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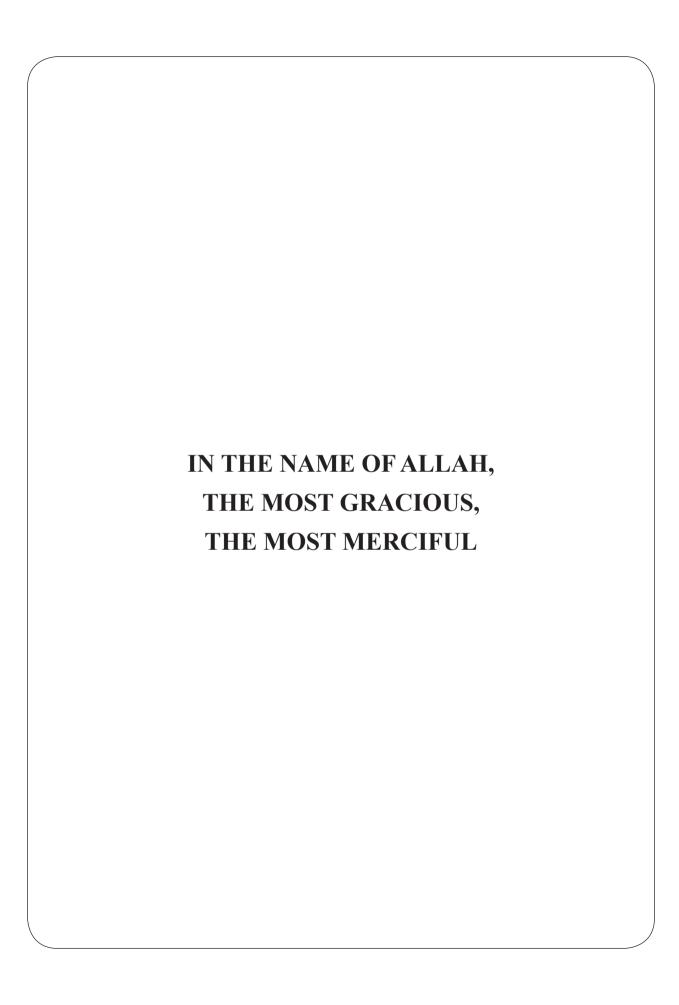
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At the outset let me express my gratitude to our beloved Rector Dr.Khalid Bin Saad Al Meqrin and Vice Rector for Graduate Studies and Scientific Research Prof.Dr.Mohammad Bin Abdullah Al-Shaaya for the trust endowed upon me.

Research is a tool for assimilation of knowledge and it facilitates learning. The ministry of Education has requested initiatives for joint research projects from the faculties of Majmaah University with prestigious Malaysian Universities. So the editorial team is welcoming scientific articles from such joint research.

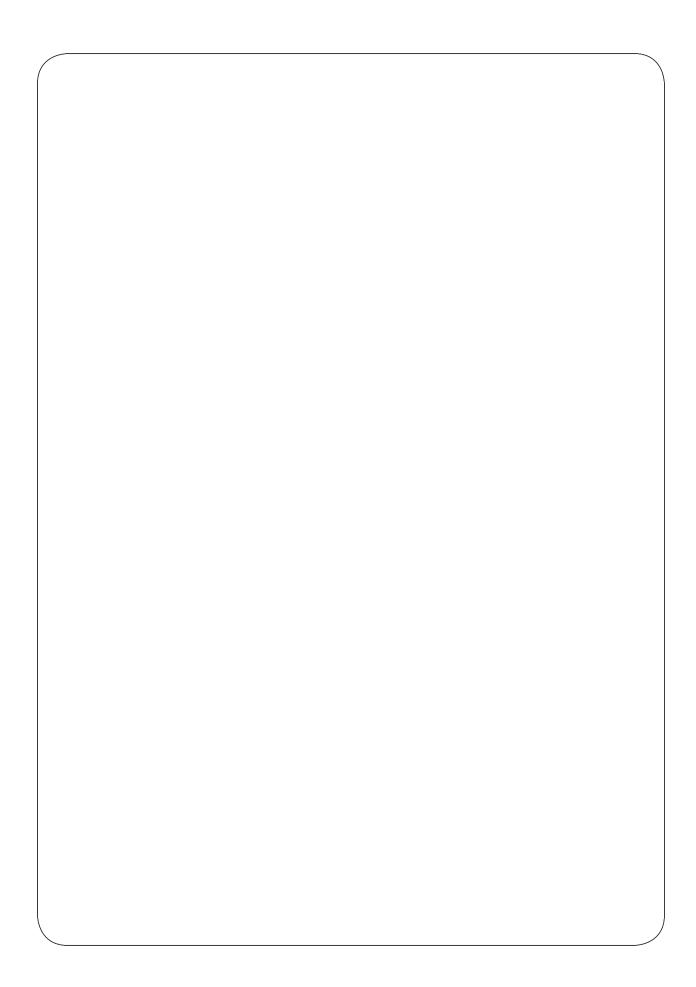
MJHS is proud to bring forth its first issue of Vol 8, 2020. The editorial team strives hard to publish the issues on time; I express my sincere thanks to the international panel of experts and new team of editorial assistants for their efforts to improve the publication process of MJHS office.

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. There are many editing services available that can help the authors improve the scientific and grammatical writing of their manuscripts. 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 Research

Profile of Children with Strabismus Managed without Surgery at a Tertiary Eye Hospital of Central Saudi Arabia

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Abstract:

Aim: To determine the causes of strabismus among Saudi children who attended a tertiary eye hospital in central Saudi Arabia.

Methods: This is a cross-section study included 112 children aged less than 16 years who attended the pediatric ophthalmology unit of King Khaled Eye Specialist Hospital (KKESH) in 2013 with complaints of strabismus, but not undergone surgical correction in the past. Demographic ocular status, refraction, fixation, visual acuity, ocular mobility status, history of eye patching, and penalization in the past were evaluated.

Results: We included 112 children with strabismus. Their mean age was 7.7 ± 2.5 years, and there were 63 boys (56%). Esotropia and exotropia were found in 99 and 13 children, respectively. Six children had hypertropia. Accommodative esotropia was found in 76 (76.8%) participants. The median angle of deviation in 99 children with esotropia was $30\Delta D$ [interquartile range (IQR) 16: 35]. The median angle of deviation in 13 children with exotropia was $25\Delta D$ (IQR 22.5: 32.5). High hyperopia, amblyopia, anisometropia, and high astigmatism were found in 65 (58%), 22 (19.6%), 2, and 16 children, respectively. Sixty-six (59%) and 82 (73%) children had undergone eye patching and refractive error in the past six months.

Conclusions: Accommodative esotropia was the main cause of strabismus. One-fifth of the participants had amblyopia. Although half of them were given medical/optical treatment in the past, failure to align eyes and address amblyopia is a matter of concern and needs further investigation.

Keywords: Strabismus; Squint; Amblyopia; Refractive Error; Childhood Blindness; Esotropia; Exotropia

الملخص

الهدف: تحديد أسباب الحول بين الأطفال السعوديين الذين التحقوا بمستشفى العيون التخصصي في المنطقة الوسطي من المملكة العربية السعودية.

طريقة البحث: تضمنت هذه الدراسة المستعرضة ١١٢ طفلاً تقل أعمار هم عن ١٦ عامًا والذين حضروا يشتكون من الحول لعيادة عيون الأطفال في مستشفى الملك خالد التخصصي للعيون في عام ١٠٠٠، ولكن لم يخضعوا لعمليات جراحية. تم أخذ بيانات عن فحص العين الشامل، قوة الابصار، فحص العيوب الانكسارية، نسبة الحول في العين، التاريخ المرضي للحول وتاريخ استخدام علاج الكسل إما بالتغطية أو باستخدام قطرات التوسيع.

النتائج: شملت الدراسة ١١٢ طفلاً يعانون من الحول. كان متوسط أعمار هم ٧.٧ ± ٢.٥ سنة، منهم ٦٣ ذكور (٥٦ ٪). كسل العين وجد عند ٢٢ (١٩.٦٪) من الأطفال بلغ عدد مرضى الحول الأنسى والوحشى ٩٩ و١٣ طفلاً، على التوالي. ستة أطفال منهم كانوا يعانون من حول فوقاني. بلغ متوسط زاوية الحول في ٩٩ طفلاً مصابًا بالحول الانسى ٣٠ درجة منشورية)١٦:٣٥ (IOR. بلغ متوسط زاوية الحول في ١٣ طفلاً مصابًا بالحول الوحشي ٢٥ درجة منشورية)٥٠ ٢٢.٥ (IOR. بلغ عدد الحول الأنسى التكيفي ٧٦ (٨ ٧٦ ٪) من أصل ٩٩ من المشاركين. طول النظر العالى وجد عند ٦٥ (٥٨٪) طفل تفاوت العيوب الانكسارية بين العينين وجد عند اثنين من الأطفال. الانحراف العالى وجد عند ١٦ (١٤/١٪) من الأطفال نسبة ٦٦٪ من الأطفال وجد ان لديهم تاريخ علاجي للكسل بتغطية احدى العينين نسبة ٧٣٪ من الأطفال تلقوا علاج بالنظارة خلال الستة أشهر الماضية. الخلاصة: هناك عدد من عوامل الخطر المسبية للكسل لوحظت عند الأطفال السعوديين الذين يعانون من الحول. أن العلاج الطبي المناسب متضمنا لبس النظارة في الوقت المناسب هو الخط الأول العلاجي عند الأطفال المصابين بالحول في السعوديين.

Introduction:

Strabismus in children is a major concern for the parents. However, lack of proper knowledge and fear of surgery result in late but frequent visits to eye care professionals[1,2]. Genetic and acquired causes are responsible for strabismus in children[3,4,5].

The prevalence of strabismus in children is [6,7] 1.2%–2.3%; however, there could be as many as 60,000 to 115,000 children with strabismus in Saudi Arabia[8]. In a study conducted in Jezan province, 37% of children attending the pediatric ophthalmology unit were diagnosed with strabismus[9]. Strabismus is responsible for ocular diseases in 6% of preschool children in Jeddah[10]. The majority of eye problems were due to refractive error and strabismus among preschoolers in a study conducted in Riyadh [11].

To the best of our knowledge, no data of strabismus are available in Saudi children less than 16 years. Routine eye screening is not performed in Saudi Arabian schools, and hence information about strabismus as one of the causes and outcome of amblyopia in young children would be of paramount importance.

The pediatric ophthalmology unit of our institution is unique as most of the children with complex ocular diseases are referred from the entire Saudi Arabian Kingdom, and most of the pediatric ophthalmologists have been qualified from our institution. Therefore, studying the profile of children with strabis-

mus at this institute would be unique and likely to be different from those managed at other institutions and complement the findings to represent all children in the Saudi Arabian Kingdom.

In the current study, we included Children with strabismus aged less than 16 years presented at a tertiary eye institution of central Saudi Arabia in 2013.

Methods:

Institutional research & ethical committee approval was obtained. A total of 1,072 children with strabismus (ICD 10 code H50.0 to H50.90) aged less than 16 years attended the pediatric ophthalmology unit of King Khaled Eye Specialist Hospital in 2013, and among them, a representative sample of 112 children was randomly enrolled in the present study based on the inclusion criteria.

One pediatric ophthalmology fellow was the field investigator. Only the children who cooperated for the measurement of vision were included in the study. The patients with a previous history of strabismus or intraocular surgery, congenital or developmental ocular diseases (e.g. cataract, glaucoma, and retinal dystrophy), ocular trauma, paralytic or restrictive strabismus were excluded. Demographic information including age at presentation and gender of child was obtained. The past history including patching, use of spectacles, and penalization of eyes in the past six months and before six months was recorded. Ocular examination including visual acuity assessment,

ocular mobility assessment, ocular fixation preference, and hand dominance was carried out as described in our previous publication [12]. If best-corrected vision in both eyes had a difference of more than 2 lines, the child was labeled as amblyopic with less vision. Cycloplegic refraction was carried out using 1% cyclopentolate eye drops. The refractive status of each eye was tested and documented in spherical and cylindrical correction, and its axis. If the spherical equivalent of both eyes had a difference of more than 2.5D, the child was defined as having anisometropia. If cylindrical refraction was more than 2.5D, even if spherical equivalent was calculated, the child was labeled as having high astigmatism[13].

On the basis of the refractive error of the worse eye, the children were grouped into the following categories: emmetropic (-0.5 to +0.5D), mild myopia (-0.5 to <-3.0D), moderate myopia (-3.0 to <-6.0D), high myopia (>-6.0D), mild hyperopia (+0.5 to +3.0D), and high hyperopia (>+6.0D)[14].

The data was collected using a pretested data collection form. It was then transferred into a spreadsheet of Statistical Package for Social Studies (SPSS 25, IBM, Chicago, USA). The qualitative variables such as gender, grades of refractive error, fixation, and dominant eye were presented as the number and percentage of the patients. The quantitative variables such as the angle of horizontal deviation and spherical, cylindrical refractive error were presented as the mean and standard deviations if their distribution was normal, and as

median and interquartile range if their distribution was not normal.

