384). Simple random sampling technique was used to include participants from outpatients of Al-Qassim primary health care centers.

#### *Tools and data collection*

The Michigan neuropathy screening instrument was translated and modified to include more questions regarding sociodemographic characteristics and diabetic history. The total score ranges from zero (0) up to (13). Total scores of 4 or more are considered as abnormal.

The data collection took place in primary health care and diabetic centers in Al-Qasim region. An electronic questionnaire form was developed via Google drive. The electronic form was used and accessed only by the investigators, the investigators did an interview with each participant and submit the answers directly to the form.

#### **Statistical analysis**

The statistical package for the social sciences (SPSS – version 21.0) were used to analyze the data. Tables and graphs were used to show the participants' responses and important findings. A new variable was computed to include all the Michigan questions to get the total scores, the mean and standard deviation was then calculated for the new variable. The Chi-square test was used to detect the significant findings.

#### *Ethical considerations*

Prior to collecting data, an ethical approval was obtained from the regional research ethics committee in Qassim province. Centres' managers were notified to gain permission for data collection. Furthermore, after explaining the nature and purpose of the study, an individual consent was gained from each participant.

#### **Results**

A total of (374) diabetic patients has been included in the analysis. The sociodemographic results showed most Saudi patients (97.1%), females represent (54%) of the total sample, about one third (33.2%) are well educated (university or higher), and more than half of our population were from Onaiza province. The mean age in our population was (53.61), with a standard deviation of (11.88), minimum age (25) and the maximum age (88) years. The screening tool for diabetic neuropathy included a total of (15) questions. The responses are demonstrated in (Table 1).

Table 1: Michigan Neuropathy Screening Instrument responses

Question	Yes	No
1. Are your legs and/or feet numb?	45.7%	45.3%
2. Do you ever have any burning pain in your legs and/or feet?	45.7%	54.3%
3. Are your feet too sensitive to touch?	26.5%	73.5%
4. Do you get muscle cramps in your legs and/or feet?	26.5%	73.5%
5. Do you ever have any prickling feelings in your legs or feet?	44.4%	55.6%
6. Does it hurt when the bed covers touch your skin?	15.5%	84.5%
7. When you get into the tub or shower, are you able to tell the hot water from the cold water?	94.4%	5.6%
8. Have you ever had an open sore on your foot?	11.2%	88.8%
9. Has your doctor ever told you that you have diabetic neuropathy?	8.6%	91.4%
10. Do you feel weak all over most of the time?	45.7%	54.3%
11. Are your symptoms worse at night?	24.3%	75.7%
12. Do your legs hurt when you walk?	41.7%	58.3%
13. Are you able to sense your feet when you walk?	90.6%	9.4%
14. Is the skin on your feet so dry that it cracks open?	36.4%	63.6%
15. Have you ever had an amputation?	2.9%	97.1%

Considering a total score of four or more as abnormal. The overall percentage of abnormal scores was (38.2%), the frequencies of diabetic neuropathy is shown in (Table 2). The mean of total scores was (3.09) with a standard deviation of (2.44).

Table 2: The prevalence of diabetic neuropathy among our sample

Total scores	Frequency	Percentage (%)
1-3	231	61.8
More than (3)	143	38.2

The prevalence of hypertension among our sample (49.5%). Smoking prevalence was (15.8%), while (8%) were ex-smokers. The duration since the diagnosis of diabetes ranged from one year up to (37) years, with a mean of (11.31) and a standard deviation of (8.28).

Upon asking about pharmacological treatment, the responses were variant with the majority indicating multidrug approach to control

diabetes (Table 3).

Significant associations of diabetic neuropathy were found with lower educational levels, presence of hypertension, use of insulin or multidrug, and higher body mass index (Fig 1).

Further analysis did not show any significant findings with smoking, age, sex or income. The analysed P-values are shown in (Table 4).

Table 3: Distribution of antidiabetic medications

Medication	Frequency	Percentage (%)
Metformin	96	25.7
Hypoglycemics agent	24	6.4
Insulin	57	15.2
Multidrug	178	47.6
I don't know	19	5.2

Fig. 1: Association of risk factors with diabetic neuropathy

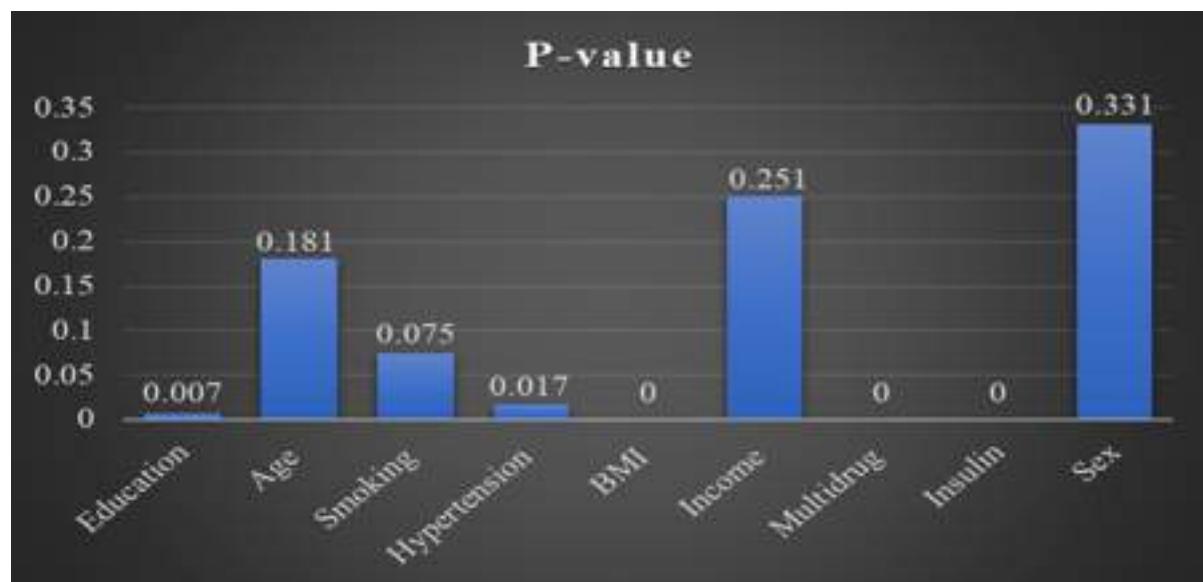


Table 4: Risk factors and its association with the presence of Diabetic Neuropathy

Variable	Test	P-value
Sex	Pearson Chi-square	0.309
Age	Pearson Chi-square	0.653
Education	Pearson Chi-square	0.031
BMI	Pearson Chi-square	0.032
Type of medication	Pearson Chi-square	0.000
Diagnosis of hypertension	Pearson Chi-square	0.009
Smoking	Pearson Chi-square	0.818
Years since diagnosis of DM	Pearson Chi-square	0.002

## Discussion

In our study, we have used the Michigan neuropathy screening instrument considering total scores of four or more as abnormal. According to Herman et al. [11] this will make the performance of the instrument better. The overall prevalence of diabetic neuropathy DN considering four or more total scores as abnormal in Herman's study was (18%). However, our study found that (38.2%) had abnormal total scores. In the UK, the prevalence was found to be (34%), which is like the overall prevalence of our study [12]. From a local perspective, the reported number was variable. In a meta-analysis done in middle east countries and North Africa, Saudi Arabia was the highest country of DN prevalence (65.3%) [13]. Moreover, among Saudi diabetics who have the disease for ten years, the preva-

lence of distal DN is (38%) [14].

This study has focused on the significant association with diabetes neuropathy. Educational level, the BMI, hypertension, use of insulin and/or multidrug approach to control diabetes were risk factors significantly associated with total scores of four or more. The mentioned risk factors are well known and have been highlighted in the literature. While few studies have not indicated any risk factors to predict DN [15], many other major studies have indicated the importance of assessing risk factors in order to suspect DN and perform nerve conduction study accordingly. Factors found to be significant in this study has been supported in addition to other factors such as hyperlipidemia [16-19]. Algeffari [20] in a multicentre cross-sectional study that was carried in Riyadh. The study

has indicated smoking and female gender as important predictors to be looked for when considering painful diabetic neuropathy. Although, a similar prevalence to Algeffari was found in our study of about one third of our population, there were no significance found with smoking or female gender on our study. Advanced age, older duration with diabetes, and insulin use are associations suggested by Wang, et al. in a cross-sectional study among Saudi population. However, our study did not show any significance with age as a cofactor for developing the disease. The explanation could rely on the number of patients with type I diabetes mellitus (DM) included in the study. Such finding is predictable in Wang, et al. study as almost (95%) of the participants had type II DM. A well-known risk factor is longer duration since the diagnosis of DM. also, DN is found to be more among patients of DM type II [21]. Thus, it is expected that longer duration with DM type II will be found in older age, which results in the accumulation of two risk factors and make the patient more prone to develop DN.

Our population has a very low percentage (2.9%) in which they have undergone amputation due to complications of DM. However, literature showed that among diabetics in Saudi Arabia (23.5%) ended doing amputation due to diabetic complications. The commonest complication is peripheral diabetic neuropathy. Furthermore, it is the most frequent complication leading to limb amputation [22-23]. In such cases, the importance of patient education and awareness must be fulfilled to prevent

foot ulcers and possible amputation [19].

## Conclusion

The prevalence of diabetic neuropathy among diabetics of Qassim region is (38.2%). Although, is considered relatively low in compare to previous studies, it is important to predict the condition and diagnose it early for a better prognosis. The common risk factors include; hypertension, high BMI, insulin use, and low education. This emphasizes the importance of implementing a health program to educate diabetic patients about possible complications and neuropathy in specific.

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## Original Article

# Relationship of insomnia, stress, and anxiety with shift work among nurses in the Kingdom of Bahrain

Danya A AlAwadhi, Aesha K Sharif, Ayat E Faraj, Sara J Mohammed, Hajar Y AlShomili, Dana K Abdulla,

Sara H Abdulla, Fawzeya A AlAhmed, Eman N AlBastaki, Aysha E AlMadani, Jamil Ahmed

Family & Community Medicine Dept. Arabian Gulf University, Kingdom of Bahrain

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Corresponding author : Dr. Jamil Ahmed

Assistant Professor - Family & Community Medicine Dept.

Arabian Gulf University P.O Box 26671 Kingdom of Bahrain

jamilmga@agu.edu.bh

### Abstract

#### Background:

Insomnia, stress, and anxiety affect the mental wellbeing and distorts the work-life balance of health workers influencing their performance at work. This study aimed to assess the relationship of shift work with insomnia, anxiety, and stress among nurses in a tertiary care hospital in Bahrain.

#### Methods:

We used a cross-sectional study design. Our study population was 345 nurses in a major tertiary care hospital in Bahrain. The sample was selected based on the population probability to size method. Nurses completed a questionnaire that contained items, including sociodemographic data, Bergen's Insomnia Scale, Perceived Stress Scale, and Shift Work Disorder scale.

#### Results:

The prevalence of insomnia was highest (85.7%) in the youngest nurses (20 to 30 years), Bahrainis (92.2%), nurses working in Surgical (85.5%) and Pediatrics (80.0%) departments, with 1 to 5 years of shift work experience (81.0%), and 1 to 3 night shifts a month (92.0%). Nurses with very high levels of stress were between the ages of 20-30 years, Bahrainis, had a B.Sc. degree, were in the Pediatrics Department, worked for 4 to 6-night shifts per month, and did not consume caffeinated drinks ( $p = <0.05$ ). The prevalence of Shift Work Disorder was 11.3% in our study.

#### Conclusion:

The prevalence of insomnia, stress, and anxiety was high in the nurses in our study, and it was significantly related to performing shift work. However, shift work disorder in those who had insomnia was low in our study although it was still higher in nurses who suffered from insomnia. Balanced working hours and support in the evaluation and treatment potential mental health challenges associated with working in shifts may improve mental wellbeing of nurses working in tertiary care hospitals in Bahrain.

#### Keywords:

Insomnia, stress, anxiety, nurses, shifts work disorder

### الملخص

#### الخلفية :

يؤثر الأرق والإجهاد والقلق على الصحة العقلية ويشوه التوازن في الحياة العملية للعاملين الصحيين مما يؤدي إلى التأثير على أدائهم في العمل. هدفت هذه الدراسة إلى تقييم علاقة العمل بنظام التوبات مع الأرق والقلق والإجهاد لدى الممرضات في مستشفى الرعاية الثالثية في البحرين.

#### طريقة البحث :

استخدمنا تصميم دراسة مقطعة (cross-sectional)، ينكون من 345 ممرض في أحد المستشفيات الرئيسية لرعاية الثالثية في البحرين. تم اختيار العينة على منهج نسبة الاحتمال إلى الحجم. أكملت الممرضات استبياناً يحتوي على العناصر التالية: البيانات الاجتماعية والديموغرافية، مقياس بيرغن للأرق، مقياس التوتر المدرك، ومقياس اضطراب العمل بنظام التوبات.

#### النتائج :

كان معدل انتشار الأرق أعلى (35.7%) لدى الممرضون الأصغر سناً (٢٠ إلى ٣٣ سنة)، البحرينيون (92.2%)، العاملون في العمليات الجراحية (80.5%) وفي طب الأطفال (80.0%)، ومع من لديهم 5-6 سنوات من الخبرة في العمل بنظام التوبات (81.0%)، ومن لديهم بين 1 إلى 3 نوبات ليالية في الشهر (92.0%). يتراوح عمر الممرضين الذين يعانون من مستويات عالية من التوتر بين 20 و30 عاماً من الأصل البحريني، حاصلين على بكالوريوس، عملوا في قسم طب الأطفال لمدة 4 إلى 6 أيام في الشهر، ولم يستهلكوا المشروبات التي تحتوي على الكافيين ( $p = <0.05$ ). دراستنا تشير إلى انتشار اضطراب العمل بنظام التوبات بمعدل 11.3%.

#### الخلاصة :

معدل انتشار الأرق، ومستوى التوتر والقلق مرتفع لدى الممرضون بالبحرين، وكان مرتبطة بشكل كبير بأداء عمل التوبات. ومع ذلك، اضطراب العمل بنظام التوبات في أولئك الذين يعانون من الأرق منخفضاً على الرغم من أنه لا يزال أعلى من أولئك الذين لا يعانون من الأرق. ساعات العمل المتوازنة والدعم في وقت التقييم وعلاج مشاكل الصحة العقلية المحتملة ستساهم في تحسين السلامة العقلية لدى الممرضون في مستشفيات البحرين.

## Introduction

Tertiary care hospital nurses frequently work in shifts that affects their own health and well-being in different ways. Some nurses may develop conditions like insomnia and anxiety because of continued shift work [1,2].

Insomnia may be defined as difficulty in sleeping as reported by the individuals themselves. It must occur at least 3 times per week for more than one month and is often associated with difficulty in falling asleep, staying asleep, or nonrestorative sleep, even in the presence of the appropriate opportunity and circumstances for proper sleep [3]. Individuals suffering from insomnia often experience daytime impairment or distress often affecting their performance at work leading to problems like committing occupational errors [4]. Insomnia has also been seen to coexist with some other mental health symptoms including anxiety and stress. Anxiety is commonly associated with stress and is a regular human emotion faced by many individuals. As defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5™), generalized anxiety disorder is a condition where the individual finds it hard to control their worry. It is associated with three of the six symptoms, including restlessness, irritability, feeling easily fatigued, difficulty concentrating, muscle tension, and/or sleep disturbance [5]. When anxiety exceeds the average threshold, it distorts the individual; leading to a non-adaptive response and a dysfunctional state. Women usually have a higher prevalence of anxiety

disorders than men, the female to male ratio of panic disorder and generalized anxiety disorder is about 2:1 [6].

Stress, on the other hand, is a more serious mental disorder compared to the anxiety and affects not only the individuals themselves, but it is also a burden on their families. Stress also has an economic impact on society because of low productivity, and it also disturbs people's quality of life [7].

Considering that the nurses work in a highly demanding and intense work environment, it is important to understand and assess their mental health. Although studies have shown that the shift work could lead to a range of psychosomatic disorders in nurses, few studies have explored such a relationship in the healthcare context of Gulf Cooperation Council countries. Shift work has been previously shown to disturb workers' health through psychosocial, behavioral, or psychological mechanisms [8]. Studies have shown that insomnia, excessive sleepiness, fatigue, anxiety, and depression are more prevalent in employees involved in shift work [9]. In the present study, we aimed to assess how shift work could be linked with insomnia and stress among nurses in a tertiary care hospital in Bahrain.

## Methods

### *Study design and sample*

This cross-sectional study was carried out between July and August 2016 at a tertiary care hospital in Bahrain. The study population included about 2150 nurses working in the hos-

pital during 2016. At least 2000 of them were involved in shift work at the time of this study. Generally, about half of the nurses in Bahrain are expatriates, and most are female. A sample size of 345 nurses, consisting of only those involved in shift work in the past year, was obtained using the sample size estimation formula for simple random sampling, with the assumptions of 95% level of confidence, 34% prevalence of insomnia and 5% bound on the error. Based on the population proportion to size sampling, we selected 90 nurses from Pediatric, 86 from Obstetrics and Gynecology, 89 from Medical, 52 from Accident and Emergency, and 28 from the surgical department. Nurses were included to participate in the study by convenient sampling. Bahraini and non-Bahraini nurses who worked either during night or day shifts were eligible to participate in the study. Data collection

Participants were approached by the data collection teams in their wards and requested to fill in the questionnaires while the data collectors waited, which ensured that participants completed the questionnaires, and if they needed any assistance with understanding any questions, the data collectors could help them. The data were collected through a validated self-administered questionnaire consisting of four sections of questions. Information was collected about the social and demographic variables, the departments where they worked, and whether they took any caffeinated drinks or medications to stay awake. Bergen's Insomnia Scale was used to diagnose insomnia<sup>[9]</sup>, and consisted of six questions, and each

had a seven-point scale where the number between 0 and 7 indicated days per week a certain symptom had been experienced. The total score ranged from 0 to 42. A score of 3 or higher on at least one of the first four questions (night-time problems), combined with a score of 3 or higher on at least one of the two last questions (daytime consequences) was regarded as the fulfillment of the insomnia criteria. The scale was based on the American Psychiatric Association DSM-IV-IR inclusion criteria for insomnia. To distinguish between participants with or without Shift Work Disorder, four questions were used. These questions were developed based on the criteria for Shift Work Disorder from the International Classification of Sleep Disorders<sup>[10]</sup>. Perceived Stress Scale was used for measuring the perception of stress by asking ten questions, which focused on the person's thoughts and feelings<sup>[11]</sup>. The data were analyzed using Statistical Package for the Social Sciences version 20.

#### *Ethical approval*

Ethical approval for the study was obtained from the Ethics and Review committee of Arabian Gulf University and the Ministry of Health Bahrain. The purpose of the study was explained to the participants, and a prior written consent was obtained before the questionnaire administration.

#### **Results**

The mean age of the nurses was  $36.8 \pm 7.7$  years, 62.9% were non-Bahraini, and 37.1%

were Bahraini. About half (50.3%) of the nurses had a diploma degree, 27.8% had done midwifery training, and 12.8% were qualified in general nursing. The females made up 98.60% of the sample, and most (94.8%) of the nurses were married. About 30% nurses used caffeinated drinks to stay awake during a shift, and only 0.60% took sleep medications. Nurses in our study had  $12.6 \pm 7.1$  years of experience of working as nurses,  $12.4 \pm 12.1$  years of shift work experience and they were involved in  $7.60 \pm 2.50$  nights of shift work in a month.

The prevalence of insomnia in our sample was

66.4%. We found a significant relationship of insomnia with age, nationality, marital status and educational level, and the department where the nurses worked. Nurses who worked in the surgery and Pediatric departments and those who had one to five years of total night work experience had the highest prevalence of insomnia. The number of night shifts per month had a significant relationship with insomnia, as nurses who had more night shifts had higher levels of insomnia ( $P<0.002$ ). In the nurses who had insomnia, 38% used caffeinated drinks (Table 1).

Table 1: Relationship of Insomnia, sociodemographic and shift work experience and stimulating hot drink-related variables among nurses in Bahrain

		Insomnia		p-value*
		Yes (%)	No (%)	
Age (Years)	20-30	66 (85.70)	11 (14.30)	<0.001
	31-40	125 (67.90)	59 (32.10)	
	41-50	27 (41.50)	38 (58.50)	
	51 and above	11 (57.90)	8 (42.10)	
Gender	Male	4 (80.00)	1 (20.00)	0.516
	Female	225 (66.20)	115 (33.80)	
Nationality	Bahraini	118 (92.20)	10 (7.80)	<0.001
	Non-Bahraini	111 (51.20)	106 (48.80)	
Marital Status	Single/Engaged	11 (91.70)	1 (8.30)	0.033
	Married	212 (64.80)	115 (35.20)	
	Divorced/Widowed	6 (100.00)	0 (0.00)	
Educational Level	B.Sc.	119 (79.30)	31 (20.70)	<0.001
	Master's degree	4 (50.00)	4 (50.00)	
	Others	106 (56.70)	81 (43.30)	
Department	Pediatrics	72 (80.00)	18(20.00)	<0.001
	Gynecology	43 (50.00)	43 (50.00)	
	Medical	56 (62.90)	33 (37.10)	
	Accidents and Emergency	34 (65.40)	18 (34.60)	
	Surgery	24 (85.70)	4 (14.30)	

Years of Experience	01-05	43 (84.30)	8 (15.70)	0.04
	06-10	62 (61.40)	39 (38.60)	
	11-15	57 (69.50)	25 (30.50)	
	16-20	44 (62.00)	27 (38.00)	
	21-25	10 (52.60)	9 (47.40)	
	26 and above	11 (57.90)	8 (42.10)	
Years of Night Work Experience	01-5	47 (81.00)	11 (19.00)	0.037
	06-10	61 (62.20)	37 (37.80)	
	11-15	62 (68.90)	28 (31.10)	
	16-20	37 (60.70)	24 (39.30)	
	21-25	8 (47.10)	9 (52.90)	
	26 and above	7 (50.00)	7 (50.00)	
Night Shifts per Month	0-3	23 (92.00)	2 (8.00)	0.002
	04-5	56 (75.70)	18 (24.30)	
	07-9	101 (59.10)	70 (40.90)	
	10-12	45 (70.30)	19 (29.70)	
Sleep Medication	Yes	2 (0.90)	0 (0.00)	0.313
	No	227 (99.10)	116 (100.00)	
Caffeinated drinks	Yes	87 (38.00)	15 (12.90)	<0.001
	No	142 (62.00)	101 (87.10)	

Perceived Stress Scale measurements showed a mean score of  $17.24 \pm 5.6$ , which indicated that most of our sample had "high level" of stress. Overall, prevalence of very high, high, average, low, and very low levels of stress was 27.8%, 40%, 16.2%, 9.3%, and 6.4%, respectively. More than half (52.3%) of the Bahraini nurses between the ages 20 and 30 years had "very high" stress level, and most nurses who only had a B.Sc. degree suffered from high to very high levels of stress ( $P<0.001$ ). On the other hand, there was no significant relationship between stress with gender or marital status ( $P>0.05$ ). Among the sample, 38.9% of

nurses who worked in the Pediatric department had very high levels of stress. Nurses with one to five years of night work experience also had the highest levels of stress ( $P<0.05$ ). Moreover, 43.2% of nurses with four to six-night shifts per month had the highest stress level. Lastly, most nurses who did not take caffeinated drinks suffered from higher levels of stress ( $P<0.001$ ) (Table 2).

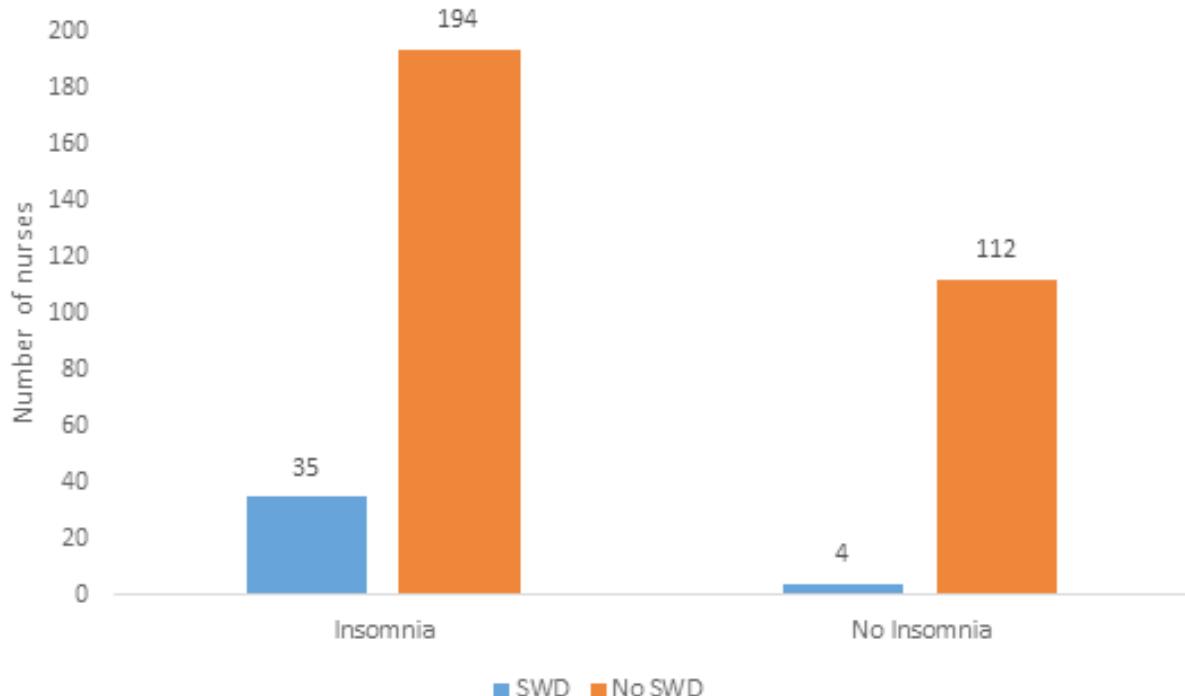
Table 2: Relationship of perceived stress levels (perceived stress scale) with sociodemographic variables of nurses in Bahrain

		Perceived stress levels					
n (%)		Very low	Low	Average	High	Very high	p-value *
		n (%)	n (%)	n (%)	n (%)		
Age	20-30	1 (1.30)	4 (5.20)	7 (9.10)	31 (40.30)	34 (44.20)	0.002
	31-40	10 (5.40)	16 (8.70)	34 (18.50)	76 (41.30)	48 (26.10)	
	41-50	9 (13.80)	10 (15.40)	11 (16.90)	22 (33.80)	13 (20.00)	
	51 and above	2 (10.50)	2 (10.50)	4 (21.10)	10 (52.60)	1 (5.30)	
Nationality	Bahraini	2 (1.60)	3 (2.30)	10 (7.80)	46 (35.90)	67 (52.30)	<0.001
	Non-Bahraini	20 (9.20)	29 (13.40)	46 (21.20)	93 (42.90)	29 (13.40)	
Marital Status	Single / Engaged	0 (0.00)	1 (8.30)	0 (0.00)	5 (41.70)	6 (50.00)	0.155
	Married	22 (6.70)	31 (9.50)	53 (16.20)	131 (40.10)	90 (27.50)	
	Divorced / Widowed	0 (0.00)	0 (0.00)	3 (50.00)	3 (50.00)	0 (0.00)	
Educational Level	B.Sc.	5 (3.30)	8 (5.30)	15 (10.00)	70 (46.70)	52 (34.70)	<0.001
	Higher Education	0 (0.00)	0 (0.00)	3 (37.50)	4 (50.00)	1 (12.50)	
Department	Others	17 (9.10)	24 (12.80)	38 (20.30)	65 (34.80)	43 (23.00)	
	Pediatric	4 (4.40)	6 (6.70)	11 (12.20)	34 (37.80)	35 (38.90)	
	Gynecology	8 (9.30)	11 (12.80)	8 (9.30)	36 (41.90)	23 (26.70)	
	Medical	4 (4.50)	9 (10.10)	26 (29.20)	31 (34.80)	19 (21.30)	0.012
	A&E	6 (11.50)	4 (7.70)	8 (15.40)	25 (48.10)	9 (17.30)	
	Surgery	0 (0.00)	2 (7.10)	3 (10.70)	13 (46.40)	10 (35.70)	
Years of Experience	01-5	1 (2.00)	3 (5.90)	5 (9.80)	19 (37.30)	23 (45.10)	
	06-10	6 (5.90)	10 (9.90)	15 (14.90)	47 (46.50)	23 (22.80)	
	11-15	5 (6.10)	7 (8.50)	17 (20.70)	31 (37.80)	22 (26.80)	0.325
	16-20	5 (7.00)	7 (9.90)	14 (19.70)	23 (32.40)	22 (31.00)	
	21-25	3 (15.80)	2 (10.50)	2 (10.50)	9 (47.40)	3 (15.80)	
	26 & above	2 (10.50)	3 (15.80)	3 (15.80)	9 (47.40)	2 (10.50)	
Years of Night Work Experience	01-5	1 (1.70)	2 (3.40)	9 (15.50)	19 (32.80)	27 (46.60)	
	06-10	6 (6.10)	11 (11.20)	12 (12.20)	47 (48.00)	22 (22.40)	
	11-15	5 (5.60)	11 (12.20)	18 (20.00)	38 (42.20)	18 (20.00)	<0.023
	16-20	5 (8.20)	4 (6.60)	14 (23.00)	18 (29.50)	20 (32.80)	
	21-25	3 (17.60)	2 (11.80)	0 (0.00)	8 (47.10)	4 (23.50)	
	26 & above	1 (7.10)	2 (14.30)	3 (21.40)	7 (50.00)	1 (7.10)	
Night Shifts Per Month	0-3	3 (12.00)	1 (4.00)	4 (16.00)	7 (28.00)	10 (40.00)	0.024
	04-5	1 (1.40)	7 (9.50)	8 (10.80)	26 (35.10)	32 (43.20)	
	07-9	10 (5.80)	15 (8.80)	29 (17.00)	76 (44.40)	41 (24.00)	
	10-12	8 (12.50)	5 (7.80)	14 (21.90)	25 (39.10)	12 (18.80)	
Caffeinated Drinks	Yes	3 (13.60)	2 (6.20)	10 (17.90)	48 (34.50)	39 (40.60)	<0.001
	No	19 (86.40)	30 (93.80)	46 (82.10)	91 (65.50)	57 (59.40)	

Our study showed a significant relationship between insomnia and Shift Work Disorder ( $P<0.001$ ). Although only 11.3% nurses had

Shift Work Disorder; however, 15.3% suffered from Shift Work Disorder and insomnia at the same time (Fig. 1).

Figure 1: Relationship of Shift Work Disorder with insomnia in nurses in Bahrain



## Discussion

We found that 66.4% of the nurses suffered from insomnia, 40.3% suffered from “high” levels of stress, and 27.8% suffered from “very high” levels of stress. A relationship between working in shifts and insomnia and stress was also a significant finding of this study. Our study showed that nurses who had worked for 1-5 years suffered from insomnia more than those who had more work experience. This could be explained by a lack of coping behavior among less experienced nurses<sup>[12]</sup>. Nurses working in the Surgical and Pediatric departments reported insomnia more frequently than those in other departments. Our results are consistent with another study on nurses in public hospitals in Greece, which also showed that insomnia was more common among the nurses who worked in the surgical departments<sup>[13]</sup>. This could be due to the fact

that surgical department nurses work within an intensive and stressful work environment compared to other departments, and they usually spend long time while assisting surgical procedures and caring for sick children.

Another finding from the present study was that 62.0% of those who did not consume any caffeinated drinks did not suffer from insomnia. A study from Brazil showed that nurses who drank more than 3 cups of caffeine drinks a day had more insomnia (39.2%)<sup>[14]</sup>. In our study, a relationship was found between the number of night shifts performed per month and insomnia, with a high prevalence in the nurses who had up to 3 shifts per month. This is consistent with a study that showed that insomnia was more common among those who worked for 2-3-night shifts per month as compared to those who did not<sup>[15]</sup>. It could be because that nurses with more night shifts may be able to cope with the disturbance in their

sleeping pattern better than those who were not as frequently disturbed.

We also found a significant relationship between insomnia and nurses' age, with the highest prevalence among nurses in the youngest age group (20-30 years). Sleep disturbances in nurses of younger age groups have also been previously reported by a study of sleep disturbance in employed women [16]. The study concluded that there was a higher incidence of sleeping disturbance in those who worked in shifts, and their age and family factors contributed more to sleep disturbances than caffeine and alcohol intake [16].

Also, 52.3% of Bahraini resident nurses suffered from very high levels of stress. In addition, the consumption of caffeinated beverages also seemed to affect the stress in nurses. The nurses who consumed such beverages had lower stress levels than those who did not. This is likely because the consumption of caffeine can stimulate the release of dopamine hormone in the brain which can improve alertness [17]. There was a statistically significant relationship between insomnia and Shift Work Disorder in our study, which is consistent with results from a study that showed that about one-third of the nurses had symptoms indicative of Shift Work Disorder, with highest prevalence in nurses working in night shifts [18]. Our study showed a significant relationship between anxiety and night shift work. A study on nurses in Norway showed how insomnia, excessive sleepiness and fatigue, anxiety, depression, and Shift Work Disorder might all be linked together in nurses with less than 11 hours' rest between shifts [10].

A similar study from Taiwan also showed a positive relationship between anxiety experienced by nurses with their age [19]. Another study with Norwegian nurses showed that about one-third of the nurses had symptoms indicative of Shift Work Disorder, with high-

est prevalence in nurses working during night shifts. Also, Shift Work Disorder has shown a significant relationship with depression and anxiety [20]. However, another study done with Greek nurses suggested that there was no such relationship between anxiety and being involved in shift work [21].

### **Strengths and limitations**

The fact that we drew the sample from all major departments, considering population in the hospital, is a strength of the study because it adds value to the sample representation and, therefore, some generalizability of the findings. Another strength was that there were no refusals in the study which ensured that all the selected and eligible nurses participated in our study. Using validated standard tools for data collection was also a strength of this study. However, our study was not without limitations. However, the nurses took their time to fill in the questionnaire while the data collectors were present in the hospital premises.

### **Conclusion**

Insomnia and stress coexisted at very high levels in nurses in the tertiary care hospital of Bahrain. Shift Work Disorder was also related to insomnia in these nurses, which indicates that including working in highly demanding departments and working in night shifts, can lead to insomnia and stress among nurses in Bahrain. To help address this problem, it is critical for nurses to maintain a healthy work-life balance. The tertiary hospitals of the region and other similar settings must also provide adequate resting opportunities for the nurses to prevent these psychological and mental health effects of shift work in nurses.

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## Original Article

# Public awareness of risk factors of gastric cancer and attitude toward disease screening in Saudi Arabia

Mohammed N Aldosari<sup>1</sup> \*, Sulaiman D Almasoud<sup>2</sup>, Ohoud A Alobaid<sup>3</sup>, Ahmed A Alrukban<sup>2</sup>, Abdulrahman K Alajlan<sup>4</sup>, Nouf Z Almutairi<sup>3</sup>, Abdullatif A Alnaaim<sup>5</sup>

1.Consultant, Assistant Professor of Family Medicine, King Abdulaziz Medical City, College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia.

2. Medical intern, College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia.

3. 5th year-medical-student, College of Medicine, Majmaah University, Majmaah, Saudi Arabia

4. 6th year-medical student, College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia

5. Medical intern, College of medicine, Olsztyn University, Olsztyn, Poland

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Corresponding author : Mohammed Nasser Aldosari, Family Medicine & PHC. Director King Abdulaziz

\*Housing City, MNGHA, College of Medicine KSAU-HS. King Abdulaziz Medical City Riyadh.

P.O. Box 22490 Riyadh 11426 Saudi Arabia.

Email Address: dosarim5@ngha.med.sa

### Abstract

#### Background:

Although incidence of gastric cancer is falling worldwide, it is the second leading cause of cancer-related mortality and the fourth most common cancer globally. The study aims to assess the public level of awareness of risk factors of gastric cancer and attitude toward disease screening among general population in Saudi Arabia.

#### Methods:

A cross-sectional study using a pre-tested questionnaire through social media applications was used to assess participants awareness of gastric cancer.

#### Results:

Total of 1410 respondents were included in this study and among them 858 (60.9%) were females and most of them were aged between 19 years to 29 years, 843 (59.8%). Respondents' perception of self-risk of gastric cancer were 693 (49.1%) had very low risk, 574 (40.7%) had low risk, 137 (9.7%) had average risk, and the remaining six respondents (0.4%) had high risk. Study participants were aware of 'chronic infection' as the most powerful risk factor, 764 (54.2%). Regarding the usefulness of regular gastric cancer screening, 1011 (71.7%) answered 'very useful' but only 30 (2.1%) undergo regular screening for gastric cancer. Respondents' age, health status, smoking habit, drinking habit, consumption of salty food, and consumption of spicy food were statistically significantly characteristics associated with their 'self-risk' of gastric cancer.

### الملخص

#### الخلفية :

على الرغم من انخفاض معدلات الإصابة بسرطان المعدة يحل سرطان المعدة ثانياً في عدد وفيات السرطان ورابع أكثر الأورام في نسبة الإصابة. تهدف الدراسة إلى قياس الوعي بين عامة الشعب السعودي لعوامل الخطر بالإصابة بسرطان المعدة ورأيه تجاه الفحص المنتظم لسرطان المعدة.

#### طريقة البحث :

تم استخدام استبيان ينشر في وسائل التواصل الاجتماعي لقياس الوعي.

#### النتائج :

عدد من أجابوا على الاستبيان ١٤١٠، كان عدد النساء فيها ٢٩١٩٨٥٨ بنسبة (٦٠,٩٪) وغالبهم في الفئة العمرية ما بين ٤٠-٥٩٪. وعي المشاركون بخطر الإصابة بسرطان المعدة كان ٦٩٣ (٤٩,١٪) ضئيل جداً، و ٤٧٣ (٤٠,٧٪) قليل، و ١٣٧ (٩,٧٪) متوسط و ٦٤ (٤,٠٪) عالٍ. يعتقد المشاركون أن التهاب المعدة المزمن هو عامل الخطر الأكثر تأثيراً بعدد ٧٦٢ (٥٤,٢٪). يعتقد المشاركون أن الفحص المنتظم لسرطان المعدة مفيد جداً بعدد ١٠١١ (٧١,٧٪) ولكن ٣٠ شخص فقط (٢,١٪) من يجري فحص منظم لسرطان المعدة. عامل العمر والتدخين والحالة الصحية واستخدام الكحول واستهلاك الأكل المملح والأكل الحار كانت عوامل مؤثرة بوعي المريض بخطر إصابته بسرطان المعدة.

**Conclusion:**

The study showed low level of knowledge of gastric cancer risk factors in Saudi Arabia, but it indicates positive attitude towards screening with only 30 respondents undergoing regular screening.