Results:

A total of 112 children with strabismus participated in our cohort study. Their mean age and male: female ratio were 7.7 ± 2.5 years and 63:49, respectively, and their age ranged from 3.2–5 years (17 children), 6–10 years (72 children), and 11–15 years (23 children). All were of verbal age and responded well to vision testing.

There were 99 (88.4%) children with esotropia and 13 (11.6%) with exotropia. In addition to horizontal misalignment, there were 6 (5.4%) with hypertropia. The further gradation of horizontal deviation suggested that there were 21 (18.8%) children with infantile esotropia, 76 (67.9%) with partly accommodative esotropia, 13 (11.6%) with intermittent exotropia, and 2 (1.8%) cases of esotropia with anisometropia.

Among the 99 children with esotropia, 13 children with exotropia, and six children with additional vertical deviation, the mean angles of deviation were 27.4 \pm 13.6 ΔD (prism diopters), 28.4 \pm 9.3 ΔD , and 6.8 \pm 2.2 ΔD , respectively.

The refractive error of the worse eye suggested that there were four (3.6%) children with emmetropia, seven (6.3%) with mild myopia, three (2.7%) with high myopia, 33 (29.5%) with mild myopia, and 65 (58%) with high hyperopia. On the basis of the relationship be-

tween horizontal deviation and refractive error, we noted that esotropia was significantly associated with high hyperopia (χ 2 = 27, DF (degrees of freedom) = 3, P < 0.001).

In 53 (47.3%) children, eye patching treatment was performed before six months. Of them, 21 (39%) children and 13 (11.6%) new children were managed by patching in the past six months. Overall, 82 (73.2%) children were given appropriate spectacles after cycloplegic refraction in the past six months. None of them had undergone penalization by atropine instillation in the past 6 months.

Considering the preference of fixating eye, 43 (38.4%) children preferred right eye, 38 (33.9%) preferred left eye, and 31 (27.7%) had no preference of eye for fixation. The degree of fixation is shown in Figure 1.

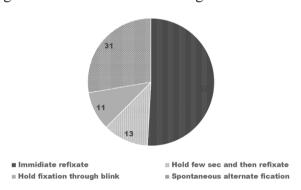


Figure: 1 The Degree of fixation for strabismus cases.

The best corrected visual acuity was similar in both eyes in 51 (45.5%) children, 40 (35.7%) children had 2 or less line difference in two eyes, while 21 (18.8%) children had more than 2 lines difference (amblyopia) in our cohort study. The functional normal vision was observed in 85 (75.9%) children and moderate visual impairment in 27 (24.1%) children.

Among the 99 children with esotropia, the right eye was the dominant (in 52) and left eye (in 46 children), and information was not available for one child. The median of spherical equivalent of refraction in 98 dominant eyes with esotropia was +3.75 D (interquartile range 2.5; 4.5). In 13 children with exotropia, right eye was the dominant in 8 and left eye in 5 children. The spherical equivalent of the dominant eyes was 0.00D (IQR -1.1; +1.4).

Discussion:

Nearly half of the children with strabismus presented at our institution had undergone medical management in the past six months. Provision of appropriate spectacles for three-fourths of the participants and patching were the main mode of management. Nearly one in five children with strabismus had amblyopia. Accommodative esotropia was the main type of horizontal strabismus.

In the absence of any reliable school- or primary healthcare-based information of ocular ailments in Saudi Arabia, hospital-based information of strabismus is used to formulate and recommend policies for eye care in the Saudi Arabian Kingdom. Although some studies are available in this context (in the province), our study based on the information from the referral center and cases dealt by pediatric ophthalmologists would be more reliable and useful to plan effective treatment strategies

The majority of the participants were afterschool aged children, which is generally considered as a late-diagnosis group. However, in the absence of information when strabismus was first detected, it is difficult to determine if the disease management is late. Mandatory eye screening of preschoolers and schoolage students are recommended for the early detection of eye problems including strabismus[15,16].

Esotropia was the main type of horizontal strabismus in our study, and 75% were of accommodative type. This is consistent with the results of another Saudi Arabian study [17] and contrast to that of another Pakistan-based study, where palsy contributed to pediatric strabismus[18]. Owing to better antenatal care and childbirth assistance in Saudi Arabian hospitals, the incidence of palsy was very low among our study participants.

The proportion of male children with strabismus was higher than female children in our study. This is different from the study of Lloyd et al[19] where the incidence of strabismus was equal in both genders, but the surgical uptake was significantly higher in females compared to males. Our study was performed in kids less than 16 years old in a country where eye care services are free of cost; therefore, comparison of gender distribution with other studies should be done with caution.

Among children with esotropia, the angle of horizontal deviation was ≤20∆D in nearly 45%. These children were managed by judicious medical management, and residual deviation was managed by botulinum toxin injection [20] or surgical correction. The best

modality of treatment for cases of exotropia is the surgical management [21].

Two-thirds of children had accommodative esotropia and hyperopic refraction. Optical management complimented with eye patching treatment with subnormal vision is recommended[22]. Although the proportion of children with exotropia was small in our study, their association with the type of refractive error was not conclusive. Among the six cases of exotropia in the study group, three had hyperopia while the other three had myopia.

In our study, one in five cases of strabismus had amblyopia, while anisometropia cases were very few. Amblyopia was caused by strabismus, anisometropia, or a combination of both of these[23]. Thus, childhood blindness can be prevented by the correction of strabismus in the study area.

In our study, 50% of the children with strabismus had previously undergone patching treatment, while another three-forth had done refractive error correction. Despite these treatments, they had strabismus when they presented to our institution, which could be due to poor compliance or late presentation. Parents' awareness about the timely treatment of amblyopia and its underlying cause is important to address this issue[24]. Generally, the staff working at the tertiary eye care centers are very busy, and hence they fail to provide adequate information for the parents regarding the importance of early eye patching and the need of good compliance. To en-

sure good compliance with the treatment, it is recommended to provide health education for parents regarding this issue. In cases with large angle deviation, prompt surgical intervention in addition to optical treatment is required. For small angle deviation and residual deviation following surgery, botulinum toxin injection of eye muscles is very effective [25, 26].

In addition to refractive error correction for accommodative esotropia, patching of the dominant eye is required if amblyopia is present; however, the child's and parent's cooperation are absolutely required for this procedure. Short-time patching and permitting the patched eyes for near work are very effective compared with one-eye patching for a long time[24]. None of the strabismus children in our study had undergone penalization using atropine eye drops.

There were a few limitations of the study. The children with strabismus were not selected randomly. Hence, extrapolation of the study results to other children with strabismus should be done with caution. The presence of positive family history of strabismus can be a risk factor for strabismus. In this study, information on family history was not collected, and hence the prevalence of familial strabismus could not be determined.

Conclusion:

This study was performed in children with strabismus who attended a tertiary eye hospital in Saudi Arabia, and the results were consistent with the previous studies in Saudi Arabia and other countries. The majority of the past treatment strategies for strabismus were not effective. Better cooperation of caregivers with the children with strabismus is required for the better outcomes of medical/optical treatment in these cases. After discussion with the parents, surgical management should be planned for cases of strabismus with a significant angle of deviation.

References:

- [1] Singh A, Rana V, Patyal S, Kumar S, Mishra SK, Sharma VK. To assess knowledge and attitude of parents toward children suffering from strabismus in Indian subcontinent. Indian J Ophthalmol. 2017;65(7):603-606.
- [2] Frazier M, Garces I, Scarinci I, Marsh-Tootle W. Seeking eye care for children: perceptions among Hispanic immigrant parents. Journal of immigrant and minority health. 2009;11(3):215-21.
- [3] Ye XC, Pegado V, Patel MS, Wasserman WW. Strabismus genetics across a spectrum of eye misalignment disorders. Clinical genetics. 2014;86(2):103-11.
- [4] Yang Y, Wang C, Gan Y, et al. Maternal smoking during pregnancy and the risk of strabismus in offspring: a meta-analysis. Acta ophthalmologica. 2018 Nov 6.

- [5] Schaal LF, Schellini SA, Pesci LT, Galindo A, Padovani CR, Corrente JE. The prevalence of strabismus and associated risk factors in a southeastern region of Brazil. InSeminars in ophthalmology 2018 Apr 3 (Vol. 33, No. 3, pp. 357-360). Taylor & Francis.
- [6] Jamali P, Fotouhi A, Hashemi H, Younesian M, Jafari A. Refractive errors and amblyopia in children entering school: Shahrood, Iran. Optometry and Vision Science. 2009;86(4):364-9.
- [7] Rajavi Z, Sabbaghi H, Baghini AS, et al. Prevalence of amblyopia and refractive errors among primary school children. Journal of ophthalmic & vision research. 2015;10(4):408.
- [8] Ministry of Health Saudi Arabia, Statistical Year Book 2017. Basic Indicators PP: 29. https://www.moh.gov.sa/en/Ministry/Statistics/book/Documents/ANNU-AL-STATISTICAL-BOOK-1438H.pdf last accessed on 16 Dec 2018.
- [9] Darraj A, Barakat W, Kenani M, et al. Common Eye Diseases in Children in Saudi Arabia (Jazan). Ophthalmol Eye Dis. 2016;8:33-9.
- [10] Bardisi WM, Bin Sadiq BM. Vision screening of preschool children in Jeddah, Saudi Arabia. Eye Care Review. 2008;2(1).

- [11] Al-Rowaily MA. Prevalence of refractive errors among pre-school children at King Abdulaziz Medical City, Riyadh, Saudi Arabia. Saudi Journal of Ophthalmology. 2010;24(2):45-8.
- [12] AlHarkan DH, Khan AO. False amblyopia prediction in strabismic patients by fixation preference testing correlates with contralateral ocular dominance. Journal of American Association for Pediatric Ophthalmology and Strabismus. 2014;18(5):453-6.
- [13] Rono HK, Bastawrous A, Macleod D, et al. Smartphone-based screening for visual impairment in Kenyan school children: a cluster randomised controlled trial. The Lancet Global Health. 2018;6(8):e924-32.
- [14] World Health Organization. Global Initiative for the Elimination of Avoidable Blindness: Action Plan 2006-2011.Geneva: World Health Organization; 2007. [Last accessed on 2018 Dec 18]. Available from http://www.who.int/blindness/ Vision2020_report.pdf
- [15] Jonas DE, Amick HR, Wallace IF, et al. Vision screening in children aged 6 months to 5 years: evidence report and systematic review for the US Preventive Services Task Force. Jama. 2017;318(9):845-58.

- [16] World Health Organization; IAPB EMR. Target population in Guidelines for School Eye Health for Eastern Mediterranean Region. 2009 page 10. https://www.iapb.org/resources/guidelines-for-schooleye-health-in-the-eastern-mediterranean-region/last accessed on 18 December 2018.
- [17] Al-Tamimi ER, Shakeel A, Yassin SA, Ali SI, Khan UA. A clinic-based study of refractive errors, strabismus, and amblyopia in pediatric age-group. Journal of family & community medicine. 2015;22(3):158.
- [18] Shaikh TS, Shaikh SP, Dareshani S, Shaikh WA. PATTERN OF SQUINT PRESENTATION IN PAEDIATRIC EYE DEPARTMENT AT CIVIL HOSPITAL KARACHI. Cell. 2015;333(3003326):021-35392255.
- [19] Lloyd ME, Gunton K. Gender and strabismus surgery. Journal of American Association for Pediatric Ophthalmology and Strabismus {JAAPOS}. 2018;22(4):e38-9.
- [20] Mahan M, Engel JM. The resurgence of botulinum toxin injection for strabismus in children. Current opinion in ophthalmology. 2017;28(5):460-4.
- [21] Yu X, Ji Z, Yu H, Xu M, Xu J. Exotropia is the main pattern of childhood strabismus surgery in the south of China:

- a six-year clinical review. Journal of ophthalmology. 2016;2016.
- [22] Lembo A, Serafino M, Strologo MD, et al. Accommodative esotropia: the state of the art. International ophthalmology. 2018:1-9.
- [23] Webber AL, Wood J. Amblyopia: prevalence, natural history, functional effects and treatment. Clinical and experimental optometry. 2005;88(6):365-75.
- [24] Jefferis JM, Connor AJ, Clarke MP. Amblyopia. Bmj. 2015;351:h5811.
- [25] Al Taisan AA, Al Shamlan FT, Al Mulhim AK, Alsomali AI, Al Owaifeer AM. Botulinum toxin; indications, success rates and complications in the management of horizontal strabismus in Saudi Arabia. Journal of Clinical Ophthalmology. 2018;2(1):32-7.
- [26] Lam CP, Chan J, Lau WW, Yam JC. Botulinum Toxin in Strabismus. Strabismus 2019 (pp. 147-157). Springer, Singapore.

Original article:

Stroke Risk Perception And Its Awareness Among Hypertensive Patients In Qassim Region Saudi Arabia

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Abstract

Background: Stroke is the most leading reasons of mortality globally and is the main cause of disability worldwide. Therefore it was necessary to study the knowledge and awareness level among the high risk population such as hypertensive concerning warning signs.

Aim: To identify the stroke risk perception and awareness among hypertensive patients in Qassim Region, Saudi Arabia.

Methods: A descriptive cross-sectional study was conducted on 203 hypertensive patients at the hypertension clinic in Buraidah central hospital. Data collection tool used in this study were socio-demographic data, past medical history, knowledge on stroke risk factors and stroke warning signs and self-reported stroke risk.

Results: The results showed that (n=117, 57.6%) of participants had elevated systolic blood pressure and (n=115, 56.7%) of them were smokers, the knowledge means of stroke risk were 10.73 ± 3.53 while the mean knowledge of warning signs was 9.276 ± 2.99 . The regressions result was statistically insignificant for the variables on the risk score; however, the age was statistically significant (p<0.001).

Conclusion: The study revealed that most of the hypertensive patients had unsatisfactory knowledge regarding risk factor and warning signs of stroke. Knowledge as a predictor for stroke risk was found not to be a significant predictor for stroke risk in this study. Increase awareness among the population to encourage primary prevention of hypertension should be the first concern by preventing smoking, reducing salt consumption, encourage physical activity, healthy diet and healthy lifestyles.

Keywords: Stroke Risk Perception, Awareness, Hypertensive Patients, Qassim Region, Saudi Arabia

الملخص

خلفية: السكتة الدماغية هي أهم أسباب الوفيات على مستوى العالم وهي السبب الرئيسي للإعاقة في جميع أنحاء العالم. لذلك كان من الضروري دراسة مستوى المعرفة والوعي بين السكان المعرضين لمخاطر عالية مثل ارتفاع ضغط الدم فيما يتعلق بعلامات التحذير. الهدف: التعرف على إدراك وخطر الإصابة بالسكتة الدماغية لدى مرضى ارتفاع ضغط الدم في منطقة القصيم، المملكة العربية السعودية. طرق البحث: أجريت دراسة لحظية على ٢٠٣ مرضى ارتفاع ضغط الدم في عيادة ارتفاع ضغط الدم في مستشفى بريدة المركزي. كانت أداة جمع البيانات المستخدمة في هذه الدراسة البيانات الاجتماعية والديموغرافية، والتاريخ الطبي السابق، والمعرفة حول عوامل خطر السكتة الدماغية وعلامات التحذير من السكتة الدماغية وخطر السكتة الدماغية المبلغ عنها ذاتيا.

النتائج: أظهرت النتائج أن 0.7.0 % من المشاركين لديهم ارتفاع ضغط الدم الانقباضي 0.7.0 % من بينهم مدخنون، وكانت متوسط المعرفة لمخاطر السكتة الدماغية 1.7.0 $\pm 0.7.0$ في حين أن متوسط معرفة علامات التحذير كان 1.7.0 $\pm 0.7.0$ كانت نتيجة الانحدار غير ذات دلالة إحصائية للمتغيرات في درجة المخاطر؛ ومع ذلك، كان العمر ذات دلالة إحصائية (0.7.0).

الخلاصة: كشفت الدراسة أن غالبية مرضى ارتفاع ضغط الدم لديهم معرفة غير مرضية فيما يتعلق بعامل الخطر وعلامات التحذير من السكتة الدماغية. تم العثور على المعرفة كتنبؤ لمخاطر السكتة الدماغية ليست مؤشرا كبيرا لخطر السكتة الدماغية في هذه الدراسة. زيادة الوعي بين السكان لتشجيع الوقاية الأولية من ارتفاع ضغط الدم يجب أن يكون الشاغل الأول عن طريق منع التدخين، والحد من استهلاك الملح، وتشجيع النشاط البدني، واتباع نظام غذائي صحي وأنماط الحياة الصحية.

الكلمات المفتاحية: تصور مخاطر السكتة الدماغية، الوعي، مرضى ارتفاع ضغط الدم ومنطقة القصيم المملكة العربية السعودية

Introduction

Stroke is one of the greatest public causes of morbidity and fatality internationally. The global incidence of stroke is predicted to be nearly fifteen million incidence strokes every year. It has been assessed that disability-adjusted life years from a stroke is approximately 90% in developing countries, which is approximately seven times the disability adjusted life years lost in developed countries. Stroke is classified as the third leading cause of mortality worldwide, with nearly six million terminal cases per year^[1].

Individuals with hypertension are at greater risk for suffering a stroke; public stroke prevention program should be focused to enhance the awareness of hypertensive people about the early warning symptoms of stroke and changeable risk factors [2].

In the kingdom of Saudi Arabia (KSA), hypertension has been predictable to be the primary risk factor for fatality. It has been assessed that nearly 25% of adults (age 15–64 years) have hypertension. High blood pressure among Saudi adults is well recognized. A massive national study found that nearly two thirds (total N = 1213) of the hypertensive patients had uncontrolled blood pressure, a terrifyingly high ratio [3].

High blood pressure is believed to be the prominent risk factor for death worldwide, initiating an expected 7.5 million deaths every year (13% of all deaths) [4]. Hypertension is the most significant risk factor for all

types of stroke. The relationship between hypertension and stroke has been approved for many years. There has been persuasive evidence for the previous 30 years that controlling blood pressure leads to the prevention of stroke [5].

Identifying of stroke warning signs is reasonably tied to taking the necessary actions to seek early emergency care. Poor recognition of stroke symptoms and risk may diminish the motivation for a modification in behavior and prolong delay of seeking emergency treatment. Investigators studying this delay have revealed that the greatest percentage of the delay exists in the pre-hospital interval of the incident: from the beginning of stroke symptoms to emergency department arrival ^[6]. The main aspects associated with this delay are a deficiency of patient and community awareness of stroke signs and symptoms and ignoring to seek emergency treatment ^[7].

Stroke is a preventable and curable illness through the control of changeable risk factors and the early discovering of stroke warning signs correspondingly ^[2]. General knowledge regarding stroke improves correct awareness, and enhance the performance of practices implemented by individuals to prevent and treat stroke. Awareness about risk factors of stroke and warning signs, appropriate action or immediate practices is essential in dealing with a stroke. In addition, the correct attitude towards stroke prevention can control both mortality and morbidity among the public and high risk groups ^[8].

Many previous studies have measured awareness in public and hypertensive patients garding stroke, its symptoms and risk factors. Some researchers have confirmed general inadequate knowledge of stroke risks and warning signs among participants [7, 9]. Other researchers have demonstrated that knowledge regarding stroke risk factors was inadequate among individuals at higher risk for stroke [10, 11]. Therefore, proper risk awareness is an essential step for the modification of risk related lifestyles. Therefore it was necessary to study the knowledge and awareness level among the high risk population such as hypertensive concerning warning signs, and changeable risk factors to prevent the event or at least discover it early. The current study aimed to identify stroke risk perception and level of awareness of stroke among hypertensive patients in Qassim region, Saudi Arabia.

Methodology

Study design

A descriptive cross-sectional study carried out from December 2018 to March 2019 to identify the stroke risk perception and its awareness among hypertensive patients in Qassim Region, Saudi Arabia.

Setting

The study was carried out in the hypertension clinic in Buraidah Central Hospital, Qassim region, KSA. It receives nearly one hundred thousand and half clients previous year 2018, approaching from different health regions of Oassim [12].

Sample

The participants included patients attending hypertension clinic on selected days from December 2018 to March 2019. Patients under the age of 18 years, non-Arabic speakers, or health professional were excluded. The calculation of sample size for stroke awareness was based on the prevalence of hypertension whereas considered a significant risk factor for stroke. The sample size was estimated using Fisher's formula: $n = \frac{Z^2P(1-P)}{d^2}$ Where n is the sample size, Z is the statistic corresponding to level of confidence, P is expected prevalence and d is precision, for estimating sample size in descriptive studies where hypertension prevalence was 15.1 % [13] and number = 197 participants and 203 participants were recruited.

Data collection and Procedure

Close ended interview questionnaire was used to collect data related to this study; it was written in a simple Arabic language developed by researchers.; A literature review was undertaken to uncover relevant items for the questionnaire, it consisted of four sections: first one; personal characteristics (age, sex, occupation, marital status, education, etc.), sources of information and previous medical history (history of hypertension, hypercholesterolemia, diabetes, smoking, cardiac disease, etc.). The second part of the questionnaire assessed the patients' awareness on stroke risk factors and stroke signs awareness which consists of 23 and 20 items addressing the risk factors, non-risk factors, signs, and non-signs of stroke. The third part self-reported stroke risk it used a six-response category scale with one being "very unlikely" and six being "very likely". The awareness questionnaire was pre tested by pilot study on 10 patients attending the hypertension clinic of Buraidah Central hospital to test the clarity of questions and to estimate the time required for using the tools. Permission to carry out the study was obtained from the administrators of the hospital and the head of Medical Education Research Center (MERC). One point was given for the correct answer and a zero was given for the incorrect answer; the individual scores were added to obtain a total score. The total knowledge was considered satisfactory if the percent score was 60% or more and unsatisfactory if less than 60% [14]. Recruited patients completed a 10-15 minutes questionnaire prior to their consultation. The fourth part was participant's record to identify the body Mass Index (BMI) and blood pressure (hypertension was classified as a blood pressure (BP) reading of 140/90 mm Hg or higher), which measured at participants' arrival to the clinic. Framingham Stroke Risk [FSR]; Stroke risk was estimated for each patient based on the adjusted FSR risk score is used to assess a participant's chance of having a stroke over ten years [15], the estimated nine risk factors: age, gender, systolic blood pressure, diabetes, antihypertensive treatment, prior heart disease, atrial fibrillation, current smoking, and left ventricular hypertrophy. The FSR was used to represent the participant's actual risk of stroke.

Statistical analyses

Data were analyzed using (Statistical Package for the Social Sciences) SPSS version 20.0. Findings were described as mean \pm standard deviation (SD) for quantitative variables and frequency (percentage) for qualitative variables. During the data analysis, one point for each correct answer was assigned, and zero for any other answer. Multiple linear regressions model was conducted to evaluate the association of relationship of the independent variables to stroke risk factors and to identify the factors influencing stroke risk and to examine the effect of each factor on the stroke risk score. Test of normality was done (Kolmogorov-Smirnov). Statistical significance was defined as p < 0.05.

Validity and Reliability

Examining the content validity of the study tools was done by 5experts by professors of nursing at the College of Nursing. Examining reliability of the suggested tools was done statistically by Cronbach's alpha test whereas 0.864 was Cronbach's alpha for awareness of stroke risk factors and 0.921 was Cronbach's alpha for awareness of stroke signs [16].

Ethical Consideration:

The study was approved by the Regional Research Ethics Committee (RREC) Qassim region, KSA prior to the beginning of the study. Aim of the study was clarified to the respondents. Informed consent was obtained from each. Respondents were informed that

they had the right to reject participation and to withdraw at any time. Confidentiality of data was confirmed.

Results

Table 1 shows the personal characteristics of the respondents, regarding age, it shows that (n=94, 46.3%) were between 25 to 45 years while (n=6, 3%) were above 65 years. The participants' average age was 41.83 ± 12.51 , the gender analysis shows that (n=104, 51.2%)

of them were male and (n=125, 61.6%) were married. The nationality of the participants shows that (n=174, 85.7%) were Saudi and (n=155, 76.4%) had enough income. Regarding education, (n=105, 51.7%) of participants reported to have higher education.

Regarding the source of information, figure 4 showed that (n=100, 49%), (n=87, 43%), and (n=16, 8%) had information from family/ friends, social media and health practitioners.

Table 1: Number and percentage distribution of participants according to their personal information

	Number	Percentage
Parameter	[N=203]	[%]
Age:	20	0.0
Less than 25	20	9.9
25 – 44	94	46.3
45 - 64	83	40.9
More than 65	6	3.0
Mean of age:	41.83=	±12.51
Gender		
Male	104	51.2
Female	99	48.8
Marital status		•
Single	55	27.1
Married	125	61.6
Divorced	18	8.9
Widowed	5	2.5
Nationality		
Saudi	174	85.7
Non Saudi	29	14.3
Income		
Enough	155	76.4

Not enough	48	23.6
Client education		
Illiterate	11	5.4
Primary	29	14.3
Secondary	58	28.6
Higher	105	51.7
Source of information		
Health practitioners	16	8
Family/friends	100	49.3
Social media	87	42.9

Figure 1: Percentage distribution of participants according to their blood pressure and Body Mass Index

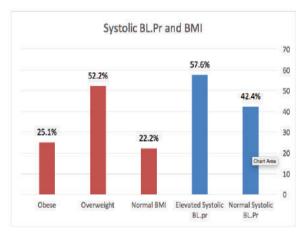


Figure 1 shows that (n=117, 57.6%) of participants suffered from elevated systolic blood pressure with average 136.72±11.30 mmgh, while in (n=49, 24.1%) of participants the diastolic blood pressure was high with average 89.57±6.43 Kg. Additionally, (n=106, 52.2%) of Participants were obese and (n=51, 25.1%) of them were morbidly obese. Normal BMI is 18.5-24.9. Values of 25-29.9 are considered overweight. Values of 30 or higher are considered obese.