**Keywords:**

gastric cancer, Saudi Arabia, Public awareness, gastric cancer screening.

**الخلاصة :**

أظهرت الدراسة قلة وعي عامة السعوديين بعوامل الإصابة بسرطان المعدة برغم رأيهم الإيجابي تجاه الفحص المنتظم، وإن كان عدد من أجروا الفحص المنظم ٣٠ شخصاً فقط.

**كلمات مفتاحية:**

سرطان المعدة في السعودية، عوامل الخطر للإصابة بسرطان المعدة، الفحص المنتظم لسرطان المعدة.

## Introduction

Although incidence of gastric cancer is falling worldwide, it is the second leading cause of cancer-related mortality and the fourth most common cancer globally. Gastric cancer has geographical differences where significantly more cases of gastric cancer were reported in less developed countries than in more developed countries<sup>[1]</sup>. Comparing nations, the highest incidence rates are observed in East Asia, East Europe, and South America, while the lowest rates are observed in North America and most parts of Africa. Gender differences were also reported with a rate of 2 to 3 folds higher in men<sup>[2]</sup>. Gastric cancer patients commonly present with vague symptoms such as dyspepsia in early stages. In advanced stages, patients might present with abdominal pain, weight loss, anorexia, or symptoms related to the site of tumor<sup>[3]</sup>. Diagnosis of gastric cancer remains a challenge as it is detected most of the time at late stages. Various diagnostic tools exist, but endoscopy and biopsy are needed to make diagnosis<sup>[4]</sup>.

In spite of high mortality and morbidity of gastric cancer, no well-established screening program has been implemented worldwide except for countries where incidence of gastric cancer is high such as South Korea<sup>[5]</sup>. Different screening programs were implemented in the past in countries with high incidence of gastric cancer. Upper gastrointestinal series, gastroscopy, Helicobacter pylori antibody and serum pepsinogen screening were used in Ja-

pan<sup>[6]</sup>. A large Japanese case-control study suggest 30% reduction in gastric cancer mortality by endoscopic screening compared with no screening within 36 months before the date of diagnosis of gastric cancer<sup>[7]</sup>. A recent meta-analysis found that an endoscopic screening for gastric cancer in Asian populations showed 40% reduction in mortality<sup>[8]</sup>.

Known risk factors of gastric cancer are previous Helicobacter pylori infection, old age, male gender, smoking, alcohol drinking, obesity, family history, and dietary habits. Dietary habits known to be a risk for gastric cancer are eating processed meat, salty or smoked food, and lack or inadequate intake of vegetables and fruit<sup>[9]</sup>. Dietary habits were believed to be responsible for the geographical variation of incidence of gastric cancer<sup>[10]</sup>. Public knowledge of warning signs and risk factors of gastric cancer hasn't been well-studied worldwide. A South Korean population-based study testing the public awareness of gastric cancer suggested that stress is believed to be the strongest factor to develop gastric cancer followed by chronic gastritis, and gastric ulcer. 60.4% Thought cancer can be prevented by lifestyle modifications such as avoidance of salty food and smoking<sup>[5]</sup>. Other study in prevalent area of gastric cancer in northern of Iran suggested that 74% of people believe that anemia is a warning sign of gastric cancer, and 91% believe that smoking is the most powerful risk factor, and cessation of smoking is the best way to prevent the cancer<sup>[11]</sup>. In addition, a recent study conducted in China to

assess people attitude toward screening, 47% showed low level of knowledge about warning signs and risk factors of gastric cancer, and 63% think that the reason for not undergoing a regular screening is lack of symptoms [12].

The incidence of gastric cancer has been studied in Saudi Arabia, but no study has been conducted to assess people knowledge of gastric cancer and its risk factors. Although gastric cancer in Saudi Arabia incidence is falling, a large retrospective study in Riyadh suggested gastric cancer to be the most frequent gastrointestinal cancer [13]. In 2013, The Saudi Arabia Cancer Incidence Report showed that gastric cancer to rank the 9th cancer among men and the 12th in women. It accounts for 2.7% of all adult cancers in Saudi Arabia, and the median age at diagnosis was 65 [14].

High morbidity and mortality of gastric cancer mandates education of Saudi population, and reduction of mortality in high-risk population was significant. Studies regarding knowledge about gastric cancer are lacking in Saudi population. This study might serve as basis for future practice and a step toward assessing quantitatively people perception of preventable risk factors and warning signs of gastric cancer and attitude toward screening and early detection.

## Methods

A cross-sectional study was conducted in September 2019 using pretested questionnaire through social media applications. The questionnaire was distributed along with structured informed consent by King Abdullah International Medical Research Centre. The calculated sample size is 1067 with 3% margin of error and 95% confidence level. The inclusion criteria were all Saudi males and females over the age of 18. The exclusion criteria were age less than 18, not living in Saudi Arabia, and

non- Saudi participants.

The questionnaire used includes questions on the following issues:

1. Sociodemographic data.
2. Perception of the self-risk of gastric cancer
3. Awareness of the attributable and preventable extent of each risk factor for gastric cancer
4. Genetic factors of gastric cancer development
5. Factors preventable by lifestyle modification
6. Value of early detection and attitudes toward regular screening

Relationship between respondents' self-risk of gastric cancer and baseline characteristics were observed by Chi-Squared test. The Significance was set at  $p < 0.05$ . The analysis was performed using the Statistical Package for Social Science (SPSS), version 24.0 (IBM, Armonk, NY, USA). The IRB was sought and approved by King Abdullah International Medical Research Centre. IRBC/1567/19

## Results

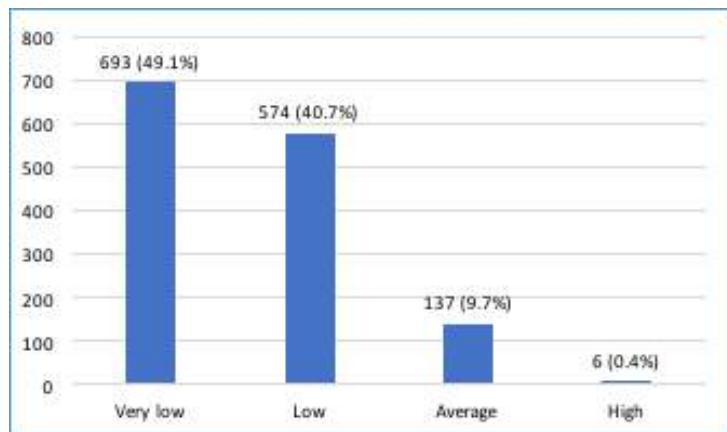
Total of 1410 respondents were included in this study and among them 858 (60.9%) were females. All respondents were adults and most of them were aged between 19 years to 29 years, 843 (59.8%). Majority of respondents had high educational level (college or above), 1093 (77.5%), reported having a good health status, 1236 (87.7%), non-smoker, 1226 (87.0%), and non-alcoholic, 1367 (97.0%) (Table 1).

Table 1: Baseline characteristics of the respondents (n = 1410)

Characteristics	Attributes	N	%
Gender	Male	552	39.1
	Female	858	60.9
Age in years	19-29	843	59.8
	30-39	197	14.0
	40-49	194	13.8
	50-59	157	11.1
	60 or more	19	1.3
Level of education	Elementary school	4	0.3
	Intermediate school	20	1.4
	High school	225	16.0
	Bachelor	1093	77.5
	Other	68	4.8
Health status	Good	1236	87.7
	Intermediate	170	12.1
	Bad	4	0.3
Smoking	Yes	184	13.0
	No	1226	87.0
Alcoholism	Yes	43	3.0
	No	1367	97.0
Consumption of salty food	Always	467	33.1
	Sometimes	774	54.9
	Rarely	161	11.4
	Never	8	0.6
Consumption of spicy food	Always	232	16.5
	Sometimes	696	49.4
	Rarely	354	25.1
	Never	128	9.1

According to respondents' perception of self-risk of gastric cancer, 693 (49.1%) had very low risk, 574 (40.7%) had low risk, 137 (9.7%) had average risk, and the remaining six respondents (0.4%) had high risk (Fig. 1).

Fig. 1: Distribution of all respondents by their perception of self-risk of gastric cancer (n = 1410)



Study participants were aware of ‘chronic infection’ as gastric cancer most powerful risk factor, 764 (54.2%), followed by ‘alcoholism’, 725 (51.4%), smoking, 707 (50.1%), and Helicobacter pylori infection, 655 (46.5%). The factors that the respondents were the least aware of were ‘vegetables or fruits’, 11 (0.8%) followed by, ‘gender’, 52 (3.7%), and ‘previ-

ous gastrectomy’, 140 (9.9%). When asked about the gastric cancer prevention if a certain factor was removed would lead to reduction of incidence of gastric cancer, the highest number of respondents recognized ‘smoking’, 722 (51.2%), then ‘alcoholism’, 623 (44.2%), and ‘H. pylori infection’, 589 (41.8%) (Fig. 2, 3).

Fig. 2: Distribution of all respondents by awareness about the factors responsible for gastric cancer, N (%) (n =1410)

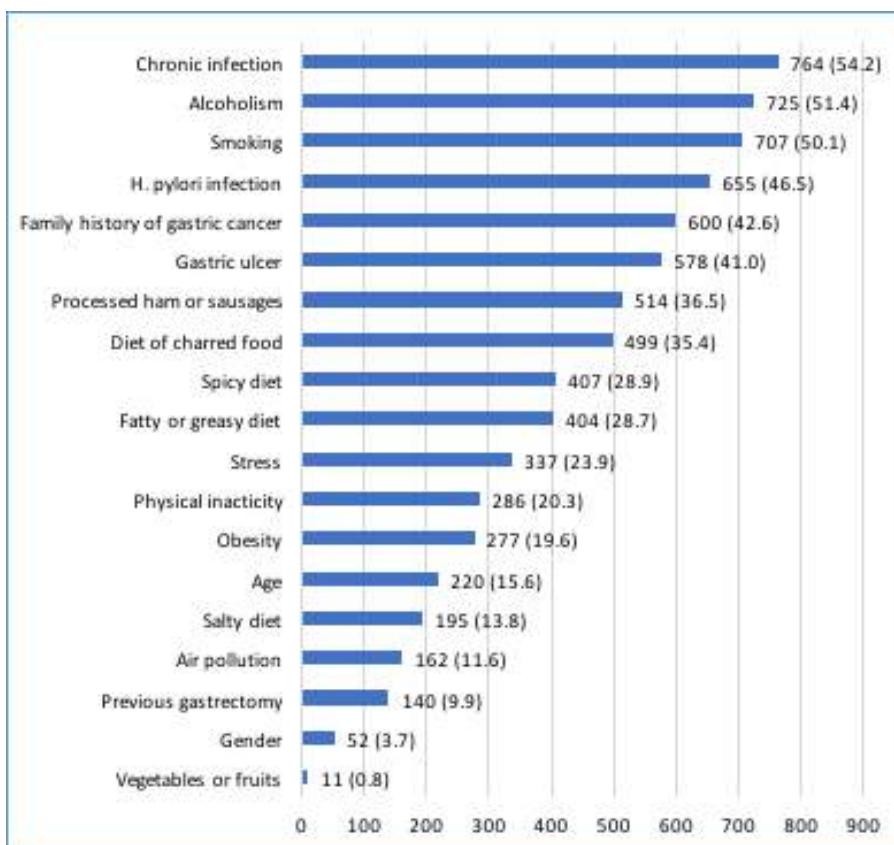
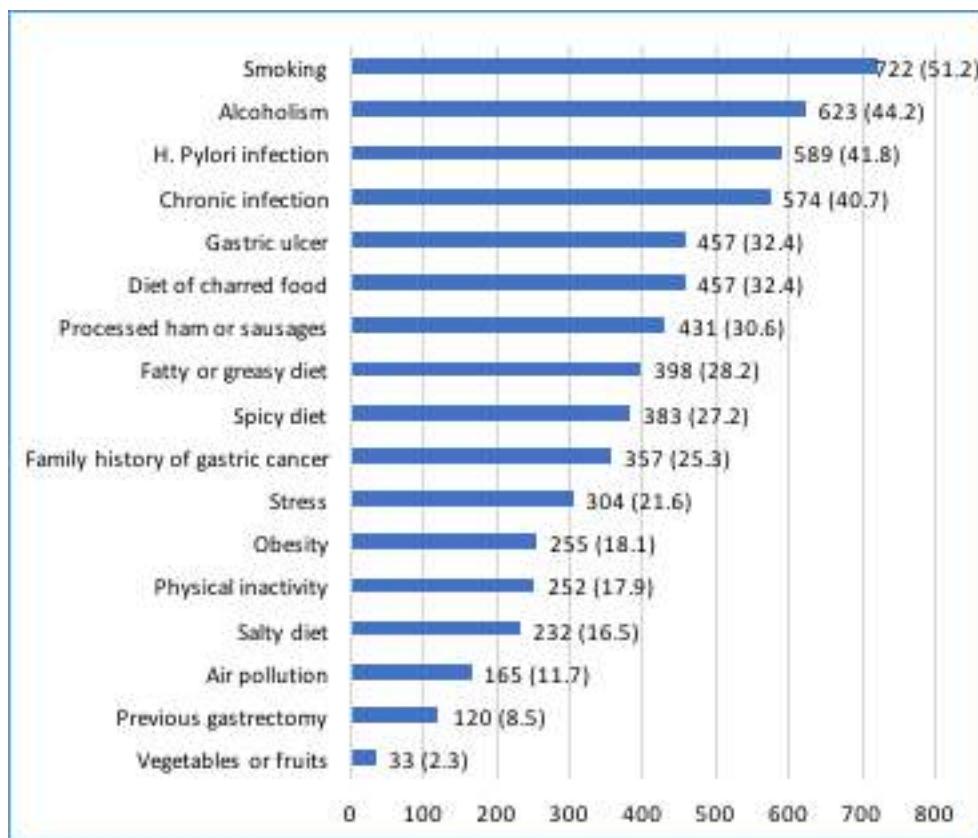


Fig. 3: Distribution of all respondents by their thought of gastric cancer prevention when a certain risk factor is totally removed, N (%) (n=1410)



About 30% of the respondents thought gastric cancer is genetically predetermined, 50% thought it can be prevented by lifestyle modi-

fication, and 50% thought gastric cancer could be fully curable (Table 2).

Table 2: Distribution of all respondents by their knowledge of genetic predisposition, lifestyle modification, and curability of gastric cancer (n = 1410)

	What % of gastric cancer do you think is genetically predetermined?	What % of gastric cancer do you think is preventable by modification of lifestyle?	What % of gastric cancer do you think is curable?
Mean	40.0525	60.4915	49.3582
Std. Error of Mean	5.75506	7.45304	0.79989
Median	30.0000	50.0000	50.0000
Std. Deviation	216.10240	279.86128	30.03589

Respondents' age, ( $p < .001$ ), health status ( $p < .001$ ), smoking habit ( $p < .001$ ), drinking habit ( $p = .008$ ), consumption of salty food ( $p < .001$ ), and consumption of spicy food ( $p < .001$ ) were statistically significantly char-

acteristics associated with their 'self-risk' of gastric cancer. However, gender, and level of education were not significantly associated with 'self-risk' of gastric cancer ( $p$  values  $> .050$ ) (Table 4).

Table 4: Relationship between respondents' self-risk of gastric cancer and baseline characteristics.

Characteristics		Self-risk				p-value
		Very low %	Low %	Average %	High %	
Gender	Male	38.7	39.0	41.6	50.0	.872
	Female	61.3	61.0	58.4	50.0	
Age in years	19-29	51.5	68.6	65.7	33.3	<.001
	30-39	16.7	12.0	8.8	0.00	
	40-49	16.2	11.3	10.9	33.3	
	50-59	14.0	7.1	13.1	16.7	
	60 or more	1.6	0.9	1.5	16.7	
Level of education	Elementary school	0.4	0.0	0.7	0.0	.088
	Intermediate school	1.6	1.4	0.0	16.7	
	High school	15.6	16.6	16.1	0.0	
	Bachelor	76.5	78.6	78.8	66.7	
	Other	5.9	3.5	4.4	16.7	
Health status	Good	92.4	84.5	79.6	33.3	<.001
	Intermediate	7.4	15.5	19.7	50.0	
	Bad	0.3	0.0	0.7	16.7	
Smoking	Yes	8.4	17.8	16.1	33.3	<.001
	No	91.6	82.2	83.9	66.7	
Alcoholism	Yes	1.6	4.2	5.1	16.7	.008
	No	98.4	95.8	94.9	83.3	
Consumption of salty food	Always	29.1	34.8	45.3	50.0	<.001
	Sometimes	54.7	57.1	47.4	33.3	
	Rarely	15.6	7.3	7.3	16.7	
	Never	0.6	0.7	0.0	0.0	
Consumption of spicy food	Always	14.4	16.4	24.8	66.7	<.001
	Sometimes	47.0	53.7	44.5	16.7	
	Rarely	26.3	23.9	24.8	16.7	
	Never	12.3	6.1	5.8	0.0	

## Discussion

Gastric cancer incidence is declining worldwide, but it remains the second leading cause of cancer-related mortality. Gastric cancer carries a very wide geographical variety where it is more common in Japan, South Korea, and China than other parts of the world<sup>[1]</sup>. Gastric cancer burden in Saudi Arabia is less where it ranks the 9th cancer among men and the 12th in women. It accounts for 2.7% of all adult cancers in Saudi Arabia<sup>[14]</sup>. The level of public knowledge about risk factors of gastric cancer has not been studied yet in Saudi Arabia.

Public awareness of gastric cancer has been studied previously in South Korea, Iran, and China<sup>[5, 11, 12]</sup>. Those three studies showed general lack of knowledge about the risk factors of gastric cancer. In our study, 54.2% of respondents chose the chronic infection as risk factor followed by alcohol drinking 51.4% and smoking 50.1%. These finding show gaps of knowledge about the role of diet, previous stomach surgery and genetics which are well-established risk factors as well<sup>[9]</sup>. Also, 49.1% and 40% of the respondents think their risk of developing gastric cancer is very low and low respectively. Surprisingly level of education was not associated with self-perception of risk of gastric cancer.

There is no nation-wide implemented regular screening program in Saudi Arabia. People who had undergone a gastroscopic screening were selective cases in which they have some symptoms or family history. Only 2.1% of respondents had undergone screening. Respondents main reason not to go for screening was having no symptoms 44% and not having an idea about screening 27%. The incidence of gastric cancer in Saudi Arabia is declining despite poor prognosis, but the burden of gastric cancer is less compared to the burden of other cancers which make the cost-effectiveness of regular screening questionable. That makes the need for spreading knowledge about risk

factors and warning symptoms is necessary for the people to seek help when they have symptoms.

The main strength of the study is number of respondents. The response rate was 100%, and 1410 have participated in the questionnaire. Which is attributed to the short survey and the questionnaire being distributed in most popular social media means in Saudi Arabia such as Twitter and WhatsApp. The study has some limitations as well. First, most of questions were answered subjectively. There were no specific definitions defining specific terms such as health status and salty, spicy, and charred food. Second, inclusion criteria involved all Saudis aged over the age of 18 and no exclusion of patients of personal history of cancer. Third, most of the respondents were aged between 19-29 and of high educational level which might explain most of participants are having a good health and low self-perception of the cancer.

## Conclusion

The study shows low level of knowledge of gastric cancer risk factors in Saudi Arabia, but it indicates positive attitude toward screening with only 30 respondents undergoing regular screening. More health awareness campaigns should be considered to improve knowledge about gastric cancer risk factors in Saudi population.

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## Original Article

# Gender Differences in Medical Students' Perception of Lecturing Skills

Ahmed Al Kuwaiti<sup>1</sup>, Arun Vijay Subbarayalu<sup>2</sup>, Ola Ibrahim Ramzi<sup>3</sup>

1. Associate Professor & General Supervisor, Department of Dental Education,  
College of Dentistry & Deanship of Quality and Academic Accreditation,  
Imam Abdulrahman Bin Faisal University

2. Assistant Professor, Quality Measurement and Evaluation Department,  
Deanship of Quality and Academic Accreditation. Imam Abdulrahman Bin Faisal University,  
Dammam 31441. Saudi Arabia

3. Assistant Professor, College of Public Health & Academic Accreditation Department,  
Deanship of Quality and Academic Accreditation,  
Imam Abdulrahman Bin Faisal University, Dammam 31441, Saudi Arabia

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Corresponding author : Ahmed Al Kuwaiti. Associate Professor & General Supervisor, Department of Dental Education, College of Dentistry & Deanship of Quality and Academic Accreditation, Imam Abdulrahman Bin Faisal University. P.O. box 40065. Al-Khobar 31952, Saudi Arabia. Tel: +966 13 3332500.  
Fax: +966 13 3330380. Mobile: +966 505843183. Email: akwaiiti@iau.edu.sa

### Abstract

#### Background:

Students' evaluations of instructors' lecturing skills have proved to be an essential component of quality management in higher education institutions (HEIs). Hence, this study intended to reveal the gender differences in medical students' perception of lecturing skills.

#### Methods:

The exploratory study design was adopted to explore the gender differences in medical students' perception of lecturing skills at Imam Abdulrahman Bin Faisal University (IAU) in Saudi Arabia. This study covers the entire population of students ( $n=570$ ) studying an undergraduate medical program at IAU during the academic year 2015-16. "Students Survey of Lecturing Skills (SSLS)" questionnaire was administered to these students using "UDQuest". The data analysis was carried out using SPSS version-20. The SEM analysis was done using Analysis of Moment Structures (AMOS) software version 5.0.

#### Results:

The SEM analysis reveals that the variables used in SSLS are positively related to the students' overall perception of lecturing skills ( $p<0.05$ ). The perception of female students towards lecturing skills is significantly better than the male students.

#### Conclusion:

Variables used in the SSLS questionnaire are adequately fit to assess the students' perception of lecturing skills. Policy-makers can use these variables to evaluate and monitor the quality of teaching at HEIs. There is a significant difference

### الملخص

#### الخلفية :

لقد ثبتت تقييمات الطلاب لمهارات الأداء التدريسي للمحاضرين أهمية هذه التقييمات التي تعد عنصراً جوهرياً في إدارة الجودة في مؤسسات التعليم العالي. تحل هذه الدراسة كيفية تطبيق النماذج لتقدير مدى كفاية المتغيرات المدرجة في استبيان استطلاع آراء طلاب الطب حول مهارات الأداء التدريسي ودراسة الفروق بين الجنسين في معرفة مهارات الأداء التدريسي.

#### طريقة البحث :

تم تبني تصميم دراسة استكشافية ومن ثم تحليل البيانات التي تم جمعها من طلاب الطبي بجامعة الإمام عبد الرحمن بن فيصل بالمملكة العربية السعودية. تم جمع البيانات من جميع الطلاب في مرحلة البكالوريوس (٥٧٠) خلال العام ٢٠١٥-٢٠١٦. تم جمع البيانات عن طريق الاستبيان. تم التحليل عن طريق SPSS.

#### النتائج :

يكشف التحليل أن المتغيرات المستخدمة في استبيان استطلاع آراء الطلاب حول مهارات الأداء التدريسي مرتبطة بشكل إيجابي بفهم الطالب الإجمالي لمهارات الأداء التدريسي، حيث يلاحظ أن فهم الطالبات (الإناث) لمهارات الأداء التدريسي أفضل بكثير من فهم الطلاب (الذكور).

#### الخلاصة :

المتغيرات المستخدمة في استبيان استطلاع آراء الطلاب حول

observed between the gender concerning the perception of lecturing skills. Although this study was conducted in a single Saudi university, given the standard regulations governing higher educational programs at institutions in the country, the findings have broader implications.

**Key words:**

Lecturing skills, Saudi Arabia, Structural equation modeling, Students perception

مهارات الأداء التدريسي ملائمة تماماً لتقدير فهم الطلاب لمهارات الأداء التدريسي، ويمكن لبعض السياسات استخدام هذه المتغيرات لتقدير ومراقبة جودة التدريس في مؤسسات التعليم العالي. ومن خلال هذه الدراسة يلاحظ أن هناك تبايناً واضحاً بين الجنسين (الذكور والإناث) فيما يتعلق بفهم مهارات الأداء التدريسي. وعلى الرغم من أن هذه الدراسة أجريت في جامعة سعودية واحدة - نظرأً للوائح العامة التي تحكم برامج التعليم العالي بمؤسسات الدولة - إلا أن نتائجها كبيرة الأثر.

**الكلمات المفتاحية :**

: مهارات الأداء التدريسي، المملكة العربية السعودية، نموذجة المعادلات البنائية، فهم الطلاب.

## Introduction

In the past few years, the quality of teaching and learning in higher education gained more attention in various countries around the globe [1,2]. The assessment of teaching quality is an extremely complex process, multidimensional, and often subjective. To carry out this task, several higher education institutions (HEIs) are taking continuous efforts to enhance the quality of teaching and learning processes through quality management systems.

One crucial component of such efforts is getting the students' feedback on teaching. The survey on 'Student Evaluation of Teaching (SET)' has been broadly studied by various researchers [3-8]. SET delivers the information to three main groups: (a) students utilize the information while selecting modules and courses; (b) teachers can make use of such information to enhance their quality of teaching; (c) managers can exploit the information to make decisions on teachers' job advancement and tenure issues and also for accountability. Therefore, HEIs have felt the need for an instrument that allows for the collection of feedback and will enable them to address the needs of all these audiences [9].

Students' feedback is an essential contributor to reflective teaching, letting lecturers improve their practice and develop their professional

skills. In order to obtain feedback, many methods can be used. Previous studies have suggested that satisfaction surveys are commonly used [10,11], and further, that the student evaluations are considered as an important tool to assess the teaching effectiveness [12-16].

For HEIs, the results of student evaluations are beneficial to administrators in helping lecturers to find exact areas for enhancing their performance [14,17] or arranging various professional development activities, which would improve their lecturing skills. Sometimes, the results of such evaluations are used to develop the key performance indices for lecturers and act as part of the staff assessment process for both job advancement and contract decisions [8,18-21]. Based on the results obtained, some policymakers may also make decisions related to pay, re-hiring, and termination of teachers. Students' evaluations of the teaching effectiveness of their lecturers, thus aid the entire institution [22].

Previous studies have evaluated students' perception of effective teaching using questionnaires or surveys [23-28]. Along similar lines, a questionnaire named Students' Survey on Lecturing Skills (SSLS) was developed by the Deanship of Quality and Academic Accreditation (DQAA) at Imam Abdulrahman Bin Faisal University (IAU) in Saudi Arabia, to capture students' perception of effective teaching.

Given the implications that poor medical education standards can have an impact on patients, the authors chose to elicit data on the perception of lecturing quality from medical students. Medical programs differ from other study programs since they offer a generally stable set of courses and use unique teaching formats such as problem-based learning and bedside teaching apart from traditional, generic teaching (lecture) formats [29]. Feedback from medical students in the past has been considered a useful tool in the evaluation of teachers' effectiveness and has been seen to enhance the quality of teaching and faculty development [30].

Student gender is one of the variables that may have a biasing effect on SET ratings [31,32]. Therefore, gender differences in students' perception of lecturing skills should also be measured using SSLS. In addition to the evaluation of gender differences, it is essential to make clear how well the variables of the SSLS questionnaire are related to overall students' perception of lecturing skills (i.e., overall satisfaction) and whether those variables are appropriate measures of the students' perception of lecturing skills. To achieve this, the present researchers adopted Structural Equation Modeling (SEM) for analysis, which is a statistical method to test hypotheses about relationships among observed and latent variables [33-35].

A few previous studies have utilized SEM to test the relationships of different variables with one another [35-41].

While exploring the literature, several other studies have been conducted to ascertain the influence of students' gender on the evaluation of teaching quality [42-47]. Two studies conducted by Dukes and Victoria and Freeman stated that there were no gender differences among students' ratings of faculty. However, the reason for this observed difference in these studies was not explained due to the nature of the research design [48,49]. In the present context, even though male and female students' study

in gender-distinct facilities at IAU, the infrastructure, facilities, and methods of teaching and learning provided to them are identical as stipulated by the Ministry of Higher Education, Saudi Arabia. Nevertheless, the perception of teaching skills in the medical program shows variation between male and female students [50,51]. This difference, therefore, necessitates a study that investigates its magnitude. Further, it may be noted that medical programs at Saudi universities are governed by common regulations and requirements set up by the Ministry of Education. Hence, a study involving the medical program at any one university may be taken to be fairly representative of the situation prevailing in such programs throughout the country.

## Methods

The exploratory study design was adopted to study the gender differences in medical students' perception of lecturing skills at IAU in Saudi Arabia. This study covers the entire population of students (N=570) studying an undergraduate medical program at IAU during the academic year 2015-2016. SSLS questionnaire was administered using an online application named "UDQuest" at the end of the semester (fall or spring) of the academic year 2015-2016. Ethical approval was obtained from the Deanship of Quality, IAU, Dammam, Saudi Arabia.

Consequently, informed consent was also acquired, and confidentiality and anonymity were assured before collecting data from the participants. Five hundred thirty-seven completed questionnaires were received, demonstrating a 94 % response rate (out of 570). Out of 537 students, 252 were male, and 285 were female.

Besides, the SSLS questionnaire consisted of five variables, with a total of 13 items and one global rating item (overall satisfaction). The level of agreement of students to those

questions in each variable was expressed in a 5-point Likert scale (1-strongly disagree, 2-disagree, 3-neutral, 4-agree, 5-strongly agree). The five variables of SSLS are: (i) Organization and Structure of the lectures (OS), (ii) Lectures Effectiveness on Learning and Understanding (LEL), (iii) Interest and Motivation (IM), (iv) Professional Interaction (PI), and (v) Presentation and Classroom Atmosphere (PC).

A previous study has already investigated the psychometric properties of SSLS [52]. In the present study, SEM was applied to propose a model based on the five variables of the SSLS questionnaire and to study how those variables of SSLS related to the overall students' perception of lecturing skills.

Data analysis was carried out using SPSS version 20. Descriptive statistics were used to find out the mean and standard deviation of the responses towards SSLS with respect to gender. The Cronbach's alpha reliability test was used to measure the internal consistency of the questionnaire. The Shapiro-Wilk test was applied to confirm the normality of collected data and it is observed that the collected data

were normally distributed ( $p>0.05$ ). The SEM analysis was done using the software AMOS (Analysis of Moment Structures) version 5.0 [53,54]. Further, an independent t-test was used to compare the perceptions of male and female medical students on lecturing skills. All statistical tests were done at the level of significance of 0.05.

## Results

### *Instrument reliability*

While examining the reliability of the SSLS questionnaire, the Cronbach's alpha value for Organization and Structure of the lectures (OS), Lectures Effectiveness on Learning and Understanding (LEL), Interest and Motivation (IM), Professional Interaction (PI) and Presentation and Classroom Atmosphere (PC) were 0.95, 0.94, 0.95, 0.94, and 0.94 respectively. Moreover, the overall item showed a Cronbach's alpha value of 0.96. As the Cronbach's alpha value of all the dimensions was observed as  $>0.90$ , the adapted questionnaire can be rated as 'excellent' [55,56]. Therefore, it is inferred that the questionnaire is a reliable one (Table 1).

Table 1. Cronbach's alpha for the variables of Students survey on lecturing skills (SSLS)

Variables	Cronbach's Alpha	No. of items
Organization and Structure of the Lectures (OS)	0.95	02
Lectures Effectiveness on Learning and Understanding (LEL)	0.94	03
Interest and Motivation (IM)	0.95	02
Professional Interaction (PI)	0.94	03
Presentation and Classroom Atmosphere (PC)	0.94	03
Overall satisfaction	0.96	01

*Structural Equation Modeling for SSLS*

SEM analysis resulted in the model depicted in Figure 1, and the following characteristics i.e., n=537, df=2 (df-degrees of freedom), Chi square=2.067, p=0.356 (p>0.05) were reported

The results showed that the value of 2.067 is found to be non-significant (p>0.05), since

it is more than the recommended value of  $\leq 3.00$  [37,57]. Therefore, it is concluded that the proposed model used in this study adequately fits the sample data. A significant positive relationship was observed between each variable with the overall item, ranging from 1.0 to 1.319 (p<0.05) (Table 2).

Figure 1. Structural equation modeling (SEM) of SSLS

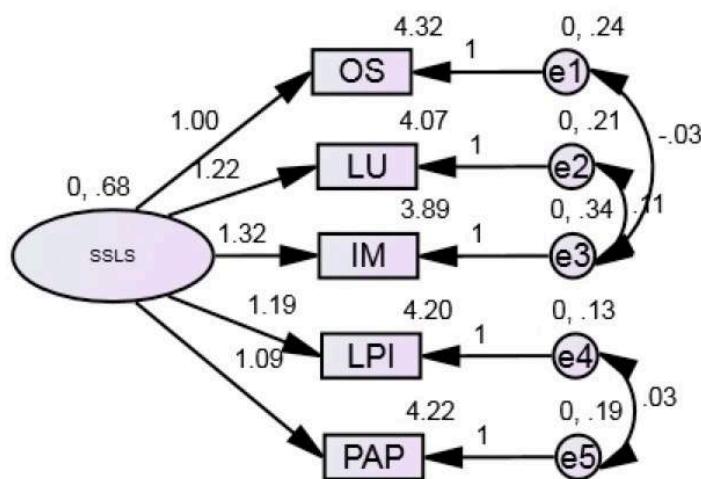


Table 2. Regression Weights

Variables	Path	Construct	Estimate	Standard Error	Critical Ratio	p value
Organization and Structure of the Lectures (OS)	<---	Overall SSLS	1.000			
Lectures Effectiveness on Learning and Understanding (LEL)	<---	Overall SSLS	1.222	0.041	29.622	p<0.05*
Interest and Motivation (IM)	<---	Overall SSLS	1.319	0.050	26.155	
Professional Interaction (PI)	<---	Overall SSLS	1.187	.039	30.235	
Presentation and Classroom Atmosphere (PC)	<---	Overall SSLS	1.092	.039	27.827	

\*Significant at 0.05 level

It is inferred that all dimensions of SSLS are positively related to the overall medical students' perception of lecturing skills. Concerning model fit indices, the recommended value for comparative fit index (CFI) is  $\geq 0.90$ , normed fit index (NFI) is from 0 to 1, relative fit index (RFI) or RHO1 is close to 1, incremental fit index (IFI) is  $\geq 0.90$ , Tucker-Lew-

is index (TLI) is  $\geq 0.95$ . These recommended values of model fit indices denote that the proposed model has a good fit with the data [37,57,58]. In this study, the values of model fit indices are observed as CFI=1 ( $p>0.05$ ), NFI=0.999, RFI=0.997, IFI=1.000, and TLI=1.000 (Table 3), and these values meet the recommended level, indicating the proposed model is a good fit.

Table 3. Model fit indices of the proposed SSLS model

Model	NFI* Delta1	RFI** rho1	IFI*** Delta2	TLI****	CFI*****
Default model	0.999	0.997	1.000	1.000	1.000
Saturated model	1.000		1.000		1.000
Independence model	0.000	0.000	0.000	0.000	0.000

\*Normed fit index (NFI), \*\*\*\*\*Comparative fit index (CFI), \*\*Relative fit index (RFI), \*\*\*Incremental fit index (IFI), \*\*\*\*Tucker-Lewis index (TLI)

Also, Root Mean Square Error of Approximation (RMSEA) for the proposed model is equal to 0.008 ( $p<0.05$ ), which is less than the

recommended value, i.e.,  $\leq 0.08$  [57,58]. This indicates that the proposed model is a good fit (Table 4).

Table 4. Root Mean Square Error of Approximation

Model	RMSEA*	LO 90	HI 90	PCLOSE
Default model	0.008	0.000	0.086	0.712
Independence model	0.751	0.729	0.774	0.000

\*Root Mean Square Error of Approximation (RMSEA)

#### Gender differences in SSLS Scores

Table 5 showed that the mean and standard deviation of variables of SSLS for gender. In addition, the results of an independent t-test were described to uncover gender differences in medical students' perception of lecturing skills. It is observed that there was a significant difference between the perceptions of male and female students on lecturing skills with respect to the variables such as 'Lectures Effectiveness on Learning and Understanding (LEL)', 'Professional Interaction (PI)', and 'Presentation and Classroom Atmosphere (PC)' ( $p<0.05$ ). This indicates that female stu-

dents have positively perceived the instructors' lecturing skills with a high mean score in terms of these dimensions when compared to male students. But in the case of variables such as Organization and Structure of the lectures (OS) and Interest and Motivation (IM), there was no significant difference between male and female students ( $p>0.05$ ). Further, a significant gender difference was observed in terms of overall satisfaction with the lecturing skills of their instructors ( $p<0.05$ ) Overall, it is inferred that female students are highly satisfied with the instructors' lecturing skills than male students.

Table 5. Comparison of variables of SSLS between gender using Independent 't' test

Variables	Males		Females		t value	p value
	Mean	Standard deviation	Mean	Standard deviation		
Organization and Structure of the Lectures (OS)	4.28	0.98	4.35	0.95	0.830	0.438
Lectures Effectiveness on Learning and Understanding (LEL)	4.00	1.18	4.13	1.04	1.402	0.019*
Interest and Motivation (IM)	3.83	1.29	3.94	1.19	1.017	0.203
Professional Interaction (PI)	4.11	1.13	4.28	0.97	1.867	0.007*
Presentation and Classroom Atmosphere (PC)	4.12	1.07	4.31	0.94	2.163	0.011*
Overall satisfaction	3.98	1.257	4.16	1.103	1.814	0.041*

\*Significant at 0.05 level (p<0.05)

## Discussion

This study aimed to identify gender differences in medical students' perception of lecturing skills in an undergraduate medical program at a Saudi higher education institution. A structured questionnaire was developed and administered within the study setting for assessing SSLS. It is a reliable instrument, as demonstrated through Cronbach's alpha reliability test. The SEM analysis proposed a model based on the five variables of the SSLS questionnaire and studied how those variables of SSLS related to the overall students' perception of lecturing skills. The results showed that the proposed model is a good fit to measure the perception of students on lecturing skills. It is also observed that there was a positive relationship between each variable and the overall item of SSLS, suggesting that all five variables are potential outcomes of SSLS. Along similar lines, Zaboli et al. analyzed the relationship between the factors affecting the teaching quality using SEM analysis and observed a good fit among the components of teaching quality [59]. In this study, the variables used in SSLS were: Organization and

Structure of the lectures (OS), Lectures Effectiveness on Learning and Understanding (LEL), Interest and Motivation (IM), Professional Interaction (PI) and Presentation and Classroom Atmosphere (PC).

### *Organization and Structure of the lectures (OS)*

This study found that the organization and structure of the lectures is one of the significant variables that assess the students' perception of lecturing skills. This is in line with the finding of previous studies that observed the instructors' organization and preparation as an influential factor of SET overall rating by students [60,61]. A study by Parmar indicated that lecturers should always keep the audience in mind while preparing and presenting the lectures. The materials should be appropriate to meet the requirements of the students [62]. Similarly, while preparing and organizing lectures, a framework planning should cover regular lectures, teaching and learning objectives, provision of relevant materials, time for interactive sessions, and also for comments on the students' achievement [63].