Figure 2: Percentage distribution of participants according to their risk factors of stroke

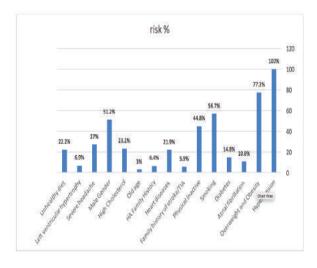


Figure 2 shows that all participants were diagnosed with hypertension and (n=157, 77.3%) of them were obese. Regarding smoking, it shows that (n=115, 56.7%) of the participants smoked and (n=91, 44.8%) of them were physically inactive and (n=45, 22.2%) of them were eating an unhealthy diet. Additionally, (n=43, 21.9%) of participants were diagnosed with heart diseases while (n=47, 23.2%) of them were diagnosed with high cholesterol and (n=22, 10.8 %) had been diagnosed with atrial fibrillation.

Table 2: Number and percentage distribution of participants according to their correct knowledge of stroke risk factors

	Number	Percentage	
Stroke risk factors Knowledge	[N=203]	[%]	
Hypertension	115	56.7	
High cholesterol	99	48.8	
Diabetes	87	42.9	
Smoking	98	48.3	
Overweight	81	39.9	
Lack of exercise	96	47.3	
Salty diet	52	25.6	
History of stroke	77	37.9	
History of neck vein disease	32	15.8	
Heart disease	77	37.9	
Alcohol	69	34.0	
Non-stroke risk factors Knowledge			
Trouble Sleeping	87	42.9	
Hypoglycemia	106	52.2	
Varicose veins	117	57.6	
Iron deficiency	105	51.7	
Low level of calcium in diet	105	51.7	
Alzheimer disease or dementia	118	58.1	
Lyme disease	115	56.7	
Stress	95	46.8	
Exposure to too much sun	116	57.1	
Living close to power plant	87	42.9	
Travel to foreign countries	126	62.1	
Total mean of risk factor knowledge	10.73 ± 3.53		

Regarding the correct knowledge of stroke risk factors table 2 explains that the mean of knowledge was 10.73 ±3.53. High blood pressure is the risk factor for stroke which was correctly chosen by (n=115, 56.7%) of the participants followed by high cholester-ol (n=99, 48.8%), smoking (n=98, 48.3%), lack of exercise (n=96, 47.3%) and diabetes (n=87, 42.9%). History of neck vein disease is the related risk factor which was least iden-

tified by the participants, there were only (n=32, 15.8%) of them who correctly answer. Regarding correct knowledge of non-stroke risk factors, it explains that traveling is not the risk factor for stroke that was correctly chosen by (n=126, 62.1%) of the participants followed by Alzheimer's by (n=118, 58.1%). Sleeping trouble was least identified by the participants, there were only (n=87, 42.9%) of them who correctly answered.

Table 3: Number and percentage distribution of participants according to their correct knowledge of warning signs of stroke

	Number	Percentage	
Stroke warning signs	[N=203]	[%]	
Double vision	86	42.4	
Dizziness	93	45.8	
Problems with speaking	84	41.4	
Vomiting	32	15.8	
Weakness or numbness of face	83	40.9	
Weakness/numbness of one side of the body	104	51.2	
Confusion	70	34.5	
Severe headache	95	46.8	
Loss of balance	86	42.4	
Weakness or numbness of arm	69	34.0	
Trouble with coordination	108	53.2	
Non-stroke warning signs			
Back pain	69	34.0	
Difficulty breathing	68	33.5	
Chest pain	60	29.6	
Swollen ankles	86	42.4	
Cold fingers /toes	86	42.4	
Cough	114	56.2	
Leg cramps	78	38.4	
Neck pain	73	36.0	
Total mean of stroke warning signs	9.276±2.99		

Regarding correct knowledge of the warning signs of stroke, table 3 shows that the mean of knowledge was 9.276±2.99, trouble with coordination is the warning sign for stroke which was correctly chosen by (n=108, 53.2%) of the participants followed by weakness or numbness of one side of the body by (n=104, 51.2%) and severe headache by (n=95, 46.8%). Vomiting is the warning sign that was least identified by the participants, there was only (n=32, 15.8%) of them who correctly answered. Regarding correct knowledge

of non-stroke warning signs, it describes that cough is not the warning signs for stroke that was correctly chosen by (n=114, 56.2%) of the participants followed by swollen ankles and cold fingers by (n=86, 42.2%). Chest pain was least identified by the participants, there were only (n=60, 29.6%) of them who correctly answered. Regarding total knowledge of stroke, it shows that (n=164, 80.8%) of participants had unsatisfactory knowledge of stroke, while only (n=39, 19.2%) of them had satisfactory knowledge of stroke.

Figure 3: Percentage distribution of participants according to their Self-Reported Stroke Risk Scores

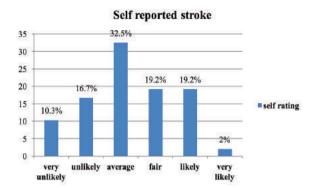


Figure 3 states the self-reported stroke risk of the participants. Whereas (n=66, 32.5%) of them estimated their risk rate as average stroke risk, (n=39, 19.2%) estimated their risk as likely stroke risk and (n=4, 2%) estimated their risk as very likely stroke risk.

Table 4: Multiple linear regressions of knowledge and demographics on total risk scores

	Unstandardized		Standardized		
Model	Coefficients		Coefficients	t	Sig.
	В	Std. Error	Beta		
(Constant)	15.226	8.156		1.867	.063
Total knowledge	151	.172058	059	874	.383
of stroke	131		038		
Gender	-1.561	1.836	058	850	.396
Age	.332	.081	.307	4.087	.000
Marital status	1.449	1.494	.071	.970	.333
Nationality	1.643	2.615	.042	.628	.531
Education	-1.554	1.062	099	-1.464	.145
Income	.564	2.132	.018	.264	.792
Self-rating	1.167	.689	.111	1.693	.092

a.Dependent Variable: total score of risk.

In the multiple regressions analysis, table 4 shows the effects of the independent variables (total knowledge of stroke, gender, age, marital status, nationality, education, income and self-rating) to total score of risk, the following were found to be non-significant predictors; total knowledge (p = 0.383), gender (p = 0.396), education (p = 0.145), marital status (p = 0.333), nationality (p = 0.531), income (p = 0.792) and self-rating (p = 0.092). Additionally, it shows that the age only variable

that was found to be significant predictors (p< 0.001), that means that the greater the age increased the risk of stroke

Discussion

According to the data gathered, the personal communication sources were found as the main source of information about stroke (49.3%), followed by social media (42.9%) and the least mentioned source was health personnel (8%). This finding was congruent with several recent studies done in numerous

countries [8, 17, 18]. During the last decades, the controlling of stroke risk factors such as arterial hypertension, atrial fibrillation, and diabetes has rapid progress [19]. Despite this improvement, stroke incidence is still high; one of the logical explanations could be the poor information of stroke risk as explained in the current study and in many studies around the world as in China [20], the United States [21], Greece [22] and the Gulf Cooperation Council countries [23].

With regards to risk factors and incongruent with the findings of previous studies, the present study revealed that all participants have hypertension which is known globally as the most common risk factors for stroke. Hypertension ranks in prevalence from 33.8% in Brazil [24], 38.4% in Australia [25] to 80.7% in Eastern Europe [26]. In addition, a large national study (n=1213) found that 63% of the hypertensive patients in Saudi Arabia had uncontrolled blood pressure, which maximizing the risk for stroke [3]. According to Kaddumukasa et al. [27], increase awareness and peoples' recognition of appropriate information, concerning stroke risk factors and warning signs may help in preventing stroke morbidity and fatality within exposed populations. Stroke risk factors mostly reported were hypertension (56.7%), high cholesterol (48.8%), smoking (48.3%), lack of exercise (47.3%) and overweight (39.9%). On the other hand, salty diet was less identified than was expected (25.6%). These findings are inconsistent with the previous studies which were carried out in various nations; in Italy [28], Canada [29]

and Australia [30]. This discrepancy may be due to the differences related to studies' setting and population.

Conclusion

The study revealed that most of the hypertensive patients had unsatisfactory information regarding risk factor and signs of stroke. This study tested knowledge of stroke risk and awareness of signs as a predictor for stroke risk. Knowledge only was detected not to be an associated predictor for stroke risk in this study. Additionally, it was found that most of the hypertensive patients had additional risk factors of stroke as obesity and smoking.

Recommendations

Increase awareness among the population to encourage primary prevention of hypertension should be the first concern by preventing smoking, reducing salt consumption, encourage physical activity, healthy diet and healthy lifestyles. Implementation of an educational program to enhance awareness of patients regarding their future risk of stroke and to change their risk factors is necessary for KSA especially to the older hypertensive patients and those with poor blood pressure control.

Limitations

The major limitations of this study are because the study sample was non probability sample, in a perspective of deficiency of mandatory data to implement accurate recruiting. The second limitation is that respondents were recruited in the hospital, which could

hinder the generalization of our findings to the general population living across Qassim region. Because the data were self-reported, the response is subject to recall bias in addition to a small sample size which may not be applicable to a larger population.

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Conflict of interest

The authors declare no conflict of interest

References

- [1] Gedefa B, Menna T, Berhe T, Abera H. Assessment of Risk Factors and Treatment Outcome of Stroke Admissions at St. Paul's Teaching Hospital, Addis Ababa, Ethiopia. Journal of Neurology & Neurophysiology. 2017;8(03).
- [2] Amen MR. Assessment of hypertensive patients' knowledge about lifestyle risk factors and warning signs of stroke. Journal of Contemporary Medical Sciences. 2016 Apr 13;2(5):28-32.
- [3] Khayyat SM, Khayyat SM, Alhazmi RS, Mohamed MM, Hadi MA. Predictors of medication adherence and blood pressure control among Saudi hypertensive patients attending primary care clinics: a cross-sectional study. PloS one. 2017 Jan 30;12(1): e0171255.
- [4] Reklaitiene, R., Tamosiunas, A., Virviciute, D., Baceviciene, M., & Luksiene, D. (2012). Trends in prevalence, awareness, treatment, and control of hypertension, and the risk of mortality among middle-aged Lithuanian urban population in 1983–2009. BMC cardiovascular disorders, 12(1), 68.
- [5] Dubow J, Fink ME. Impact of hypertension on stroke. Current atherosclerosis reports. 2011 Aug 1;13(4):298-305.
- [6] Centers for Disease Control and Pre-

- vention (CDCP). Prehospital and hospital delays after stroke onset--United States, 2005-2006. MMWR. Morbidity and mortality weekly report. 2007 May 18;56(19):474.
- [7] Zeng Y, He GP, Yi GH, Huang YJ, Zhang QH, He LL. Knowledge of stroke warning signs and risk factors among patients with previous stroke or TIA in China. Journal of clinical nursing. 2012 Oct;21(19pt20):2886-95.
- [8] Ibrahim RA. Soliman FE. The Effect of Educational Program for High Risk People about Stroke Prevention. 2016 5(4), 83-89
- [9] Hickey A, O'Hanlon A, McGee H, Donnellan C, Shelley E, Horgan F, O'Neill D. Stroke awareness in the general population: knowledge of stroke risk factors and warning signs in older adults. BMC geriatrics. 2009 Dec;9(1):35.
- [10] Gill R, Chow CM. Knowledge of heart disease and stroke among cardiology inpatients and outpatients in a Canadian inner-city urban hospital. Canadian Journal of Cardiology. 2010 Dec 1;26(10):537-41.
- [11] Sloma A, Backlund LG, Strender LE, Skånér Y. Knowledge of stroke risk factors among primary care patients with previous stroke or TIA: a questionnaire study. BMC family practice. 2010 Dec;11(1):47.

- [12] Ministry of Health Qassim Health. Outpatient clinics in Buraidah Central Hospital receive more than 141 thousand references during 2018[internet]. 2019 [cited 15 February 2019]. Available from: (http://qh.gov.sa/?p=45354).
- [13] El Bcheraoui C, Memish ZA, Tuffaha M, Daoud F, Robinson M, Jaber S, Mikhitarian S, Al Saeedi M, AlMazroa MA, Mokdad AH, Al Rabeeah AA. Hypertension and its associated risk factors in the kingdom of Saudi Arabia, 2013: a national survey. International journal of hypertension. 2014;2014.
- [14] Sloma A, Backlund LG, Strender LE, Skånér Y. Knowledge of stroke risk factors among primary care patients with previous stroke or TIA: a questionnaire study. BMC family practice. 2010 Dec;11(1):47.
- [15] Cushman M, Cantrell RA, McClure LA, Howard G, Prineas RJ, Moy CS, Temple EM, Howard VJ. Estimated 10 year stroke risk by region and race in the United States. Annals of Neurology. 2008 Nov;64(5):507-13.
- [16] Hinton PR, McMurray I, BrownlowC. SPSS explained. Routledge; 2014 Mar21. 351
- [17] Nansseu JR, Atangana CP, Petnga SN, Kamtchum-Tatuene J, Noubiap JJ. Assessment of the general public's knowledge of stroke: A cross-sectional study in

- Yaoundé, Cameroon. Journal of the Neurological Sciences 378. 2017. 123-129.
- [18] Pothiban L, Khampolsiri T, Srirat C. Knowledge and Awareness of Stroke Impacts Among Northern Thai Population. Pacific Rim Int J Nurs Res 2018; 22(3) 212-222.
- [19] January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC, Conti JB, Ellinor PT, Ezekowitz MD, Field ME, Murray KT. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. Journal of the American College of Cardiology. 2014 Dec 2;64(21):2246-80.
- [20] Yang J, Zheng M, Chen S, et al. A survey of the perceived risk for stroke among community residents in western urban China. PLoS One 2013;8: e73578.
- [21] Boden-Albala B, Carman H, Moran M, et al. Perception of recurrent stroke risk among black, white and Hispanic ischemic stroke and transient ischemic attack survivors: the SWIFT study. Neuroepidemiology 2011; 37:83-87.
- [22] Ntaios G, Melikoki V, Perifanos G, Perlepe K, Gioulekas F, Karagiannaki A. et al. Poor Stroke Risk Perception de-

- spite Moderate Public Stroke Awareness: Insight from a Cross-sectional National Survey in Greece. Journal of Stroke and Cerebrovascular Diseases, Vol. 24, No. 4 (April), 2015: pp 721-724.
- [23] Kamran S, Bener AB, Deleu D, Khoja W, Jumma M, Al Shubali A, et al. The level of awareness of stroke risk factors and symptoms in the Gulf Cooperation Council countries: Gulf Cooperation Council stroke awareness study. Neuroepidemiology. 2007;29(3-4):235-42.
- [24] Meira F, Magalhães D, DaSilva L, Mendonca-E Silva AC, Silva GS. Knowledge about Stroke in Belo Horizonte, Brazil: A Community-Based Study Using an Innovative Video Approach. Cerebrovasc Dis Extra. 2018;8(2):60-69. doi: 10.1159/000488400.
- [25] Grady A, Carey M, Sanson-Fisher R. Assessing awareness of appropriate responses to symptoms of stroke. Patient Education and Counseling. 95. 2014. 400–405
- [26] Oldgren J, Healey JS, Ezekowitz M, Commerford P, et al. Variations in Etiology and Management of Atrial Fibrillation in a Prospective Registry of 15,400 Emergency Department Patients in 46 Countries: The RE-LY AF Registry, Circulation. 2014; 129:1568-1576.
- [27] Kaddumukasa M, Kayima J, Kaddu-

- mukasaMN, Ddumba E, Mugenyi L, Pundik S, Furlan AJ, Sajatovic M, Katabira E. Knowledge, attitudes and perceptions of stroke: a cross-sectional survey in rural and urban Uganda. Kaddumukasa et al. BMC Res Notes. 2015. 8:819.
- [28] Baldereschi M, Di A, Bullet C, Vaccaro C, Biancamaria B, Inzitari D, Stroke knowledge in Italy. The Promotion Implementation of Stroke Care in Italy Project Working Group, Neurol. Sci. 36 (3).2015 Mar. 415–421.
- [29] Metias M, Eisenberg N, Clemente M, Wooster E, Dueck A, Wooster D, Roche-Nagle G, Public health campaigns and their effect on stroke knowledge in a high-risk urban population: a five-year study, Vascular 1. 2017 Jan. Available at https://doi.org/10.1177/1708538117691879
- [30] Spark JI, Blest N, Sandison S, Puckridge PJ, Saleem HA., Russell DA, Stroke and transient ischemic attack awareness, Med. J. Aust. 195 (1) .2011 Jul 4. 16–19.

Original Article

Haematobium Schistosomiasis Prevalence Among School Age Children In Irrigated Schemes At Shendi Locality, River Nile State, Sudan: Implication Of Behavior And Risk Factors

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Abstract

Background: Schistosomiasis categoried as water-based diseases transmit by skin contact with the contaminated water. Children at school age are the highly vulnerable victims of the disease. The aims of the study was to measure the schistosomiasis prevalence and determine the influence of ecological and behavioral factors associated with the situation of the disease prevalence.

Methods: In this cross-sectional study the multi-stage cluster random method was used to select a sample size of 1188 children, aged six to18 years, from 16 villages located around the agricultural schemes in the Shendi locality. The data were collected using structured questionnaires, observation and laboratory investigation for the urine samples of the selected children. In addition, checklists lists were used to drive the levels of knowledge about the schistosomiasis.

Results: The results showed 33.3% positive cases. Males reported higher prevalence (35.1%) than females (27.5%), this difference was associated with the dominant culture in the area, that male responsible for providing family needs, and they were more exposed to the disease incidence. The prevalence of schistosomiasis was highest (59.8%) among age groups of 11-15 years. The bridges to cross over the irrigation canals also was one of the important risk factors enhancing it spread in the area. A highly significant association was found between the schitosomiasis prevalence, behavioral and ecological factors.

Conclusion: The urinary schistosomiasis representing a public health problem in the area. Environmental and cultural factors were significantly associated with the prevalence of the disease in the locality.

Keyword: Haematobium Schistosomiasis, Public health, Infectious-disease, Water-based disease

الملخص

خلفية: البلهارسيا هي واحدة من أكثر الأمراض المرتبطة بالماء انتشارا والتي تنتقل عن طريق ملامسة الجلد بالماء الملوث بالأطوار المعدية للمرض. الأطفال هم أكثر ضحايا تلك الأمراض في البلدان النامية. تهدف هذه الدراسة لقياس انتشار البلهارسيا وتحديد تأثير البيئية والعوامل السلوكية المرتبطة بحالة المرض.

طريقة البحث: هذه الدراسة مقطعية وتم جمع العينات بإتباع نموذج العينات المتعددة المراحل العشوائية العنقودية لاختيار حجم عينة من ١٦٨ طفل، تتراوح أعمارهم بين ٦ إلى ١٨ سنة، من ١٦ قرية تقع حول المخططات الزراعية في محلية شندي. تم جمع البيانات باستخدام الاستبيانات المحكمة، وعن طريف الملاحظة والتحاليل المختبرية لعينات البول من الأطفال المختارين في الدراسة. بالإضافة إلى ذلك، تم استخدام قوائم التحقق المراجعة لقياس مستويات المعرفة حول البلهارسيا.

النتائج: أظهرت النتائج أن نسبة الحالات الإيجابية ٣٣,٣ ٪. حيث وجد أن معدل انتشار أعلى في الذكور (٣٥,١ ٪) مقارنتاً بالإناث (٢٧,٥ ٪). أظهرت الدراسة أن معدل انتشار البلهارسيا (٩٩,٨ ٪) بين الفئة العمرية ١١-١٥ سنة وكانت أعلى نسبة إصابة بالمقارنة مع كل الفئات العمرية الأخرى. عدم وجود أو/ وبعد الجسور لعبور قنوات الري كانت أيضا واحدة من عوامل الخطر الهامة التي تعزز فرص الإصابة وانتشار المرض في المنطقة.

الخلاصة: وجدت الدراسة علاقة قوية بين انتشار مرض البلهارسيا والسلوكيات والعوامل البيئية، حيث أظهرت العوامل البيئية والثقافية أقوى مؤثر مرتبط بحدوث المرض في المنطقة.

Introduction

Schistosomiasis also known as Bilharzia caused by a group of helminths parasites (1) The disease is transimitted by snail, its endemic in most rural areas and more spread in tropical biomes and subtropical ecosystems (2). Schistosomiasis is the most prevalence one of the water-based diseases group. It is one of the greatest risks impair the public health, specially in the rural agriculture areas of developing countries for example in sub-Saharan Africa where approxi-mately 200,000 deaths per year are associated with the schistosomiasis prevalence(3).

Schistosomiasis is amongst the majorcause of high morbidity in developing countries. The diseases are considered the most common and decrease the productivity of the affect humans and incapacitating the livestock. Healthrelated quality of life (HrQoL) total score was significantly lower in villages with high prevalence rate of S. haematobium (24.0%, p,0.001) and within the lower socioeconomic quartiles (22.0%, p,0.05). A greater effect was seen in the psychosocial scales as matched to the physical function scale. In villages with the moderate prevalence, detection of any parasite eggs in the urine was associated with a significant 2.1% (p,0.05) reduction in total score as reported by Terer CC, et al 2013 (5). The schistosomasis endemic is limited in 78 counries (5) and may conservative increase with particular agricultural activities. Recent estimation reveals that, It has been anticipated that, in 2013, there were approximately 261

million people – including about 240 million cases in Africa – who required preventive chemotherapy because they were at risk of schistosome infection (6). In our study area, Schistosomiasis expected to be increased due to the historical presence of the disease in this area and the establishment of the new investment agricultures schemes. Thus, the Schistosomiasis assessment could be one of the most useful indicators to evaluate the public health of the children. The aims of our study was to measure the schistosomiasis prevalence and determine the ecological and behavioral factors associated with the schistosomiasis prevalence,.

World Health Organization (WHO) reported that in 2009 the global prevalence of schistosomiasis has some changed, and it has been eliminated from many countries. However, the cost of schistosomiasis still high, and it contributes to co-morbidity with other health problems, such as human immunodeficiency virus (HIV), hepatitis, and malaria, in regions where these diseases are endemic (7).

Schistosomiasis considered one of the globally, neglected tropical diseases (NTDs) (3), although they are further most common diseases among the poor people, especially in rural area (7). Schistosomes is classified as the second most common prevalent (NTDs) helminths after the soil-transmitted helminthiasis (hookworm) (8). Recent studies of the schistosomiasis disease incidence show that the occurrence of symptoms and the cost in disability-adjusted life years is growing and

abundant greater than it was formerly (4). Therefore, it concludes that the Schistosomiasis are still a health problem in developing countries, especially among the children in rural area and villages located close to openwater resources.

There are two core schistosome types that cause infection to human in Africa they are Schistosoma mansoni, causes intestinal schistosomiasis infection, and Schistosoma haematobium, which causes urogenital schistosomiasis. Schistosoma intercalatum and Schistosoma guineensis are rarely reported and have limited distribution (3,10,11).

It was reported in 1996 that, around 500 to 600 million people were at risk of being infected with the schistosomiasis largely in rural areas, often as work-related disease. Schistosomiasis primarily affects people who are incapable to avoid touching with infested water, either because of their occupation for examples, agriculture and fishing, or due to the lack of other reliable source of drinking water, using infected water for bathing and washing. As a result of a of immunocompromize and rigorous contact with contaminated water during playing or swimming, young school children aged 10 to 17 years are among the most vulnerable to the schistosomiasis infection(12). WHO reported in 2004 that, schistosomiasis is found to be endemic in 76 countries and regions worldwide (13). Schistosomiasis is a chronic, long lasting disease, leading to a burden of 3.3 million cases worldwide disability-adjusted life-years (DALYs) (10,11). Researchs results showed that wider distribution and usage of praziquantel drug, improved drinking water supply and sanitation status, result in slightly decrease of Schistomosiasis prevelances(14). African sub-Saharan region was reported for 93% (192 million) of the cases globally. Most reported cases were subclinical symptomatic infections, with mild complication such as anemia and malnutrition(15).

Although 46 African countries reported schistosomiasis active transmission, however Asia account the more pathogenic type of disease. There is growing difference between sub-Saharan Africa and the rest of the world in terms of transmission and control (16)

In Sudan, the prevalences of urinary Schistosomiasis were common in all the Nile banks from Halefa to Nemoli village on the Sudanese. The disease spread to all the agricultural development schemes which were inaugurated after the Gezira such as Managil, Rahad and sugar cane schemes in Jinaid, NewHalfa, Asalaya and Kinana (17).

A study was conducted in Elkriab primary school, near ELslait irrigation scheme Sudan to determine the prevalence rates and intensity of infection with the schistosomiasis disease among school pupils. The results displayed that the prevalence of schistosomiasis in this area was 28% of school children. The result also showed that in 74% out of 97 children infected with S. haematobium, the intensity exceeded 500eggs/10 ml of urine (9).

School-age children frequently have the highest incidence and intensity of infection. Amuta et al reported that, The age-related prevalence showed (70.5%,) in the 11-15 year old children than those in 1-5 year old group (44.9%,). A significant variance was saw in the prevalence between the age groups (P=0.014). Males were more infected (60.6%,) than females (47.7%,). (18).

Schistosomiasis is found in poor sanitation areas where humans are in contact with water contaminated by human waste (urine, genital tract excretions and faeces) as part of their daily lives activities, during recreational or professional activities (18).