### *Lectures Effectiveness on Learning and Understanding (LEL)*

The use of appropriate teaching methods by instructors aids the students to learn effectively [64,65]. Further, the learning environment should be engaging and aided by the use of audio-visual material to ensure that students are highly alert in the classrooms and actively participate in learning activities. This would lead to enhancing the level of retention, understanding, and comprehension. Therefore, proper uses of audio-visual aids not only develops teachers but also augments the students' level of motivation and interest in classroom teaching and other learning activities, and promotes the achievement of desired learning outcomes [66]. Moreover, this study revealed that the instructors' lectures having a demonstration with examples and audiovisual aids for drawing attention, better learning, and understanding of students are related to the students' perception of lecturing skills.

#### *Interest and Motivation (IM)*

Motivation is considered as vital in students' learning, and such motivated students, in turn, possess high achievement [67]. Hence, teachers should consistently teach students to become self-motivated rather than giving rewards. Moreover, this study observed that the interest and motivation of students is an essential element for assessing the students' perception of lecturing skills. A study by Lalla et al. has also included an item dealing with motivation and interest aroused by the instructor in their SET questionnaire [68]. Feistauer and Richter stated that stimulating the students' interest in the subject area is one of the facets of teaching effectiveness in the higher education environment [27]. Further, motivation is considered as one of the key components of effective teaching, and it might influence the students' ratings of their instructors [69,70].

#### *Professional Interaction (PI)*

Student-lecturer interaction is associated with overall student academic and social develop-

ment, irrespective of where the interaction occurs in the university [71]. Students' satisfactory educational experiences can be improved with constructive and close interactions between lecturers and students and result in enhanced academic and personal development [72]. Feistauer and Richter revealed that the student-lecturer interaction showed a significant influence on SET scores [27]. Previous studies have found that SET overall rating is related to the dimensions such as class interactions, enthusiasm, and relationship with students [60,61,73-75]. This study also observed that the lecturer's professional interaction and support towards students are related to the students' perception of lecturing skills.

#### *Presentation and Classroom Atmosphere (PC)*

Classrooms that strengthen emotional well-being make a conducive environment for both learning and emotional development. Educational research indicates that an environment of mutual respect needs to be promoted, where students feel comfortable to share their ideas and raise questions [76]. Moreover, Classroom environment and presentation are considered as one of the key features of good teaching [69]. Otani et al. recognized that the clarity of the lecturer's explanation and positive learning environment are the most influential areas in the overall perception of university students of effective teaching. In this study, presentation and classroom atmosphere are found to be related to the students' perception of lecturing skills [6].

In the present study, the perceptions of male and female students on lecturing skills were compared using an independent t-test, and the results revealed a significant difference between gender with respect to overall satisfaction and the variables such as LEL, PI, and PC ( $p<0.05$ ). It is inferred that the female students showed a more positive perception of LEL, PI, and PC when compared to male students. This finding is consistent with a study by Lavin et

al. which revealed that there were differences between female and male student ratings of teaching effectiveness. It was noted that females rated statistically higher than males towards the instructor's characteristics, such as professionalism, clear presentations, concise explanations, enthusiastic, responsiveness, and encouragement given [77]. Overall, this study observed that female students are highly satisfied than male students with respect to their instructors' lecturing skills. This is in accord with the finding of Korte et al. who found that female students provided high overall ratings than male students to their instructors regarding teaching effectiveness [44]. Previous studies also found that female students generally gave higher ratings when compared with male students in terms of teaching effectiveness [42,44,78]. In contrast, few studies found no gender difference in students' ratings of teaching effectiveness [48,49]. Notably, Suarman observed that there was no gender difference between the perception of Riau University in terms of the relationship between lecturer and students and students' satisfaction on teaching quality [79].

The present study showed no significant difference between gender concerning the variables such as OS and IM. In contrast, Lavin found that female students paid more attention to organization and preparedness of lectures and engaging when compared to male students [77]. Kumar reported that female dental and medical students were found more attentive for over 70% of the time of lectures than male students [80].

It is noteworthy to mention that there is a uniform teaching plan that exists at IAU and it is implemented across both male and female sections. All faculty members at IAU, either male or female, have to follow a unique course specification while delivering the lecture. The course specification clearly stipulates the methods of teaching to be adopted in each course and the utility of audiovisuals

while giving lectures. Students belonging to both male and female sections are taught using the same lesson plan, which is approved and monitored by a common academic coordinator. The adherence of the course instructors to this course specification is regularly monitored in the form of course report prepared at the end of each course

Besides these uniform practices exist at the study setting, this study attempted to reach certain generalization by adopting the theory of stereotyping where students might have specific characteristics either to male or female faculty, who are the stereotypical university faculty members. As such, this study captured the perception of male and female medical students towards the lecturing skills of faculty members, irrespective of their gender.

Our results indicated that female students have a more positive attitude towards lecturing skills of teaching staff than male students. Stereotyping may have its influence on observed results, where it denotes a generalization made with similar characteristics assumed virtually over a group of members irrespective of actual difference observed among them [81]. Besides these stereotyping gender-specific characteristics of lecturers, lecturing skills of faculty members might differ, and it is influenced by other factors such as their knowledge, professional interaction, and presentation skills & classroom atmosphere. Conformance with our argument, a more recent study also concluded that the gender of the lecturer truly does not matter, whereas the personality and lecturing skills of lecturers were considered as more important [82]. Understanding the influence of these individual factors on the lecturing skills of teaching staff is beyond the scope of this study as restricted by the study design. Hence, further research is warranted to address this issue by comparing student's perceptions towards the lecturing skills of the same faculty members at both male and female sections.

## Conclusion

Gender-wise comparisons indicated that the female students in the medical program at IAU have a more positive attitude towards lecturing skills than male students. In addition, the SEM analysis revealed that the proposed model with five variables and 14 items used in SSLS are adequate to assess the perceptions of students on lecturing skills of faculty members in the undergraduate medical program offered at IAU. This study adds value to the literature by providing a questionnaire for assessing faculty members' lecturing skills and gender differences among medical students' ratings of lecturing skills.

## Limitations and Recommendations

This study is limited to the students of a single program in a higher educational institution. Nevertheless, the method employed, and the instrument developed suggests that the study can be extended to various other courses and programs in similar settings in the future. In the present study, since the survey was conducted at the end of the semester of an academic year and it might lead to the recall bias, where the students' responses can be biased with the most recent lectures delivered by faculty. Future research can be conducted by distributing a similar survey among students at the end of each module to ascertain student's perception of lecturing skills.

This study demonstrated a 100% response rate, particularly through an online system, which is less likely to happen in reality. Several reasons attributed to this high response rate viz. (i) Policy adopted at IAU where the survey completion by students deemed mandatory and all the students are strictly adhering to such practice; (ii) extensive campaigning carried out across all the colleges at IAU where all the students highly motivated to register their response and (iii) mode of administration of online sur-

vey where students can record their response through mobile phones, and it can be assessed through university E-service platform via My-IAU application. Despite these practices, it is noteworthy to mention such a high response rate might result in response bias in the form of higher ratings by students towards lecturing skills of faculty members, and it is considered as one of the limitations of this study. Further, the instructor's gender-bias on students' ratings of teaching effectiveness can be measured in future research. In the Saudi Arabian context, the gender difference in student ratings of lecturing skills can also be evaluated with respect to other faculty characteristics, including ethnic differences since the teaching staff comprises both Saudi and non-Saudi faculty. In a similar line, additional research is warranted to study gender differences concerning other student characteristics such as cultural background, personality type, psychosocial dynamics, and domain-specific vocational interests.

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## Original Article

# Effect of Bariatric Surgeries on Cardiovascular Risk Factors: Single Institution Retrospective Study

Marya Alsuhaibani <sup>1</sup>, Amjad Alharbi <sup>1</sup>, Abdullah A. Alshehri <sup>2</sup>, Essam A. Alghamdi <sup>2</sup>

Raneen K. Aljehani <sup>2</sup>, Soha Elmorsy <sup>3</sup>, Jasser Alshehri <sup>3</sup> and Ali Almontashery <sup>3</sup>

1. College of Medicine, Qassim University, Qassim, Saudi Arabia.

2. College of Medicine, Umm-alqura University, Makkah, Saudi Arabia

3. King Abdullah Medical City (KAMC), Makkah, Saudi Arabia.

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Corresponding author :Maryya Alsuhaibani, MBBS. College of Medicine, Qassim University, Qassim, Saudi Arabia. Email: alsuhaibanima@gmail.com . Phone No.: 00966503132488

Address: Saudi Arabia, Alqassim. King Abdulazizz Rd, AlNahdha Neighborhood

House number: 301. POBox: 85 ZIP code: 59169

## الملخص

### Abstract

#### Background:

Recently bariatric surgeries became trend for obese individuals. As known obesity is major risk factor for cardiovascular diseases. We Aim to describe effect of bariatric surgeries on cardiovascular risk factors including glycemic control, lipid profile, blood pressure, and weight for patients registered at tertiary center in Saudi Arabia.

#### Methods:

Retrospective cohort including obese patients who underwent bariatric surgeries at King Abdullah Medical City, Makkah between 2013 and February 2016.

#### Results:

Total of 566 patients aged  $34.8 \pm 10.2$  years at time of operation. More than half were females (58.1%). Almost all patients underwent laparoscopic sleeve gastrectomy (95.9%). Diabetes and hypertension were the most prevalent comorbidities (24.8% and 18.9%, respectively). There is significant reduction in mean Body Mass Index from 47.6 kg/m<sup>2</sup> to 31.8 kg/m<sup>2</sup> and in Glycosylated Hemoglobin from 6.8% to 5.7%. At 24 months of follow-up ( $p < 0.001$  for both parameters). Baseline High Density Lipoprotein (44.4 mg/dl), non-HDL cholesterol (147.1 mg/dl) and triglyceride (123.6 mg/dl) improved significantly to reach 52.3 mg/dl, 137.7 mg/dl and 78.5 mg/dl, respectively at one-year post-operative follow-up. Out of 79 hypertensive patients, 57 patients had remission of hypertension in last follow-up ( $p < 0.001$ ). Among diabetic patients, seventy-one (18.8%) had complete remission, and 21

#### الخلفية :

في الآونة الأخيرة تشهد عمليات السمنة انتشاراً واسعاً بين كافة طبقات المجتمع عامةً ومرضى السمنة خاصةً. وتتعدد الدوافع للجوء إلا أن الغالب هو العلاجية منها، حيث تعد السمنة عامل خطير للإصابة بأمراض القلب والأوعية الدموية.

تهدف هذه الدراسة لوصف واستقصاء تأثير عمليات السمنة على مختلف عوامل الخطورة المؤدية للإصابة بأمراض القلب والأوعية الدموية كالوزن، نسبة سكر الدم، نسبة دهون الدم وضغط الدم بين مرضى السمنة المسجلين في أحد مراكز المملكة العربية السعودية المرجعية.

#### طريقة البحث :

تعد هذه الدراسة دراسة استعرافية وتشمل جميع مرضى السمنة المسجلين في مدينة الملك عبد الله الطبية من منطقة مكة المكرمة والذين قاموا بإجراء أحد عمليات السمنة خلال المدة الزمنية ما بين بداية السنة الميلادية لعام ٢٠١٣ ولغاية شهر فبراير من السنة الميلادية ٢٠١٦.

#### النتائج :

شملت العينة البحثية ٥٦٦ مريضاً بلغ متوسط أعمارهم  $٤٠,٢ \pm ٣٤,٨$  سنة، غالبيتهم من النساء بنسبة ٥٨,١ %. وأظهرت نتائج الدراسة أن النوع الأكثر انتشاراً لعمليات السمنة بين المرضى هي عملية تكميم المعدة الطولي بالمنظار الجراحي بنسبة ٩٥,٩ %. قدّرت نسب مرض السكري ومرض ارتفاع ضغط الدم كأكثر الأمراض انتشاراً بين هؤلاء المرضى بنسبة ٢٤,٨ % و ١٨,٩ %، على التوالي. أفادت الدراسة بوجود انخفاض ملحوظ بعد سنتان منذ وقت العملية الجراحية في متوسط كتلة الجسم من ٤٧,٦ كجم/م<sup>٢</sup> إلى ١٨,٩ كجم/م<sup>٢</sup> ومعدل سكر الدم التراكمي من ٦,٨ % إلى ٥,٧ % من جانب آخر أثبتت الدراسة وجود تحسن في نسب كلاً من: الدهون البروتينية عالية الكثافة من ٤٤,٤ ملجم/ديسيلتر إلى ٥٢,٣ ملجم/ديسيلتر، الكوليستيرون من ١٤٧,١ ملجم/ديسيلتر إلى ١٣٧,٧ ملجم/ديسيلتر، والدهون الثلاثية من ١٢٣,٦ ملجم/

(5.6%) had partial remission from diabetes in the last follow-up. Significant decrease shown in predicted ten-years risk of cardiovascular disease from 7.4% to 5.5% ( $p<0.001$ ).

### **Conclusion:**

Obesity-related cardiovascular risk factors can be controlled significantly after bariatric surgeries. It also decreasing ten-years predicted cardiovascular disease risk within short term follow-up.

### **Key words:**

Bariatric Surgeries, Cardiovascular Risk, Diabetes, Hypertension

ديسياتر إلى ٧٨,٥ ملجم/ديسياتر وذلك بعد مرور عام على وقت العملية الجراحية. سبعة وخمسون مريضاً من المصابين بارتفاع ضغط الدم تماثلوا للشفاء التام من بين ٧٩ مريضاً إثر إجراء عمليات السمنة. على صعيد آخر، قدرت نسبة الشفاء الكلي من مرضي داء السكري ١٨,٨٪ بما يعادل ٧١ مريضاً، و ٥,٦٪ كشفاء جزئي بما يعادل ٢١ مريضاً. وتکللت الدراسة ببيان أن نسبة الإصابة بأمراض القلب والأوعية الدموية المتوقعة في العشر سنوات قد تناقصت من ٥,٥٪ إلى ٣,٤٪ بعد إجراء عمليات السمنة.

### **الخلاصة:**

أثبتت الدراسة أن عمليات السمنة بين المصابين بالأمراض المزمنة قد أدت إلى تحسن ملحوظ في كلّ من: عوامل الخطورة المرتبطة بالسمنة المؤدية إلى أمراض القلب والأوعية الدموية ونسبة الإصابة بأمراض القلب والأوعية الدموية المتوقعة في العشر سنوات القادمة، مثبته بدلالة إحصائية.

## **Introduction**

Obesity is a common disease and is associated with many cardiac risk factors such as hypertension, dyslipidemia, and diabetes. Cardiovascular diseases (CVD) contribute to 31% of all deaths worldwide and 45% of deaths in the Gulf Council Countries (GCC)<sup>[1-4]</sup>. Studies conducted in Saudi Arabia have revealed that the prevalence of the cardiac risk factors is increasing<sup>[5-7]</sup>.

Despite changing the lifestyle in terms of diet and exercise or using drug treatments to reduce obesity, weight is usually regained within a year<sup>[8]</sup>. Currently, bariatric surgeries are more widespread between obese individuals and believed to play an important role in the cure and control of cardiovascular risk factors<sup>[9]</sup>. There are different types of bariatric surgeries including sleeve gastrectomy and gastric bypass. The extent of weight loss depends on the type of the surgery used. Gastric bypass operation (Roux-en-Y Gastric bypass) cause excess weight loss of around 60-80 %<sup>[10]</sup>. According to Lee et al., the mean body weight loss was 31.4% for sleeve gastrectomy and 37.1% for mini-gastric bypass one year after each surgery<sup>[11]</sup>.

In gastric sleeve surgery, the effect of surgery on glycemic control may be achieved

by increasing insulin sensitivity and decreasing insulin resistance<sup>[12]</sup>. But, in the case of biliointestinal bypass, glycemic control may be achieved by decreasing the fasting blood glucose three months after the surgery by decreasing fat absorption which subsequently leads to reduce insulin hypersecretion and improve insulin sensitivity<sup>[13]</sup>. In addition, it has been reported that 59% of patients who did laparoscopic gastric sleeve showed evidence of diabetes remission<sup>[14]</sup>.

Moreover, it has been demonstrated that recovery from diabetes, hypertension, and hypertriglyceridemia can be achieved 2 years post-operatively<sup>[15]</sup>. Carson et al. noticed that 54% of hypertensive patients recovered from hypertension and 22% had improvement in their blood pressure readings<sup>[16]</sup>. Lipid profile was also found to become normal in most of the cases (84%) who had successful weight loss after bariatric surgery<sup>[17]</sup>.

Although bariatric surgeries are on the rise in Saudi Arabia, only a few studies have reported the follow-up of such patients. Our study focuses on bariatric surgery patients from a tertiary health care center in Makkah, Saudi Arabia. In our study, we describe the effect of bariatric surgeries on different cardiovascular risk factors.

## Methods

### *Data source*

This retrospective cohort study including a patient who underwent bariatric surgery at King Abdullah Medical City (KAMC) in Makkah, Saudi Arabia between January 2013 and February, 2016. KAMC is considered as a tertiary care center and a referral hospital that receives patients from a wide area of western Saudi Arabia. Patients of both genders were included in this study, but those aged less than 18 years at the time of surgery were excluded. Prior to start the study, ethical approval was gained from the Institutional Review Board at KAMC. Data was collected from all the patients' files and then entered into an SPSS database.

### *Data collection*

The following data was collected: height, weight, blood pressure, fasting blood glucose (FBG), lipid profile, and glycosylated hemoglobin (HbA1c). Baseline data were collected from the pre-operative medical assessments done a few days before surgery. Post-operative data were collected from bariatric clinic follow-up records at 3, 6, 12, and 24 months after surgery.

The comorbidities were defined by the following criteria: diabetes was defined by a HbA1c  $\geq 6.5\%$  as many patients had not done the FBG test, hypertension by the use of anti-hypertensive medications, and dyslipidemia by a total cholesterol  $>239$  mg/dl, triglyceride (TAG)  $\geq 200$  mg/dl, low-density lipoprotein (LDL) cholesterol  $\geq 160$  mg/dl, or high-density lipoprotein (HDL) cholesterol  $<40$  mg/dl. Remission of hypertension was defined by the patient quitting anti-hypertensive medications. For dyslipidemia, remission was defined as the return of lipid profile values to normal as per guidelines. For diabetes, the remission criteria of the American Diabetes Association was used, where HbA1c  $<6\%$  without any drugs defined as a complete remission, HbA1c

6–6.5 % without any drugs defined as a partial remission, and HbA1c  $> 6.5\%$  with or without drugs defined as no remission [18]. The predicted ten-years risk of CVD score was calculated using the age in years, gender, systolic blood pressure measurement, total cholesterol value, HDL cholesterol value, use of anti-hypertensive medications, cigarette smoking, and presence of diabetes according to Framingham heart study (2008) [19].

### **Statistical analysis**

Analysis was performed using SPSS, version 21.0 (IBM Inc.). Body Mass Index (BMI) was calculated using height and weight using the below formula:

$$\text{BMI} = \text{weight (kg)} / \text{height}^2 (\text{m}^2)$$

Other weight loss parameters were calculated through the following equations: Absolute weight loss = Weight at baseline – weight at each time point (3, 6, 12, 24 months).

$$\text{Percentage of weight loss} = [(\text{Weight at baseline} - \text{weight at each time point}) / (\text{Weight at baseline})]$$

$$\text{Percentage of excess weight loss} = [(\text{Weight at baseline} - \text{weight at each time point}) / (\text{excess weight})], \text{ where}$$

$$\text{excess weight} = \text{Actual weight} - \text{ideal body weight}$$

$$\text{Percentage of excess BMI loss} = [(\text{BMI at baseline} - \text{BMI at each time point}) / (\text{excess BMI})], \text{ where excess BMI} = \text{Actual BMI} - \text{the ideal BMI}$$

Numeric data presented as mean  $\pm$  standard deviation (SD). Differences between baseline values and values at 3, 6, 12, 24 months post-operative were assessed by ANOVA with repeated measures. The paired t-test was used for pre-operative and 12 months post-operative values. For variables with non-normally distributed data, non-parametric repeated measure tests, such as sign test, were used. For comparing categorical variables, the chi-square test was used. Two-sided alpha was set as 0.05.

## Results

A total of 566 patients records fit the eligibility criteria. The mean age of the included patients was  $34.8 \pm 10.2$  years (18.04 – 78.2 years). Most of the patients were females (58.1%; n=329), Saudis (93.5%; n=529) and non-smokers (67%; n=379). Table 1 summarizes the characteristics of the patients. Diabetes mellitus patients (24.8%; n=118) and patients with hypertension (18.9%; n=107) were on the top of the obesity-related co-morbidities. Only 3.9% (n=22) of the patients had chronic heart disease, but 12.3% (n=62), 37.7% (n=191), 14.6% (n=71), and 11.1% (n=56) of the patients had hypercholesterolemia, low HDL, high LDL and hypertriglyceridemia, respec-

tively.

Regarding the type of surgery, 95.9 % of the patients (n=543) underwent laparoscopic sleeve gastrectomy, 2.5% (n=14) underwent laparoscopic Roux-en-Y gastric bypass, and 1.6% (n=9) underwent laparoscopic mini-gastric bypass. Patients underwent laparoscopic sleeve gastrectomy developed some complications during and after the surgery such as: two patients had leakage, two patients got bleeding, ten patients developed gastro-esophageal reflux disease, and six patients developed other complications such as obstruction, ulceration, perforation, post-gastric surgery syndrome, and incisional hernia. Furthermore, two patients developed anastomotic ulcer and obstruction post laparoscopic mini-gastric bypass.

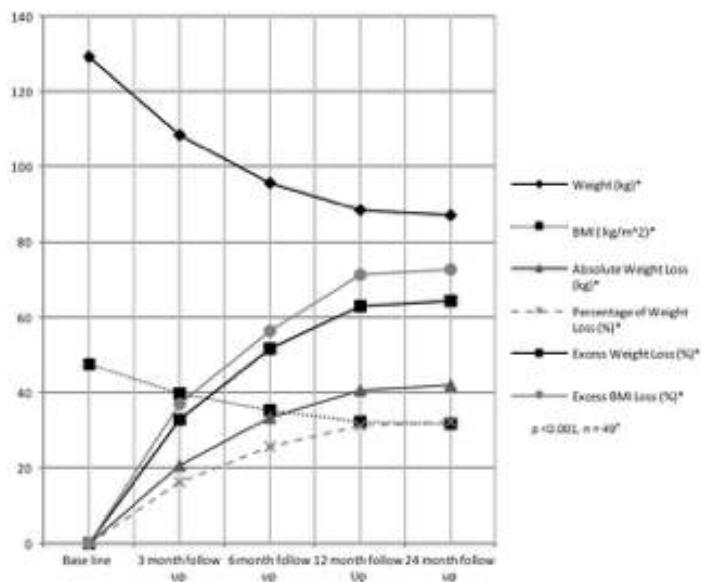
Table 1 : Characteristics of the studied patients

	Characteristic	n (%)
Gender n=566	Male	237 (41.9)
	Female	329 (58.1)
Smoking n=566	Smoker	152 (26.9)
	Ex-smoker	35 (6.2)
	Non-smoker	379 (67.0)
Type of surgery n= 566	Laparoscopic sleeve gastrectomy	543 (95.9)
	Laparoscopic Roux-en-Y gastric bypass	14 (2.5)
	Laparoscopic mini gastric bypass	9 (1.6)
Comorbidities	Diabetes (n= 475)	118 (24.8)
	Hypertension (n= 566)	107 (18.9)
	Chronic Heart Disease (n= 566)	22 (3.9)
	Hypercholesterolemia (n= 504)	62 (12.3)
	Low HDL (n= 506)	191 (37.7)
	High LDL (n= 485)	71 (14.6)
	Hypertriglyceridemia (n= 506)	56 (11.1)

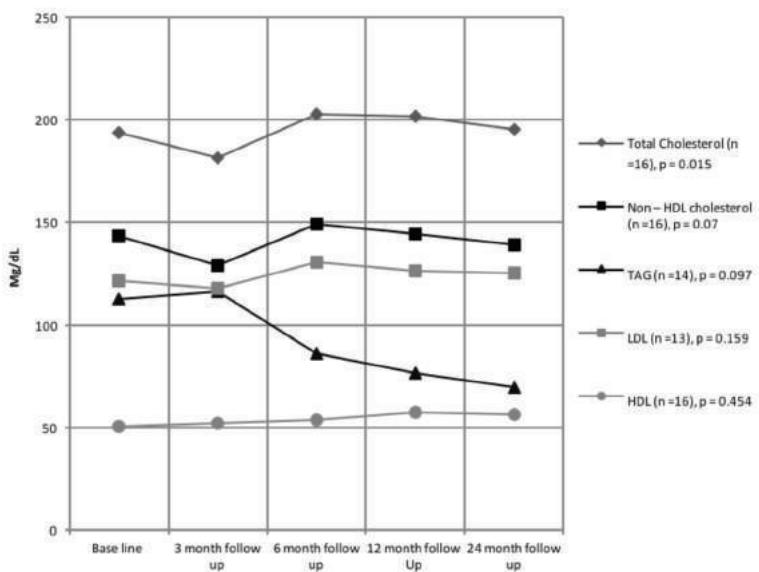
n number of patients with available data for each parameter

Figures 1.1 and 1.2 show the changes in weight and lipid profile parameters over time. The number of patients who had regular post-operative follow-up at 3, 6, 12, 24 months was small. Weight and BMI recordings were available for 49 patients, and these variables showed a statistically significant decrease from  $129.1 \pm 20.1$  kg and  $47.6 \pm 7.6$  kg/m<sup>2</sup> at baseline to  $87 \pm 15.5$  kg and  $31.8 \pm 6$  kg/m<sup>2</sup>, respectively, at 24 months ( $p < 0.001$ ). This was

coupled with a statistically significant increase in weight loss parameters (absolute weight loss, percentage of weight loss, percentage of excess weight loss and Percentage of excess BMI loss). The decrease in weight and BMI and the increase in weight loss parameters were the steepest initially and approached a plateau at one-year post-operative, after which the rate of changes reduced.



**Fig. 1.1** Change in weight and BMI over 24 months of post-operative follow up

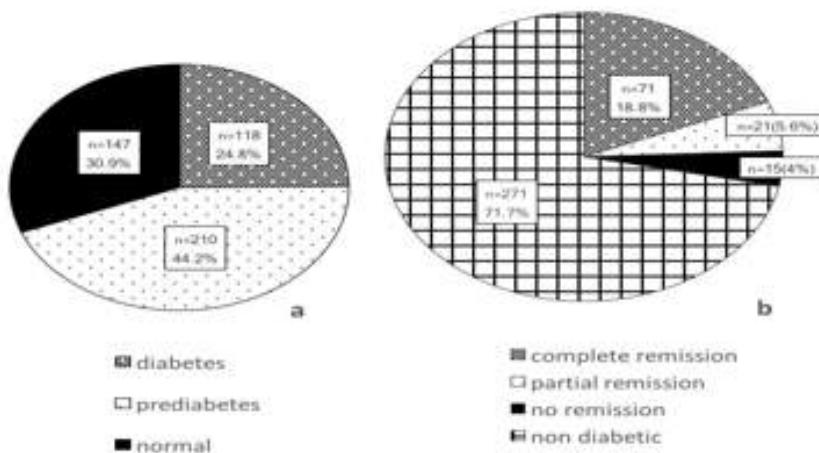


HDL high density lipoprotein, LDL low density lipoprotein, TAG triglyceride, n number of patients with available data for each parameter

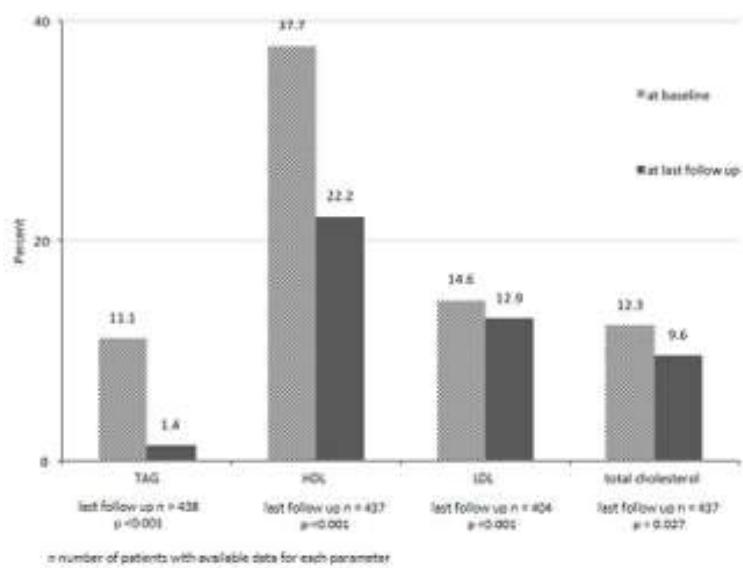
**Fig. 1.2** Change in Lipid Profile over 24 Months of Post-operative Follow Up

Changes in lipid profile were less consistent over time as shown in Figure 1.2 Total cholesterol showed an overall statistically significant decrease ( $p=0.015$ ). Although statically significance could not be achieved with other lipid profile parameters, the TAG decreased from  $112.7 \pm 46.1$  mg/dl to  $69.7 \pm 31.6$  mg/dl ( $n=14$ ,  $P=0.09$ ) and the HDL increased from  $50.4 \pm 14.4$  mg/dl to  $56.5 \pm 11.8$  mg/dl ( $n=16$ ,  $P=0.45$ ). Although regular HbA1c values were

completed only in 11 patients, there was a statistically significant decrease from  $6.8 \pm 1.3\%$  at baseline to  $5.7 \pm 0.4\%$  at 24 months ( $p<0.001$ ). The blood pressure measurements were available for 19 patients and showed a mild reduction for both systolic and diastolic readings from  $132.8 \pm 14.1$  mm Hg to  $125.5 \pm 17.9$  mm Hg for systolic blood pressure ( $P=0.28$ ) and from  $70.3 \pm 10.7$  mm Hg to  $66.3 \pm 11.2$  mm Hg ( $P=0.17$ ) for diastolic blood pressure over 24 months follow-up after surgery.



**Fig. 2.1 a** Diabetic status at baseline, **b** Postoperative diabetic status



**Fig. 2.2** Percentage of patients with abnormal lipid profile variables at pre-operative and post-operative measurements

completed only in 11 patients, there was a statistically significant decrease from  $6.8 \pm 1.3\%$  at baseline to  $5.7 \pm 0.4\%$  at 24 months ( $p < 0.001$ ). The blood pressure measurements were available for 19 patients and showed a mild reduction for both systolic and diastolic readings from  $132.8 \pm 14.1$  mm Hg to  $125.5 \pm 17.9$  mm Hg for systolic blood pressure ( $P=0.28$ ) and from  $70.3 \pm 10.7$  mm Hg to  $66.3 \pm 11.2$  mm Hg ( $P=0.17$ ) for diastolic blood pressure over 24 months follow-up after surgery.

Table 2 focuses on changes captured at 12 months of follow-up and so it makes use of the relatively bigger number of cases with available follow-up values. There were only a few patients with FBG measurements as it was not done routinely for each patient during

their follow-up. Lipid profile of patients improved significantly at one year of post-operative follow-up as the mean HDL increased to 52.3 mg/dl and the mean non-HDL cholesterol decreased to 137.7 mg/dl.

Out of 79 patients who were hypertensive at baseline, 57 (72.2%) became normotensive and quit their medication by the time of the last follow-up, within two years after surgery ( $p < 0.001$ ). It can be seen from the data in Figure 2.1.b that 18.8% ( $n=71$ ) of patients had complete remission from diabetes two years postoperative. Many patients with dyslipidemia had their lipid profile normalized Figure 2.2. Also, the ten-years predicted cardiovascular risk decreased from  $7.4 \pm 8.1\%$  to  $5.5 \pm 5.3\%$  ( $n=96$ ,  $p < 0.001$ ) by the time of the last follow-up.

Table 2 Comparison between Cardiovascular Risk Factors at Baseline and at 12 Months Post-operative.

Test	Baseline (Mean $\pm$ SD)	12 Months Follow-Up (Mean $\pm$ SD)	Mean difference	P value
Weight (kg) $n=274$	$127.9 \pm 23.8$	$85.8 \pm 17.6$	42.1	<0.001*
BMI (kg/m <sup>2</sup> ) $n=273$	$47.3 \pm 7.4$	$31.8 \pm 6.4$	15.5	<0.001*
Systolic BP (mm Hg) $n=175$	$129.8 \pm 14.2$	$125.5 \pm 16.3$	4.3	0.005*
Diastolic BP (mm Hg) $n=175$	$71.0 \pm 13.4$	$70.5 \pm 13.9$	0.5	0.076
HbA1c (%) $n=207$	$6.4 \pm 1.4$	$5.4 \pm 0.6$	1.05	<0.001*
FBG (mg/dl) $n=7$	$126.0 \pm 36.0$	$86.3 \pm 9.4$	39.7	0.020*
Total cholesterol (mg/dl) $n=222$	$191.6 \pm 35.5$	$190.0 \pm 32.4$	1.6	0.257
Non – HDL cholesterol (mg/dl) $n=222$	$147.1 \pm 35.8$	$137.7 \pm 31.2$	9.3	<0.001*
HDL (mg/dl) $n=223$	$44.4 \pm 12.3$	$52.3 \pm 13.0$	(-7.9)	<0.001*
LDL (mg/dl) $n=191$	$121.9 \pm 33.2$	$120.5 \pm 29.6$	1.4	0.596
Triglyceride (mg/dl) $n=221$	$123.6 \pm 83.4$	$78.5 \pm 31.5$	45.1	<0.001*

BP Blood pressure, HbA1c Glycosylated hemoglobin, FBG Fasting Blood Glucose, HDL High density lipoprotein, LDL Low density lipoprotein, \*statistically significant, n number of patients with available data for each parameter, SD standard deviation

## Discussion

Surgical treatment of obesity dates back to 1953 when the first induced malabsorption for weight loss was performed. This procedure resulted in marked weight reduction; nevertheless, it sometimes resulted in nutritional complications. The bariatric surgery field has grown over the past 50 years, and weight loss has almost been outshined by the effects of obesity-related comorbidities such as hyperlipidemia, hypertension, and diabetes. Recently, the interest in finding the impact of weight loss achieved by surgical methods on cardiovascular risk factors using different biomarkers has increased [20].

In this study, we reviewed the effect of bariatric surgery on different cardiovascular risk factors. The obtained data clearly showed 23% reduction in the overall BMI at one year after surgery. In diabetics, there were also great reductions in HbA1c. These results are consistent with the results described by Gulliford et al. in a study that included diabetic patients, and in which they found that the mean HbA1c reduced from 8% to 6.8 % and 6.5 % at one and two years, respectively, after bariatric surgery [21]. Similarly, Mihmanli et al. stated that the HbA1c after laparoscopic sleeve gastrectomy decreased to 5.5% on the 6th month and 5.2% on the 12th month [22]. Other diabetes measurements in the present study also showed great reductions such as the mean fasting blood sugar which decreased from 126 to 86.3 mg/dl by the 12th month. Similarly, Mihmanli et al. found that fasting plasma glucose decreased to 92.29 mg/dl six months after laparoscopic sleeve gastrectomy and to 87.94 mg/dl one year after surgery [22].

In this study, there was a clear improvement in lipid parameters as well. This result is similar to what was found by Vogel et al. [23] and Buchwald et al. who showed a remarkable effect of bariatric surgery on lipid levels among patients with hyperlipidemia [24]. With regard

to the arterial blood pressure, a significant decrease was achieved only in systolic blood pressure after 12 months follow-up in the present study. The decline in diastolic blood pressure and the changes over 2 years may have needed a bigger study sample to achieve statistical significance. Yet, there was a general trend of reduction in the arterial blood pressure. Vogel et al. found that the blood pressure measurement among 109 obese patients revealed a significant decline in systolic and diastolic blood pressure from 133 mmHg and 80 mmHg to reach 116 mmHg and 71 mmHg, respectively [23].

The results obtained through this study revealed that the 10-year predicted cardiovascular risk by Framingham score decreased from 7.4% to 5.5%. This impressive reduction following bariatric surgery sheds light on the significant impact of bariatric surgeries on comorbidities prevention. In a large study comparing cardiovascular outcomes between obese individuals treated with bariatric surgery and non-surgically treated individuals, Sampalis et al. revealed a notable reduction in the treatment of different cardiovascular situations such as ischemic heart disease among those who treated surgically. [25]. Many other studies found great reductions in the 10-year risk factor as those done by Torquati et al. [26], Batsis et al. [27] and Eliasson et al. [28].

Long-term effects after bariatric surgery should be examined as obesity is a chronic disease [29]. The 2-years follow-up data obtained through this study revealed that 72.2% of the hypertensive patients quit their medication completely ( $P<0.001$ ), and 18.8% of patients had complete remission from diabetes. Furthermore, there was a great improvement in the lipid profile for the patients. Similarly, Sjöström et al. in their non-randomized matched study found that all the 2-year rates of improvement for the studied risk factors were better in the surgery group compared to the control group [15]. They observed that gas-

tric bypass surgery has a significant effect on the rate of diabetes and mortality [30].

It is obvious that bariatric surgery has a more influential impact than those achieved by other methods. the effects of medications are reliant on patients' compliance, and the benefits may achieve persevere during the period of treatment. In general, surgical intervention is considered a good choice for obese individuals and should be considered as a life-saving and preventive intervention in preference to a cosmetic surgery.

There were some limitations to our study. The available literature does not show clear criteria to examine obesity comorbidities. Some articles used laboratory data for diabetes and blood pressure measurements for hypertension; however, others used patient history and medications for diagnosis. Another limitation was that not all the patients were available for regular post-operative follow-up. Moreover, the literature reported the data on weight loss and co-morbidity in several and variable formats using descriptive and non-numeric data which hinder the comparison of the obtained results in this study with others. The maintenance of all these changes needs a longer time of follow-up.

## Conclusion

Bariatric surgeries are significantly effective for remission and controlling of obesity-related cardiovascular comorbidities, including diabetes, hypertension, and dyslipidemia, and decreases its 10-year predicted risk within a 24 months follow-up period.

It is obvious that a set of standardized formats for reporting such data related to weight loss and comorbidities is needed. In addition, future studies should focus on the biochemical verification for resolution or reduction of obesity-related comorbidities. Also, further prospective studies are recommended with strict follow up to detect which type of patients ben-

efit more and which risk factors are associated with less benefit after bariatric surgery.

Studies to compare the advantages of each type of bariatric surgery are needed with longer follow-up periods.

## Conflict of Interest

The authors declare no conflict of interest.

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## Original Article

# Nutrition Label Use in Relation to Obesity Among Female College Students at Taibah University

Rola A Jalloun<sup>1</sup> and Magda H Youssef<sup>2</sup>

1. Assistant Professor of Nutrition and Food Science Department, Taibah University, Madinah, 42353, Kingdom of Saudi Arabia.

2. Professor of Physiology, Taibah University, Madinah, 42353, Kingdom of Saudi Arabia.

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Corresponding author :1. Rola A Jalloun. Assistant Professor of Nutrition and Food Science Department, Taibah University, Madinah, 42353, Kingdom of Saudi Arabia. Email: rajalloun@taibahu.edu.sa

### Abstract

#### Background:

Nutrition labels are a basic requirement for every prepackaged food product. In the last decades, nutrition labels have been used as a tool to help people choose healthy foods to control body weight. The objective of the study was to estimate the prevalence of nutrition label users and to assess the effect of using nutrition labels on body mass index and body fat percentage among female students at Taibah university.

#### Methods:

A cross-sectional study was performed with 552 university students aged 18-24 years who were randomly selected from two different colleges at Taibah University in Madinah. A self-administered questionnaire was given, and BMI and body composition were measured.

#### Results:

The outcomes of this study indicated that over 60% of the participants were not using nutrition labels. The prevalence of not using nutrition labels was significantly higher among participants who were from colleges of arts and humanities, unmarried, and obese. More than half (58.8%) of the participants reported that they looked at the number of calories listed on the nutrition labels first. Students' responses showed that 62% of the participants wanted to take classes on how to read nutrition labels, and because of that, 40.7% participants did not read nutrition labels. After adjusting for demographic characteristics, obesity was significantly associated with nonuse of nutrition labels; the prevalence of obesity was 1.74-times higher in those who did not use nutrition labels than in those who used them (aOR 1.74 and 95% CI: 1.07- 2.81, P<0.000).

#### Conclusion:

This study showed the need to raise awareness about the importance of using nutrition labels among females. Health policy makers should implement nutritional guidance at all levels to encourage healthy eating habits among the young population. Regardless of BMI status, female college students would benefit from using nutrition labels.

#### Keywords:

Nutrition label, Health, body mass index (BMI), body composition (BC), body fat percentage (BF%), visceral fat level (VFL).

### الملخص

#### خلفية:

تعتبر البطاقة الغذائية مطلبًا أساسياً لكل منتج غذائي معيناً مسبقاً. على مدار العقود الماضية، استخدمت البطاقة الغذائية كأداة لمساعدة الأشخاص لاختيار الأغذية الصحية للحفاظ على وزن الجسم. هدفت هذه الدراسة إلى معرفة مدى انتشار قراءة البطاقة الغذائية الموجودة على الأغذية المعلبة وعلاقتها بمؤشر كثافة الجسم ونسبة الدهون في الجسم ومستوى الدهون الحشوية بين الطالبات في جامعة طيبة.

#### طريقة البحث:

هذه دراسة مقطعة، تم اختيار عينة الدراسة من كليةين بجامعة طيبة في المدينة المنورة، حيث بلغ عدد أفراد العينة ٥٥٢ طالبة تراوحت أعمارهن ما بين ٢٤-١٨ سنة، كما تم إعداد استبيان بهدف معرفة مدى انتشار قراءة البطاقة الغذائية وجمع القياسات الجسدية لمؤشر كثافة الجسم وقياس نسبة الدهون ومستوى الدهون الحشوية بالجسم.

#### النتائج:

أشارت نتائج هذه الدراسة إلى أن أكثر من (٦٠٪) من المشاركات لا يقرأن البطاقات الغذائية. كما أوضح أن النسبة الأعلى لغير القراءات للبطاقات الغذائية هي من كلية الآداب والعلوم الإنسانية وغير المتزوجات والمصابات بالسمنة. كما أفادت الدراسة أن أكثر من نصف المشاركات (٦٢٪) يطلعون على عدد السعرات الحرارية كأول معلومة موجودة في البطاقة الغذائية، وأنهارت ردة الطالبات أن (٦٠.٢٪) أردن أخذ دروس عن كيفية قراءة البطاقة الغذائية وللهذا السبب فإن (٤٠.٧٪) منها لا يقرأن البطاقات الغذائية. وعند استخدام الانحدار اللوجستي للتتبؤ بمدى تأثير عدم قراءة البطاقة الغذائية على مؤشر كثافة الجسم، فانخفض ارتفاع معدل انتشار السمنة بين المشاركات الغير قارئات للبطاقات الغذائية عند مقارنتهن بقارئات البطاقات الغذائية.

#### الخلاصة :

استنطقت الدراسة عدداً من التوصيات أبرزها الحاجة إلى رفع مستوى الوعي حول أهمية استخدام البطاقات الغذائية بين الإناث. كما يجب على واضعي السياسات والبرامج الصحية زيادة التوعية بالبطاقات الغذائية على جميع المستويات لتحسين عادات الأكل الصحية بين فئة الشباب. فيغض النظر عن حالة مؤشر كثافة الجسم، هناك فوائد عديدة لطالبات الجامعة من استخدام البطاقات الغذائية.

#### الكلمات المفتاحية :

البطاقة الغذائية، الصحة، مؤشر كثافة الجسم، مكونات الجسم، نسبة دهون الجسم، ومستوى الدهون الحشوية

## Introduction

Obesity is defined as a medical condition in which excess body fat accumulates to the degree that causes negative health effects, leading to an increase in health problems and a reduction in the average life expectancy of the individual. Obesity is a major preventable cause of death globally and is common or increasingly common among adults and children worldwide<sup>[1]</sup>. In 2016, the World Health Organization (WHO) reported that more than 650 million adults were obese and more than 1.9 billion were overweight<sup>[2]</sup>. In the Kingdom of Saudi Arabia (KSA), the predictions of earlier secular trends indicate that over 75% of adult women and over 40% of adult men would be obese by 2022<sup>[3]</sup>.

Research on the relationship between obesity and health problems has indicated that being overweight or obese might increase the risk of other diseases, such as cardiovascular disease (CVD), diabetes mellitus (DM), and cancer<sup>[4]</sup>. According to the Health Awareness Information Center at the Ministry of Health (MOH), the rapid growth in the rate of CVD accounted for 42% of noncommunicable disease deaths in 2010 due to obesity and other health issues<sup>[5]</sup>. Moreover, compared to nonobese adults, obese adults have a higher DM rate, possibly due to the dietary habits and greater physical inactivity of Saudis<sup>[6-8]</sup>. Most populations in the developed world are affected by obesity, and cancer is also often associated with obesity<sup>[9,10]</sup>. For instance, the prevalence of overweight and obesity was reported to be significantly higher among Saudi breast cancer patients than among healthy controls<sup>[11]</sup>.

There are many factors that may influence the risk of obesity. Diet composition is one of the important factors that should be considered in obesity processes<sup>[12]</sup>. Nutrition labels or food labels are often displayed as a panel or grid and include information on energy in kilojoules (kJ) and kilocalories (kcal), fat, saturat-

ed fat, carbohydrates, sugars, protein, and salt<sup>[13,14]</sup>. Other nutrition information that must be on the label is the name of the food, the list of ingredients, the quantity of certain ingredients, instructions for use, storage conditions and/or conditions of use, name or business name, address of the food business operator, place of origin or provenance, and food allergens. The main purpose of nutrition labels is to educate customers about the food they purchase to help them make informed decisions. Education about food also enables the safe storage and use of food<sup>[15]</sup>.

One way of reducing the prevalence of overweight and obesity is by encouraging consumers to use nutrition labels. In 2004, the WHO recommended using a nutrition label to help people make healthy choices by knowing the content of food items<sup>[16]</sup>. In 2010, the European Union (EU) also listed the use of nutrition labels in the "Strategy for Europe on Nutrition" for the same reason<sup>[17]</sup>. To our knowledge, only one study among 400 consumers in the KSA reported that most of the participants did not use nutrition labels<sup>[18]</sup>. Therefore, the present study was formulated to assess the knowledge, attitudes, and practices of female college students at Taibah University regarding nutrition label use and to predict the effect of nutrition label use on BMI.

## Methods

A cross-sectional study was conducted at Taibah University, KSA, during the spring of 2019. This study has been approved by the committee of research ethics at Taibah University and the number of this ethical approval is TUCDREC/20180420/ JALLOUN. A total of 662 students aged 18-24 years who attended Introduction to Health and Nutrition class (GS 135) in different two colleges, were invited to participate in the study, among them 552 students participated in the present study based on the inclusion criteria. All underweight,

pregnant, and lactating subjects were excluded from the study. A written consent form was used. Participants were informed with a brief description of the study, along with instructions on how to fill out the questionnaire. Demographic data collected included: college name, age, status, smoking habits, and physical activity. The questionnaire was designed to study student attitudes, knowledge, and practices regarding nutrition labels. In the last part of the questionnaire, we provided a picture of a nutrition label and asked the participants if they understood the picture. The questionnaire was piloted for validity, and subsequently, minor modifications were made.

**Anthropometrics:** After completion of the questionnaire, height was measured to the nearest 0.1 cm using a standard stadiometer, and anthropometric measurements, body fat percentage (BF%) and visceral fat level (VFL) were assessed using a bioelectrical impedance analysis (BIA) device (Omron Healthcare Co. Ltd., Kyoto, Japan; BF 501). Measurements were collected with the subjects in either socks or barefoot, and all heavy items were removed from the participants. Body mass index (BMI) was computed as weight/height (weight in kilograms and height in centimeters)<sup>[2]</sup>. According to the values given by the Omron Healthcare catalog based on sex and age, subjects were classified as underweight (BMI  $\leq 18.0$ ), normal (BMI = 18.5–24.9), overweight (BMI = 25.0–29.9), or obese

( $BMI \geq 30.0$ ). BF% was categorized as low ( $BF\% < 21.0\%$ ), normal ( $BF\% 21.0\text{--}32.9\%$ ), high ( $BF\% 33.0\text{--}38.9\%$ ), and very high ( $BF\% \geq 39\%$ ). VFL was classified as normal (VFL = 1–9), high (VFL = 10–14), and very high (VFL = 15–30).

**Statistical Analysis:** The Statistical Package for Social Sciences (SPSS Ins., Chicago, IL, USA) version 23 was used to enter and analyze the data on a personal computer. Demographic characteristics of the study population were calculated as frequencies and percentages. The chi-square test was used for categorical variables. Multiple logistic regression was performed to determine the significant differences among the different variables. All reported p-values are based on two-tailed tests. Statistical significance was set at 0.05.

## Results

As indicated in Table 1, of the 552 respondents, 68.2% were from the College of Arts and Humanities, and 31.8% were from the College of Science. Most of the participants (52.8%) were aged 18–20 years and had normal body mass indexes (BMIs). Most of the participants were not married and did not smoke. Regarding physical activity, 60.7% of the respondents were physically inactive. In addition, only 63.5% of the total students reported not using nutrition labels.

Table 1: Demographic characteristics of the study population (n = 552) and their correlation with attitudes toward nutrition labels.

Variables	Frequency	Percent
College		
College of Arts and Humanities	377	68.2
College of Science	175	31.8
Age (years)		
18–20	292	52.8
21–22	180	32.6
$\geq 23$	80	14.6

Marital Status		
Single	476	86.2
Married	76	13.8
BMI		
Normal	354	64.2
Overweight and obese	198	35.8
Smoking		
Yes	17	3.1
No	535	96.9
Physical Activity		
Yes	217	39.3
No	335	60.7
Do you always read nutrition labels?		
Yes	201	36.5
No	351	63.5

According to Table 2, our results showed that 56.4% of the participants believed products' nutritional labels were not truthful. Regarding the question of "what is the first thing you look at?", over half of the participants (58.8%) were looking for the calorie count on the labels. In contrast, they were less concerned with "serving size", "fats and cholesterol", and "product claims". When we asked the participants if they were interested in enrolling in a class on how to understand nutrition labels, 62.5% of them were interested. Most of the participants were not using nutrition labels because either they did not take a class on how to read the

labels (29.7%) or they were not interested in using nutrition labels (40.7%). The rest of the sample population indicated that the reason for not using the nutrition label was either that they did not have time to read it (13.9%) or the information was too complicated (7.4%). Finally, 8.3% of the participants mentioned that the reason for not using nutrition labels was that the information was not important.

Table 2 : The respondents' nutrition labeling choices, N (%).

* Students' knowledge and attitude regarding nutrition labels					
Do you think the nutrition label information is truthful?	Yes 88 (43.6%)	114 (56.4%)			
* Information that consumers are looking for on the nutrition labels					
When looking at nutrition labels, what is the first thing you look at?	Serving size 20 (7.5%)	Calories 98 (58.8%)	Ingredients 55 (20.6%)	Fat & cholesterol 20 (7.5%)	Claims 9 (5.6%)

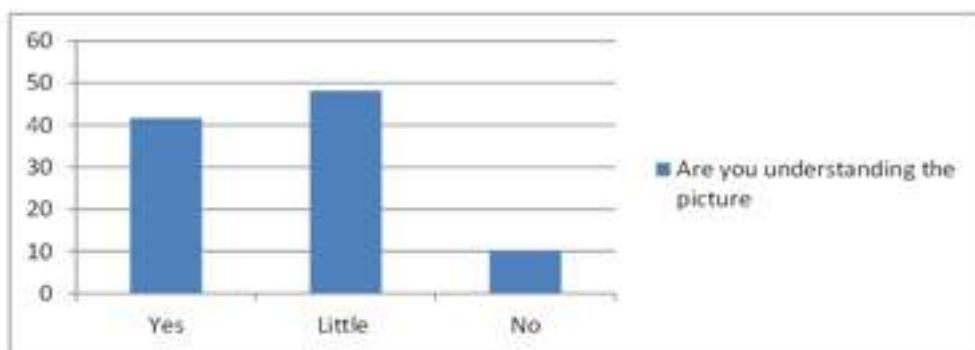
* Information that consumers are looking for on the nutrition labels					
Do you want to take a class on how to understand and use the nutrition facts label?		Yes 311 (62.5%)		No 241 (37.5%)	
Why are you not using nutrition labels?	Not interested 225 (40.7%)	Information is not important 46 (8.3%)	Did not take a class 164 (29.7%)	Information is too complicated 40 (7.4%)	No time 77 (13.9%)

\* Only nutrition label users were respondent (202)

\*\* Whole participants were respondent (552)

When we showed a picture of the nutrition label for a product and asked the participants if they understood it, most of them reported either "yes" or "a little", and 10.1% reported "no" (Fig 1).

Figure .1. Respondents on Picture Understanding



\* Values are percentages

Over half of the participants had normal BMI, high BF%, and low VFL. Regarding the correlation between body composition (BMI, BF%, and VFL) and attitude towards nutrition

labels, BMI and BF% were significantly correlated with the participant's attitude towards nutrition labels, while VFL was not significantly correlated (Table 3).

Table 3 Correlations between body compositions (BMI, BF%, and VFL) and attitude towards the

nutrition labels		
Do you read a nutrition label?		
Body Composition	Yes (N = 227) N (41.1%)	No (N = 325) N (58.9%)
- BMI		
Normal	145 (63.8%)	209 (64.3%)
Overweight	53 (23.3%)	70 (21.5%)
Obese	29 (12.9%)	46 (14.2%)
p-value	0.005	

- BF%		
Low	4 (1.8%)	5 (1.6%)
Normal	67 (29.5%)	97 (29.8%)
High	156 (68.7%)	223 (68.6%)
p-value	0.029	
- VFL		
Normal	226 (99.5%)	323 (99.5%)
High	1 (0.5%)	1(0.5%)
p-value	0.112	

Stepwise multiple regression was performed on BMI categories, with unadjusted and adjusted odds ratios shown in Table 4. Adjustments were made for BF%, VFL, smoking, weekly allowances, college, age, and physical activity. The contributions of BMI were observed after using normal body weight as a reference, and both overweight and obese individuals had higher odds ratios. In overweight participants, the odds ratio was 1.4-times higher in those who were not using nutrition labels than

in those who were using nutrition labels (OR 1.42, 95% CI 1.025- 2.77, P<0.003). The prevalence of obesity was significantly associated with nonusers of nutrition labels; the prevalence of obesity was 1.74-times higher among those who were not using nutrition labels (OR 1.74, 95% CI 1.79- 2.81, P<0.000). Moreover, not using nutrition labels increased the risk of having high levels of BF% by 2.5-times compared to those who used nutrition labels (OR 2.52, 95% CI 1.21- 3.98, P<0.031).

Table 4 Odds ratio of not using nutrition labels among BMI categories by multiple logistic regression

Variables	p-value	OR	95% CI for adjusted OR	
			Lower	Upper
BMI	References			
BMI1	0.003	1.429	1.025	2.779
BMI2	0.000	1.743	1.079	2.815
BF%	0.031	2.524	1.211	3.987
VFL	0.479	1.823	0.346	9.598
Smoking	0.552	0.773	0.264	2.036
Weekly allowances	0.216	1.049	0.972	1.131
College	0.432	1.332	0.073	2.343
Age	0.238	1.144	0.890	2.541
Physical activity	0.543	1.376	0.981	2.561

\* significant at 5% level of significance. OR: odds ratio; CI: confident interval.

\*\* BMI categories; BMI; Normal Body Weight, BMI (1); Overweight, BMI (2); Obese

Tested by multivariable logistic regression analysis (adjusting for covariate variables such as BF%, VFL, smoking, weekly allowances, college, age, physical activity).

## Discussion

The objective of the present study was to examine awareness of food labeling and the association between food label use and BMI and body composition among female college students in the KSA.

The current data demonstrated that 36.5% of the students reported using nutrition labels. These findings were consistent with the results of similar studies in African countries. For instance, the prevalence of self-reported use of nutrition labels was 40.5% in Lesotho [19] and 48% in South Africa [20]. In contrast, these prevalence estimates were lower than those observed in prior studies in other Middle Eastern, Asian, and some Western countries. In the Arab Gulf countries, the prevalence of respondents who read nutrition labels was 92% of 430 participants in Bahrain [21] and 89.5% of 1200 consumers in the United Arab of Emirates (UAE) [22], and 63.2% of 500 participants reported “sometimes to always” using nutrition labels in the UAE [23]. In Malaysia, the corresponding percentage of consumers who read nutrition labels was 85.1% out of 2690 consumers, while in China, consumers who reported using nutrition labels accounted for approximately 66.4% of 500 consumers [24]. Moreover, only 78% of African Americans reported using nutrition labels [25]. Another study conducted among 1,450 adult residents of Washington State found that 80% read the nutrition information on labels [26]. A review of research in 15 European countries reported the following prevalence of nutrition label use among European consumers: France, 63%; Sweden, 50%; and the United Kingdom, 52% [27]. Even though the participants in the present study were all women, all of the above-mentioned studies reported that women tend to read nutrition labels more than men. This finding may reflect that women are more likely to engage in household shopping and/or to be more health conscious than men [23].

It is well documented that education is one of the most relevant factors for using nutrition labels. The majority of these studies reported significant associations between consumer education and nutrition label use [28,29]. For example, a self-reported survey of 658 African Americans found that a high level of education was significantly associated with self-reported nutrition label use, even after adjusting for demographic characteristics and health-related variables in a multivariate model [25]. A random-digit-dial telephone survey selected a group of 1,450 adult residents of Washington State and found that education level was associated with self-reported food label use [26]. Our research indicated that education is not a factor that affects the association between education and nutrition label use, and this could be due to either the lack of knowledge of how to read nutrition labels or not knowing the reason for having nutrition information on the label. However, the SFDA is working hard towards the 2030 deadline by designing nutrition campaigns on many topics, and one of these campaigns focuses on how to read nutrition labels. Unfortunately, these campaigns are implemented only in large cities in the country (Riyadh, Jeddah, and Dammam), but it may now be the time for the SFDA to raise awareness in more cities such as Madiyah, Makkah, Al-Ahsa, Taif, Tabuk, and other cities throughout the country.

Data from the present study demonstrated that nearly 30% of the students were overweight and obese. The overweight participants represented 22.2% of the sample, whereas 13.6% were obese. These outcomes were similar to the results of similar studies conducted in the KSA and Arab Gulf countries. In the KSA, the prevalence of overweight and obesity among female students in the eastern region of the country was 54.2% and 17.4%, respectively [30]. In southwestern Saudi Arabia, a study reported that approximately 23.8% of female students were in the overweight and obese cat-

egory [31]. In Riyadh, which is located in the center of the KSA, the prevalence of overweight and obesity among female college students was 31.5% and 18.83%, respectively [32]. According to research conducted at King Faisal University, the prevalence of obesity/overweight among students was 29.7% [33]. In the United Arab Emirates, the corresponding percentages of obese and overweight individuals were 17.6% and 6.9% [34], respectively, while in Bahrain, the prevalence of obesity was 19.4% [35]. In a study conducted at Kuwait University, the prevalence of obesity was reported to be 8.9% [36]. These findings indicated the severity of obesity among the female population.

The analysis showed that the majority of the participants did not use the nutrition labels, which might have affected their body composition. Significant relationships were found between BMI and nutrition label usage. The results indicated that over half of the students had a normal body weight with a high level of BF%. The findings of our study were consistent with those reported in studies conducted in some Western countries [37–39]. BF% represents a risk factor for mortality [40,41] and other health problems [42], such as CVD [43–47], even if the participants had a normal BMI. Moreover, nutrition label use was significantly lower among participants, which might elevate the risk of high levels of BF% [48]. This indicates the dire need to raise awareness about the importance of using nutrition labels to reduce health problems.

We confirmed the reports of many international and large -scale studies that the use of nutritional labels plays a role in reducing obesity among users, notably among women globally [48–53]. However, a study demonstrated that nutritional label use did not have an effect on BMI [54]. This could be attributed to the technique that was used, which was a propensity score matching technique.

Adolescents and young adults accounted for

30% of the 33.5 million Saudis [55]. In recent years, poor self-awareness of nutrition label usage and increased unhealthy food consumption may explain the increase in diet-related diseases in the KSA [18]. The risky behaviors of the young population contribute to the occurrence of most chronic diseases [56]. One way of reducing the burden of these diseases is early interventions such as awareness campaigns and health programs in schools and universities that educate young adults about the importance of using and understanding nutrition information on food labels.

Because of the large size of our sample and the prevalence of young people using nutrition labels, the results of the survey of the present study can be considered representative of the whole female college population. Students who participated in the study, in fact, were mainly young female adults with a normal BMI. These elements let us assume that the sample analyzed includes people who are sufficiently aware of the health-diet relationship, who are interested in keeping their diet balanced and who are more likely to use food labels as a tool to guide their decisions in food and beverage selection.

This study has two limitations. First, the cross-sectional study design did not allow us to causally link the impact of the use of nutrition labels on obesity. Second, the data on nutrition label use was based on the self-report of the respondents and their use of information on nutrition labels, which might have resulted in biased answers in some cases.

## Conclusion

The results indicated that most respondents were not using nutrition labels. In addition, more than half of them wanted to take a professional class on how to read nutrition labels. This study showed that there was a statistically significant positive association between BMI and the use of nutrition labels among

female college students. Not using nutrition labels might be a risk factor for being obese. These findings may have important implications in terms of health outcomes and preventive methods. One suggestion is to provide education and awareness programs through the nutrition labeling campaign in the KSA about how to read nutrition labels and be familiar with the terminology and language written on nutrition labels. Further studies among the Saudi population on using nutrition labels should quantify the harmful effect of not using nutrition labels.

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## Original Article

# Haematological profiles of Sudanese Traditional Bakery workers exposed to biomass burning hazards

Ahmed Mohammed Elnour Elkhalifa<sup>1,2</sup>

1. Department of Public Health, Collage of Health Sciences, Saudi Electronic University,

College of Health Sciences, KSA.

2. Department of Haematology, Faculty of Medical laboratory Sciences,

University of El Imam El Mahdi, Kosi, Sudan.

Tel.: 00966501976641, 00249122467181

E-mail: a.alkhalifa@seu.edu.sa ; ahmedelnour2003@yahoo.com

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Corresponding author :Dr. Ahmed Mohammed Elnour Elkhalifa- Associate Professor

1. Department of Public Health, Collage of Health Sciences, Saudi Electronic University,

College of Health Sciences, KSA.

2. Department of Haematology, Faculty of Medical laboratory Sciences,

University of El Imam El Mahdi, Kosi, Sudan.

Tel.: 00966501976641, 00249122467181

E-mail: a.alkhalifa@seu.edu.sa ; ahmedelnour2003@yahoo.com

## Abstract

### Background :

Approximately one-third of the world's population in the developing countries are still dependent on Solid Biomass Fuel for cooking, heating and other household activities. This study aims to determine the Haematological profiles of Sudanese Traditional Bakeries workers exposed to wood-burning and compared with the non-exposed.

### Methodology :

A case-control study conducted at Kosti, Rabak, and Kenana, during the middle of 2017. Two hundred participants recruited in this study. One hundred traditional bakeries workers represented the case group and another hundred non-exposed apparent healthy matching individuals were chosen as a control group. 2.5 ml venous blood was collected into an EDTA container and the two groups were exposed to full blood counts (FBC).

### Results :

The mean of Haemoglobin, Haematocrit, Mean Cell Volume, Mean Cell Haemoglobin Mean Corpuscular Haemoglobin Concentration, Platelet counts, and Neutrophil count values among bakeries group compared to control group were statistically significantly decreased ( $12.58 \text{ g/dl}$  ( $\pm 2.15$ ) vs.  $15.5 \text{ g/dl}$  ( $\pm 0.95$ );  $42.71 \text{ l/l}$  ( $\pm 6.14$ ) vs.  $44.72 \text{ l/l}$  ( $\pm 4.15$ );  $83.49 \text{ fl}$  ( $\pm 6.43$ ) vs.  $89.18 \text{ fl}$  ( $\pm 7.15$ );  $27.72 \text{ pg}$  ( $2.83$ ) vs.  $29.41 \text{ pg}$  ( $\pm 1.88$ );  $30.75\%$  ( $\pm 2.64$ ) vs.  $32.33\%$  ( $\pm 2.26$ );  $205.29 \times 10^3/\text{l}$  ( $\pm 51.49$ ) vs.  $238.11 \times 10^3/\text{l}$  ( $\pm 59.56$ );  $49.59\%$  ( $\pm 16.43$ ) vs.  $57.36\%$  ( $\pm 13.93$ ) respectively. The mean of TWBC counts  $6.77 \times 10^3/\text{l}$  ( $\pm 1.71$ ) vs.  $6.17 \times 10^3/\text{l}$

## الملخص

### مقدمة:

لا يزال حوالي ثلث سكان العالم في البلدان النامية يعتمدون على الوقود الحيواني لأغراض الطهي. والتدفئة وغيرها من الأنشطة المنزليه المختلفة وتهدف هذه الدراسة لمعرفة صورة الدم الكاملة للعاملين في المخابز السودانية التقليدية المعرضين لدخان الناتج من استخدامهم حرق الأخشاب ومقارنتها بصورة الدم الكاملة مع أشخاص أصحاب غير معرضين لدخان الأخشاب.

### طريقة البحث:

أجريت الدراسة الحالية في السودان في مدن كوسٰي وربك وكشانة خلال منتصف العام ٢٠١٧ بمشاركة مائة من عمال المخابز التقليدية متلوا مجموعة الدراسة، وتم اختيار مائة شخص آخر كمجموعة ضابطة متطابقة مع مجموعة الدراسة في الجنس والعمر حيث تم عمل صورة دم كاملة للمجموعتين.

### النتائج:

أظهرت نتائج الدراسة أن متوسط قيمة الهيمو غلوبين، الهيماتوكريت، متوسط حجم الخلية، متوسط تركيز الهيمو غلوبين في الدم، تركيز الهيمو غلوبين وتعداد الصفائح الدموية لدى عمال المخابز التقليدية أقل وذات دلالة إحصائية جوهرية مقارنة بالمجموعة الضابطة بينما أظهر متوسط تعداد الخلايا الليمفاوية ومتوسط تعداد كريات الدم البيضاء قيم أعلى وذات دلالة إحصائية جوهرية لدى عمال المخابز التقليدية في حين لم يتم ملاحظة أي

( $\pm 1.50$ ) and Lymphocyte counts 36.21% ( $\pm 13.52$ ) vs. 29.98% ( $\pm 5.70$ ) were statistically significantly increased in bakeries. No significant differences were observed in the RBC counts between the study group and control group.

#### Conclusion :

There was a clear and significant effect of exposure to wood-burning smoke on most of the haematological values, among workers of the traditional bakeries.

#### Keywords :

Wood-burning, RBCs counts, Hb, TWBCs counts, Platelet count, Sudan.

## Introduction:

Biomass burning has its origins since ancient times. In spite of mass urbanization of the world, a large section of residents of rural areas in developing countries continue using biomass burning in Traditional Cook Stoves (TCS). [1, 2] Most rural households (approximately one-third of the world's population in developing countries- around three billion people) are still dependent on Solid Biomass Fuel (SBF) from materials including wood, sawdust, crop residue, dunk cake or coal for cooking, heating and other household energy needs.<sup>[3-6]</sup> Dependence on SBF (40%) leads to Indoor Air Pollution (IAP) which is recognized as a major threat to human health. [2, 7] Short-term exposure to emissions from wood combustion is known to be harmful to health from the combustion of fossil fuels. These include at least 28 pollutants in smoke from solid fuel use which are toxic, including 14 carcinogenic compounds and 4 cancer-promoting agents.<sup>[5]</sup> Several health-hazardous pollutants released by Burning of SBFs included Particulate Matters (PM), which have been declared carcinogenic by the International Agency for Research on Cancer. Examples are Carbon Monoxide (CO), Volatile Organic Compounds (VOCs) and, certain hydrocarbons including Polycyclic Aromatic Hydrocarbons (PAHs) in the environment. [8-10] Numerous studies have mentioned that, (PM2.5) product of incomplete SBF combustion, is a component asso-

цииated with climatic impacts and health effects. [3, 11] Concerning the systemic effects of human health, air pollution represents around 6% of the burden of disease. However, the World Health Organization (WHO) estimates that more than 4.3 million deaths annually are caused by smoke-induced diseases. This is more than deaths caused by tuberculosis and malaria, which makes it one of the leading causes of deaths worldwide. According to the report by World Health Organization (WHO) in 2018, high levels of exposure to PM2.5 may be responsible for approximately 3.8 million premature deaths annually which includes deaths due to respiratory and heart diseases.<sup>[12]</sup> Also, CO is a colourless gas which has serious effects, causing tissue hypoxia due to high binding capacity to haemoglobin; continuous exposure may result in neuropsychiatric impairment. [13-15] Workers in traditional bakeries, women, and children are the most vulnerable group being exposed to burning emissions in the kitchen area during cooking hours. [7, 8] Therefore, the impact of the concentration of pollutants from indoor biomass burning depends on many factors such as stove characteristics, kitchen characteristics, type and quantity of fuel, method of cooking and ventilation influencing the household indoor air quality (IAQ). [16, 17] Indoor air pollution from biomass combustion, such as exposure to wood smoke represent a major source of mortality and morbidity worldwide. It has been associated with irritation of the mucous

membranes, physiological and neurological effects in humans and may be responsible for reduced lung function, increased risks of cardiovascular disease, stroke, lung cancer, chronic obstructive pulmonary disease, acute lower respiratory infections, ischemic heart disease, low birth weight, preterm birth, still-birth, stunting, cataracts, and all-cause mortality. [5, 18-22] Most of the Sudanese in rural areas use biomass fuel (mainly wood) in their traditional bakeries. So, the current study aimed to determine the alterations and changes with regards to haematological profiles to detect if there was any significant difference between traditional bakery workers, who worked more than three continuous years using wood and were exposed to burning smoke and healthy individuals. It is important to note that, this type of study has not been conducted in Sudan before.

### **Methods:**

**Study Design and study setting:** A case-control study was done at White Nile State, Kosti, Kenana and Rabak towns, Sudan, from the period of June to November 2017 in order to study the effects of exposure to wood-burning smoke on complete blood counts among Sudanese traditional bakery workers exposed to burning smoke for more than three consecutive years. **Participants and sample size:** One-hundred traditional bakers were chosen randomly according to Inclusion and Exclusion Criteria to participate in this study as a case group and another hundred healthy age and sex-matched individuals were chosen as a control group.

**Inclusion and Exclusion Criteria:** All bakery workers working in Kosti, Rabak; and Kenana being exposed to wood-burning smoke for more than three continuous years were included in this study. Participants who had cardiovascular disease, presence of concurrent blood diseases, concurrent drug usage effect on Complete blood counts (CBC), smokers,

alcoholism, children, work period less than or equal to consecutive three years and those who refused to participate were excluded.

**Data Collection:** Structured questionnaire was used to collect data. It included personal and clinical information along with laboratory investigations. **Laboratory Analysis:** 2.5ml venous blood samples were collected from each participant into Ethylene Diamine Tetra Acetic Acid (EDTA) containers, labelled, mixed, and checked for absence of clots, and examined immediately for full blood counts (FBC) using automated haematology analyser (XK-21 Sysmex®, Tokyo, Japan). Peripheral blood films were stained with Giemsa for morphology and differential counts were done microscopically. **Statistical analysis:** Laboratory and demographic data were analysed by Statistical Package for the Social Sciences (SPSS), IBM version-25. Mean, standard deviation and Frequency distribution were performed. The comparison was done by applying two-tailed Student's t-test to know the difference between traditional bakery workers' haematological values and the healthy control group laboratory results. The alpha error of 0.05 and P-value  $\leq 0.05$  was considered as a level of significance. **Ethical considerations:** Each participant completed the informed consent form before the collection of specimen. Ethical approval was obtained from the research and ethics committee at the University of El Imam El Mahdi, Faculty of Medical Laboratory Sciences.

### **Results:**

100% of the study participants were male because normally females in Sudan don't work in bakeries and fuel stations. [27] The findings of the current study showed that, 50% of the study group and controls were between 30-39 years old, 32% between 20-29 years old, and the remaining 18% between 40-49 years old. (Table 1) The results of haematological pa-

rameters indicated that the mean of Hb, HCT, MCH, MCHC, MCV, platelet counts, and Neutrophil count values among bakers' group were statistically significantly decreased compared to the control group. The mean of the Haemoglobin (Hb) ( $12.58 \pm 2.15$  g/dl vs.  $15.15 \pm 0.95$  g/dl;  $P < 0.001$ ), Haematocrit(HCT) ( $42.71 \pm 6.14$  l/l vs.  $44.72 \pm 4.15$  l/l ; $P < 0.001$ ), Mean Cell Haemoglobin (MCH) ( $27.72 \pm 2.83$  pg vs.  $29.41 \pm 1.88$ pg;  $P = <0.001$ ), Mean Cell Haemoglobin Concentration (MCHC) ( $30.75 \pm 2.64\%$ vs.  $32.33 \pm 2.26\%$ ;  $P = <0.001$ ), Mean Cell Volume (MCV) ( $83.49 \pm 6.43$ fl vs.  $89.18 \pm 7.15$  fl;  $P < 0.001$ ), platelet counts ( $205.29 \pm 51.49 \times 10^3$ /l vs.  $238.11 \pm 59.56 \times 10^3$ /l;  $P = <0.001$ ), Neutrophil count ( $49.59 \pm 16.43\%$  vs.  $57.36 \pm 13.93\%$  ; $P = <0.001$ ).

(Table 2, 3, 4). However, the mean of TWBCs counts ( $6.77 \pm 1.71 \times 10^3$ /l vs.  $6.17 \pm 1.50 \times 10^3$ /l;  $P = 0.007$ ), and the mean of lymphocyte counts ( $36.21 \pm 13.52\%$  vs.  $29.98 \pm 5.70\%$ ;  $P = <0.001$ ), were statistically significantly increased in bakers group (Table4). The mean of Red Blood Cells (RBCs) counts ( $4.89 \pm 0.6 \times 10^{12}$  vs.  $4.90 \pm 0.42 \times 10^{12}$ ;  $P < 0.001$ ), had no statistically significant difference between bakers and apparently healthy control group (Table 3). The blood morphology of the traditional bakery workers showed that,37% of the participants' RBCs had a normocytic normochromic picture, 34% normal with stomatocyte cells, 17% dimorphic picture, 6% normal with target cells, and 4% normal with spherocytes and 2% showed a microcytic hypochromic picture. (Table 5)

Table 1: Traditional bakers (exposed to wood burning) and controls age and address

Parameter	Category	Frequency	percent
bakery workers' age range	20-29	32	32%
	30-39	50	50%
	40-49	18	18%
	Total	100	100%
bakery workers' Addresses	Kosti	63	63%
	Rabak	21	21%
	Kenana	16	16%
	Total	100	100%

Table 2: Haemoglobin concentration (Hb) and haematocrit blood test (HCT) values among Traditional bakers (exposed to wood burning) and controls.

Parameter	Study group traditional bakeries n=100				Control group apparent healthy individuals n=100				t- value	P-value*
	Category	Frequency	percent	Category	Category	Frequency	percent	Mean ±SD		
Hb concentration	12-17 g/dl	52	52%	12.58±2.15 g/dl	12-17 g/dl	87	87%	15.15±0.95 g/dl	10.924	<0.001
	<12 g/dl	48	48%		<12 g/dl	9	9%			
	>17 g/dl	0%	0%		>17 g/dl	4	4%			
	Total	100	100%		Total	100	100%			
HCT	45.5 l/l- 41.5 l/l	59	59%	87%	45.5 l/l- 41.5 l/l	93	93%	44.72±1.05 l/l	5.605	<0.001
	<41.±.5 l/l	37	37%		<41.±.5 l/l	5	5%			
	>45±.5 l/l	4	4%		>45±.5 l/l	2	2%			
	Total	100	100%		Total	100	100%			

\*Significance at the level  $\leq 0.05$

Table 3: RBCs counts and red cell indices (MCV, MCH, and MCHC) values among Traditional bakers (exposed to wood burning) and controls.

Parameter	Study group traditional bakeries n=100				Control group apparent healthy individuals n=100				t- value	P-value*
	Category	Frequency	percent	Mean ±SD	Category	Frequency	percent	Mean ±SD		
RBCs counts	3.8-5.5 × 10 <sup>12</sup>	52	52%	4.89±0.61 ×10 <sup>12</sup>	3.8-5.5 × 10 <sup>12</sup>	85	85%	4.90±0.42 × 10 <sup>12</sup>	0.068	0.946
	<3.8× 10 <sup>12</sup>	31	31%		<3.8× 10 <sup>12</sup>	12	12%			
	>5.5 × 10 <sup>12</sup>	17	17%		>5.5 × 10 <sup>12</sup>	3	3%			
	Total	100	100%		Total	100	100%			
MCV	92.0±9 fl	48	48%	83.49±6.43 fl	92.0±9 fl	87	87%	89.18±7.15 fl	5.919	<0.001
	<83fl	52	52%		<83fl	11	11%			
	>101fl	0	0%		>101fl	2	2%			
	Total	100	100%		Total	100	100%			
MCH	29.5±2.5 pg	53	53%	27.72±2.83pg	29.5±2.5pg	91	91%	29.41±1.88 pg	4.974	<0.001
	<27 pg	42	42%		<27 pg	6	6%			
	>32 pg	5	5%		>32 pg	3	3%			
	Total	100	100%		Total	100	100%			
MCHC	33±2.5 %	49	49%	30.75±2.64%	33±2.5 %	83	83%	32.33±2.26%	5.605	<0.001
	<30.5 %	43	43%		<30.5 %	5	5%			
	>35.5 %	8	8%		>35.5 %	12	12%			
	Total	100	100%		Total	100	100%			

\*Significance at the level ≤0.05

Table 4: TWBC counts, PLTs counts, Neutrophil counts, and Lymphocyte counts values among Traditional bakers (exposed to wood burning) and controls.