The overall prevalence of urinary schistosomiasis, is high in the White Nile River basin, Sudan, and is strictly associated with frequencies of contactwith water, bathing, swimming, and wading the stream (19).

A study in Ethiopia, among the moderaterisk community for urinary schistosomiasis, revealed that; sex, father's occupation and living separately from parents were found to be associated with the disease infection (20). Knowledge, behavior and practices are key factors in schistosomiasis prevalence. knowledge about the schistosomiasis cause, transmission, symptoms and prevention among the rural population in Yemen was found to be inadequate, and that this could be a challenging obstacle to the elimination of schistosomiasis in these communities (21).

Altahir, 2009 (22), revealed that knowledge,

attitude, was significantly improved, and also reveals reduction of Schistosomiasis infection after health education intervention. According to World Health Organization (WHO) reports, based on a study conducted by Balola and Abdul Raheem, 2014 (23). In the study of the schistosomiasis prevalence among school children, in Khartoum state, knowledge of the disease among the interviewed was, 57.1% of the population had poor knowledge about the symptoms of intestinal Schistosomiasis, while 67.1% had poor knowledge about the urinary Schistosomiasis complications, and 69.6% had poor knowledge about intestinal disease complications. The same conclusions also was determined in in Shendi locality by Elawad, 2005 (24)

Ahmed, (2006) (11), reported that, occupation linked to water-contact activities such as fishing, farming, bathing and laundering show high exposure to the diseases. A study conducted by (Eline and Henry,2006) to determine the current status of schistosomiasis infections in the Gazera – Managel Scheme and the impact of the new irrigation system on transmission in Sudan reported that the significant risk factors were farming as the paternal occupation, living in houses built with material other than red bricks, proximity to a water canal, unavailability of water supply and latrines, and past history of infection and treatment (25).

Jember TH., 2014 in Southern Ethiopia, and **Altaher (2009)** in his study about the epidemiology of Schistosomiasis in Kordufan –Su-

dan. He revealed high prevalence of S. haematobium among males (22). Huang, 2005, also reviewed that at an individual level, sex, age, educational level and ethnicity are all associated with different patterns of water use and water contact behaviour thereby affecting infection rates (27). Huang, 2005 also reported that, S. japonicum risk of infection is also influenced by the dominant local environment, including both the distance of house location from the snail-colonized water sources, access to safe drinking water, and the improvement of sanitation status.

Material and Methods

The main objective of this cross-sectional study was to measure Schistosomiasis prevalence among school children in Shendi locality and determine the factors associated with the disease burden

Sample size include 1188 school-age children were randomly selected from the household. Multistage cluster random method was followed to determine the units of the study from their homes in the villages around agricultural schems

Below equation used to derive the sample size:

$$N = Z2 \times PO \div d2$$

N = the desired sample size.

Z = the standard normal deviate, usually set at (1.96) or more simply at (2.0)

P = the proportion in the target population

estimated to have a particular characteristic, (it there are no reasonable estimate, than use 50% or 0.50).

$$Q = 1.0 - P$$

d = the degree of accuracy desired, usually set at 0.05 or occasionally at 0.02

The data were collected by the questionnaires and laboratory investigations of urine. All the study uints (school-age children) were introduced for the study purposes and a written consents taken before the data collection. The collected data were processed, and analyzed using the statistical package for sciences (SPSS). Frequency, Cross tables, parcharge and pie charge used to present the results. The statistical analysis Qui-squier test was used to examin the significant of association between prevalence of schistosomiasis, their influencing factors and potential risk factors.

Results

Among the examined children, 33.3% were found to be infected with haematobiums Schistosomiasis (Figure 1). The infection was higher among males.

Figure (1): Haematobium Schistosomiasis Prevalence by gender among School Age Children in Irrigated Schemes at Shendi locality, Sudan

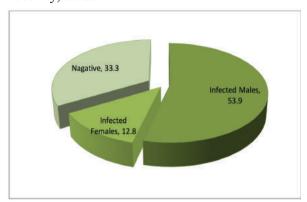


Table (1) shows that the level of knowledge among the Children was poor. About 70.5%, of the children did not know the causative agents. Furthermore, most of the children lacked knowledge about the effects of the diseases, mode of transmission, asymptom of schistosomiasis, predisposing factors, control, prevention measurement, treatment, and factors enhancing the spread of the disease in a percentage crosponding to; 88.5%, 83.4%, 89.7, 88. 7%, 92.2%, 89.1%, 87.2%, and 91.9% respectively.

Table (1): Level of knowledge about Schistosomiasis among the children at school age in Shendi locality, Sudan

		Good		Acceptable		Poor		None	
Children knowledge	No.	%	No.	%	No.	%	No.	%	
Causative agents	4	0.3	160	13.5	187	15.7	837	70.5	
Effects of Schistosomiasis	2	0.2	31	2.6	104	8.8	1051	88.5	
Mode of transmission	7	0.6	23	1.9	167	14.1	991	83.4	
Symptom of Schistosomiasis	7	0.6	16	1.3	99	8.3	1066	89.7	
Schistosomiasis predisposing factors	5	0.4	17	1.4	112	9.4	1054	88.7	
Schistosomiasis control measures	5	0.4	16	1.3	72	6.1	1095	92.2	
Prevention measurement	6	0.5	21	1.8	102	8.6	1059	89.1	
Treatment	3	0.3	45	3.8	104	8.8	1036	87.2	
Factor influence disease spread	1	0.1	14	1.2	81	6.8	1092	91.9	

Table (2) shown that the prevalence of Schistosomiasis was highest among the children those, their families jobs related contacting polluted water by (45.5%), followed by farmers and the least prevalence was among other jobs which did not associ-

ate contact with water. A highly significant association was found between occupation and the prevalence of the schitosomiasis, P-value (0.000)

Table (2): The association between types of occupation for the family head and the prevalence of schistosomiasis in Shendi locality

		Urine Exa	m Results			
Occupation	Positive Negative		ative	Total	P-value	
	No.	%	No.	%		
Farmer	188	39.0%	294	61.0%	482	
Employee	70	45.5%	84	54.5%	154	000
Others	138	25.0%	414	75.0%	552	.000
Total	396		792		1,188	

Table (3) shows that children aged 11-15 years reported the highest prevalence among the other age groups. Most of them contact

canals either for the purpose of playing or help their families.

Table (3): Age distribution for the prevalence of Schistosomiasis in Shendi locality RiverNilestste Sudan

		Urine Exa				
Children age	Positive		Negative		Total	P-value
	No.	%	No.	%		
5-10 years	45	20.5%	174	79.5%	219	
11-15years	276	38.9%	434	61.1%	710	000
16-20 years	75	29.0%	184	71.0%	259	.000
Total	396	33.3%	792	66.7%	1188	

Table (4) shows that children living with compared to those living with only father parents reported highest infection (34.7%) (5.7%) or mother (16.1%).

Table (4): Association between the social status of the children and the prevalence of Schistosomiasis in Shendi locality

Children living status	Pos	sitive	Negative		P-value
	%	No.	%	No.	
Children living with parent	389	34.7%	733	65.3%	
Children living with Father only	2	5.7%	33	94.3%	
Children living with Mather only	5	16.1%	26	83.9%	
Total	396	33.3%	792	66.7%	< 0.000

Figure (2) report that the incidence of the disease increase among the children whom still at school (35.5%) compared to the children whom left the school (26.5%) this might be linked to the nearest distances of the most school from the contaminated water sources.

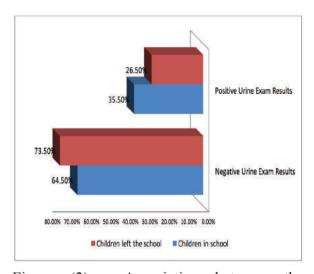


Figure (2): Association between the educational status of children and the prevalence of Schistosomiasis in Shendi locality, Sudan

Table (5) shown that the distances between the bridge which used to cross-over the canal was highly significant in the prevalence of schistosomiasis. Most of the near bridges were poorly constructed by the villagers' member, using local materials such as stones and branches of trees, the children contact with the channel's water while using these types of the bridges to crossover to the other side of the canal. While the well-constructed one which used for crossover found at far distances more than 100 from the residential area of the children. exposure due to canal cross-Regading the over the study revealed that the children those use the good-constructed bridges were found more protected (37.1%) from getting infected compared to those who use the conventional local constructed bridges (62.9%). The distances between the well-constructed bridge schools and village positions were highly significantly associated with the schistosomiasis P-value (0.000)

Table (5): Association from home to open water sources and the distance of the available bridge compared with the prevalence of schistosomiasis in Shendi locality, Sudan

Distance from home to open		Urine Exam Results vs nearest available bridge				Urine Exam Results vs home to open water sources			
water sources and available bridge	Positive		Negative		Positive		Negative		
bridge	No.	%	No.	%	No.	%	No.	%	
>50 meters of distance of the nearest bridge to cross the canals	34	40.5%	50	59.5%	140	38.9%	220	1.3 cm	
50-100 meters of distance of the nearest bridge to cross the canals	215	46.9%	243	53.1%	205	41.8%	285	58.2%	
<100 meters of distance of the nearest bridge to cross the canals	147	22.8%	499	77.2%	51	15.1%	287	84.9%	
Total	396 ((33.3%)	792 (6	66.7%)	396 (3	33.3%)	792 (66.7%)	

Table (6) shown highly significant difference was found between the rates of infection and the frequencies of contact with the canal's

water P-value (< 0.000). The more frequencies contact with the canal water, lead to increase infection among the children.

Table (6): Association between the frequencies of contact with open water sources and the prevalence of Schistosomiasis in Shendi locality, Sudan

Frequencies of open water		D volvo			
Trequencies of open water	Pos	itive	Neg	P-value	
contact	No.	%	No.	%	
Do not contact open water	36	19.3%	151	80.7%	
daily contact	106	31.7%	228	68.3%	
weekly contact	138	38.3%	222	61.7%	
monthly contact	68	30.2%	157	69.8%	
Others period of contact	48	58.5%	34	41.5%	
Total	396	78%	792	22%	< 0.000

Discussion:

The prevalence of schistosomiasis diseases among the pupils seems to be increasing in the River Nile state which might be due to increase the number of investments in irrigated agriculture schemes in the area. Altahir MN, 2009 revealed the same finding from his study conducted among primary school children determined that; the prevalence rate among the pupils was found to be 37.5%. The high prevalence of schistosomiasis expects to burden hard effects upon the student health and their productivity levels (22).

The results in table (1) refelect that most of children lacked knowledge about the effects of the diseases, mode of transmission, asymptom of schistosomiasis, predisposing factors, control, prevention measurement, treatment, and factors enhancing the spread of the disease. These results are going with the Elawadb KH, 2005 mentioned (24). WHO, 2014 re-

ported (25), the same results about knowledge of schistosomiasis, symptoms, and complications. This report also concluded that the disease prevalence in Khartoum was very high, even though knowledge about the disease was poor. The same conclusions also were determined by Jember TH, 2014 (26), and Huang y, 2005 (27), but some results observed that sometimes exposure was occurring not due to poor or lack of knowledge only, but could be linked with the lack of other safe or protected alternatives.

The occupations of the family in Shendi were enhancing the spread of schistosomiasis infection. Contact with the open-water of the irrigation channels is the main sources of the disease infection. Table (2) results go with what Afifi A, Ahmed AA, Sulieman Y, Pengsakul T, reported (2009) (11), that, occupation related to water-contact activities such as fishing, farming bathing and laundering showed

high exposure to the diseases. The same results presented by (Eline and Henry, 2006) reported that the significant risk factors were farming as the paternal occupation (25).

The higher prevalence of the disease among males compared to females in the area showed in figure (1) may be associated with social and cultural factors. This result is similar to the results reported by (Tadesse, 2014) (28), Altahir MN(22). reported 2009 and similar to what Huang y, 2005, reported which showed that males had high levels of both prevalence and intensity (27).

As in Table (3) the distribution of the disease by age was highly significant P-value (0.000). (22) Altahir MN, 2009 reported similar results (22). Elawadb KH, 2005 (24), from his study conducted among primary school children also conducted that; the higher infestation was found among the 10-14 group, and 5-9 came next 28.9%, followed by the age group greater than 15 years 26.1%. Similar findings stated by Huang y, 2005 (27), Altahir MN.,2009(22) and Tadesse, 2014 (28).

Table (4) shown that the social status of the Children were highly significant P-value (0.000) associated with the disease prevalence. When the child lives with one of the parents, he/she knew that the care of the child exclusively his responsible, while when he lives with the parents, each depends on the other to care about the child.

Figure (2) report that, educational status was very significantly associated with the preva-

lence of the disease P-value (0.003)

Results in Table (5) & Table (6) were similar and sometimes identical with what was reported by Huang, 2005 (30), Elawad, 2005 and also goes with what reported by, (22) Altahir MN., 2009 (22) and Tadesse, 2014 (28).