Parameter	Study group traditional bakeries n=100				Control group apparent healthy individuals n=100				t- value	P-value*
	Category	Frequency	percent	Mean ±SD	Category	Frequency	percent	Mean ±SD		
TWBC counts	4-10 ×10 <sup>3</sup> /l	95	95%	6.77±1.71 ×10 <sup>3</sup> /l	4-10 ×10 <sup>3</sup> /l	97	97%	6.17±1.50 ×10 <sup>3</sup> /l	2.740	<0.007
	<4×10 <sup>3</sup> /l	4	4%		<4×10 <sup>3</sup> /l	2	2%			
	>10 ×10 <sup>3</sup> /l	1	1%		>10 ×10 <sup>3</sup> /l	1	1%			
	Total	100	100%		Total	100	100%			
PLT counts	170-450×10 <sup>3</sup> /l	88	88%	205.29 ±51.49 ×10 <sup>3</sup> /l	170-450×10 <sup>3</sup> /l	93	93%	238.11± 59.56 ×10 <sup>3</sup> /l	4.168	<0.001
	<170 ×10 <sup>3</sup> /l	12	12%		<170×10 <sup>3</sup> /l	5	5%			
	>450 ×10 <sup>3</sup> /l	0	0%		>450 ×10 <sup>3</sup> /l	2	2%			
	Total	100	100%		Total	100	100%			

Neutrophil counts	40-80%	64	64%	49.59 ±16.43%	40-80%	89	89%	57.36 ±13.93%	3.607	<0.001
	<40%	36	36%		<40%	9	9%			
	>80%	0	0%		>80%	2	2%			
	Total	100	100%		Total	100	100%			
Lymphocyte counts	20-40%	50	50%	36.21 ±13.52%	20-40%	83	83%	29.98±5.70%	4.246	<0.001
	<20%	9	9%		<20%	6	6%			
	>40%	41	41%		>40%	11	11%			
	Total	100	100%		Total	100	100%			

\*Significance at the level  $\leq 0.05$

Table 5: Red Cell Morphology among traditional bakers.

Red Cell Morphology	Frequency	Percent
Normocytic normochromic	37	37.0
Dimorphic	17	17.0
Microcytic hypochromic	2	2.0
Normal with stomatocyte	34	34.0
Normal with target	6	6.0
Normal with spherocyte	4	4.0
Total	100	100

## Discussion:

The exposure to biomass smoke and PAHs induces oxidative stress, represents an imbalance between pro-oxidant and antioxidant systems causing haemolysis which leads to release of free heme, which acts as pro-oxidant and contributes to inflammatory events by increasing the expression of vascular adhesion molecules during haemolysis. However, recent studies have provided evidence of the association between wood-smoke emissions mainly PAH exposure and probable impairments on blood parameters in humans. [23-26] The traditional bakeries workers used wood as a fuel and were exposed to both air pollutants and high temperature. The findings of this study go in line with previous studies done in Ghana in 2019 by Dadzie EK. and his colleagues [28] who indicated low haemoglobin, low MCV, low MCH, low MCHC, and low GRAN which is significantly associated with exposure to

wood smoke, and a study done in Pakistan in 2016 by Kamal A, and his colleagues [29] who found low haemoglobin level (Hb) in subjects who had prolonged exposure to combustion of large amounts of fuelwood and coal smoke. Also, it is in agreement with another study done in India by Padhy PK. and his colleagues who in 2009 [30] reported that the children who live in households using traditional biomass fuels for cooking had low Hb levels. But this is not in agreement with regards to neutrophil counts which were found to be increased in the traditional biomass fuel exposed people. In contrast, the study was done on Tandoor occupants in Pakistan in 2014 by Nabi G, et al. [31] stated, high Hb, high HCT, high MCV, High MCHC, High RBCs counts, high lymphocyte counts, and high Platelet counts among Tandoor Occupants who exposed to Wood Smoke when compared to healthy control persons, however the results regarding decreased neutrophil counts, increased lymphocyte counts

and increased TWBCs counts were in agreement with this study. On the other hand, the results concluded by Rabha R. and his colleagues in India during 2018, [32] revealed that platelet counts had a significant positive association with results from emissions released during cooking with fuelwood while haemoglobin had a negative association. The mean of TWBCs counts ( $6.77 \pm 1.71 \times 10^3/l$  vs.  $6.17 \pm 1.50 \times 10^3/l$ ; P=0.007), and the mean of lymphocyte counts ( $36.21 \pm 13.52\%$  vs.  $29.98 \pm 5.70\%$ ; P<0.001), were statistically significantly increased in bakers (Table4). Similar results were recorded in previous studies [30, 31, 32] with high white blood cell counts also concluded in a previous study done in Pakistan in 2016 by Kamal A, and his colleagues [29]. Regarding high lymphocyte counts the current study findings agree with the previous study done in Ghana in 2019 by Dadzie EK and his colleagues [28]. The mean of RBCs counts ( $4.89 \pm 0.6 \times 10^{12}$  vs.  $4.90 \pm 0.42 \times 10^{12}$ ; P<0.001), had no statistically significant difference between bakers and control group (Table 3). These results are in contrast with the study done in India by Padhy PK and his colleagues in 2009 [30] who reported low red blood cell (RBC) among wood smoke exposure and study done in Tandoor in 2014 by Nabi G, et al. [31] who stated high RBCs count. The blood morphology of the traditional bakeries workers showed that 37% of the participants RBCs had normocytic normochromic picture, 34% showed normal morphology with presence of stomatocyte cells, 17% showed dimorphic picture, 6% showed normal morphology with presence of target cells, 4% showed normal morphology with presence of spherocyte, and 2% showed microcytic hypochromic picture (Table5). Changes in hematologic parameters in this study are like the findings, in a study conducted by Lal et al. in 2011[33] who measured haematological parameters in rodents, exposed to cow dung smoke for around 12 months. The possible reasons for the similar-

ties and differences in blood parameters in different populations may be due to the length of exposure and the nature of the biomass used. The blood morphology of the traditional bakery workers showed that, 37% of the participants' RBCs had a normocytic normochromic picture, 34% normal with stomatocyte cells, 17% dimorphic picture, 6% normal with target cells, and 4% normal with spherocyte, and 2% showed a microcytic hypochromic picture. (Table 5) This morphological change may be due to long exposure to wood-burning and according to the blood parameters, mainly RBC indices.

#### Conclusion:

The present study results showed apparently significant effects in approximately all haematological parameters among traditional bakers exposed to wood-burning smoke including the mean of Haemoglobin, Haematocrit, Mean Cell Volume, Mean Cell Haemoglobin, Mean Corpuscular Haemoglobin Concentration, Platelet counts, Neutrophil counts, Total White Blood Cell counts and Lymphocyte counts.

**Conflict of Interest:** The author declared no conflict of interests.

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## Original Article

# Prevalence of Laser Vision Correction Among Qassim Medical Students

Omar A. Alrobaish<sup>1</sup>, Ahmad F. Alhumaid<sup>1</sup>, Muath A. Alduayji<sup>1</sup>, Ahmad M. Alaraj, MD<sup>2</sup>

1. From College of Medicine, Qassim University, medical intern, Saudi Arabia.

2 . Assistant professor, Ophthalmology Department, College of Medicine, Qassim University, Saudi Arabia.

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Corresponding Author : Ahmad M. Alaraj, MD, Assistant professor, Department of Ophthalmology, college of medicine, Qassim University, PO Box 6655, Buridah 51452, Kingdom of Saudi Arabia. Telephone: +966-16-380-0916; Fax: +966-16-380-1228; Mobile phone: +966506153620. Email: aaraj@qumed.edu.sa.

### Abstract

#### Background:

Laser vision correction is considered one of the most common optional eye surgeries done worldwide. It includes a variety of procedures with changing indications in modern ophthalmology. The aim of this study is to determine the prevalence of laser vision correction (LVC) among medical students at the college of medicine, Qassim University, Saudi Arabia and to assess their level of satisfaction.

#### Methods:

Cross-sectional observational randomized questionnaire study. The questionnaire was distributed to 200 medical students randomly selected from each academic year, where the self-reported response was recorded.

#### Results:

Responses were completed by 195 out of 200 subjects. Of the 195 subjects, 104 (53.3%) reported that they had refractive errors. Myopia was the most prevalent type of refractive errors. Of the 104 students with refractive errors, only 10 (9.6 %) had undergone refractive surgery. Eight out of ten were females, and the two were males. The 94 of 195 participants who did not do LVC were satisfied with glasses or contact lenses while a few of them were afraid of postoperative complications. More than 90% of those who underwent refractive were satisfied after the refractive surgery.

#### Conclusion:

The prevalence of refractive errors among medical students of Qassim University is comparable to general population. The prevalence of LVC among them is also comparable to international published reports.

#### Keywords:

Laser vision correction, Refractive errors, Myopia.

### الملخص

#### خلفية:

يعد تصحيح النظر بالليزر أحد أكثر العمليات الإختيارية شيوعاً في العالم. يشمل تصحيح النظر عدة أنواع مختلفة من العمليات لأسباب متغيرة في طب العيون الحديث. الهدف من هذه الدراسة هو معرفة مدى إنتشار عمليات تصحيح النظر بالليزر بين طلاب كلية الطب في جامعة القصيم وقياس مدى رضاهم من هذه العمليات.

#### طريقة البحث:

: دراسة مقطعة رصدية مبنية على إستبيان عشوائي. الإستبيان وزع على ٢٠٠ طالب طب عشوائياً من كل سنة دراسية و تم تسجيل إجاباتهم وحفظها

#### النتائج:

أكملت الإجابات بعدد ١٩٥ من أصل ٢٠٠. من أصل ١٩٥ ، ١٠٤ (٥٣.٣٪) أجابوا بأن لديهم عيوب إنكسارية. قصر النظر كان أكثر الأنواع انتشاراً. عشرة (٦٪) فقط من أصل ١٠٤ الذين كانت لديهم عيوب إنكسارية قاموا بعملية تصحيح النظر. ثمانية من أصل هؤلاء العشرة كانوا إناث وإناث كانوا ذكور. أربعة وتسعمون من المشاركون ١٩٥ الذين لم يخضعوا للعمليات تصحيح النظر كانوا بالمجمل راضين مع استخدامهم للنظارات والعدسات وقليل منهم كانوا خائفين من مضاعفات العملية. أكثر من ٩٠٪ من المشاركون كانوا راضين بعد قيامهم بعملية تصحيح النظر.

#### الخلاصة :

معدل انتشار أخطاء العيوب الإنكسارية بين طلاب الطب في جامعة القصيم مقارب لعامة السكان بالمملكة. كما أن معدل انتشار عمليات تصحيح النظر بين الطلاب مقارب لإنتشارها عالمياً.

## INTRODUCTION:

Refractive errors are the most common cause of vision loss after cataract in different age groups and are leading cause of visual impairment [1]. Moreover, previous researches have shown that children and adults who have refractive errors commonly do not get the ideal level of vision correction [1]. Refractive errors may cause difficulties in a person's daily life activities related to vision [2]. Glasses and contact lenses are considered the first line option for refractive errors correction in all age groups [3]. In the last two decades, laser vision correction (LVC) has got more popular and nowadays the most popular optional surgery in the world [3].

The prevalence of myopia is increasing notably in Asians [4]. It has reached 70% in some Asian countries, 50% in England and 25% in North America [4]. Other than geographic differences, gender and race may affect the risk of myopia [4,5]. Previous studies showed that the prevalence of myopia among medical students in selected universities in Saudi Arabia was 53.5% [6].

Refractive errors have social, economic and educational impact, and its economic impact is substantial in the world [7]. Furthermore, the average annual cost of myopia for every 12 to 17-years-old student in Singapore can reach up to 148 U.S. Dollars [8].

With the use of improved ophthalmic instruments, LVC has shown a noticeable increase in the safety and efficacy of surgical results [9]. Types of laser vision correction can be grouped as either surface treatment like photorefractive keratectomy (PRK), in which the epithelium is removed before the cornea is subjected to laser, or laser in situ keratomileusis (LASIK), in which a corneal flap is fashioned and flipped before laser is applied to the underlying cornea, and then the flap is replaced back [10,11]. Selection of procedure type depends on detailed history and complete ocular exami-

nation for candidacy status. One of the very important post-operative risk to be considered is post Lasik ectasia in which the cornea gets thinned with increasing irregular astigmatism and deterioration of visual acuity [19]. In this study we are looking for the prevalence of LVC among medical students of Qassim University and their postoperative satisfaction.

## METHODS:

This is a cross-sectional observational study conducted in the month of April 2019. The study population included all students of Qassim University College of medicine in Qassim province, Saudi Arabia. Total students were 707 (450 Males, 257 Females). Stratified random sampling was taken from each year. The sample size was 200 (73 Females and 127 Males). With predicted prevalence of 8% the confidence interval was 4% and alpha level of 0.05, which was verified by a statistician.

Questionnaire was used as a printed copy and distributed to all participating students in a private and anonymous manner. The participants were given the option to withdraw at any time during the survey. Questions were designed to elicit information in a concise and objective manner. In addition, logics were used in the question so the subsequent answer would base on prior response. Questions included 3 main categories, which elicit 12 responses in demographic, candidacy status and satisfaction rate.

Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 21 (IBM, SPSS, Chicago, IL, USA). In all analyses,  $P \leq 0.05$  was considered statistically significant.

### *Ethical approval and informed consent:*

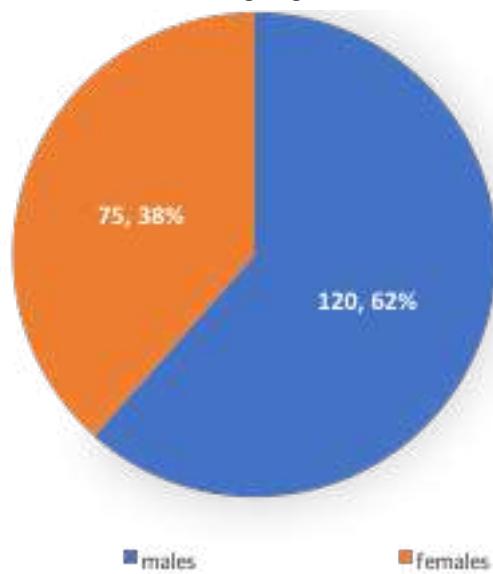
This study was approved from the institutional review board at research center in college of medicine, Qassim University. Informed consent was taken from all participants. Survey

was optional and participants were able to withdraw any time.

## RESULTS:

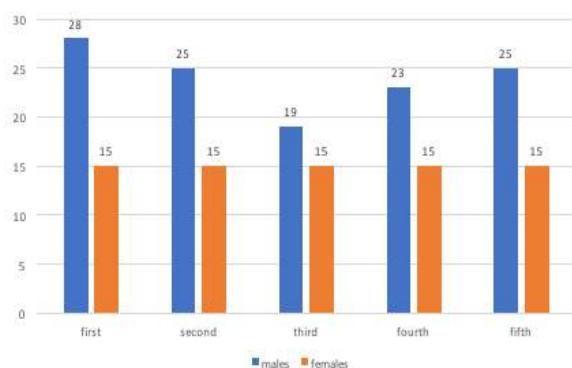
Participants received a hard copy of the questionnaire by the data collectors, this method insured that most participants responded. Of the 200 students from different academic years, 195 responded, 120 (61.5%) were males, and 75 (38.5%) were females as represented in Figure 1.

Figure 1. the distribution of Participants according to gender.



The breakup of students selected from each academic year is summarized in Figure 2.

Figure 2. The distribution of participants in each academic year



## Distribution of Refractive Errors in the Overall study

Of the 195 participants, 91 (46.7%) reported they had no refractive errors and 104(53.3%) reported they do have. Sixty-six participants (33.8%) had myopia. Only 24 (12.3%) reported having astigmatism, and 8 (4.1%) had hyperopia. Lastly, 6 (3.1%) reported they don't know their refractive errors.

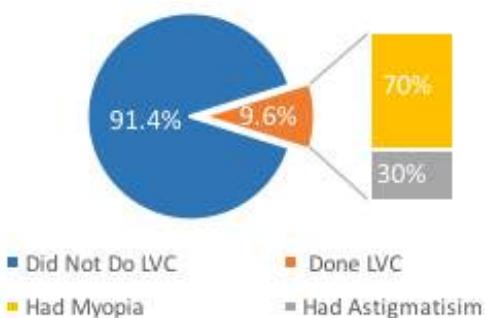
### Rates of Laser Vision Correction

Out of 104 participants who had refractive errors, only ten (9.6 %) had undergone a refractive surgery. Eight out of ten were females and the two were males. Out of the total 195, only (5.1 %) had a refractive surgery.

The procedure of choice for majority 5 (50%) was LASIK, whereas 3 (30%) underwent PRK, the remaining 2 (20%) did not know the type of procedure.

The most prevalent refractive error among participants who had LVC was myopia as seen in Figure 3.

Figure 3. The distribution of participants who had refractive errors



### Distribution of reasons for not having LVC

The 98 of 195 participants who provided reasons for not having the refractive surgery are represented in Table 1.

Table 1. Reasons for those with refractive errors and not having Refractive Surgery.

Reasons	N	Percent
Fear of complications	12	12.8%
High cost	14	14.9%
Waiting for better alternatives	6	6.4%
Satisfied with glasses or contact lenses	46	48.9%
Timing issue	13	13.8%
Other	3	3.1%
Total	94	100.0%

First reason was satisfaction with glasses or contact lenses in 46.9%, second was high cost in 14.3%, and closely followed by timing issue 13.3% and fear of complications in 12.2%, waiting for better alternatives 6.1% and other reasons were 7.1%.

#### *Satisfaction Rates*

The participants who had refractive surgery were asked about their satisfaction, 7 (70%) were completely satisfied and 3 (30%) were mostly satisfied and only one of these 30 percent not satisfied who reported having a complication. When we asked the participants "Are you better off having had the refractive surgery" all answered yes.

#### **DISCUSSION:**

The prevalence of LVC of refractive errors in Saudi adult population is not well known. The variation in refractive errors usually accounts for environmental, geographic, cultural, economic and demographic variables [12-14]. Few studies reported the prevalence of refractive errors in Saudi adult population. In these studies, the proportion of myopia ranging from 24.4% to 53.7%, astigmatism ranging from 9.5% to 15% and hyperopia ranging from 2.2% to 15% as seen in table 2 [15-18].

Table 2. Comparison of refractive errors prevalence studies in Saudi adults.

Study	Sample size	Emmetropes	Myopia	Astigmatism	Hyperopia
Al-Rashidi, et al. study	162	41.3%	53.7%	1.2%	3.7%
Alsaqr A, et al. study	998	44.5%	53.3%	15%	2.2%
Parrey M, et al. study	966	54.2%	24.4%	9.5%	11.9%
Alsaif B, et al. study	338	45.6%	47.9%	Not mentioned	6.5%
Current study	200	46.7% + 3.1% Did not know	33.8%	12.3%	4.1%

In the current study myopia accounts for 33.8%, astigmatism 12.3% and hyperopia 4.1%, which is comparable to previously reported publications in Saudi adult population. In the current cross-sectional study, self-reported prevalence of LVC was obtained from participants. Findings indicated that 9.6% reported having LVC and majority of them having myopia. To best of our knowledge this is the first reported prevalence of LVC in Saudi Arabia. Comparing our results to international published report from United State where the estimated overall prevalence of LVC was 13.1% of general population<sup>[13]</sup>.

Kezirian GM. et al and his colleagues presented a prospective randomized study on prevalence of LVC in ophthalmologists who perform refractive surgery<sup>[12]</sup>. They found 62.6% of ophthalmologist who were candidate for the surgery underwent LVC. This is about 4 times more in comparison to the reported 13.1% prevalence of LVC among general U.S population<sup>[13]</sup>. This increase might be attributed to the increase awareness and safety of the procedure among ophthalmologist who perform refractive surgery. In the same study 37.4% of ophthalmologist who were candidate did not undergo LVC. About 92.5% of them prefer to wear glasses or contact lenses and 5% had concern or fear of complication. Ninety percent of our participants who had refractive errors did not undergo LVC. About 46.9% were satisfied with glasses or contact lenses, 14.3% had concern regarding high cost of procedure, and 12.2% reported fear of complication. This will emphasize the necessity for increased awareness program among general population and in particular those in medical and paramedical field. Fifty percent of our participants who had got LVC reported that they did LASIK, 30% underwent PRK, and 20% were not sure what type of procedure they did. In comparison, the ophthalmologist study reported 65.7% underwent LASIK and 34.3% did PRK<sup>[12]</sup>. Although our result is comparable to

international published report, we emphasize and stress on proper patient selection for type of procedure since we have increasing number of keratoconus cases and post LASIK ectasia in Saudi Arabia<sup>[19]</sup>.

Satisfaction rate among our participants with LVC was high with 70% were completely satisfied post-surgery and 30% were mostly satisfied. When we ask our participant “Are you better off having had the refractive surgery” All answered yes. This again emphasizes their satisfaction. This agrees with other published report by J. Lellouch et al on evaluation of vision quality after laser vision correction in healthcare professionals<sup>[14]</sup>. Ninety percent were satisfied with postoperative vision quality, 92.8% would have the procedure again, and 94.6% would recommend it to their family and patients.

This study does have limitation. All participants were from one place with narrow age range, so the results cannot be generalized. The degree to which the students in this study can be representative to all medical students is not known. These limitations should be considered in the interpretation of the results, which cannot be overcome.

### Conclusion:

refractive surgery is safe procedure with very high satisfaction rate among our participants, which is comparable to international reports. Proper preoperative counseling and patient selection is needed to prevent post LASIK ectasia. This necessitates increase awareness program about safety and efficacy of LVC.

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## Original Article

# Intrinsic Investigations of Physiological Interaction for Pulsatile Rotary Blood Pumps

Mohsen Bakouri<sup>1,2,\*</sup>

1. Department of Medical Equipment Technology, College of Applied Medical Science, Majmaah University, Majmaah City, Saudi Arabia, 11952 E-mail: m.bakouri@mu.edu.sa

2. Department of Physics, College of Arts, Sebha University, Traghen, Libya

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Corresponding Author : m.bakouri@mu.edu.sa;

Tel.: +966-533231905

### Abstract

#### Background:

One of the major concerns with the use of circulatory assist devices (CADs) is their performance during the transition from supine to standing position. In standing position, vasodilatation of veins occurs in the legs, which decreases left ventricular end-diastolic pressure, and, in turn, the preload to the CAD. This research numerically studies the physiological interaction of pulse left ventricular assist devices (LVADs) in relation to cardiac output and stroke volume under systolic and diastolic situations.

#### Methods:

A cardiovascular system (CVS) model was used to configure the output of heart failure (HF) status by changing system parameters in one cardiac cycle, whereas LVAD pump was configured to change the fixed rotational speed. The terms of the pump cannulae model, real-time detection of aortic valve status, left ventricular stroke volume analysis, and LVAD control method were designed and analyzed.

#### Results:

The results showed that end-diastolic left and right ventricular volumes – pressures in heart failure condition were reduced from 183 mL to 164 mL with continuous fixed speed RBP support, Alongside with a corresponding increase in ejection fraction (16%).

#### Conclusion:

The results show that LVADs are more sensitive to preload than afterload when operating at a fixed speed.

#### Keywords:

Heart Failure; Rotary Blood Pumps; Cardiac Output; Cardiovascular System.

### الملخص

#### خلفية:

أحد أهم المشاكل الرئيسية المتعلقة بمضخات القلب (مضخات الدم الوراء) هو ردة فعل المضخة عند رجوع الدم إلى القلب عن طريق الأوردة. عندما يتغير الوضع الجسماني للمريض من وضع الجلوس إلى وضع الوقوف، تتم زيادة حجم الدم في عروق الساق بسبب توسيع الأوعية الدموية، وبالتالي رجوع الدم عن طريق الأوردة إلى الأذين الأيمن وبالتالي نقله إلى الأذين الأيسر. وينتج عن هذا انخفاض في الضغط الانبساطي البطيني الأيسر، وبالتالي التحميل (المسيق) لمضخة الدم الدوراة. في هذا البحث تمت دراسة التفاعل الفيزيولوجي للنقط النقيبية النبضية فيما يتعلق بحالات الانقباض والانبساط الناتج من القلب أثناء تدفق الدم.

#### طريقة البحث:

في هذا البحث سيتم استخدام النموذج الرياضي لنظام القلب والأوعية الدموية لتكوين إنتاج يماثل قصور القلب عن طريق تغيير معاملات النظام عند سرعة دوران ثابتة أثناء عمل المضخة.

#### النتائج:

أظهرت النتائج أن أحجام البطين الأيسر والأذين الانبساطي بالنسبة لضغط الدم أثناء حالات القصور القلبي نقل من 183 مل إلى 164 مل مع دوران ثابت السرعة لمضخة القلب ومع زيادة مقابلة في جزء الطرد الطرد بنسبة 16%.

#### الخلاصة :

وعليه نخلص إلى أن مضخات الدم الدوراة (مضخات القلب) هي أكثر حساسية للتحميل المائي من التحميل اللاحق عند التشغيل بسرعة ثابتة.

## Introduction

Heart failure (HF) is a severe health condition that occurs when the heart does not pump enough blood to support the body organs. Over the last decade, this disease has been associated with a significant population worldwide [1, 2]. In the United States, there are approximately 5.3 million people with HF condition, yet less than 0.05% receive heart transplants annually [3]. Similarly, in Australia, the annual prevalence of heart failure is approximately 2% of the population [4]. The continuous intravenous inotropic support is used as a short-term treatment, and although this may improve symptoms, mortality may worsen. This sets the stopwatch for patients receiving inotropic therapy as survival rates after a year is only 10% to 30% [5]. Despite the small number of patients receiving an appropriate treatment through the health management of this disease, heart transplantation is becoming a useful option for affected individuals. However, the shortage of donor hearts has compelled mechanical circulatory assistance (MCS) to mitigate the severity of the heart failure situation [5].

MCS has proven to produce more favorable outcomes for the end-stage HF patients than for optimally medically treated HF patients [6]. For this reason, the use of MCS is expected to increase significantly, with the indications expanding to include both bridge to recovery (BTR) patients and destination therapy (DT) patients who were previously not considered transplant candidates. The location of the inflow cannula is a factor that may aid this treatment strategy, with atrial cannulation and ventricular cannulation favoring BTR and DT, respectively. These mechanical devices fall into two categories: constant flow rotary and pulsatile ventricular assist devices (VADs). Recent investigations on these two types of VADs indicate that patients have a higher chance of survival with rotary or constant flow

support because they allow higher reliability, reduce sepsis, and decrease incidence of the right heart and end-organ failure [2]. These results are reflected in the U.S. Food and Drug Administration (FDA)'s recent approval of the rotary Heartmate II as a destination therapy [7]. The ability of constant flow support to provide optimal safety is likely to be due to the small size of devices, less implantation procedural time, and reduced device complexity, although the effect of the ventricles' interactions with either type of device is largely unknown [7]. There are many devices that support blood circulation in patients with HF condition, with the main distinguishing feature related to their mode of outflow, i.e., pulsatile or continuous [8, 9]. Although physiological pulsatility in the middle cerebral arteries was developed in patients with continuous axial ventricular support, the debate continues on the benefit of maintaining flow pulsatility [10]. In the cardiovascular system, the pulsatile rotary blood pumps (RBPs) have the benefit of generating physiological stress and flow. These devices can be useful in enhancing microcirculation and preventing gastrointestinal circulation complications [11]. However, the excessively large size and unreliable mechanical function of these devices far outweigh the advantages of pulsatile flow. The rotary pumps can overcome these problems by offering smaller and more reliable devices; however, the reduced operation of the pulse can be harmful to the vasculature and/or end-organ perfusion. For instance, Nishimura et al. discovered that extended non-pulsatile RBPs decreased the aortic wall thickness and smooth muscle cell size ratio [12]. Pulsing the velocity of an RBP to induce pulse pressure using a rotary pump is therefore an appealing control approach; however, the timing and operation advantages of this model are not clear [12].

The ability to regulate the velocity of continuous flow or RBP may allow the development of a simulated pulse, but until now, circulatory

assistance is traditionally provided at a steady mean rotational speed, which despite the sensitivity to left ventricular and aortic pressure, constantly decreases pulse pressure [13, 14]. In addition, the insensitivity of the device to the altering hemodynamic environment in which it operates can predispose the left ventricle (LV) to collapse [14] or regurgitate the pump flow [15]. Vandenberge et al. conducted the simulation of synchronous and asynchronous ventricular assist with phase shifting. They found that the synchronous pulsing could maximize stroke volume and ventricular pressure, whereas asynchronous pulsing led to highly unphysiological hemodynamic [16]. However, the best timing of the pulses to favor interaction between heart and RBP was not decided until an accurate triggering of pulses was achieved. On the other hand, Rüschen et al. developed a simulation model to investigate the effect of pulsatility phase timing on the left ventricular stroke work (LVSW). However, this study was limited due to the computational environment in which it was conducted [17]. The purpose of this study was to investigate the physiological interaction of LVADs with cardiac output (CO) on both sides of the heart (left and right ventricular atria) in terms of volume and pressure during an HF. Furthermore, this work evaluated the systolic and diastolic reactions to find the most appropriate timing strategy to minimize the potential of a ventricular suck-down, enhance aortic pulse pressure, and improve the degree of ventricular washout or unloading.

## Methods

### *Cardiovascular System Model Description*

A cardiovascular system (CVS) software model was developed in conjunction with an LVAD to simulate a wide range of cardiovascular and pump operating conditions. The CVS model consists of 12 coronary, pulmonary, and sys-

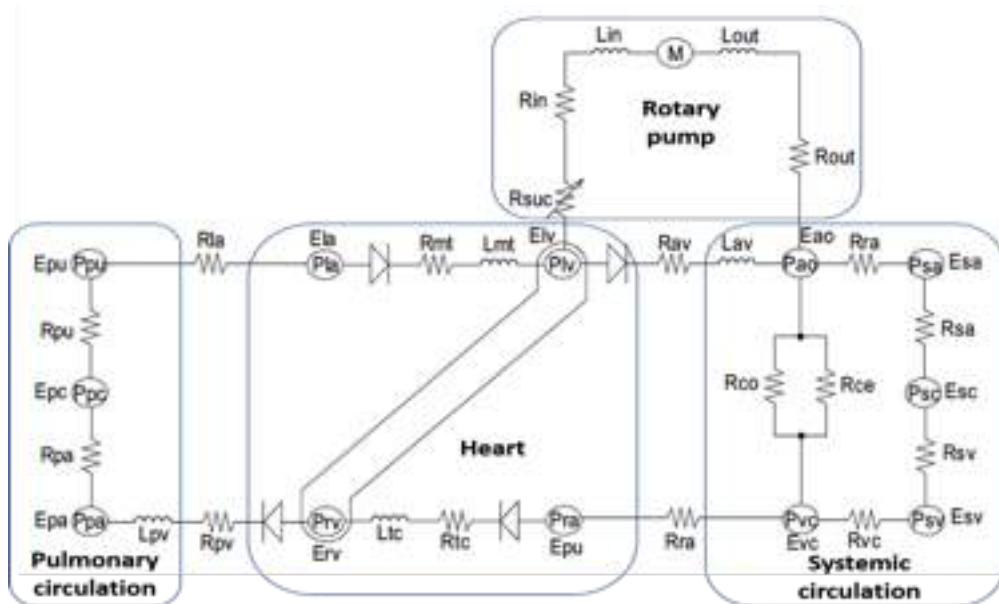
temic circulations on the left and right sides as shown in Fig. 1. The model also contains interventricular septum and pericardial interaction formulations. This model was validated using the literature data. A more detailed description of the model formulations is presented in [15, 18]. Three differing equations model the pump: an electric engine winding equation, an electric torque transfer, and a hydraulic pump equation. The input and output cannulae are also modeled on a constant flow resistance (in- and outlet), resulting in a decrease in pressure and inductive series of fluctuations (in- and outlet). A third resistance is included in the simulation of the suction events before cannula input. The amount of this variable force depends on the pressure of the LV.

### *Pump control and parameters adjustment procedure*

To ensure that the LVAD flow was maintained at a safe level, a proportional–integral–derivative (PID) controller was introduced to vary the pump speed as required. The controller featured a negative feedback loop that compares the independent LVAD pump flow to the target flow. The error between the two signals is then fed into the PID controller that can then alter the pump speed to minimize the error signal. The gains of 1.2, 0.75, and 1 were initially used for the PID controller [19]. A saturation blow was used to ensure that the speed of the pump did not leave the safe operating region of 1800 rpm to 2800 rpm. The displacement of the hub was held constant at 0 mm.

During this analysis, the model parameters were carefully modified to ensure correct simulation of heart output, aortic pressure, and left aortic pressure. Table 1 shows the hemodynamic variables of the model for both healthy and heart failure patients. The model parameters were set as required to configure the simulation study. The pump rotational speed of LVAD was adjusted until the pump outlet flow was 5 L/min. The steady-state pilot

Fig.1. Electrical equivalent circuit analog of CVS - LVAD interaction. Rin: inlet cannulae resistances; Rout: outlet cannulae resistances; Lin: inlet cannulae instances; Lout: outlet cannulae instances; Rsuc: suction resistance; thor;1 & Pthor;2: intrathoracic pressures



simulations were performed to find the pressure head and flow of the LVAD at a particular speed. The inlet pressure was increased from 0 mmHg, and the resulting outlet pressure and pump outlet flow were recorded. The outlet resistance valve was then adjusted as per the cannulae response to maintain the outlet pressure at 100 mmHg, and the corresponding pump outlet flow was recorded. The pump was then configured with pulse peaks in systo-

le or diastole to alter the rotational speed. The hemodynamic results were reported, such as left ventricular pressure/volume aortic pressure, pump outflow, and ventricular volumes.

## Results

Under widely varying physiological conditions, the LVAD with the scheduled PID controller was tested using computer simulations.

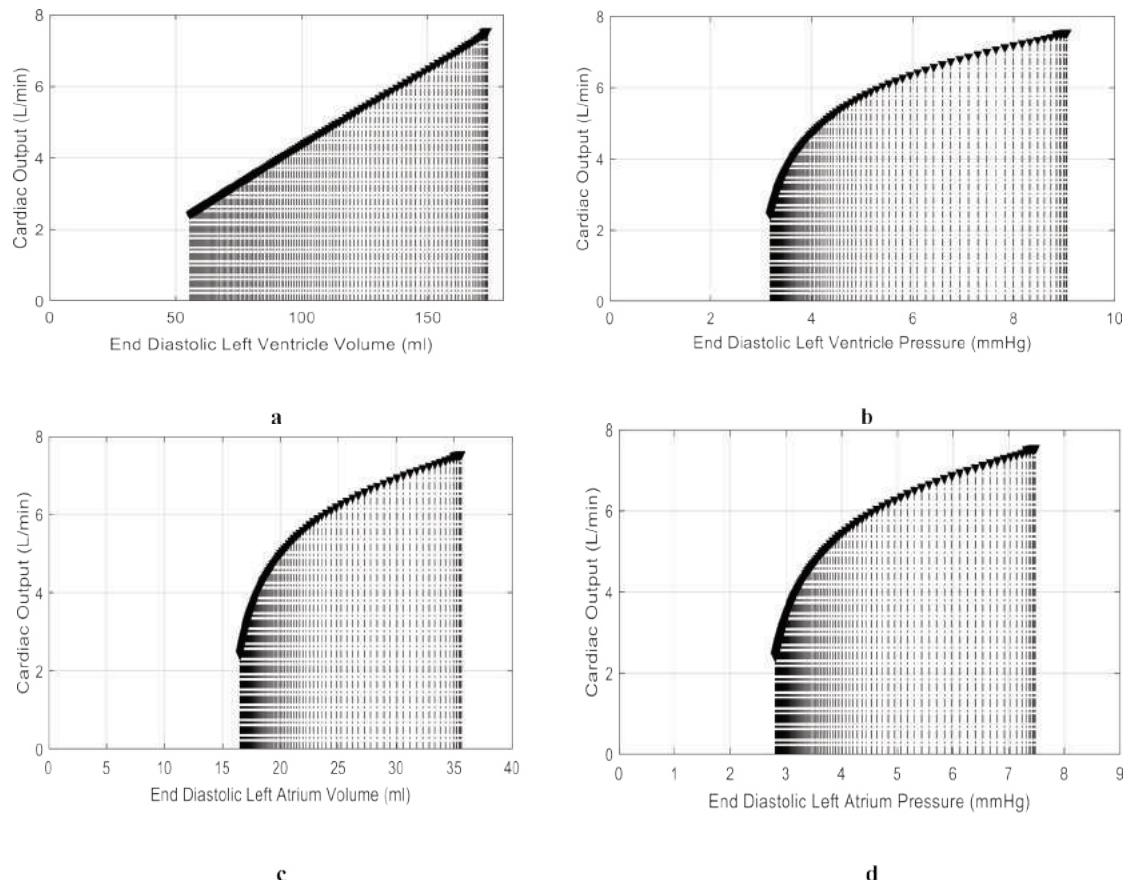
Table 1. Hemodynamic variables of the model for both healthy and heart failure patients

Model Parameter	Unit	Healthy		Heart Failure	
		Rest	Exercise	Rest	Exercise
Heart rate (HR)	bpm	70	150	85	120
Aortic resistance ( $R_{ao}$ )	mmHg/mL/s	0.48	0.16	0.36	0.72
Systemic arterial resistance ( $R_{ar}$ )	mmHg/mL/s	0.5	0.17	0.25	0.5
Systemic venous resistance ( $R_{vr}$ )	mmHg/mL/s	0.22	0.07	0.11	0.22
Vena cava resistance ( $R_{vc}$ )	mmHg/mL/s	0.08	0.03	0.04	0.08

The simulation scenarios ranged in both rest and heavy practice from the healthy heart to HF where the heavier LVAD load. In the simulation the pulse rate was 60 beats per minute and the LVAD parameters were set as required. Fig. 2 illustrates the changes in CO for the left side. Fig. 2a indicates the relationship between CO and the end-diastolic left ventricular volume (LVEDV). The volume of CO with LVAD support was linearly changes from 2.5L/min to 4.5L/min. Fig. 2b shows that the variations in CO was non-linear changing in relation

with the end-diastolic left ventricular pressure (LVEDP). For the left atrium, the CO was non-linearly changing in terms of both end-diastolic left atrium volume (LAEDV) and the end-diastolic left atrium pressure (LAEDP) (Fig. 2, a and b). In comparison to the right side of heart, the variation in CO has the same behavior in left side where the changes with the end-diastolic right ventricular volume (RVEDV) has linear relationship as shown in Fig. 3a. In the other hand, the end-diastolic right ventricular pressure (RVEDP), end-diast-

Fig. 2. End-diastolic left ventricular volumes–pressures vs cardiac output: (a) End-diastolic (left ventricle volume vs cardiac output; (b) End-diastolic left ventricle pressure vs cardiac output; (c) End-diastolic left atrium volumes vs cardiac output; (d) End-diastolic left atrium pressure vs cardiac output.



tolic right atrium volume (RAEDV), and the end-diastolic right atrium pressure (RAEDP) have non-linear behavior with the CO (Fig. 3, b, c and d). The changes for end-systolic volume and stroke work (SW) are summarized in Table 2 in terms of systole, continuous

and diastole.

## Discussion

The alteration of the speed of the pump to induce pulsatility in RBPs was found to in-

Fig. 3. End-diastolic right ventricular volumes–pressures vs cardiac output: (a) End-diastolic right ventricle volumes vs cardiac output; (b) End-diastolic right ventricle pressure vs cardiac output; (c) End-diastolic right atrium volumes vs cardiac output; (d) End-diastolic right atrium pressure vs cardiac output.

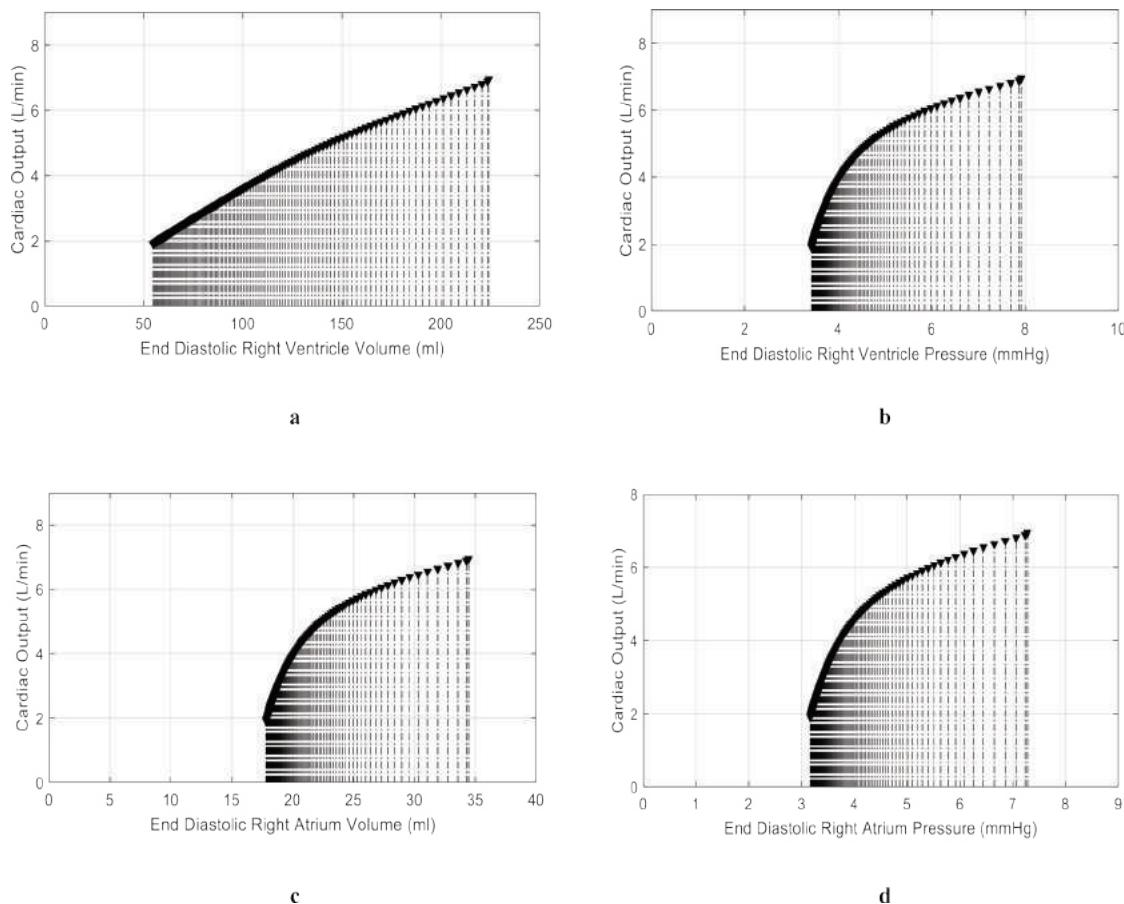


Table 2. Summary of results for hemodynamic variables.

Parameters	In Systole	Continuous	In Diastole
End-diastolic Left ventricle volume	163 mL	144 mL	147
end-diastolic Left ventricle pressure	22.5 mmHg	10 mmHg	8.2 mmHg
Stroke Work	0.19 J	0.18 J	0.16 J
Aortic Pulse Pressure	21 mmHg	10mmHg	7.5mmHg
Ejection Fraction	19%	16%	14%

fluence the end-diastolic left and right ventricular pressure and volume. Among three situations: constant speed, pulse peak in systole, and pulse peak in diastole, the pulse peak in diastole demonstrated the largest end-systolic volume (ESV) and the smallest SW and aortic pulse pressure, as shown in Table 2. These findings suggest that pulsing the RBP

in diastole can create a potentially ideal environment for myocardial recovery because the load on the heart is minimized. Furthermore, the reduced pulse pressure from the continuous operation mode, while not intuitively beneficial to the end-organ perfusion, may, in fact, benefit recovery. This is due to the maintenance of a higher diastolic aortic pressure,

and thus, the coronary blood flow is expected to increase as observed in other counter-pulsation devices [20, 21].

On the other hand, placing the pulse peak in systole created the largest pulse pressure by effectively amplifying the remnant ventricular pressure. This may be beneficial to improve the end-organ perfusion, particularly, under exercise conditions. The resulting reduction in the ESV, while predisposing the ventricle to the suck down events and thus the ventricular washout [22, 23].

The pulsatile output from an RBP might be beneficial for microcirculation, however, the effect on the coronary circulation should also be considered. With good aortic pressure autoregulation maintained between 60 to 200 mmHg, normal coronary blood flow is usually maintained despite changes to coronary perfusion pressure. However, due to the extravascular pressure, the endocardium is more susceptible to ischemia, especially at lower perfusion pressures [24, 25].

Therefore, the care should be taken to maintain a diastolic pressure of greater than 60 mmHg. In addition, the lowest trough of ‘pulse peak in systole’ could easily cause the diastolic aortic pressure to be lower than the minimum diastolic pressure for normal coronary blood flow (60 mmHg). Although the ‘pulse peaks in diastole’ maintained the largest diastolic aortic pressure, the timing of this pressure may not coincide with ventricular relaxation due to the phase delay caused by the cannula [26, 27].

## Conclusion

The physiological interaction of RBPs in terms of left ventricular/atrium volume–pressure and right ventricular/atrium volume–pressure with CO was investigated. The volume of the pump flow changed frequently in diastole, whereas it did not change in systole at varying blood pressures or pump speeds. This indicated that diastole would be more demanding for

a high preload sensitivity compared to systole. Therefore, RBPs reduced outflow with a further small reduction in preload and thus left ventricular pressure (LVP) to prevent the abnormal reduction of ESV and even ventricular collapse so as not to suck much blood from the ventricle.

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## Original Article

# Effect of invasive hemodynamic monitoring training program on nurses' knowledge and practice in cardiac centers in Sudan

Mudathir Mohamedahmed Eltayeb<sup>1\*</sup>, Suad Ahmed Mohamed Salahen<sup>2</sup>, Waled Amen Mohammed Ahmed<sup>3</sup>

1. Assistant Professor of Nursing,

2. Assistant Professor of Nursing & Head, Medical Nursing Department, Faculty of Nursing Sciences,  
University of Khartoum - Sudan.

3. Associate Professor of Nursing, Nursing Department, Faculty of Applied Medical Sciences,  
Albaha University - Saudi Arabia

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Corresponding Author : Mudathir Mohamedahmed Eltayeb

Assistant Professor of Nursing, Medical Nursing Department, Faculty of Nursing Sciences,

\*University of Khartoum - Sudan , Email: mudathireltayeb@gmail.com

Mobile phone: +249123115855

### Abstract

#### Background:

The critically ill patients often complain of complex medical or surgical conditions need a continuous assessment for their circulatory system using a well-established monitoring system in diagnoses and management. Thus invasive hemodynamic monitoring is quiet necessary and considered one of essential competences for the critical care nurses.

#### Aim:

This study aimed to assess the effect of invasive hemodynamic monitoring training program on nurses' knowledge and practice in governmental cardiac centers in Sudan during the period 2015 to 2018.

#### Methods:

quasi-experimental study, the training program was designed and applied in four selected Sudanese governmental cardiac centers through proportional random sampling method of the participants ( $n = 61$ ), an official permission was obtained from National Ribat University, Federal Ministry of Health, then the data was collected by validated questionnaire and checklist, then managed by SPSS v.20, only values less than 0.05 was considered significant, with a confidence interval of 95%.

#### Results:

Participants' overall knowledge before the interventional program was 54.3% increased to 92.0% after the interventional program, and 93.4% in the follow up phase. Participant's mean practice before applying of the program was 34.2% increased to 80.9% after the interventional program and 84.0% in the follow up phase. These results indicated significant improvement in nurses' competences before and early after interventional program by one month ( $P = 0.004$ ), before and late after 3 months in the follow up phase ( $P = 0.003$ ).

### الملخص

#### خلفية:

المرضى الذين يعانون من حالات طبية وجراحية حرجة يحتاجون إلى تقييم مستمر لنظام القلب والأوعية الدموية للتشخيص والعلاج، لذلك مراقبة الورقة الدموية من داخل الوعاء الدموي لمؤازلة المرضى أمر بالغ الأهمية وتعتبر واحدة من الكفاءات الرئيسية الازمة لممرضى الرعاية الحرجة.

#### الهدف:

دراسة أثر البرنامج التدريبي على مدى معرفة ومهارة ممرضى الحالات الحرجة فيما يتعلق بمراقبة قياسات الورقة الدموية من داخل الوعاء الدموي بوحدات الرعاية الحرجة بمراكيز القلب السودانية الحكومية للأعوام ٢٠١٥-٢٠١٨.

#### طريقة البحث:

دراسة تطبيقية، البرنامج التدريبي صمم ونفذ لأربع مراكز قلب سودانية حكومية، عن طريق جمع العينة العشوائية التناصي (العدد ٦١)، تمأخذ التصريح من جامعة الرباط الوطني، ووزارة الصحة الاتحادية، كما تمأخذ آذن شفاهي من المشاركين في الدراسة. تم جمع البيانات عن طريق الاستبيان وقائمة التحقق، حيث تمت معالجة البيانات باستخدام الحزمة الإحصائية للعلوم الاجتماعية الإصدار ٢٠ فقط القيم الأقل من ٥٠٠٥ اعتبرت ذات قيمة إحصائية.

#### النتائج:

أشارت النتائج أن نسبة المعرفة الشاملة للمشاركين قبل البرنامج التدريبي كانت ٥٤,٣٪ ارتفعت إلى ٩٢,٠٪ بعد تنفيذ البرنامج التدريبي، و ٩٣,٤٪ في فترة المتابعة. كما أشارت أن نسبة التطبيق العملي الصحيحة الشاملة قبل البرنامج التدريبي كانت ٣٤,٢٪، ارتفعت إلى ٨٠,٩٪ بعد التنفيذ و ٨٤,٠٪ في فترة المتابعة. كما أشارت هذه الدراسة إلى وجود تحسن ملحوظ في كفاءة الممرضين قبل وبعد البرنامج التدريبي، مقارنة بقبل وبعد البرنامج التدريبي بمدة واحد شهر ( $P = 0,004$ ), قبل البرنامج التدريبي وبعد بمنتهى ٣ أشهر خلال فترة المتابعة ( $P = 0,003$ ).

**Conclusion:**

Baseline level of critical care nurses' competences about invasive hemodynamic monitoring in the Sudanese cardiac centers was not satisfactory. There was a considerable improvement in nurses' competences when they received a structured educational program on invasive hemodynamic monitoring.

**Keywords:**

invasive hemodynamic monitoring, knowledge, practice, training, nurses

**الخلاصة :**

المستوى الأساسي لكفاءة ممرضى الحالات الحرجة لقياسات مراقبة الدورة الدموية من داخل الوعاء الدموي بمراكيز القلب السودانية الحكومية لم تكن مرضية، كما أوضحت وجود أثر وتحسن في كفاءة الممرضين عند تلقيهم لبرنامج تدريبي معتمد فيما يتعلق بقياسات مراقبة الدورة الدموية من داخل الوعاء الدموي.

**كلمات مفتاحية:**

مراقبة قياسات الدورة الدموية من داخل الوعاء الدموي، المعرفة، مهارة، برنامج التدريبي.

## Introduction

Hemodynamic monitoring is a practice on monitoring machines to measure cardiovascular parameters of patients. Monitoring definitely affects patient care positively, and the critical care nurses must be eligible to interpret all parameters on the clinical setting parameters from error and keep in mind the all pharmacological, biochemical, or physiological data for the changes observed on the clinical setting as well. Therefore the competent nurses have a tremendous impact on patient outcome as technology in the critical care setting has been used in both diagnostic and therapeutic decision making purposes<sup>[1, 2]</sup>.

Critical ill patients physiologically are unstable, so; they need for a well-secured vascular access for both therapeutic purposes to give fluids and essential medications, or diagnostic hemodynamic monitoring purposes. Furthermore; critically ill patients usually need rapid medical interventions pointed in supporting compromised vital organ, and standardizing their response to that therapy<sup>[3, 4]</sup>.

The access line is the therapeutic cornerstone in the critical care setting. All patients must have a well-secured access line, even without current use as receiving infusion therapy, also the need for that vascular access lines must be frequently weighed against the need, cost, and risk of potential complications<sup>[3, 5, 6]</sup>.

There are different intensity levels of inva-

sive hemodynamic monitoring focusing on the clinical needs; the simplest level includes monitoring heart rhythm, central venous pressure, and arterial blood pressure. Patient who has a low cardiac output after acute myocardial infarction needs more intense level of surveillance, so, it required to use pulmonary artery catheter "Swan Ganz", which provides hemodynamic information that includes intra-cardiac pressures, direct measurement of cardiac output, and if necessary it provides a direct measurement of pulmonary arterial oxygen saturation<sup>[7,10]</sup>. The study aimed to assess the effect of Invasive Hemodynamic Monitoring Training Program on nurses' knowledge and practice in cardiac centers in Sudan.

## Methods

*Design:* A quasi experimental study that was conducted as pretest and posttest one group design.

*Study population:* All nurses who work in the governmental cardiac centers' critical care units in the Sudan with at least one year experience and registered at the Sudanese National Medical and Health Professional Council were taken as target population of this study. Sampling and sample size calculation: Probability simple random sampling method was used. The study sample was composed of 61 nurses in four governmental cardiac centers in the Sudan. The sample size required to meet

this objective was calculated using the following formula (curtesy of the Department of Mathematics; College of Science, University of Khartoum):

$$N = \frac{(Z_1 - \alpha + Z_1 - \beta) 2}{\Delta^2} + \frac{(Z_1 - \alpha) 2}{2}$$

Distribution of critical care nurses working in the Sudanese governmental cardiac centers (2015 - 2018)

No	Cardiac center name	Frame	Proportionate sample	%
1	Sudan Heart Center	45 nurses	19	31.1
2	Ahmedgasim Specialized Hospital	24 nurses	10	16.4
3	Shaab Teaching Hospital	33 nurses	13	23.0
4	Madani Heart Center	45 nurses	19	29.5
	Total	147 nurses	61	100

### Instruments

1. Structured self administered questionnaire was designed by the researchers and utilized for data collection. The Cronbach's alpha was used to assess internal consistency and validity of the designed questionnaire. Based on sample of 10 nurses, the level of Cronbach's alpha was above acceptable level, which indicates the validity and reliability of questionnaire. First: to find out the general characteristics of the study sample, it contains basic data related to their general characteristics such as nurses' gender, level of education, years of experience, attendance of invasive hemodynamic monitoring courses, availability of written protocols in their unit, (reviewed by expert academics for reliability and modifications were made as well as 10 nurses excluded from the sample for validity test).

Second: to assess nurses' knowledge regarding variables of invasive hemodynamic monitoring that includes questions about knowledge related to phlebostatic axis; central line removal position, etc.

The questionnaire composed of 31 questions using a scoring system of the phrases (correct = 1, incorrect = 0), the interval score was used for evaluation of the scores for the level

of knowledge items which was evaluated by: poor (less than 50%), fair (50% - 75%), good (more than 75%).

2. Observational checklist was used by researchers. It was composed of main ten observed items, the scale for checklist was scored into (done = 1, not done = 0).

### Data analysis:

The collected data was arranged into a master sheet, coded separately and then entered into the software (SPSS) Statistical Package for Social Science version 20.

### Ethical consideration:

- Approval from The National Ribat University, Faculty of Graduate Studies and Scientific Research.
- Approval from the Federal Ministry of Health - Sudan (Scientific Researches Committee) toward the study areas.
- A written consent from the nurses under study.

### The training program procedure:

Nursing educational programs in healthcare institutions improve nurses' knowledge and practice that will improve their quality of care which result in better patient outcome; also it improves satisfaction for the nurses, physicians, clients, and their families (11).

*Contents of the program:*

The researchers prepared a training program to be delivered to the intervention group. The training program contents were:

- Lectures that included: (power point presentation, videos, and photos).
- Group discussion.
- Practical demos.
- Practical supervision.
- Posters and Handouts.

*Theoretical framework:*

Many theories in health education and health promotion seek answers to the fundamental question of why people behave the way they do. Furthermore; the improvement in health care, education, and lifestyle are amazing achievement in which intended to meet the demand of the future to produce the intelligent, independent people as reported by Combs 1972 cited in Candy 1991 [12]. The educational sessions of this study educational program were conducted in order to improve the nurses' knowledge and practice regarding invasive hemodynamic monitoring, by keeping the adult learning theory of Malcolm Knowles (Theory of Andragogy) in mind [13-15]. The TRA model (theory of reasoned action behavior) illustrates that human behaviors can be predicted from behavioral intentions, attitude, and influences by subjective social norms [16].

*Materials of the program:*

- Laptop presentations that included power point presentation, photos, videos, and wall posters for theoretical part.
- Half manikin with full invasive hemodynamic monitoring kit for practical part.

**Results:**

In the Sudan, most of critical care nurses who work in the governmental cardiac centers are working in four major cardiac centers; three of them are in the capital of the Sudan which is Khartoum state, and one center in the middle of the country which is Gezira state.

The demographic characteristics of participants was shown in Table 1, most of participants were females (67.2%), and less than 30 years old (77%), almost of them have bachelor qualification (90.2%) and their experience was less than 5 years (62.3%). Table 1 also showed that there was no written protocol in the units (82%) and most of nurses (93.4%) did not attend any formal training.

Table 2 and Figure 1 and Figure 4, showed the participants' global mean knowledge before the interventional program which was 54.3% increased to 92.0% after the interventional program, and 93.4% in the follow up phase. Participant' global mean of practice before applying of the program was 34.2% increased to 80.9% after the interventional program and 84.0% in the follow up phase. These results indicated significant improvement in nurses' competence before and early after interventional program by one month ( $P = 0.004$ ), before and late after 3 months in the follow up phase ( $P = 0.003$ ), Table 3 and Figure 2 and Figure 3.

Table (1):Characteristics of nurses working in the Sudanese cardiac centers critical care units (n=61).

Character	N	%
<b>Gender:</b>		
Males	20	32.8
Females	41	67.2
<b>Age in years:</b>		
< 30	47	77.0
≥ 30	14	23.0
<b>Nursing qualifications:</b>		
Diploma	0	0
Bachelor	55	90.2
Master	9.8	9.8
PhD	0	0
<b>Nursing experience:</b>		
Less than 5 years	38	62.3
More than 5 years	23	37.7
<b>Availability of formal written protocol in the unit</b>	:	
Yes	11	18.0
No	50	82.0
<b>Attendance of formal training program:</b>		
Yes	4	6.6
No	57	93.4

Table (2): Knowledge of the population regarding preparation, procedure, and complications of the invasive hemodynamic monitoring system in the Sudanese cardiac centers before and after attendance of the training program (n=61).

Item		Pre		Post (early)		CI 95%		P
		Mean	SD	Mean	SD	Lower	Upper	
<b>preparation of the system</b>	Preparation of the invasive system	1.0	0.76	2.0	1.18	0.14	0.85	0.007
	Allen test	2.0	0.10	2.0	0.0	0.87	1.43	0.006
	Preparation for CVC	2.0	0.14	2.0	0.0	-0.05	0.02	0.319
	Invasive homodynamic monitoring	2.0	0.11	2.0	0.4	-0.48	-0.01	0.040
	The best line for CVP connection	2.0	0.1	2.0	0.0	-0.81	-0.27	0.002
	The pressure in the pressure bag	2.0	0.2	2.0	0.1	-0.71	-0.21	0.006
	Standard zeroing intervals	1.0	0.4	2.0	0.8	-0.11	0.27	0.001
	Phlebostatic axis	1.0	0.1	2.0	1.0	0.93	1.46	0.002
	The dicrotic notch	2.0	0.1	2.0	1.2	0.73	1.34	0.004
	Sudden shooting in BP, nursing intervention	2.0	0.2	2.0	0.3	-0.55	-0.14	0.007
	Sudden dropping in BP, nursing intervention	2.0	0.3	2.0	0.0	-0.48	-0.15	0.002
	Total	2.0	0.22	2.0	0.45	0.53	0.56	0.036

<b>procedure</b>	Confirmation of the actual invasive readings	2.0	1.1	2.0	0.3	-0.31	0.14	0.004
	Repeated zeroing of the invasive system	2.0	0.1	2.0	0.5	0.49	0.06	0.005
	The level of the transducer affects the reading	2.0	0.3	2.0	0.4	0.16	0.06	0.008
	Insurance of the function of the pressure bag with flushing solution	2.0	0.6	2.0	0.7	-0.11	0.08	0.005
	CVP is indicated to measure the preload	1.0	0.1	2.0	0.0	0.07	0.29	0.001
	Do you think that the arterial waveform on the monitor is important	2.0	0.1	2.0	0.0	-0.02	0.05	0.319
	Do you think that the CVP waveform on the monitor is important	2.0	0.2	2.0	0.0	-0.01	0.08	0.156
	Total	2.0	0.3	2.0	0.2	0.16	0.10	0.071
<b>Complications</b>	The best position for CVC removal	2.0	0.7	2.0	0.2	-0.82	-0.36	0.003
	The commonest site for CVC related infection	2.0	1.0	2.0	0.8	0.29	0.83	0.008
	Pneumothorax related to CVC insertion	2.0	0.4	2.0	0.5	-0.38	0.12	0.002
	Standard dressing intervals of the CVC	2.0	0.7	2.0	0.3	-0.29	0.09	0.003
	Your duty as a nurse to know the age of the CVC	2.0	0.2	2.0	0.0	-0.01	0.10	0.080
	Total	2.0	0.6	2.0	0.3	0.35	0.30	0.010

Table (3): Study population according to their practice in the Sudanese cardiac centers before and after application of the training program (n=61).

Item	Pre		Post (early)		C/I 95%		P
	Mean	SD	Mean	SD	Lower	Upper	
Checked the pressure bag and the flushing solution	1.0	0.9	2.0	0.0	0.55	0.79	0.004
Leveled the transducer to the phlebostatic axis	1.0	0.8	2.0	0.0	0.16	0.39	0.004
Made zeroing of the invasive system in the beginning of the shift	1.0	0.2	2.0	0.2	0.60	0.84	0.002
Changed the stopper after every use	1.0	0.3	2.0	0.3	0.33	0.62	0.003
Kept the access line always dressed	1.0	0.6	2.0	0.0	0.15	0.37	0.009
Used hand hygiene methods during handling	1.0	0.7	2.0	0.0	0.11	0.32	0.009
Used alcohol swap for the 3 way stopcock pole	1.0	0.5	2.0	0.5	0.52	0.79	0.002
Kept the 3-way stopcock always covered	1.0	0.7	2.0	0.0	0.36	0.62	0.006
Performed the fast flush squire test	1.0	0.8	2.0	0.0	0.95	1.02	0.002
Removed the access line properly	1.0	0.5	2.0	0.5	0.16	0.39	0.004
Total	1.0	0.6	2.0	0.15	0.38	0.57	0.004

Figure (1): Participants' knowledge percentage regarding invasive hemodynamic monitoring in the Sudanese cardiac centers before application of the training program by hospitals (n = 61).

(I):

( = ١١).

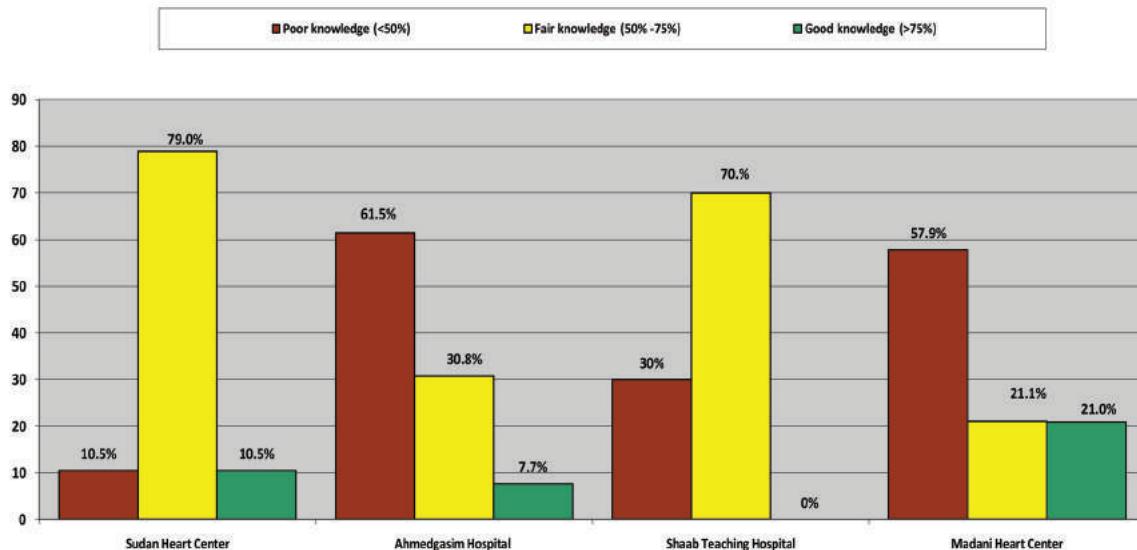


Figure (2): Distribution of participants' total practice percentage regarding invasive hemodynamic monitoring in the Sudanese cardiac centers before application of the training program (n = 61).

(f):

( = ١١).

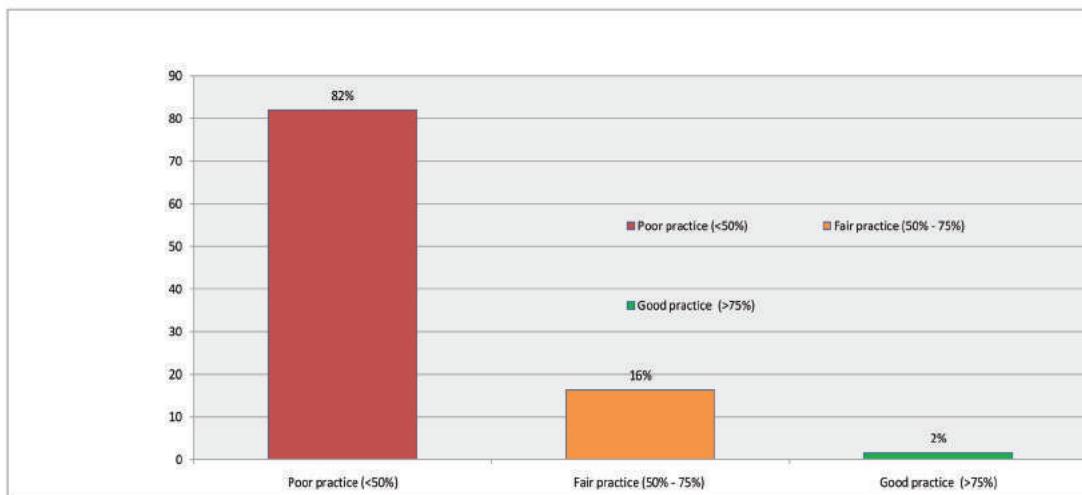


Figure (3): Participants' practice percentage regarding invasive hemodynamic monitoring in the Sudanese cardiac centers before application of the training program by hospital (n = 61).

(P):

( $n = 11$ ).

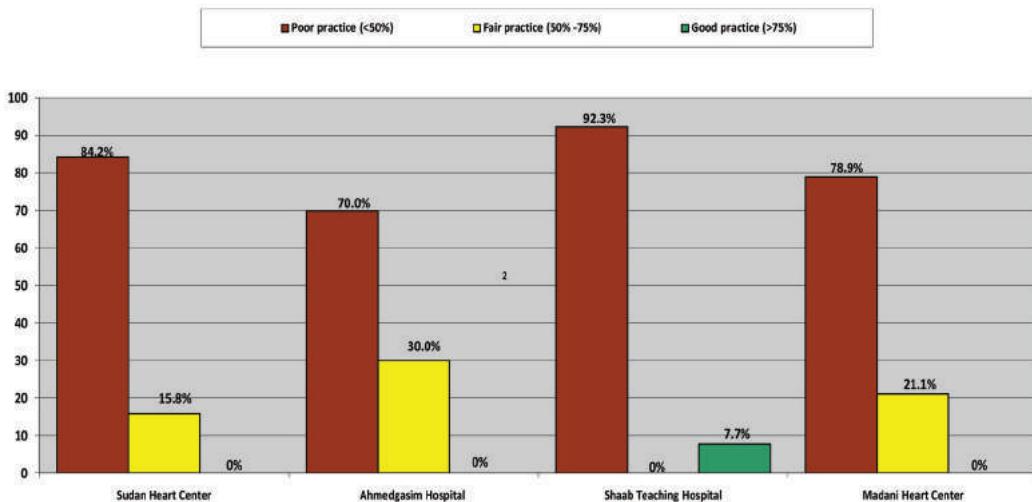
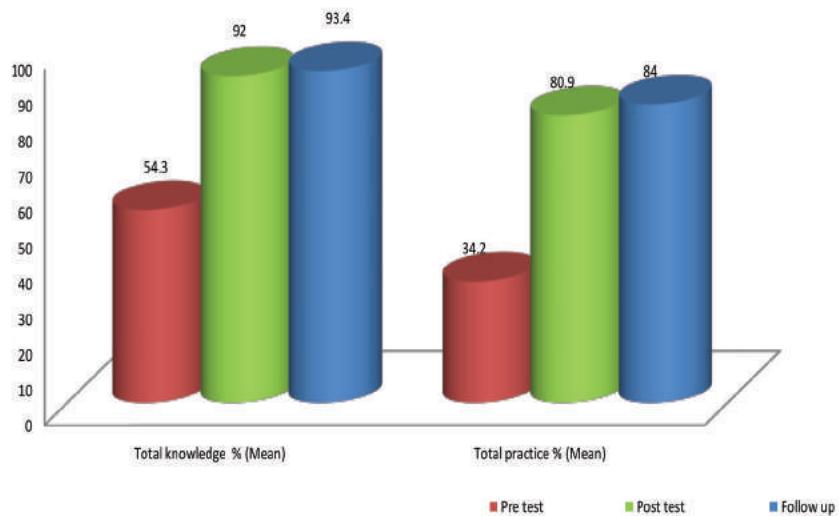


Figure (4): Participants' mean total knowledge and practice before and after the interventional training program (n = 61).

(E):

( $n = 11$ ).



## **Discussion:**

Education is crucial element for critical care nurses, particularly in countries where there is lack of formal and well organized programs, despite the limited resources in undeveloped countries such as the Sudan, still have to deal with complex issues related to enforcement of standard programs<sup>[11, 17]</sup>. The present study included 61 nurses, most of them were female nurses (67.2%), and the most were less than 30 years old (77.0%), furthermore; majority (90.2%) had a bachelor degree in nursing besides (62.3%) had clinical nursing experience less than 5 years. These results are similar to a study made in Oman in 2015 to study improving of nurses' knowledge to reduce catheter related bloodstream infection<sup>[18]</sup>.

Regarding the training program, this study educational program was based on the educational theory of Andragogy by Malcolm Knowles (13). It found that majority of nurses (93.4%) did not get any training program before related to this study, or has a written protocol in their critical care unit (82.0%) related to invasive hemodynamic monitoring. These findings were similar as studies found that training programs were required to target the specific needs of nursing staff working at different care settings<sup>[19, 21]</sup>. On the same line a study done in England in 2017 stated that quality should begin with education and end with education<sup>[34]</sup>. For these reasons enhancing nurses' performance as a result of applying an educational program was noticed and supported by lots of researches, these findings also congruent with researchers found that nurses' knowledge is enhanced by professional training and well education<sup>[22, 27]</sup>.

Regarding level of education, this study has found that; there were no statistical significant difference between nurses' total knowledge and practice and their level of education where the p values were more than 0.05, these results may be due to most of the studied nurses were in the same age group, and majority were also

in the same educational level. These results are contradicted with studies found a significant relation between nurses' knowledge, and practice, and participants' level of education<sup>[24, 26]</sup>.

Regarding the age of participants, these results clarified that there were no statistical significant difference between nurses' practice and their age groups. These findings are resembled with a research done in Arizona in 2011, concluded that there were no significant statistical differences between practice score and nurses' age, and between nurses' practice and nurses' age<sup>[26]</sup>.

Regarding years of experience the results of the current study showed that most of studied nurses had years of clinical nursing experience less than 5 years (77.0%); these findings were contradicted with a study done in Egypt in 2011, it revealed a positive statistically correlation between years of experience and practice<sup>[25]</sup>. Lastly these results agreed with a study done in Egypt in 2012 reported that there were no statistically significance relation was found between nurses' practice and their age, and years of experience<sup>[24]</sup>.

Participants' baseline mean practice regarding invasive hemodynamic monitoring before application of the interventional program was 38.4% which was reflected as poor results, these results are similar to a descriptive study done in Sudan in 2014 to study critical care nurses knowledge and practice about invasive hemodynamic monitoring that found nurses' knowledge was fair and nurses' practice was poor<sup>[28]</sup>. There was a noticeable improvement on overall nurses' practice after their receipt of the structured interventional program.

Statistically, this study found that; nurses' practice has improved from 34.2% to 80.9% after the interventional program which was considered as good results, mean p value was 0.0045. These results are similar to a study done in Oman in 2015 to study improving of nurses' knowledge to reduce catheter related

bloodstream infection<sup>[18]</sup>. There were no statistical significant changes in nurses' practice in this study in post interventional period and follow up phase, where the mean p value of nurses' practice mean p value was 0.368. These results are similar to a study take place in Egypt in 2014 to investigate the effect of structured educational program on nurses' practice<sup>[23]</sup>. The present study is unique in several ways, first; the type of study; that included nurses practice in very critical area, second; the area of the study that was critical care units in un developed country, third; this study identified key determinants of nurses' practices; rather than simply documenting what nurses do and what demographic factors relate to these knowledge and practices<sup>[29, 31]</sup>.

The findings of this study have implications for problem solving interventions to increase nurses' competences on invasive hemodynamic monitoring that will enhance the quality of nursing care, patient safety and outcome, also it has a relevance for the educational programs in healthcare institutions that will improve nurses' practice thus will lead to save lives, result in better patient outcomes, reduces blood stream infection rates, improve satisfaction for nurses, physicians, clients and their families, and is cost efficient to implement. Furthermore this study has implications for social change in practice that will consider as an opportunity to create a quality improvement project for the critically ill patients<sup>[9]</sup>.

The present study has provided evidence and database for conducting studies in invasive hemodynamic monitoring in critical care units in the Sudan. Advantages are that it is a multicentre carried out in four main governmental specialized cardiac centres in the Sudan; also it has been carried out in an undeveloped country that does not have previous or similar interventional studies to compare with to fill the gap. Limitations of this study include lack of generalization, and the small sample size.

### **Conclusions:**

The baseline level of critical care nurses' knowledge and practice regarding invasive hemodynamic monitoring in the Sudanese cardiac centers' was not satisfactory. There was a considerable improvement in nurses' level of knowledge and practice after the receipt of a structured educational program on invasive hemodynamic monitoring.

### **Competing on interest:**

We declare that this study is one of our own works. We also declare that we have no competing interests related to this study.

### **Financial support of the study:**

The researchers did not receive any financial support from any authority, and the entire expenses towards implementation of this study were provided by the researchers only.

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#### Annexes:

##### 1- Questionnaire:

#### SECTION (A)

Basic information about nurses under study

Please make a tick around the appropriate answer (ONLY ONE):-

1. Your hospital is:

1. Sudan Heart center
2. Shaab Teaching Hospital
3. Ahmedgasim Hospital
4. Madani Heart Center

2. Your gender is:

1. Male
2. Female

3. Your age is:

1. Below 29 years
2. 29 to 35 years
3. More than 35 years

4. Your scientific qualification in nursing is:

1. Diploma
2. Bachelor
3. Master
4. Doctorate

5. Your clinical experience in nursing is:
1. Less than one year
  2. 1 to 5 years
  3. More than 5 years
6. Do you have a written protocol about invasive hemodynamic monitoring in your critical care unit?
1. Yes
  2. No
7. If you have a written protocol, is it always applied in practice?
1. Yes
  2. No
8. Have you ever attended any training program about invasive hemodynamic monitoring?
1. Yes
  2. No
4. Invasive hemodynamic monitoring is done for:
1. Heart rate & respiratory rate
  2. Noninvasive Blood Pressure
  3. ECG rhythm strip
  4. CVP, ABP, & PAP
5. When you have a triple central line (three lumens) and you need to measure the central venous pressure, best line of connection:
1. The proximal line
  2. The median line
  3. The distal line
  4. I don't know
6. The pressure in the pressure bag should always be:
1. 100mm/Hg
  2. 200mm/Hg
  3. 300mm/Hg
  4. I don't know

1. Preparation of the invasive hemodynamic monitoring needs:

1. Monitor and Transducer
2. Monitor and ECG cable
3. Monitor and peripheral cannula
4. None of the above

2. Allen test is done to:

1. Test central line patency
2. Test arterial collateral perfusion
3. Test the pressure bag pressure
4. Test the actual blood pressure.