Conclusions

Prevalence of schistosomiasis is increasing among the population in the Shendi locality. The prevalence of schistosomiasis was highest among males and age group of 11-15 years. The gender variation in the prevalence of schistosomiasis was associated with the dominant culture in the area, that male responsible for providing family needs and they were more exposed to the risk factors of the disease incidence (e.g., contact with polluted water).Lack of knowledge about the disease among children and their families, living near open water sources and the distance of bridge from schools and houses was most influencing factors for the disease prevalence. We can conclude that, ecological and behavioral factors are very significantly associated with the schistosomiasis prevalence.

Institutions are recommended to support for the local schitosomiasis control program and raise awareness of the community in infested villages to improve their lifestyle and to prevent the incidence of schitosomiasis. Environmental factors manipulations need to take top priority for the local schitosomiasis control program such as building bridges and provide other sanitation measures to prevent the contact with contaminated water.

References

- [1] Parija SC. Textbook of Medical Parasitology ... 2014;6(1):58–59. [PMC free article] [PubMed]
- [2] AfricaTawanda Manyangadzea,*, Chimbaria MJ, Gebreslasieb M, Mukaratirwac S. Risk factors and micro-geographical heterogeneity of Schistosomahaematobium in Ndumo area, uMkhanyakude district, KwaZulu-Natal,South Africa. Acta Tropica 159 (2016) 176–184
- [3] WHO, schistosomiasis fact sheet; 2014. Available from:http://www.who.int/mediacentre/factsheets/fs115/en [accessed 10.11.15].
- [4] Terer CC, Bustinduy AL, Magtanong RV, Muhoho N, Mungai PL, et al. Evaluation of the Health-related Quality of Life of Children in Schistosoma haematobium-endemic Communities in Kenya: A Cross-sectional Study. PLoS Negl Trop Dis 2013; 7(3): e2106. doi:10.1371/journal.pntd.0002106 Editor: Amadou Garba, Ministe`re de la Sante´ Publique et de la Lutte contre les Ende´mies, Niger
- [5] Schistosomiasis: number of people treated worldwide in 2013. Wkly Epidemiol Rec 2015; 90(5):25–32. PMID: 25638822
- [6] Colley DG, Bustinduy AL, Secor WE, King CH. Human schistosomiasis. Lancet. 2014 Jun 28;383(9936):2253–64.

- doi: http://dx.doi.org/10.1016/ S0140-6736(13)61949-2 PMID: 2469848.
- [7] King CH. Toward the elimination of schistosomiasis. N Engl J Med 2009; 360(2): 106-9
- [8] Okwori AEJ, Sidi M, Ngwai YB, Obiekezie SO, Makut MD. Prevalence of schistosomiasis among primary school children in gadabuke district,toto lga, north central nigeria. BMicroRJ 2014; 4(3): 255-261.
- [9] Agrawal MC. Schistosomes and schistosomiasis in south asia. springer india 2012.
- [10] Afifi A, Ahmed AA, Sulieman Y, Pengsakul T. Epidemiology of Schistosomiasis among Villagers of the New Halfa Agricultural Scheme, Sudan. Iran J Parasitol 2009; 11(1) 110-115.
- [11] WHO. Informal consultation on expanding schistosomiasis control in Africa. Geneva: World Health Organization 2015;, http://www.who.int/schistosomiasis/epidemiology/PZQ_WHO_report. 2015.
- [12] Ying-Si L, et al. Spatial distribution of schistosomiasis and treatment needs in sub-Saharan Africa: a systematic review and geostatistical analysis, The Lancet Infectious Diseases 2015; 15 (8) 927–940
- [13] WHO, Health education in the control of schistosomiasis. Geneva: world health

organization 1999.

- [14] [15] WHO, Regional Office for the Eastern Mediterranean. Annual report of the regional director (1 January–31 December 2003). Cairo: WHO EMRO. 2004.
- [15] Garcia LS. Practical guide to diagnostic parasitology. 2nd Ed. 2009; USA.ISBN 978-1-55581-454-0. Library of Congress Cataloging-in-Publication Data.
- [16] Hotez PJ, Kamath A. Neglected Tropical Diseases in Sub-Saharan Africa: Review of Their Prevalence, Distribution, and Disease Burden. PLoS Negl Trop Dis 2009; 3(8): e412. doi:10.1371/journal.pntd.0000412
- [17] Amuta EU, Houmsou RS. Prevalence, intensity of infection and risk factors of urinary schistosomiasis in preschool and school aged children in Guma Local Government Area, Nigeria. Houmsou/Asian Paci J of Tropic Medi 2014;34-39
- [18] Ismail HAHA, et al. Prevalence, risk factors, and clinical manifestations of schistosomiasis among school children in the White Nile River basin, Sudan. Parasites & Vectors 2014; 7:478 http://www.parasitesandvectors.com/content/7/1/478
- [19] Geletal S, Alemu A, Getie S, Mekonnen Z, and Erko B. Prevalence of urinary schistosomiasis and associated risk factors among Abobo Primary School children in Gambella Regional State, southwestern Ethiopia: a cross sectional study. Geleta et

- al. Parasites & Vectors 2015; 8:215 DOI 10.1186/s13071-015-0822-5
- [20] Sady H, et al. Knowledge, attitude, and practices towards schistosomiasis among rural population in Yemen. Parasites & Vectors, 2015; 8:436 DOI 10.1186/s13071-015-1050-8
- [21] Altahir MN. The prevalence of Schistosomiasis Among Basic schools pupils in Kejara –south Kordofan State: a thesis submittedin partial fulfillment for the degree of MPEH (Public health) 2009; U of K.
- [22] Balola1 HA, and Abdul raheem EM. Assessment of knowledge and attitude among khartoumpopulation regarding schistosomiasis. Int j of pure and appl sci and technol 2014; 1-7.
- [23] Elawadb KH. The Prevalence of Schistosomiasis among primary School Children in Barakat area-Gezira State 2005; U of K, Sudan
- [24] Eline B, Henry M. Irrigation and Schistosomiasis in Africa: Ecological Aspects., 2006. ISBN 978-92-9090-631-5 by IWMI.
- [25] Jember TH. Review Challenges of schistosomiasis prevention and control in Ethiopia: Literature review and current status. J Parasitol Vector Biol 2014; 6(6): 80-86.
- [26] Huang y. The social and economic

context and determinants of schistosomiasis japonica. Acta tropica, 2005; 223-231

[27] Grimes JET, Tadesse G, Mekete K, Wuletaw Y, Gebretsadik A, French MD, et al. (2016) School Water, Sanitation, and Hygiene, Soil-Transmitted Helminths, and Schistosomes: National Mapping in Ethiopia. PLoS Negl Trop Dis 10(3): e0004515. doi:10.1371/journal. pntd.0004515

Original Article

Prevalence of Major Depression Among Types II Diabetes: A Cross Sectional Study In Riyadh, Saudi Arabia

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Abstract:

Background: Depression is the second most prevalent disorder seen by the doctors of the primary care. Early diagnosis and proper management of this depression significantly reduce its adverse effects.

Aim: To determine the prevalence of major depressive symptoms among patients with type II diabetes, compare the prevalence between diabetic and non-diabetic patients and determine the associated factors.

Methods: It is a cross-sectional study that was conducted in Al Imam Mohammed Ibn Saud Islamic University medical center in Riyadh, during the interval from November 2017 to January 2018. In which we used a patient health questionnaire-9 that was administered to randomly selected diabetic and non-diabetic patients. This survey included 200 diabetic type II and 241 non-diabetic participants who anonymously completed the questionnaires. Data were analyzed using SPSS-16 and chi-square test was used to assess the statistical association.

Results: The percentage of major depression among diabetics was 38.5%, whereas it was 26% among non-diabetic participants with odds ratio of 1.7 (p = 0.007). The percentage of diabetic females suffering from major depression was higher (45%) than the percentage of diabetic males suffering from depression (32%). Diabetic patients who were living alone were more liable to have depression than those who were living with their spouses (OR 2.97; p = 0.001)

Conclusion: Over than one third of diabetics and one fourth of non-diabetics were detected to have major depressive symptoms. Diabetes type II and being single are significantly associated with the prevalence of depression.

Keywords: depression, Major depressive symptoms, type-II diabetics.

الملخص

خلفية: الاكتئاب هو ثاني الأمراض الأكثر شيوعاً التي يراها الأطباء بوحدات الرعاية الأولية، خصوصاً بين مرضى السكري. إن التشخيص المبكر والعلاج لهذا الاكتئاب يقلل من آثاره السلبية بشكل كبير.

الأهداف: تهدف الدراسة الى تحديد مدى انتشار أعراض الاكتئاب الرئيسية لدى مرضى السكري من النوع الثاني مقارنة بأولئك الذين لا يعانون من مرض السكري. وكذلك معرفة العوامل التي تؤدي لحدوث ذلك الاكتئاب

طريقة الدراسة: هذه در اسة مقطعية اعتمدت على استبيان خاص بصحة المرضى والذي تم توزيعه على مجموعة من المرضى والذي تم توزيعه على مجموعة من المرضى والذين لا يعانون يعانون من مرض السكري من النوع الثاني وكذلك الذين لا يعانون منه، والذين تم اختيار هم عشوائياً. أُجريت هذه الدراسة بالمركز الطبي لجامعة الإمام محمد بن سعود الإسلامية بمدينة الرياض، وذلك خلال الفترة من نوفمبر ٢٠١٧ إلى يناير ٢٠١٨. اشتملت الدراسة على ٢٠٠ مريض يعانون من مرض السكري من النوع الثاني، و ٢٤١ مريض لا يعانون من مرض السكري. تم تجميع البيانات وتحليلها ودراسة العلاقات الإحصائية بينها.

النتائج: بلغت نسبة انتشار أعراض الاكتئاب الرئيسية لدى مرضى السكري (٣٨,٥٪، بينما بلغت ٢٦٪ في المشاركين الذين لا يعانون من مرض السكري (القيمة الاحتمالية ٢٠،٠٠٠). معظم النساء المصابات بمرض السكري يعانين من الاكتئاب مقارنة بالرجال حيث كانت نسبة الاحتمال ٢٠،٠ والقيمة الاحتمالية ٢٠٥٠. وجدت الدراسة أن مرضى السكري الذين يعيشون بمفردهم أكثر عرضة للإصابة بالاكتئاب مقارنة بأولئك الذين يعيشون مع أزواجهم حيث كانت نسبة الاحتمال ٢٠,٠٠٠

الخلاصة: يعاني أكثر من ثلث مرضى السكري وكذلك ربع المرضى الذين لا يعانون منه من النوع الثاني الذين لا يعانون منه من النوع الثاني وكذلك الحياة بدون شريك بشكل كبير على معدل انتشار الاكتئاب. الكلمات المفتاحية: الاكتئاب، الأعراض الأساسية للاكتئاب، مرض السكرى من النوع الثاني.

Introduction

Depression is the second most prevalent chronic disorder seen by the doctors of the primary care. [1,2] In the United States, nearly seventy five percent of individuals who require care for depression, go to the doctors of primary care instead of mental health professionals. Persons who are suffering from major depressive symptoms may develop impairment of functional activities and this leads to decrease their productivity power. There is increase in their health care expenses and they are more liable to suicide. Complaints as sleep disruption, exhaustion and general pain are the most prevalent presentations of depressed patients seen by family physicians. [3] Recognizing depression among patients in a primary care centers may be difficult issue because patients, especially men, rarely talk about their emotional problems. [4] Therefore, family physicians may be unsuccessful to detect about 30 to 50% of patients suffering from major depressive episodes. [5, 6] Studies have shown that early diagnosis and proper management significantly reduce the adverse effects of depression in most patients. [7]

Previously, it was proposed that there is a relation between depression and the risk of diabetes. This relation has been confirmed in the recent times by Eaton et al. [8] and Kawakami et al. [9] whom studies confirmed elevation of the incidence of type II diabetes in those patients who were suffering from the symptoms of depression initially. Both studies suggest that depression may occur before the onset

of type II diabetes and possibly has a role in its occurrence. These studies confirmed that major depressive symptoms may progress to type II diabetes i.e. they have a major role in its development.

The ability of the body to deal with excess carbohydrate may be impaired by the increased release of counter-regulatory hormones that occurs in depression, and this could increase the risk type II diabetes development. Major depressive symptoms may increase the risk of evolving type II diabetes either through changes in eating habits or physical activities or due to the drugs used for their treatment. [8]

A well-established way to measure major depression is by a survey which is usually achieved by short, easily administered questionnaire that provides information and insight on patients' symptoms. The aim of this study was to evaluate the prevalence of depression in patients suffering from diabetes type II as well as non-diabetic patients who presented to the clinics of family physicians.

Patients And Methods

This is a cross sectional study that has been approved by the Family Medicine Research Committee and the IRB of Al-Imam Muhammad Ibn Saud Islamic University, in session number 21, the number of this ethical approval is 23-2019. It was performed during the period of November 2017 - January 2018 at the family medicine clinics of Al Imam Mohammed Ibn Saud Islamic University medical center in Riyadh. Confidentiality of the pa-

tients was highly respected and therefore no identifying marks were in the questionnaire. An informed consent has been obtained from each participating patient before sharing in this study and their role in sharing by filling the questionnaire has been explained to them.