3. To prepare for central line insertion you need:
  1. Dressing set
  2. Alcohol swap
  3. Central venous catheter
  4. All of the above

7. Zeroing of the system should be:

1. Every hour

2. Every shift

3. Not important

4. I don't know

8. The phlebostatic axis is:
1. Point marker on the neck
  2. point of leveling transducer
  3. Point of arterial line puncture
  4. I don't know it
9. The dicrotic notch is seen in:
1. Central venous pressure waveform
  2. Arterial waveform
  3. Electrocardiogram waveform
  4. I don't know it
10. Your patient on invasive monitor, he suddenly developed shooting in systemic blood pressure (e.g. 240/180) the first nursing action you should do is to:
1. Notify the physician
  2. Start glycerin infusion
  3. Check the invasive system first
  4. Do nothing
11. Your patient on invasive monitor , he suddenly developed dropping in systemic blood pressure ( 60/40) the first nursing interventions you will do is:
1. Notify the physician
  2. Start Noradrenaline infusion
  3. Check the invasive system first
  4. Doing nothing
12. Confirmation of the actual monitor readings is best done by the:
1. Resident physician
  - 2 . C a r d i o l o g i s t
  3. Nurse in charge
  4. Anesthesiologist
13. Repeated zeroing is not necessary in the recognition of the accurate reading:
1. Yes
  2. No
14. The level of the transducer affects the actual reading:
1. Yes
  2. No
15. To ensure pressure bag with flushing solution is well functioning you test it by:
1. Make zeroing
  2. pressing the flushing devise
  3. Notify the physician
  4. I don't know
16. CVP is indicated to measure the preload:
1. Yes
  2. No
  3. I don't know.
17. The best position for removing of the central line is:
1. Sitting position
  2. Supine position
  3. Trendelenburg position
  4. I don't know
18. The commonest site for central venous catheter related infection is:
1. External jugular
  2. Internal jugular
  3. Femoral
  4. I don't know
19. Do you know the central line catheter related infection bundle?
1. Yes
  2. No
20. Pneumothorax related to central line insertion is more common in the:
1. External jugular site
  2. Internal jugular site
  3. Subclavian site
  4. I don't know

- 21.Standard dressing of the central line intervals should be:
1. Every shift
  2. Every day
  3. Every 2 days.
  4. I don't know
- 22.Is it your duty to know the age of the central venous line of your patient?
- 1.Yes
  2. No
  3. I don't know
- 23.Do you think that the arterial waveform on the monitor is important?
- 1.Yes
- 24.Do you think that CVP waveform on the monitor is also important?
- 1.Yes
  2. No
  - 2-
  - 3-

**Annexes:**

**2. observational check list:**

Observation	Done	Not Done
Checked the pressure bag and the flushing solution		
Leveled of the transducer to phlebostatic axis		
Made zeroing of the system in the beginning of the shift		
Changed the stopper after every use		
Kept the access line always dressed		
Used hand hygiene methods during handling		
Used alcohol swab for the three way stopcock		
Kept the three way stopcock always covered		
Performed the fast flush squire test		
Removed the access line properly		

## Review article

# Computed Tomography Dose Reduction in Children: Review Paper

Nouf Hussain Abuhadi<sup>1</sup>

1. Diagnostic Radiology Department, College of Applied Medical Sciences, Jazan University, Jazan, KSA  
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Corresponding Author:

Nouf Hussain Abuhadi. Diagnostic Radiology Department, College of Applied Medical Sciences, Jazan University, Jazan, KSA. P.O. Box 114, 45142. Email: nabuhadi@jazanu.edu.sa  
n\_pasint@hotmail.com. Mobile: 00966558271718

### Abstract

#### Background:

Increasing the needs of Computed Tomography (CT) for children is quietly augmented over the last decades, although it's one of the most important modalities in diagnostic finalization. However, it carries a higher risk for the patient in term of radiation dose and cancer risk due to higher sensitivity to radiation than the adult.

#### Aim:

This study was conducted to review the multiple methods of dose reduction technique as presented by different authors where the different scanning protocols, machine and types of the studies were presented

#### Methods:

Here, more studies and books were selected, where they are carefully summarized and outlined into different categories for which the result stated that; the most frequent examination done in the CT department is head, neck, and sinuses in which where taken as an example of dose reduction methods.

#### Results:

The use of the most modern technical advances was recommended in order to optimize the dose level, comfortable, constants (anesthesia if required) position and using low number of phases as possible according to the pathology of interest (low phases with better visualizations), scanning with thin collimation and view thicker as possible, increasing pitch, automatic exposure control, only the area of interest should be examined, with low tube voltage and using of tube current modulation system can give better result of dose reduction and there were multiple methods presented here.

#### Conclusion:

Where is most important for radiologist, technicians, and the person who conduct such studies to increase their knowledge in radiation protection, technical advances and how to interpret the different CT protocols.

#### Keywords:

Radiation, Children, Dose Reduction, computed tomography.

### الملخص

#### خلفية:

ازدادت الحاجة الى التصوير المقطعي (CT) للأطفال بشكل ملحوظ خلال العقود الماضية؛ وعلى الرغم من أنها واحدة من أهم الطرق لوضع المسارات الأخيرة على التشخيص، لكنها تحمل الكثير من المخاطر على المريض من حيث جرعة الإشعاع ومخاطر السرطان بسبب الحساسية العالية للإشعاع مقارنة بالبالغين.

#### هدف الدراسة:

تهدف الدراسة الحالية لمراجعة الطرق المتعددة لتقنية تخفيف الجرعة كما قدمها كثير من الباحثين والمؤلفين، حيث تم استعراض بروتوكولات المسح المختلفة، وألة المسح المستخدمة، ونوع الدراسات التي تم تطبيقها.

#### طريقة البحث:

طرقتنا في المنهجية الى الكثير من الدراسات والكتب، حيث تم تلخيصها وترتيبها بعناية في فئات مختلفة كما هو موضح في النتائج. والفحص الأكثر شيوعاً الذي تم اجراؤه في قسم التصوير المقطعي المحسوب شمل الرأس والرقبة والجيوب الأنفية، حيث تمأخذ مثال على طرق تخفيف الجرعة.

#### النتائج:

توصي الدراسة باستخدام أحدث التطورات التقنية من أجل تحسين وضع الجرعة، وتوفير الراحة، والثبات (التخدير إذا لزم الأمر)، واستخدام عدد قليل من المراحل قدر الإمكان وفقاً لمتطلبات علم الأمراض الذي يهم بعدد المراحل القليل مع تصورات أفضل، والتصوير المتوازي الريفي، ورؤية أكثر سماكاً بقدر الإمكان، وزيادة درجة الاهتزاز، والتحكم التلقائي في التعرض الإشعاعي، ويجب فحص مجال الاهتمام فقط، مع الجهد المنخفض للأنبوب واستخدام نظام تعديل جهد تيار الأنبوب، والذي يمكن أن يعطي نتيجة أفضل لتخفيف الجرعة، حيث عرضنا أكثر من طريقة ضمن هذه الورقة البحثية.

#### الخلاصة :

من المهم بالنسبة لأخصائيين الأشعة والفنين والشخص الذي يجري مثل هذه الدراسات السعي لزيادة معرفتهم في الحماية من الإشعاع والتقديم التقني وكيفية تفسير البروتوكولات المختلفة.

**Introduction:**

A variety of doses has been reported for computed tomography investigations of the same area. Such variations caused by using different scan procedures as well as different dose units. Increasing the values of CT in diagnosis of a majority of body disease in case of CT brain, chest abdomen and neck in addition to the bony structure of the body in both cold and urgent cases, leads to increasing the use of CT over other routine x-ray and MRI examination. Therefore, with increasing the number of scans needs for such case where contrast scan additional to the routine axial scan could resulting for more radiation exposure dose due to multi and high doses scans. Thus, dose reduction technique allows for acceptable image quality and lower radiation doses<sup>[1]</sup>.

Many researches of minimizing radiation exposure during CT scans concluded the possibilities of using decreased dose in imaging of high contrast as in case of lung scans with same image performances and no any loss of information effecting the diagnosis<sup>[2]</sup>. Still not yet clear if low dose protocols could be used in areas of low contrast CT studies as in cases of intracranial brain constructions. In similar cases of child brain abnormalities, a reduction of ‘standard’ image considerations due to lower dose protocols could be occurred and possible in such CT investigations<sup>[3]</sup>.

**Image technicalities.**

Its main aim must be to gain a high-quality image performance rather than only optimizing a protocol with a decreased radiation exposure to the child. In addition to implementation of ALARA principle with good image quality. Inappropriately, up to now no stablished intensities of CT noise descriptions have been believed adequate for investigative dedications, particularly in children.

*Minimum stages and collimation:*

avoidance of multistage and dependence of pre-contrast imaging is important; If further characterization of a lesion by multiple pre- and post-CM phases is indicated, these scans should be kept to a minimum, and a low dose technique often will suffice<sup>[4, 5]</sup>. Furthermore, other imaging modalities such as US or MRI should be used if possible. On other hand; Small children need thin collimation, but this will increase the image noise and as small children usually lack visceral fatty tissue, less noise can be tolerated than in adolescents and adults. Therefore, the choice of collimation depends on the clinical question and size of the patient and should balance the necessary z-axis resolution, gain in three-dimensional (3-D) reformatting possibilities, noise level and low radiation dose level. The higher noise level usually can be solved by using the “scan thin view thick” approach while interpreting the images. Also using small FOV as possible that gives higher spatial resolution, as the pixel size decreases with smaller FOV.

*Pitch:*

An increase in the playing field outcomes in a shorter scan time and (in some scanner types) in a dose reduction for the patient. But this is not the best option in MDCT; this is explained by the negative dose effects of the so-called over-ranging which will be exaggerated by increasing the pitch. Furthermore, the spatial resolution will decrease by increasing the pitch. In those scanner types in which effective mAs is used, an increase in pitch will result in an increase in the tube current. Therefore, it is usually more dose efficient to keep the pitch as low as possible (<1) and if needed manually decrease the tube current, in order to achieve a similar tube current/pitch ratio (effective mAs) as would be the case with a higher pitch.

*Tube Power (voltage - kVp):*

According to the reduced size of children, lower voltage with maintaining the image quality is required. In most children a tube voltage of 80–100 kVp will suffice, especially in children with a body weight <45 kg. Adolescents, a tube voltage of 100 kVp for the thorax and 120 kVp for the abdomen is usually sufficient. However, the scanner-related parameters, such as, scanner geometry, tube filtration, detector design and efficiency, sometimes negatively influence the image quality with lower tube voltages, for instance by inducing artifacts. Recent studies with phantoms suggest that the optimal tube voltage in children may be even lower (approximately 60 kVp), at least for some indications.

*Current of the Tube (mA):*

decreasing the tube current will directly decrease the dose. But increasing the noise is a major drawback, but so the adapted selection of noise is acceptable<sup>[6]</sup>. Although several studies in phantoms have shown that the mA can be halved for each 3.5- to 4-cm reduction in body diameter (half value layer, HVL), in clinical practice a less stringent HVL of 4–6 cm is used in children. This is because small children usually lack large amounts of visceral fatty tissue and, therefore, less image noise is desirable. Based on the aforementioned, several body size or weight-based pediatric CT protocols have been suggested<sup>[7, 8, 5, 9]</sup>.

*Tube spinning:*

Majority of recent MDCT scanner models with a tube rotation times of 0.3 -to- 0.5 seconds giving a shorter investigation time. This is beneficial to children by reduction in movement and respiration artifacts. Nevertheless, minding that a shorter spins period can produce a reduced number of profiles that will

be used in image rebuilding, concerning the increase of the noise image. Then a spinning time of 0.5 seconds is the option of choice for image quality. Concerning the procedures of radioactive dose modulation, approximately all recent MDCT scanners are now fitted out with some type of programmed exposure control (AEC) or Automatic Tube Current Modulation (ATCM) system. Such a systems are acting as a dynamic tube current controller during the process of scanning then adjustable and modified to the body building constructed geometry. By this way, an improved image performances and quality can be gained because of the decreasing of constant noise level and radiation exposure. Variation in models is conceivable for axial horizontal plane (XY-modulation as well as angular), or joined systems<sup>[10]</sup>.

The procedure and settings of various models are different<sup>[10,11]</sup>. Some medical systems recommended using the old good quality images as quality control for new investigations. By using ATCM methods, a drop of radiation exposure received by individual patient is commonly achievable<sup>[12,13]</sup>. Depending on operators the dose will optimized. For example, if ATCM is used in the upper body the tube current will rise in the shoulder and liver area to keep a constant noise level.

**Exposure Lessening in Head and PNS CT of Kids:**

A report by Brenner et al., (2001) estimated the mortality risk for cancers as (0.18% and 0.07%) for pediatric CT abdominal and head CT respectively, which is 10-fold huger than for adult individuals (14). Their findings strongly recommended dropping the CT dosage exposure for children to the lower possible level, and not applying the same CT protocols of adults for the youngsters' population, as was a common trend at that time<sup>[15]</sup> While the CT image excellence and quality mainly dis-

tinguished X-ray fluency dependent; accordingly, pediatrics CT method factors should be reduced compared to those of adults, due to the fewer X-ray attenuation by smaller bodies of children. Consequently, similar scan performances and quality must be provided even with lower dose methodology. Furthermore, CT energy values for pediatrics are always less than for grown person<sup>[16]</sup>. Cranial CT is the investigations of high frequency in children. Around 30% of neonate's bone marrow is located in the skull, while only about 10% in adults. The marrow-absorbed high radiation exposure even more than the chest or abdomen<sup>[17]</sup>. Chan, et al., (1999) demonstrated the possibility of using lower tube current for a pediatric brain CT scan with the same image performances and quality<sup>[18]</sup>. No change in image performances recorded for seven anatomical regions with low dose image procedure. Maximum antero-posterior diameter (MAPD) was used by Wong, et al., (2001) as a respectable principle for tube current assortment to measure child head diameters<sup>[19]</sup>. Boone et al., (2003) recommended using CT system charts which depends on the body size and circumference of the child with reduced dose scanning protocols<sup>[20]</sup>. All measured statistics were taken via phantom chambers with different thicknesses. An exponential relation among X-ray diminution versus patient diameters leads to a significant dose drop in the smallest body sizes as kids<sup>[20]</sup>. Diagnostic reference levels (DRL) could be useful for modification of dose to age agreement. Such alike surveys in Europe are now in hand<sup>[21] [22]; [23]</sup>. In case of CT brain of pediatric, extra dose exposure lessening practice could be held for some signs and indications as hydrocephalus assessment<sup>[12]</sup>: a standard dose procedure is used for 'higher dose' suggestions: trauma, encephalopathy, seizure, congenital anomalies and acute neurologic deficit. Low dose CT is highly recommended even for 10-15 yrs old patient.

### **Dose adaptation & Lessening of CT Skull and Neck Area:**

In a CT study of skull phantom done by (24) with 120 kV tube voltages, six set of investigations were done with 50 percent of mAs reduction every time. Similar research also handled with 28-fold dose reduction for coronal scan, and other of 60 volunteers in a same way subdivided to six groups each of them undergone coronal CT as for the phantom. 30 patients were scanned with lower mAs; same procedure was followed also for the phantom. The gained CT scan results were of high-quality image performances in diagnostic point of view for the lowest dose procedures. Some latest researches agreed with the finding of the earlier ones concerning the excellent and diagnostic clearness results of the low dose CT protocols<sup>[25], [26]; [27]; [28]</sup>. Conversely a modern CT system can provide an outstanding diagnosable image quality with low dose levels<sup>[27], [21]</sup>. Also mentioned, the effect of high contrast in sinus CT could allow the use of low dose protocol easily. The only challenging point is the comparison between various CT scanners because they are not suppling extra dose descriptors as CTDI or effective dose. Then, straightly comparing mAs values alone, cross-wise studies with different scanners, has restrictions<sup>[29]</sup>. Also Tack et al., (2003) calculated the effective dose of these earlier described low-dose CT studies of the sinuses<sup>[1]</sup>. At eight different sinus nasal anatomical locations in mucosal deformities study, weighty divergence comments reported by three different reviewers, while the image result outcome by different dose levels showed no significant variances. This could be explained, observational dissimilarities concomitant with the reduction in dose levels, although they concluded and decided that low dose MDCT should be deliberated as routine procedure for the evaluation and assessment of chronic sinusitis. the Pediatrics Academy of USA on (2001)

recommends replacing the routine use of sinusitis imaging in case of not improved patients or/and deteriorates during treatment in addition to the event of recurrent illness (due to lack of sensitivity). CT use is almost limited to children who have very tenacious or recurrent sinus infections, not reactive to medical managing and whereby surgical procedure is considered, and for those of acute sinusitis. CT exams provide a much well detailed scan of the anatomy of sinus, which will be useful guide of surgical treatment. Aforementioned studies already presented the imprecision of radiographic diagnosis of children sinusitis in comparison to CT exams. More than 70% of the results were not in agreement with each other in around 40% of normal radiographs patients, there were signs of pathology showed on CT scans and vice versa.

While in 35% of suspicious abnormality in radiographs the CT results were normal. [30]. Another weakness of sinus radiograph is the huge variability in the interpretation and clarification between radiologists [31]. The use of sedation was often essential in youngsters to accomplish a good quality CT exam.

Many other organs could be visualized at the same time of CT sinuses as middle ear, mastoids and adenoids. Using and performing this technique of CT the whole ear, nose and throat section could be displayed in one inspection, which is impossible in radiographic exam. A weakness in sinusitis imaging is the high prevalence of soft tissue variations. [32]; [33]. Recently the Use of the tube current modulation systems in CT has been publicized for dose reduction purposes. Will significantly reduce the dose by 20-60% [34].

Cone Beam CT in the Head and Neck area: This is a new modality which is provide a dose reduction procedure and 3 dimensional images for bones of head and neck areas, also found to be very useful for follow up of cochlear implantations [35]. Other studies were used for evaluation of lung parenchyma, and

lung cancer surveying programs using a significantly reduced dose protocols<sup>[36]</sup>.

### Interpretations of the literature:

Contemporary research indicates that (CT) procedures are a major cause of radiation exposure for patients when conducted repeatedly in the course of healthcare treatments and therapies, especially for those with chronic health conditions<sup>[37]</sup>. Demonstrative organ absorbed doses in CT are significantly lower than threshold doses for the instruction of deterministic effects. However, extended exposure following the advent of helical, fluoroscopic and multi-slice techniques exposes patients to the same levels of radiation repeatedly within different procedures, thereby significantly increasing their overall levels of radiation exposure, [38]. Furthermore, the use of CT scanning has also increased through new applications including cardiac CT, CT colonography, angiography and urology<sup>[39]</sup>. The increased frequency in the use of CT investigations from 4% to 15% of procedures along with the rise in the diagnostic radiation dose received by patients from 40% to 75 has led to a statistically important increase in malignance occurrence related to scanning<sup>[14], [39], [40], [37]</sup>.

According to Dougeni et al., (2012) most physicians underestimate the exposure risk for patients, as evidenced by the increased use of CT scans on children and the limited implementation of exposure parameters considering the clinical question under investigation and the patients' size<sup>[39]</sup>. Hence, dose reduction in pediatric CT scanning demands significant attention to prevent high-risk radiation exposure among children<sup>[40]</sup>. Alarmingly, only 43% of image departments acknowledge having adjusted CT parameters for children<sup>[41]</sup>. Furthermore, the reasons for conducting pediatric CT scans sometimes fail to confirm their necessity. According to Donnelly (2005), unnecessary pediatric CT scans are a public health

problem in America<sup>[41]</sup>.

In their study, Hollingsworth et al., (2003) discovered that 11–26% of CT examinations of children younger than nine years of age were done using more than 150mA, while 20–25% of radiologists did not adequately understand the specific parameters for the helical CT scans of the body they oversaw<sup>[42]</sup>. Ironically, pediatricians have limited power to effectively manage the levels of radiation exposure their patients receive when undergoing CT scans since it remains the role of the radiologists conducting the scan<sup>[43]</sup>. Consequently, pediatricians mainly focus on educating the patient's family on the potential dangers of CT scanning and limit recommending its use until an absolute necessity<sup>[43]</sup>.

Bischoff et al., (2009) argue that radiation doses of 6.4–27.8mSv are adequate for spiral CT angiography image acquisition<sup>[44]</sup>. However, the international Prospective Multicenter Study on Radiation Dose estimates of Cardiac CT Angiography I maintains the optimal median dose-length-product as 885mGy. cm, with an effective radiation dose of 12mSv. The technical considerations in radiation dose management generally focus on optimizing the trade-offs between noise, artefacts, scanning speed and contrast<sup>[45]</sup>. There are several factors worth considering when determining dose reduction measures during CT scans in paediatric care. According to Yu et al., (2011), the process depends on the size of the patient and the diagnostic task being conducted. The main limitations are the scanner speed and the power limits of the CT scanner<sup>[45]</sup>. In their study, critically evaluated the use of automatic exposure control and optimal tube potential in improving image quality and reducing the radiation dose in pediatric CT examinations. They argue that low tube potential improves contrast enhancement and reduces radiation exposure for children, even though their use increases noise output during the process<sup>[5]</sup>, [45]. One effective strategy for reducing the ra-

diation dose in pediatric CT scanning involves hybrid interactive reconstruction. Singh et al., (2009) compared the effectiveness of hybrid interactive reconstruction and the conventional filtered back projection and determined that hybrid interactive reconstruction such as hybrid adaptive statistical iterative reconstruction (ASIR) reduced the radiation dose significantly without adversely affect the quality of the images or diagnostic confidence when analyzed.

Similarly, Lee et al., (2012) compared radiation dose reduction among pediatric patients undergoing chest CT scans when using ASIR and filtered back projection. They found that the CT dose index decreased by 60.3% from 18.73 to 7.43 mGy, the dose-length product decreased by 56.2% from 307.42 to 134.51mGy x cm and the effective dose decreased by 55.2% from 4.12 to 1.84 mSv compared to the filtered back projection results<sup>[46]</sup>.

Contrastingly, Lee et al., (2012) analyzed the effectiveness of a kilo-voltage (Kvp)-lowering strategy in mitigating dose reduction on chest CT scans for children, where Kvp was reduced from 120 to 80 for children below 15 kg and reduced to 100 for children 15–60 kg at a reduced mA rating of 65–55 mA. The CT dose index, dose-length product and effective dose reduced by 73%, 75% and 73%, respectively, for children below 15 kg. The measures declined by 45%, 44% and 48%, respectively, for children 15–60 kg<sup>[46]</sup>.

Another innovative strategy for radiation dose reduction in pediatric CT scanning is model-based iterative reconstruction (MBIR). According to GE Healthcare (2012), MBIR is superior to both filtered back projection and ASIR due to its capacity to develop multiple iterations using multiple models. Unlike filtered back projection, MBIR analyses the x-ray beam in three different ways: at its focal spot, as it passes through the body and at the level of the x-ray detector. It uses these three points to create three-dimensional representa-

tions of the areas scanned using multiple iterations. The MBIR algorithm models two parts of the CT system: the system statistics, including noise and system geometry or optics. Moreover, CT scanning using MBIR can take from 5–40 minutes, depending on the amount of data required and the complexity behind reconstructing an image from the data beam analysis [48]. Hence, the image quality is superior to both ASIR and filtered back projection.

### Conclusions:

There was greater challenge meeting us in CT for the babies where the adjustment of protocols to implement the better imaging sequence with low dose to the patient, where it need much knowledge and carful parameter selection in addition to the use of advance technical improvement as mentions can lead to the safe scan with better quality of imaging and diagnosis.

### Key points:

- CT is one of sensitive tools for diagnosing many of child's disease, more frequently than other method medical imaging (e.g. Brain CT). so increasing the sensitivity of radiations among baby's lead to increase the cancer risk so dose reduction techniques should be considered.
- Children are more sensitive to radiation than adults they need significant dose reduction (low dose) and separate CT protocols for each part of the baby body. (Low dose CT is highly recommended even for 10-15yrs old patient).
- Small size, with accurate collimations, low mAs as possible, lower Kvp and increasing pitch they consider important in philosophy of dose reductions.
- Using of new technological advances such as effective mAs, ASIR, and automatic tube current modulations ATCM are greatly reduce the amount of received dose by child's body.
- Reducing the number of scans and specifying the dose into its specific area is consider

significant in term of radiation induced soft tissue toxicity.

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## Review article

# Tertiary Hyperparathyroidism: A Narrative Mini-Review

Saad Mansour Alqahtani<sup>1</sup>

1. Department of Surgery, College of Medicine, Majmaah University, Majmaah 11952, Saudi Arabia

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Corresponding Author:

Saad Mansour Alqahtani, MD, Assistant Professor and Head, Department of Surgery, College of Medicine, Majmaah University, PO Box 66, Majmaah 11952, Kingdom of Saudi Arabia.

Telephone number: +966-504786646; Fax: +966-16-4042500. Email: drsaadalhabib@hotmail.com.

### Abstract

Tertiary hyperparathyroidism (THPT) is characterized by persistent secondary hyperparathyroidism following successful kidney transplantation. In this case, there is an autonomous proliferation of the parathyroid glands and an over secretion of the parathyroid hormone, which is less likely to recover spontaneously. If untreated, this disease will affect patient survival and renal allograft. Classically in THPT; there is hyperplasia of all parathyroid glands; single or double adenomas are seen in 20% of patients.

### Aim:

review the features of THPT, its pathophysiology, the risk factors, complications and treatment options.

### Keywords:

Parathyroid gland; Parathyroid hormone; Tertiary hyperparathyroidism; Kidney transplantation.

### الملخص

#### خلفية:

يتميز فرط نشاط جارات الدرق الثالثي (THPT) باستمرارية فرط نشاط جارات الدرق الثانوي بعد زرع الكلية الناجح. في هذه الحالة يوجد نمو مستقل لعدد جارات الدرق مع فرط إفراز لهرمون جارات الدرق، والذي من النادر أن يتحسن تلقائياً. في حالة عدم معالجة المرض سيؤثر ذلك على الكلية المزروعة وحياة المريض. عادة ما يكون السبب في فرط نشاط جارات الدرق الثالثي هو فرط تصنيع لجارات الدرق الأربع (hyperplasia)، وفي حوالي ٢٠٪ من الحالات يوجد ورم غدي(adenoma) مفرد أو متعدد.

#### الهدف :

التعرف على الملامح السريرية لهذا المرض، علاماته المرضية، عوامل الخطورة ومعرفة المضاعفات المحتملة له وكذلك مناقشة طرق العلاج المتاحة له.

## Introduction

In chronic kidney disease, 90% of patients will develop secondary hyperparathyroidism (SHPT). This is due to hyperphosphatemia and diminished production of calcitriol (the active form of Vitamin D) which will eventually lead to hypocalcemia and high parathyroid hormone (PTH). Prolonged hyperphosphatemia, hypocalcemia and low Vitamin D will end up with parathyroid chief cell hyperplasia and excessive PTH production. Thus, successful renal transplantation reverses and corrects the metabolic, physiologic and mineral abnormalities observed in SHPT (e.g., uremia, acidosis, hyperphosphatemia, hypoc-

alcemia, reestablishment of calcitriol production and reversal of skeletal resistance to PTH and vitamin D). During the first three months post renal transplantation, there is a significant decline in serum PTH, and then followed by a progressive reduction in the next nine months. Also, there is a decrease in the parathyroid function mass<sup>[1, 2]</sup>. In most post kidney transplantation patients, a spontaneous improvement occurs as the glomerular filtration rate (GFR) normalizes. The degree of parathyroid hyperplasia is highly considered in defining the ability for this resolution. In nodular hyperplasia or adenomatous transformation, this regression is difficult to happen<sup>[2, 3]</sup>. There are about 17–50% of transplanted patients will re-

main to have hyperparathyroidism at one year post successful kidney transplantation; this condition is known as tertiary or autonomous hyperparathyroidism. Autonomous HPT refers to the unresponsiveness of the parathyroid gland to negative feedback mechanisms. THPT is not only developed in patients with renal failure; it can also occur with any condition which leads to long-standing hypocalcemia such as gastric malabsorption or chronic dialysis use [4-7].

#### *Clinical Presentations*

The clinical features of THPT are listed in Table 1 [4, 8, 9]. Body systems involved are many and include gastrointestinal tract, central nervous system, cardiovascular system, renal sys-

tem, as well as skin and soft tissues. Overall, the signs and symptoms are mostly attributable to the organ dysfunction caused by the high PTH and resultant high calcium levels. Thus, hypercalcemia can result in nausea, vomiting, constipation, abdominal pain, pruritus, calcification of soft tissues/cardiac valves/vascular structures, kidney stones, altered mental status and various metabolic derangements of carbohydrate and lipid metabolism. Moreover, the low level of calcium in bones, particularly, contributes to the undesired osteoporosis, pathological fractures, bone pain and muscle weakness.

Table 1. Clinical Presentation of Tertiary Hyperparathyroidism

Bone and muscles	Bone pain and Muscle weakness - Pathological fractures - Osteopenia
Skin and soft tissue	Pruritus - Soft tissue calcifications
Renal	Nephrolithiasis
Gastrointestinal Tract	Peptic ulcer disease - Pancreatitis
Central Nervous System	Mental status changes
Cardiovascular system	Hypertension and cardiomyopathy - Vascular calcifications Calcifications of cardiac valves
Others	Impaired graft function Metabolic abnormalities of carbohydrate and lipid metabolism Organ calcifications

## **Problems After Kidney Transplantation**

#### *Persistent hyperparathyroidism and hypercalcemia*

There are many factors that attribute to the persistent hyperparathyroidism such as duration of dialysis, the size of the parathyroid gland and formation of nodular and/or monoclonal hyperplasia of parathyroid glands. On the other hand, the possible causes of the hypercalcemia are resorption of extra-skeletal calcifications, phosphorus depletion or the gradual recovery of the normal calcemic activity of PTH after transplantation.

In most patients, the hypercalcemia resolves

in a few months post kidney transplantation. It can persist after the first year but resolves gradually within 2 to 5 years in 5–10% of patients. This persistent mild hypercalcemia is usually well endured and not associated with graft dysfunction. On the other hand, a small percentage of unfortunate patients who still maintain persistent hypercalcemia will require parathyroidectomy (PTx) (1–5%). The surgery will reduce the risk of renal dysfunction, nephrocalcinosis, pancreatitis and vascular calcifications [8, 10].

#### *Hypophosphatemia*

Hypophosphatemia after kidney transplantation is due to the reduction of phosphorus re-

absorption. THPT as well as some concurrent medications (e.g. immunosuppressives and diuretics) can cause urinary phosphorus wasting. Patients can experience muscle weakness and osteomalacia if plasma phosphate level drops below 1.4 mg/dl, and if it is less than 0.9 mg/dL, this can result in hemolytic anemia, rhabdomyolysis, decreased myocardial contractility and respiratory failure. One of the major sequelae of persistent phosphorus wasting after kidney transplantation is bone mineral density reduction, which in turn increases the risk of pathological bone fractures [4, 8, 10].

#### *Bone diseases*

In the first six months post renal transplantation, there is a quick rate of bone loss (i.e., 1.5% per month at the lumbar spine). Immunosuppressive medications, renal phosphorus wasting and hypophosphatemia and calcitriol deficiency collectively increase the probability of pathological bone fractures [4].

#### **The Risk Factors**

There are several risk factors that contribute to the development of persistent hyperparathyroidism such as long duration of dialysis as well as high serum levels of intact parathyroid hormone, calcium, phosphorus and/or alkaline phosphatase at the time of transplantation. Furthermore, parathyroid gland size (by ultrasound), renal insufficiency, calcitriol deficiency, immunosuppressive medications (including steroids), high body mass index and female gender are also reported [4, 8, 9, 11].

#### **Complications**

The consequences of the autonomous proliferation of the parathyroid glands and high secretion of parathyroid hormone are hypercalcemia and hypercalciuria, both of which lead to dysfunction and loss of the renal allograft [8, 9,

[12-15]. Furthermore, acute tubular necrosis, osteoporosis, cardiovascular diseases and bone fractures (particularly in the first five years post transplantation) have been reported [9, 16-18].

#### **Preoperative Imaging**

The most common preoperative imaging modalities used are neck ultrasound and  $^{99m}\text{Tc}$  sestamibi scintigraphy. Both provide the site and size of the biggest parathyroid glands. In contrast to primary hyperparathyroidism in which the preoperative imaging studies localize the abnormal gland (i.e., adenoma), these radiological investigations are not routinely done in patients with SHPT or THPT, except in ectopic or re-operative cases

[4, 13, 14]. It is published that bilateral neck exploration is needed in SHPT and THPT; thus, the utility of preoperative imaging is technically unnecessary [15]. In the case of re-operative PTx for THPT, Triponez and colleagues suggest starting with neck ultrasound and  $^{99m}\text{Tc}$  sestamibi scintigraphy. If both preoperative imaging studies are inconclusive, then magnetic resonance imaging (MRI) and fine needle aspiration of the suspicious lesion—with measurement of parathyroid hormone in the aspirated fluid—are advised. Additionally, in the case of persistent or recurrent hyperparathyroidism, if neck ultrasound,  $^{99m}\text{Tc}$  sestamibi scan and MRI are negative or equivocal, then selective venous sampling is indicated [4]. On the other hand, Karipineni et al. support the routine utilization of preoperative localization images [16].

#### **Management**

In THPT, the most favorable management remains unclear. Overall, in comparison to medical treatment, surgical intervention has higher cure rates. In a systemic review in 2017, the vast majority of studies on cinaclet in THPT

were limited to 22 small-sized observational studies and only two randomized controlled trials. Medically, cinacalcet is the most frequently used drug. Mechanistically, cinacalcet is a calcimimetic agent that increases the sensitivity of the calcium-sensing receptor and thus, decreases the circulating parathyroid hormone level. It can achieve normocalcemia in around 80.8% of patients with THPT. Cinacalcet is a fairly safe and successful drug which is an alternative option to PTx in post-transplant hyperparathyroidism patients, especially if there are contraindications for surgical intervention or potential complications following PTx [17, 18, 23, 24]. Accumulating evidence suggest that PTx is superior than cinacalcet in normalizing parathyroid hormone and calcium levels [23, 25] with low complication rates

[5, 18]. Furthermore, PTx improves bone density, symptomatic relief, patient survival and renal allograft function [14, 18, 26, 27].

In a review by Dulfer et al., it was concluded that no study reported data regarding the efficacy of surgical or medical treatment on cardiovascular complications in patients with THPT. However, in patients with SHPT, several published studies confirmed the reduction in cardiovascular events and mortality after PTx when compared to conservative management. Additionally, PTx far improves bone density compared to cinacalcet [18].

There are no evidence-based guidelines for indications of surgery in THPT; however, there were several proposed indications. Persistent hypercalcemia (more than 3–12 months after renal transplantation) is the only major criterion. Other reported indications include persistent hypercalciuria, renal phosphorus wasting (including hypophosphatemia), low bone marrow density, nephrocalcinosis, pruritus, parathyroid glands weighing more than 500 mg (as evaluated by ultrasound), severe renal osteopathy, calcification of tendons and soft tissue, calciphylaxis, progressive extra skeletal calcifications, severe bone pain or fractures

and formation of renal stones in grafted kidney [4, 7, 28-31].

Total parathyroidectomy (TP) with or without auto transplantation and subtotal parathyroidectomy (SP) plus/minus thymectomy are satisfactory and well-accepted surgical options in patients with THPT [13, 18]. Both procedures have persisted and recurrence rates (4% and 8.9%, respectively) [18] with a lower incidence of hypocalcemia in the latter [12]. Furthermore, it was reported that TP with forearm autograft was a proper surgical technique for patients with THPT [32]. On the other hand, Triponez et al. recommended SP in patients with THPT and concluded that limited parathyroidectomy has a higher risk of persistent/recurrent HPT [33]. This conclusion was also supported by another study by Abouchacra et al. in which the authors concluded that SP had excellent outcomes with favorable metabolic control and preservation of allograft function, without an increase in the rate of acute rejection [3]. Another study by Dulfer et al. recommended the SP surgical approach as it had low incidences of postoperative hypocalcemia and persistent hyperparathyroidism [23]. Moreover, it was observed that the impairment of kidney graft function was less with SP [29]. The gamma probe was used as an adjunct to PTx with high cure rates [34]. A limited parathyroidectomy (i.e., removal of enlarged parathyroid glands only) is rarely used. However, the rate of persistence and recurrence reaches up to 90% [18, 33, 35].

Thymectomy is routinely done by some surgeons, while others recommend it in certain situations (Table 2) [4]. Unlike primary hyperparathyroidism (PHPT), the role of intraoperative PTH monitoring in SHPT and THPT remains uncertain. Its accuracy rate reaches up to 95% in PHPT [4,13].

Table 2. Indications for thymectomy (Triponez et al. )

1	If the inferior gland is not found in its location.
2	If the intrathyroidal gland has been found by preoperative localizing techniques
3	In patients with higher risk of recurrent HPT (in patients with decreased renal function and in young patients with a long life expectancy).

Kidney transplantation is the most suitable treatment option for patients with end stage renal disease (ESRD)-related THPT, as kidney transplantation is projected to eliminate the underlying cause of HPT<sup>[36]</sup>. However, spontaneous regression of hyperparathyroidism following kidney transplantation does not take place in all patients. In a study of roughly 1700 patients with hyperparathyroidism undergoing kidney transplantation, Lou et al. showed 70% and 43% of patients had persistent THPT at one- and two-years post kidney transplantation<sup>[37]</sup>. The most appropriate time for THPT patients to undergo kidney transplantation continues to be a topic of controversy<sup>[36]</sup>.

The time of surgery is different from center to another. As published before, most centers recommend the delay of parathyroidectomy till after renal transplantation up to one year, in order to give a chance for the glands to regress<sup>[4]</sup>. Conversely, institutes suggest the surgery to be done at three months<sup>[8]</sup>.

Data showed that PTx (either TP or SP) itself could impair kidney graft function<sup>[29, 32]</sup> and unfavorably decrease the glomerular filtration rate<sup>[26]</sup>. In patients with THPT, several studies demonstrated a stable renal graft function along with a concurrent cinacalcet use

<sup>[20, 38, 39]</sup>. On the other hand, a reduction in the glomerular filtration rate<sup>[40]</sup> and an increase in the serum creatinine level<sup>[41]</sup> were reported, too. The effect of percutaneous ethanol injection therapy (PEIT) after SP was studied in patients with recurrent SHPT. However, this technique is useful and effective, especially if the cinacalcet and cryopreservation are not attainable<sup>[42]</sup>. On the contrary, it has side effects such as nerve paralysis and adhesions, which could complicate parathyroidectomy<sup>[43]</sup>.

## Conclusion

The management of THPT is challenging. The hyperparathyroidism alone is not an indication for PTx; thus, other associated factors should be thought of (i.e., hypercalcemia and its symptoms). Although cinacalcet is helpful and safe, PTx is indicated for refractory cases. Prospective multicenter studies should be considered as this will help to resolve the controversies concerning the best surgical approach and the indications of parathyroidectomy in patients with THPT.

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## Review article

# A review of worldwide distribution of Acanthamoeba from drinking water sources

Esam S. Al-Malki

Assistant Professor, Department of Biology, College of Science in Zulfi,

Majmaah University, Majmaah 11952, Saudi Arabia - E.mail: e.almalki@mu.edu.sa

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Corresponding Author:

Dr. Esam S. Al-Malki, E.mail: e.almalki@mu.edu.sa

### Abstract

Acanthamoeba species are free-living amoebae (FLA) that inhabit a diversified environmental source such as air, soil, and water. These FLA can also act as an opportunistic pathogen to cause infections in both healthy and immunocompromised individuals, including granulomatous encephalitis, keratitis, cutaneous lesions, and sinusitis. Thus, information's about Acanthamoeba distribution in environmental samples is very important in parasitology research. Therefore, this review aimed to analyze the incidences of Acanthamoeba in different types of water sources that are open to public accesses every day of life. Besides, this review endorses safety measures to avoid Acanthamoeba contamination in water.

### Keywords:

acanthamoeba, trophozoites, cysts, drinking water, granulomatous amebic encephalitis

### الملخص

#### خلفية:

تتبع انواع الakanthamibya جنس الطلائعيات وهي من الامبيات الحرة وتنتاج في مصادر بيئية متنوعة مثل الهواء والتربة والمياه. يمكن أن تعمل هذه الانواع أيضاً كأمراضات انتهازية لإحداث التهابات في كل من الأفراد الأصحاء والذين يعانون من نقص المناعة، بما في ذلك التهاب الدماغ الحبيبي والتهاب القرنية والامراض الجلدية والتهاب الجيوب الأنفية. وبالتالي، تعد المعلومات المتعلقة بتناول هذه الانواع في العينات البيانية مهمة جداً في أبحاث الطفيلييات. لذلك، تهدف هذه المراجعة البحثية إلى تحليل تواجد مثل هذه الانواع المختلفة في مصادر المياه المتاحة للبشر والتي تستخدم كل يوم في حياتنا اليومية بالإضافة إلى أن هذه المراجعة البحثية تدعم تدابير السلامة لتجنب تلوث الماء بأنواع الakanthamibya.

#### كلمات مفتاحية:

الakanthamibya ، التروفوزويت ، الطور المتكيس ، مياه الشرب ، التهاب الدماغ الامبيي الحبيبي.

## Introduction

Microbial contamination in water sources is one of the significant problems concerning the proper sourcing of water reservoirs used for drinking water supply, recreational facilities, and harvesting seafood due to possible contamination by pathogenic bacteria, protozoa, and viruses. In the past three decades, there had been intense contamination of drinking water by pathogenic parasites, transferred by water, which is causing many diseases in humans<sup>[1]</sup>. Free-living amoebae (FLA) are one of the protozoa most common habitants in the environment, such as water, sewage water, air, soil, dust, sewage water, and sediments<sup>[2]</sup>. The genera of free-living amoeba include Naeg-

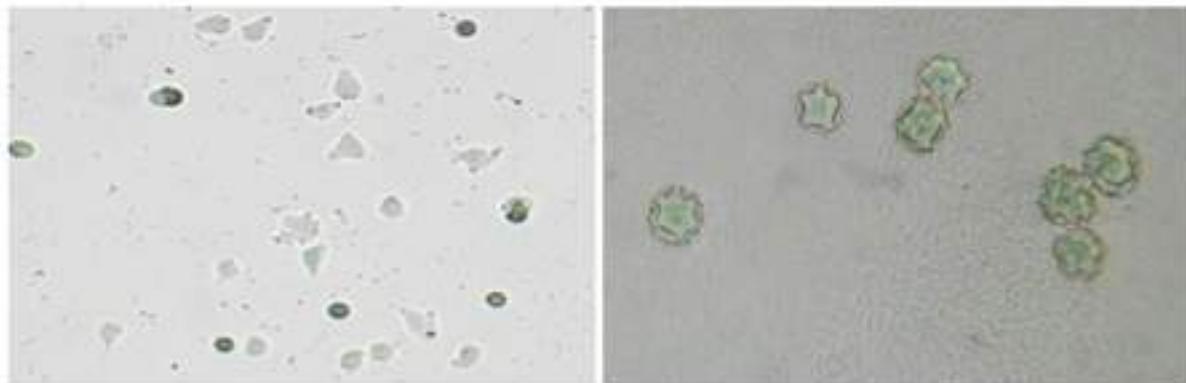
leria fowleri, Acanthamoeba spp, Balamuthia mandrillari, Sappinia diploidea, which cause a dangerous infection in human<sup>[3]</sup>.

Even though there are many parasites in water samples, Acanthamoeba is considered to be the most important protozoan pathogen because of its opportunistic nature. This opportunistic parasite can be found in diversified natural environments such as dust, soil, ambient air, potable water sources, sea, and recreational facilities (home aquaria, swimming pools) sources<sup>[2,5]</sup>. The bacteria-phagocytosing protozoa has been proved as one of clinical free-living amoeba not only present in the natural soil and water bodies, and it is also found in the man-made environment as a

secondary decomposer. It was found that the abundance of Acanthamoeba is more common in water sources such as water systems, rivers, and swimming pools to which humans are frequently exposed<sup>[6]</sup>. Acanthamoeba has adopted to withstand diverse environmental conditions by switching their phenotype (infective trophozoites form and resistant cyst

form) (Figure 1)<sup>[7]</sup>. The infection occurs to humans by inhalation of contaminated water or dust particles containing trophozoite and cyst. The infective trophozoites can infiltrate to the respiratory tract and cause nasopharyngeal infections and also skin infections. Particularly some pathogenic strains cause serious diseases in humans, such as keratitis in the eye and granulomatous amebic encephalitis

Figure 1. Acanthamoebae cysts isolated from water samples



<sup>[8,9]</sup>. The existence of Acanthamoeba in aquatic sources could be a dual danger because some of these are pathogenic and could also harbor pathogenic microorganisms such as Legionella, Pseudomonas, and Helicobacter<sup>[10]</sup>. Thus, parasitologist must know the distribution of Acanthamoeba in water samples and their control measures. Hence, the aim of this review is to analyze the distribution of Acanthamoeba incidence, especially in drinking water samples reported worldwide.

### History of Acanthamoeba

Acanthamoeba is a unicellular parasite with bearing centrosome, in Order of Acanthopodida, Class Centramoebia, Phylum Discosea, Amoebozoa clade in Amorphea domain of Eukaryotic organisms. In Greek, expressing the term “Acanth” is ‘spike’ which represents noticeable sub-pseudopodia while “amoeba” implies alteration, which represents change their shapes often. Acanthamoeba spp. Was first documented as a microbial culture con-

taminant along with Cryptococcus pararoseus by Castellani in 1930. Initially, the organism was named Hartmannella castellanii, and subsequently, a year later, it was renamed as Acanthamoeba spp. As of its irregular ectocyst appearance with double-wall nature, which is distinct from Hartmannella spp (round & smooth cyst wall)<sup>[11]</sup>.

### Acanthamoeba – adaptations

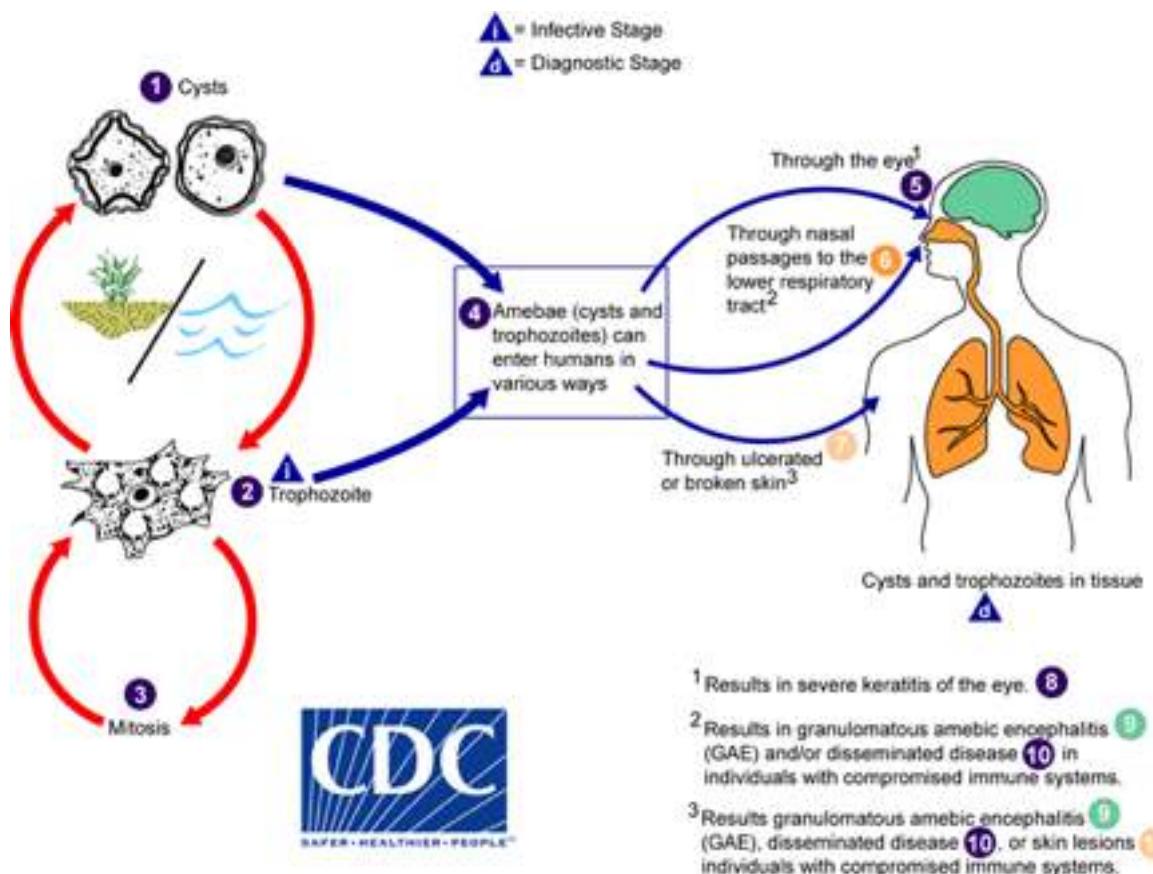
Acanthamoeba spp. Exhibits two different forms of life cycle (Figure 2). In rich nutrient conditions, in growing stat is in the form of trophozoites, and later in the dormant stage, it changed into cyst form. The size of Trophozoite is 25 to 40 µm, and it is an infectious stage with amoeboid motility. The size of this FLA's cyst roughly 13 to 20 µm is a dormant stage against tough environments such as high temperature and pH imbalance, malnutrition, or the presence of anti-amoebic agents<sup>[12]</sup>. Anwar et al. analyzed the cell wall biochemical characteristics and found that one-third of the

strength of the cyst wall might come from a polymer of glycosidic linkages between saccharides while another 2/3 are protein and other components, respectively [13]. Various researchers reported Acanthamoebae adaptations, and it acts as a possible source or vector of human-pathogenic bacteria, fungi, or viruses while endosymbiont and Acanthamoeba-resistant organisms also are identified [12,14]. Lately Corsaro et al. described more than 25 species were documented in NCBI taxonomy database, and 20 genotypes were published, which T4 is a major genotype associated with human infections [15].

## Epidemiology of Acanthamoeba in drinking water samples

Acanthamoeba species can transmit through waterborne, especially acquired through forceful inhalation of surface waters from poorly maintained swimming pools and other aquatic sources. Even though there are many reports available in various water sources worldwide, this review concentrates only on drinking water sources. Acanthamoeba, a protozoan parasite, is most found in soil and water environments throughout the world [2]. These FLVs have been isolated from a variety of sources, including water sources from the Antarctic [16], packaged drinking water, swimming pools [17], and even from dust in the atmosphere [18]. Prevalence of Acanthamoeba in various types

Figure 2. Life cycle of Acanthamoeba and waterborne infections  
(Image credit: Centers for Disease Control and Prevention, Atlanta, Online access from : [https://www.cdc.gov/parasites/images/acanthamoeba/Acanthamoeba\\_LifeCycle.gif](https://www.cdc.gov/parasites/images/acanthamoeba/Acanthamoeba_LifeCycle.gif))



of water sources reported worldwide listed in Table 1. The rate of prevalence varying based on region-wise, sample size, and sources. Go'rnik and Kuz'na-Grygiel from Poland found that at least 50% of the swimming pools contaminated with Acanthamoeba. This high frequency being recognized not only to the amoebae's resistance to chlorination but also

transfer by humans. In studies carried out on various water sources in Jamaica, amoebae with pathogenic potential were detected in 26.4%, 36.1%, and 49.6% of the samples of river water, tap water, and seawater, respectively, clearly representing a health risk [19]. Recently Tanveer et al. (2015) reported that pathogenic Acanthamoeba predominantly

Table 1: Prevalence of Acanthamoeba in different types of water in worldwide

Country	Year	Type of water source	Number of samples processed	Prevalence of Acanthamoeba	Authors
USA, Oklahoma	1995	Pond, running water	2016	63%	John and Howard [19]
Saudi Arabia	1998	River water	40	36.7%	Al-Herrawy et al., [20]
Thailand	2001	Water samples	95	18.9	Nacapunchai et al. [21]
USA	2003	James river water	330	7%	Ettinger et al.,[6]
Malaysia	2003	Domestic tap water	42	2.4%	Anisah et al. [22]
	2010	Swimming pool	840	46.2%	Init et al. [23]
Poland	2004	Swimming pools	NA	59.7%	Gronik et al., [24]
Jamaica	2005	Tap water & sea water	2004	43.3%	Lorenzo-Moraes et al. [25]
Brazil, Porto alegre	2009	Swimming pools	13	20%	Caumo et al., [17]
Iran	2010	Cold and warm water	94	45%	Bagheri et al., [26]
Brazil, Rio Grande do sul	2011	Tap water	136	9.5%	Winck et al.,[27]
Turkey	2012	Fountains, hot springs, wells	250	4.4%	Ozçelik et al., [28]
Pakistan	2013	Drinking water	35	92%	Tanveer et al., [5]
Turkey	2013	Tap water	150	22%	Coskun et al.,[29]
Egypt	2013	Nile river	NA	56 %	Al-Herrawy et al., [30]
	2014	Swimming pools	NA	60%	Al-Herrawy et al., [31]
Iran	2014	Environmental water	34	73.5	Mohammadi Manesh et al.,
		Tap water	59	45.16	[32]
The Philippines	2014	Tap water	3	33.3	Onichandran et al. [33]
India	2015	Tap water	100	14%	Khurana et al., [34]
Uganda	2016	Tap water	84	42.9	Sente et al [35]
Pakistan	2017	Drinking water supplies	20	35%	Yousuf et al [36]
Saudi Arabia	2018	Drinking water, fountains, well water	57	17.5%	Vijayakumar [37]
Malaysia	2019	Tap water	181	24.9%	Gabriel et al. [38]

NA – Not available

present in various water sources in Pakistan and pointed that Acanthamoeba as a potential transmission vehicle of pathogenic bacteria in different environmental sources and causes an additional threat to humans<sup>[20]</sup>. There are various authors published many research studies in the distribution of Acanthamoeba in water samples and their pathogenicity<sup>[21-39]</sup>. The prevalence of Acanthamoeba in water samples varies worldwide, in the literature search noticed in the range of 2.4% to 90%. The variation of percentage of Acanthamoeba is due to the sampling method, culture processing, and changes in ecological factors.

Very recently, Bunsuwansakul et al. documented a review on the prevalence of pathogenic Acanthamoeba among the Southeast Asian Nations and recognized a different range of certain supporting determinants such as distribution, the demographic profile of the patients, potential source of the parasite, method of transmission and treatment<sup>[40]</sup>.

### **Effects of Acanthamoeba contamination in drinking water**

Acanthamoeba has adopted to withstand diverse environmental conditions by switching their phenotypes, and it can grow in the water at various temperature and also act as a carrier for different microorganisms to humans, working as a medium for the circulation of pathogens between the environment and humans (Huws et al., 2008). Dry Acanthamoeba cysts can persist to many years and are isolated frequently from natural water sources, swimming pools, soil, sewage, freshwater fish, brackish water, ocean sediments, dust, air, and even packaged mineral water, or contact lens cleaning and soaking solutions. Therefore the public can easily access the Acanthamoebic infections by accidentally and forcibly inhaling water.

The major infection by Acanthamoebic cysts

contaminated water is corneal ulcer/keratitis. Acanthamoeba keratitis recognized as a vision-threatening corneal infection and can occur in healthy persons but most often reported in contact lens wearers<sup>[41]</sup>. These infections are repeatedly a result of direct eye exposure to contaminated water or solutions such as contact lens soaking and cleaning fluids. However, commensal bacteria present on the eyelids, the conjunctiva may have an additional role in the pathogenesis of Acanthamoeba corneal infections. Kilvington et al. investigated and proved that domestic tap water could be a source for Acanthamoeba, causing keratitis. The study revealed that the domestic tap water outlets of almost 89% (24 of 27) of patient homes, of which eight samples contained Acanthamoeba, indicated that this is a significant source of these organisms<sup>[42]</sup>. Another study by Vesaluoma and his associates analyzed the swimming pool water sample in Finland revealed the high possibility of amoebic and bacterial keratitis linked with swimming or bathing in properly cleaned public pools. Subsequently, they recommend that the contact lens wearers should not swim or bathe in public pools with contact lenses, which may increase the chances chance of getting Acanthamoeba keratitis<sup>[43]</sup>. Additionally, Acanthamoeba may occur as a commensal in the nasopharynx of apparently healthy normal individuals<sup>[42]</sup>. The infiltration of the amoebae into the central nervous system (CNS) is possibly by hematogenous spread from a primary focus in the lower respiratory tract, skin, or open wounds, but the amoebic trophozoites or cysts can reach the CNS directly through the olfactory neuroepithelium.

Regarding the brain infection, *A. polyphaga* is the first species that causes granulomatous amoebic encephalitis, which leads to hemorrhagic and necrotic encephalitis that is generally seen only in debilitated or immunodeficient persons. Early symptoms include

drowsiness, intense headaches, nausea, vomiting, fevers, and coma. Additionally, cutaneous acanthamoebiasis is a Cutaneous infection caused by Acanthamoeba and is most common in patients with AIDS, with or without CNS involvement [44].

### **Pathogenic Species**

Currently, about 25 species of Acanthamoeba have been described, and eight of them frequently linked with eye infections, the most prevalent Acanthamoeba genotype from clinical and environmental samples are the T4 genotype [45]. As mentioned before, Acanthamoeba has mostly been linked with granulomatous amoebic encephalitis (GAE), amoebic keratitis (AK), cutaneous lesions, and sinusitis in people. Eight species of Acanthamoeba (*A. castellanii*, *A. polyphaga*, *A. culbertsoni*, *A. hatchetti*, *A. rhysodes*, *A. lugdunensis*, *A. quina* and *A. griffini*) have been previously reported by researchers as causative agents in Acanthamoeba keratitis which is very common in individuals using dirty contact lenses as well as those washing and bathing with contaminated water. [41,42,46]

### **Control Measures**

The most influencing factors that lower the consequences of Acanthamoeba contamination and infections to public health are proper hygiene practices, availability of sufficient good quality water, appropriate sanitary conditions, and suitable disposal of human and animal excreta.

Various authors suggested effective control measures of 'Acanthamoeba' infection by water exposure which are collectively listed below

1. Good personal hygiene: As per CDC guidelines, people can protect themselves against waterborne Acanthamoebic infections by following proper personal hygiene, which in-

cludes frequent hand-washing prior cooking and consuming food, after using the restroom, after changing diapers, and before and after attending to someone who is sick [47].

2. Proper storage and use of water: Due to the ubiquitous nature of Acanthamoeba, water can be easily polluted by users at the household level through inappropriate use. Therefore, the water tanks shoud be kept clean and covered; it is also necessary to cleanse and disinfect them routinely [48,49].

3. Avoid long term storage water: Water stored in the water tanks for household usage should not be stored for a long time, and also proper cleaning and disinfection should be done for each refilling and avoid exposure/touching of hand to the water [50].

4. Public awareness: According to the US EPA Office of groundwater and drinking water, the public should be aware of how necessary it is to protect the source of water supply from the contamination of pathogenic protozoa. They should also accept liability for the safety of the water they utilize. It is highly essential to dispose of human waste matters and sewage materials away from any sources of water supply and construction of lavatories according to the requirements to avoid any possible contamination [51].

5. Filtering water by a water purification system is one of the important aspects of hygiene and plays an significant role in preventing the entry of Acanthamoeba at a household level. If people do not afford purification system, boiling is the most reliable way of getting water that is free from microbial pollution. The boiling of drinking water is one of the commonest methods to avoid microbial infections in many developed countries. Most importantly, after boiling, the water must be stored in a clean, germ-free container with a tight cover, and refrigerated [52,53].

6. The ophthalmologist should instruct their patients to follow appropriate hygiene practices while using and handling contact lenses to

avoid Acanthamoeba keratitis [54].

7. While Acanthamoebic trophozoites are considered to be susceptible to many chemical agents, however the cysts shown resistant to many chemicals. It has been documented in several research studies that the cysts exhibited tolerance to quaternary ammonium compounds, biguanides, chlorine & chlorine dioxide, and hydrogen peroxide. Only a few studies documented the strategies to control Acanthamoebic cysts by effective disinfection and investigated their virulence factors [55].

## Conclusion

The literature review indicates that there is a limited number of epidemiological surveys of Acanthamoeba infections that occurred worldwide, especially the local incidences from water sources. However, based on the available information, there is a steady increase in the number of infections caused by Acanthamoeba. Therefore, the local epidemiological survey on the occurrence of Acanthamoeba in drinking and public access water sources worldwide is a need of the hour.

## Key Point box

- Acanthamoeba is considered important because it is an opportunistic protozoan pathogen, is ubiquitous in nature
- Acanthamoeba cysts can withstand several years in water and adapt both trophozoites and cyst in extensive environmental conditions
- Acanthamoeba is the causative agents of granulomatous amoebic encephalitis, a fatal disease of the central nervous system, and amoebic keratitis, a painful sight-threatening disease of the eyes.
- This review highlighted the occurrences of Acanthamoeba in various aquatic environments in particular drinking water sources worldwide.
- This review recommended the control meas-

ures of Acanthamoebic infections by contaminated water.

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## Review article

# Retinal detachment in Stickler syndrome: A review of surgical outcomes and prognosis

Nayef F Alswaina

Ophthalmology Department, College of Medicine, Qassim University, Kingdom of Saudi Arabia

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Corresponding Author: Nayef F Alswaina

nayef529@hotmail.com - Nayef F Alswaina, Ophthalmology Department,  
College of Medicine, Qassim University, Kingdom of Saudi Arabia

### Abstract

Stickler syndrome is an inherited disorder of the collagen connective tissues with ophthalmic, orofacial, auditory, and articular manifestations. The risk of retinal detachment in Stickler syndrome is very high, and it is considered to be the most common cause of retinal detachment in children. Repair of retinal detachment in Stickler syndrome is challenging with variability in surgical and visual outcomes. Early diagnosis, close follow up and prompt intervention is necessary to prevent serious complication of retinal detachment and visual loss. Here we are reviewing the retinal detachment in Stickler syndrome, surgical outcomes and prognosis.

### Keywords:

Stickler syndrome, retinal detachment in Stickler syndrome, prognosis of Stickler retinal detachment.

### الملخص

#### خلفية:

متلازمة ستيكلر هي اضطراب وراثي للأنسجة الضامنة للكواليجين مع وجود مظاهر وتغيرات في العيون، ومنطقة الفم، والقناة السمعية، وكذلك المفاصل. إن خطر انفصال الشبكية في مرضي متلازمة ستيكلر مرتفع للغاية، ويعتبر السبب الأكثر شيوعاً لأنفصال الشبكية عند الأطفال. عملية إصلاح انفصال الشبكية في متلازمة ستيكلر تمثل تحدياً مع وجود تباين في النتائج الجراحية والبصرية. بعد التشخيص المبكر والمتابعة عن كثب والتدخل الفوري ضروريين لمنع المضاعفات الخطيرة لأنفصال الشبكية وفقدان البصر. في هذه المادة تمت مراجعة انفصال الشبكية في متلازمة ستيكلر وكذلك النتائج الجراحية والتشخيص

### Introduction:

Stickler syndrome (also known as hereditary arthro-ophthalmopathy) was first described by Stickler et al in 1965 [1]. It is an inherited progressive disorder of the collagen connective tissues with multi-systemic association. It is predominantly presented with ophthalmic, orofacial, auditory, and articular manifestations. The incidence of Stickler syndrome is estimated of about 1:7500 to 1:10000 live births, and it is considered to be the most common cause of inherited and childhood retinal detachment [2, 3, 4].

### Genetic findings:

Stickler syndrome is a disorder caused by gene

mutations affecting the formation of different types of collagen (types II, IX, and XI). These proteins are involved in building and function of the eye, articular and hyaline cartilages, and other connective tissues [5]. Because of genetic heterogeneity, there is diversity of phenotypes, and affected individuals present with variable expression. There are at least five subgroups of Stickler syndrome, based on its underlying genetic collagen defect [3, 6, 7, 8, 9, 10, 11]. Autosomal dominant forms of Stickler syndrome caused by mutation in COL2A1 gene(type I), CO-L11A1 gene (type II), and COL11A2 gene(-type III ,non-ocular form ). While, mutation in COL9A1 gene(type IV) and COL9A2 gene(-type V) are the autosomal recessive forms of Stickler syndrome [7, 9, 11, 12, 13, 14]. Type I Stickler

syndrome is the most common type, affecting more than 80% of patients [6, 15].

#### Clinical features and diagnosis:

Ocular manifestations present in 95% of Stickler syndrome patients include, congenital abnormality of vitreous, high myopia , anterior chamber drainage abnormality with high risk glaucoma , cortical cataract, and retinal lattice degeneration with high risk of retina breaks formation [16,17]. Non-ocular findings include orofacial malformation (e.g. maxillofacial hypoplasia and cleft palate ), hearing loss, as well as numerous skeletal malformations(e.g. premature osteoarthritis, epiphyseal dysplasia and joint hypermobility [18,19,20]. Although diagnosis of Stickler syndrome is confirmed by genetic analysis, careful systemic examination is essential and continue to have a major role for clinical suspicion and to help in genetic screening [6].

#### Rhegmatogenous retinal detachment(RRD) in Stickler syndrome:

Rhegmatogenous retinal detachment (RRD) is caused by a retina break which permit accumulation of fluid in the potential space between neuroretinal layers and the retinal pigment epithelium (RPE), and potentially leading to vision loss. RRD risk in Stickler syndrome patient is very high, and it was reported that over 50% to 65% of clinical diagnosis patient of one of the Stickler syndromes had retinal detachment [16, 17, 21, 22]. The risk reach to 70% of genetically confirmed type 1 Stickler syndrome, and almost 50% of them had bilateral detachment [21]. In type 2 Stickler syndrome, the percentage of retinal detachment is less and it was suggested to be between 40–50% of patients [23].

In Stickler syndrome, RRD occurs relatively early in life, often in the second and third decades of life. Giant retinal tear (GRT), which at least 3 clock-hours of peripheral retinal in-

volvement, considered to be a major cause of retinal detachment, it predisposed by the vitreoretinal changes associated with the syndrome [5, 16, 24, 25, 26]. In different studies , they showed that retinal detachment in Stickler syndrome is caused by a single retinal break in about 18% of cases, multiple retinal breaks range between 30-50%, and in between 31-50% of cases had GRTs [25, 27]. Lattice degeneration was found in about 75% of patients of Stickler patients, which further increase the risk of retinal breaks formation [25]. 50% to 75% of Stickler syndrome patients will develop proliferative vitreoretinopathy (PVR) at any point of their life [25, 27]. PVR is a main cause of retinal detachment repair failure, it is a disease process which result in periretinal membrane formation and traction, due to the proliferation of various cells (e.g RPE, glial cells , inflammatory cells) in the vitreous and/or periretinal area in patients with rhegmatogenous retinal detachments [28,29].

#### Management and prognosis:

Retinal detachment repair and maintaining the final success outcome in Sticklers syndrome patient is difficult and challenging although the advancement in surgical techniques. This complexity because of multiple factors, including the presence of multiple retinal tears, GRTs, the young age of presentation, the liquefied abnormal vitreous, and the high prevalence of PVR seen in these patients [25, 27]. Scleral buckle, vitrectomy, and combined vitrectomy and scleral buckle procedures with silicon oil or gas tamponade are the surgical options for RRD repair in Stickler patients, and all show anatomical successful outcomes. Silicon oil tamponade show superiority compare to gas tamponade in the term of decrease of the recurrence rate of RRD, and it was shown that the combined vitrectomy and scleral buckle procedure with silicone oil tamponade could be the treatment of choice for treating RRD in

patients with Stickler syndrome [25, 27, 30, 31].

### **Outcome of visual acuity:**

The visual acuity (VA) outcome after successful surgical intervention for RRD in Stickler syndrome is varies, showed improvement of VA in between 31%-63% of cases, 28%-40% of cases maintain VA, while 7%-37% showed decrease in VA [25, 27, 30]. In patients with complete re-attachment of the retina, Snellen VA was 20/200 or better in 61% to 76% of patients, and it was 20/40 or better in 16% to 45% of patients [25, 30]. There are multiple factors may impact the final visual outcome in Stickler patients, including young age of presentation, which may result in delayed diagnosis and more advanced findings, amblyopia, band keratopathy, cataract, high incidence of macula involvement and PVR changes [25, 30].

### **Success rate of surgery and complications:**

The final success rate for retinal reattachment in Stickler syndrome patients was ranging between 75%-100% [25, 27, 30, 32]. The success rate of primary surgery was ranging between 59 % and 78 %, with an average of 63.5%,70.5% and 75% after scleral buckling with cryotherapy, pars plana vitrectomy, and combined scleral buckling and pars plana vitrectomy, respectively [25, 30, 32]. The average time to re-detachment after the primary procedure was ranging between 2.6 months and 9.2 months [25, 27, 30]. The achievement of success retinal reattachment in Stickler syndrome may require multiple surgeries with average of 3.1 surgeries [27]. Most common complications noticed after retinal re-attachment surgery were proliferative vitreoretinopathy (PVR)( 50-75%), cataract ( 26-43%), raised intraocular pressure ( 14-27%), band keartopathy ( 8-25%), epiretinal membrane ( 7-11%) ,and intraocular hemorrhage (1-7%) [25, 30].

### **Prophylactic interventions:**

There are multiple prophylactic procedures were used to secure retina and to prevent ret-

inal detachment in Sticklers patients, such as cryotherapy, laser therapy and scleral buckling. Because of safety and clinical effectiveness issues, there are no general agreement for the ideal practice and clear guidelines on prophylactic interventions. There are several studies have demonstrated that the prophylactic retinopexy is safe and markedly reduces the risk of RRDs in Stickler syndrome patients and may be eliminate the risk of bilateral retinal detachment [21, 33]. Other studies were inconclusive and showed that the final outcomes of eyes that received prophylactic retinopexy were not statistically significant differences compared with eyes that did not receive any prophylactic treatment [3, 25].

### **Conclusion:**

Stickler syndrome is an inherited disorder presented with multi-systemic manifestations and high risk of RRD. Repair of RRD in Sticklers syndrome patient is complex with highly variable in surgical and visual outcomes. Despite controversy, several studies showed that the prophylactic retinopexy is safe and markedly reduces the risk of RRDs in Stickler syndrome patients. Because of younger age of presentation, as well as the challenges of surgical procedures and visual outcomes, this emphasizes the importance of early recognizing, close follow up, and prompt intervention for preventing the severe retinal complications and visual loss in these patients.

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## GUIDELINES FOR MANUSCRIPT PREPARATION

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Manuscripts submitted in this category are expected to be concise, well organized, and clearly written. The maximum length is 5000 words, including the abstract, references, tables, and figure legends. The maximum length is 5000 words, including the abstract, references, tables, and figure legends.

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- The title must not exceed 130 characters.
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- References should not exceed a maximum of 100.
- The abstract must be organized as follows:
  - Background & Aims
  - Methods
  - Results
  - Conclusions
  - Do not use abbreviations, footnotes or references in the abstract.
  - An electronic word count of the abstract must be included.
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The manuscript must be arranged as follows:

- Title page
- Abstract
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- Results
- Discussion
- Acknowledgements
- References
- Tables
- Figure legends
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- Review articles must be accompanied by a title page and a summary.

- Reviews should include at least one Key Point Box, with a maximum of 5 bullet points, that briefly summarizes the content of the review.

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- For mathematical symbols, Greek letters, and other special characters, use normal text. The references must be in accordance with the Vancouver reference style (see References).
- Approved nomenclature for gene and protein names and symbols should be used, including appropriate use of italics (all gene symbols and loci, should be in italics) and capitalization as it applies for each organism's standard nomenclature format, in text, tables, and figures.
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"HVPG was measured by hepatic vein catheterization using a balloon catheter according to a procedure described elsewhere [14, 15] and used as an index of portal hypertension [16]."

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[14] Merkel C, Bolognesi M, Bellon S, Zuin R, Noventa F, Finucci G, et al. Prognostic usefulness of hepatic vein catheterization in patients with cirrhosis and esophageal varices. *Gastroenterology* 1992;102:973-979.

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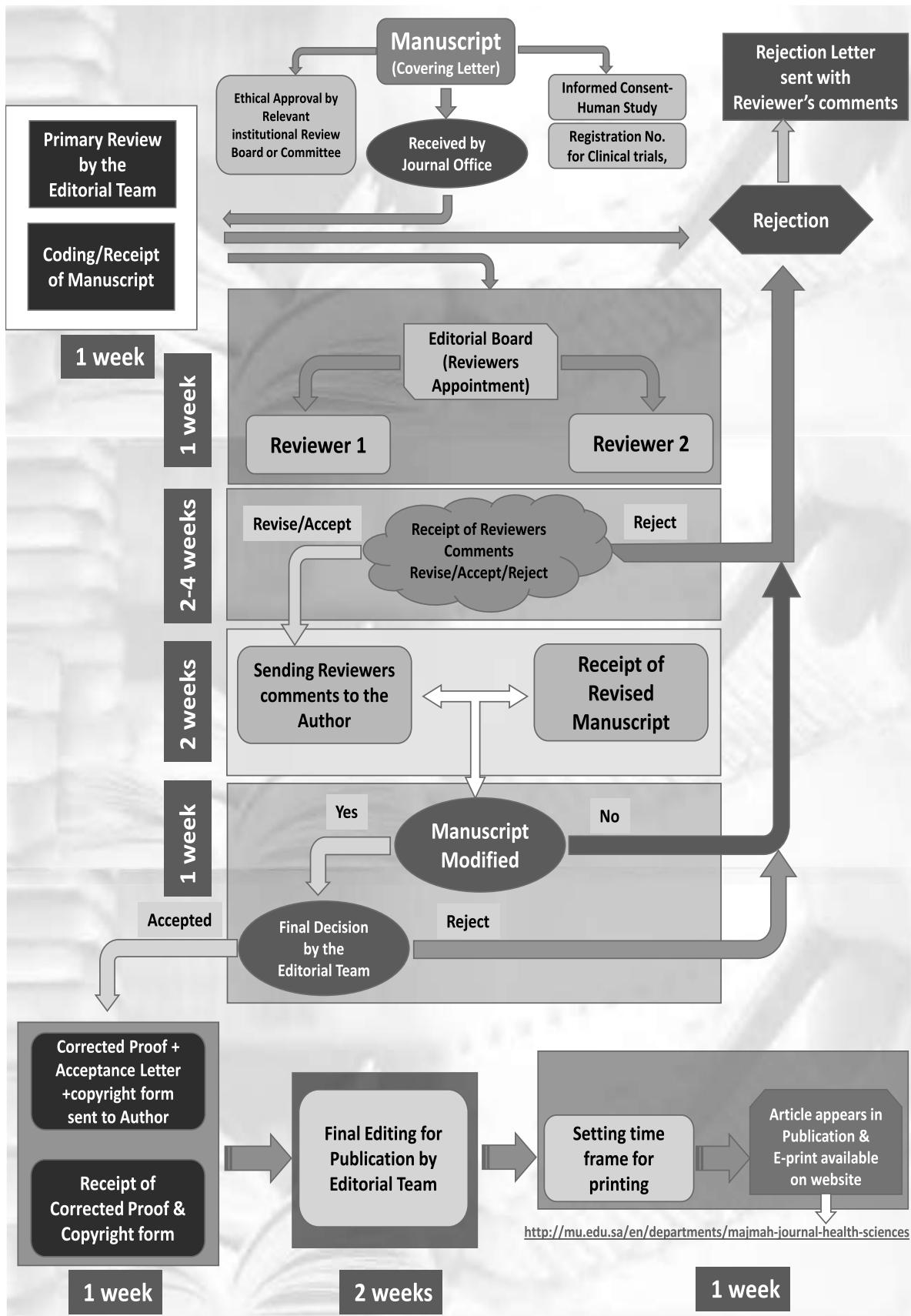
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The manuscripts should include a complete and detailed description of what was done. This includes a description of the design, measurement and collection of data, the study objective and major hypotheses, type and source of subjects, inclusion and exclusion criteria and measures of outcome, number of subjects studied and why this number was chosen. Any deviation from the study protocol should be stated. The baseline characteristics of any compared groups should be described in detail and -if necessary -adjusted for in the analysis of the outcome.

For randomized clinical trials the following should also be clearly documented: treatments, sample size estimation, method of random allocation and measures taken for maintaining its concealment including blinding, numbers treated, followed-up, being withdrawn, dropping out, and having side effects (numbers and type). The statistical methods used should be relevant and clearly stated. Special or complex statistical methods should be explained and referenced.

Complex analyses should be performed with the assistance of a qualified statistician. Unqualified use of such analyses is strongly discouraged. The underlying assumptions of the statistical methods used should be tested to ensure that the assumptions are fulfilled.

For small data sets and if variable distributions are non-normal, distribution free (non-parametric) statistical methods should be used. The actual p values - whether significant or not - should always be presented (not NS). Confidence intervals convey more information than p values and should be presented whenever possible. Continuous variables can always be summarized using the median and range which are therefore preferred. Only in the infrequent case of a Normal distribution are the mean and standard deviation (SD) useful. Complex analyses (including Cox and logistic regression analysis) should be presented in sufficient detail: i.e. variable scoring, regression coefficients, standard errors and any constants. Odds-ratios or relative risks are not sufficient documentation of such analyses. The handling of any missing values in the data should be clearly specified. The number of statistical tests performed should be kept at a minimum to reduce spurious positive results. Explorative (hypothesis generating) analyses without confirmation using independent data are discouraged. Figures showing individual observations e.g. scatter plots are encouraged. Histograms may also be useful. Tables should indicate the number of observations on which each result is being based





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