A total of 441 adult subjects were chosen randomly by using systematic random technique by odd numbers of diabetic and non-diabetic patient's list. The American Diabetic Association criterion was used for the diagnosis of Diabetes mellitus. [10]

Participating patients were interviewed by well-trained medical students after their acceptance to share in the study.

The first portion of the questionnaire consisted of demographic data including (age, gender, marital status, education level, is the patient diabetic or not, and diabetes duration). In the second part, Patient Health Questionnaire-9 was used for diagnosis of depressive symptoms. The 9 items in this instrument are based on the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV) diagnostic criteria. [11] We used English as well as Arabic versions of Patient Health Questionnaire-9, which has been validated and tested in primary care settings in Arab countries. [12]

Each one of the 9 questions were scored from 0 to 3 which means (not at all) and (nearly every day) respectively. So, PHQ-9 score ranges 0 to 27, which has been used as a measure for the severity of disorder. We used the cut

points of 5 which means mild disorder, 10 which means moderate disorder, 15 which means moderately severe disorder and 20 which means severe depression. They have been used to assess the threshold of depression. Major depression is diagnosed when the patient has a total score of 10 or more and so it is an indication for the need to start treatment. [13]

Data were entered and analyzed by Statistical Package for Social Sciences (SPSS) with statistical significance at P value (<0.05) a confidence level of 95%. Descriptive analysis including frequencies, percentages of the study variables were carried out. Chi-square test was used to measure statistical association.

Results

Among 441 patients, the ratio of male to female was 1:1.4 (41.5% Vs 58.5%) in non-diabetics while it was 1:1 (50% Vs 50%) in diabetics.

The total diabetic patients were 200 (45.4%) with the mean age of 49.4 (SD 11.2) ranging to 28 – 77 years, whereas the average age of 241 (54.6%) non-diabetic participants was 42.4 (SD 11.8) ranging 23-75 years. Further characteristics of participants are revealed in **table 1**

Table 1: Demographic Information of study population

Characteristics	Diabetic patients (n=200)	Non-Diabetic patients (n=241)
Age		
Mean ±SD	49.4±11.2	42.48±11.8
Marital status		
Single	13 (6.5%)	42 (17.5%)
Married	156 (78%)	162 (67%)
Widow	24 (12%)	24 (10%)
Divorced	7 (3.5%)	13 (5.5%)
Education		
Illiterate	60 (30%)	37 (15.4%)
Educated	140 (70%)	204 (84.6%)
Depression as per PHQ-9 score criteria	77(38.5%)	63(26%)

Out of 200 diabetic patients, 77 (38.5%) of 10 or higher), while 35.5% had minimal screened positive for clinically signifidepressive symptoms (PHQ -9 score less than 10) as revealed in **table -2**.

Table 2: Different levels of depressive disorder among diabetic patients, as per PHQ-9 severity score

Provisional Diagnosis	N (%)
Community normal	52 (2(0/)
(PHQ-9 scores <5)	52 (26%)
Mild depressive symptoms	71 (25 50/)
(PHQ-9 scores 5 - <10)	71 (35.5%)
Major depression, Moderate symptoms	21 (10.5%)
(PHQ-9 scores 10 - 14)	21 (10.5 %)
Moderately severe Major depression	40 (20%)
(PHQ-9 scores 15 - 19)	40 (20 /0)
Severe Major depression	16 (90/.)
(PHQ-9 scores ≥20)	16 (8%)
Total	200 (100%)

Of those who have significant depressive symptoms, 21 (10.5%) had PHQ-9 scores between 10 and 14 (moderate depressive symptoms), 40 (20%) had scores between 15 and 19 (moderately severe major depression) and 16 (8%) had scores of 20 and above (severe major depression) as shown in table 2.

Seventy-seven (38%) diabetic patients were depressed as compared with 63 non-diabetic patients (26%) p=0.007 and odds ratio 1.7

(95% C.I. 1.16 - 2.7). Most of diabetic females (45%) were suffering from depression as compared to diabetic males (OR 1.7) but this difference was not statistically significant (p=0.059) (95% CI 0.94 – 3.22). Depression was also significantly more common among diabetic patients living alone as compared to those diabetics who were living with their spouses (52.9% Vs 33%); P=0.001, as shown in table 3.

Table 3: Prevalence of depression among diabetics and non-diabetic patients and factors related with depression among diabetic patients

Major Depression	No Major		P				
(%)	Depression		1				
Participants (n=4	41)						
77 (38.5%)	123 (61.5%)	1.76	0.007				
63 (26%)	178 (74%)] 1./6	0.007				
Gender of diabetics(n=200)	•					
45 (45%)	55 (55%)	1.74	0.059				
32 (32%)	68 (68%)	1./4	0.059				
ion of diabetes in ye	ears (n=200)						
22 (40.75%)	32 (59.25%)	1 1 4	0.603				
55 (37.7%)	91 (62.3%)	1.14	0.692				
abetic's Age in years	s (n=167)						
48 (38.4%)	77 (61.6%)	1 22	0.420				
14 (33.3%)	28 (66.7%)	1.33	0.439				
Diabetic's Education(n=200)							
24 (40%)	36 (60%)	1.00	0.775				
53 (37.9%)	87 (62.1%)	7 1.09	0.775				
Diabetic's Spouse Company(n=167)							
18 (52.94%)	16 (47.06%)	2.07	0.001				
44 (33%)	89 (67%)	7 2.97	0.001				
	(%) Participants (n=4) 77 (38.5%) 63 (26%) Gender of diabetics(45 (45%) 32 (32%) ion of diabetes in years 22 (40.75%) 55 (37.7%) hetic's Age in years 48 (38.4%) 14 (33.3%) iabetic's Education 24 (40%) 53 (37.9%) etic's Spouse Compa	Company (n=200) Participants (n=441) 77 (38.5%) 123 (61.5%) 63 (26%) 178 (74%) Gender of diabetics(n=200) 45 (45%) 55 (55%) 32 (32%) 68 (68%) ion of diabetes in years (n=200) 22 (40.75%) 32 (59.25%) 55 (37.7%) 91 (62.3%) abetic's Age in years (n=167) 48 (38.4%) 77 (61.6%) 14 (33.3%) 28 (66.7%) iabetic's Education(n=200) 24 (40%) 36 (60%) 53 (37.9%) 87 (62.1%) etic's Spouse Company(n=167) 18 (52.94%) 16 (47.06%)	Correction Cor				

Discussion

Depression is a common medical problem that frequently coexists with Diabetes Mellitus (DM). [14] Reports indicated that >25% of

patients with DM reached clinical criteria for depression. [15] Many explanations account for this finding that have been integrated into 3 hypotheses. [16, 17] The first one is that the disease severity and different management mo-

dalities represent a load on patients and affect their normal daily life. The second one is that the long-term duration of the disease and its associated complications produce a chronic continuous stress on the patient, which affects the quality of his life. The third one is that DM and depression are portions of a related group of metabolic disorders. Individuals suffering from depression have negligence of self-care, which in result leads to low compliance with receiving their diet and treatments. Diabetes mellitus is an illness that needs significant compliance to diet, medications and exercise and these needs are potentially ignored by depressed patients.

In this primary clinic-based study, we observed a high risk of developing depression individuals suffering from diabetes. The prevalence rate of depression in those patients was 38.5%, which is in accordance with other studies. [18, 19] Study in a western region of Saudi Arabia showed 34% prevalence of depression among diabetic patients. [20]

The results of this study, in alignment with the reported results by Keita [21], showed that the prevalence of depression was higher among women than men. It prevalence is two folds higher in women than men. This statistic has also been observed among women with Diabetes in this study but it was not statistically significant (p-value =0.059). There are some biological and socioeconomic factors that clarify the reason of higher prevalence of depression in the female group such as hormonal changes during pregnancy, postpartum and

premenopausal periods, Genetic vulnerability and being dependent to others. [21]

The educational level is another factor which is associated with the prevalence of depression; where it helps to protect against it. It seems that educated people tend to use health care services more than those who are illiterate. [22] Education would help to lower their trend to unhealthy behaviors such as smoking, obesity and fewer tendencies to crime committing. [23, 24] The study performed by Bjelland I et al [23] showed that high level of education is a protective agent against anxiety and depression although in this study we did not find any relation between depression and the level of education (p-value=0.775).

The study conducted by Palizgir et al [25] revealed that younger individuals had higher level of depression and anxiety than the older ones. This is closely related to the amount of the patients' experience in coping with different situations such as their concerns about their treatment procedure and the challenge of diabetes. The influence of disease on physical and psychological functioning and decreased quality of life resulting from the disease are the factors that increased the ratio of depression and anxiety among younger patients. [25] A study conducted by Zhao et al.[26] to investigate the relationship between the age and depression and it showed that younger adults were more likely to have adolescence-onset diabetes and the prevalence of depression was three folds higher than in the adolescences without diabetes.

But in this study, we have not found any significant correlation between diabetic patient age, duration of diabetes and the prevalence of depression among them.

Another interesting finding is the higher prevalence of depression among patients who are living alone in comparison with those living with a partner (OR = 2.97, P = 0.001).

Conclusion

More than one third of diabetics and one fourth of non-diabetics were found to have major depressive symptoms. Diabetes type II and living alone is significantly associated with depression. These findings reflect the importance of screening such patients for depression and educational efforts directed to medical team who treat patients with diabetes mellitus type-II

The study recommends that early detection of depression among diabetics. Prompt intervention by treating depressed diabetic patients would improve the overall outcome among those patients.

Current evidence-based guidelines are required to be applied in order to guide practitioners in the detection and treatment of depression in diabetic patients.

Family physicians should work "hand in hand" with the psychiatrist to improve detection and treatment of depression among diabetics and the population in general. Further research should focus on the impact of depression and how it impairs functioning, quality of life, the development and exacerbation of diabetic complications.

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Conflict of interest

I have no conflict of interest with any one regarding this research to declare.

References

- [1] Wells KB. Caring for depression. Cambridge, Mass.: Harvard University Press, 1996
- [2] Grandinetti A, Kaholokula JK, Crabbe KM, Kenui CK, Chen R, Chang HK. Relationship between depressive symptoms and diabetes among native Hawaiians. Psychoneuroendocrinology. 2000 Apr;25(3):239-46
- [3] Preboth M. Clinical review of recent findings on the awareness, diagnosis and treatment of depression. American family physician. 2000 May 15; 61(10):3158-60.
- [4] Suh T, Gallo JJ. Symptom profiles of depression among general medical service

- users compared with specialty mental health service users. Psychol Med 1997; 27:1051-63.
- [5] Weissman MM, Leaf PJ, Tischler GL, Blazer DG, Karno M, Bruce ML, et al. Affective disorders in five United States communities. Psychol Med 1988; 18:141-53.
- [6] Simon GE, VonKorff M. Recognition, management, and outcomes of depression in primary care. Arch FAM Med 1995; 4:99-105.
- [7] Coulehan JL, Schulberg HC, Block MR, Madonia MJ, Rodriguez E. Treating depressed primary care patients improves their physical, mental, and social functioning. Arch Intern Med 1997; 157:1113-20.
- [8] Eaton W, Armenian H, Gallo J, Pratt L, Ford DE: Depression and risk for onset oftype II diabetes. Diabetes Care 19:1097–1102, 1996
- [9] Kawakami N, Takatsuka N, Shimizu H, Ishibashi H: Depressive symptoms andoccurrence of type 2 diabetes among Japanese men. Diabetes Care, 1999; 22:107–116.
- [10] American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care. 2010 Jan; 33(Suppl 1): S62–S69.
- [11] American Psychiatric Association.

- The Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV). 1400 K Street, N.W., Washington, DC 20005. Chapter 5: Mental Disorders Due to a General Medical Condition, p.165-74.
- [12] Becker S, Al Zaid K, and Al Faris E: Screening for somatization and depression in Saudi Arabia: a validation study of the PHQ in primary care. Int J Psychiatry Med 2002; 32:271-283
- [13] Ramona S DeJesus, Kristin S Vickers, Gabrielle J Melin, Mark D Williams. A System-Based Approach to Depression Management in Primary Care Using the Patient Health Questionnaire-9, Mayo Clinic Proceedings 2007; 82: 1395- 1403.
- [14] Gavard JA, Lustman PJ, Clouse RE. Prevalence of depression in adults with diabetes: an epidemiological evaluation. Diabetes Care 1993; 16: 1167-1178
- [15] Lustman PJ, Anderson RJ, Freedland KE, de Groot M, Carney RM, Clouse RE. Depression and poor glycemic control. Diabetes Care 2000; 23: 934-942.
- [16] Peyrot M, Rubin RR. Levels and risks of depression and anxiety symptomatology among diabetic adults. Diabetes Care 1997; 20: 585-590.
- [17] Talbot F, Nouwen A. A review of the relationship between depression and diabetes in adults. Diabetes Care 2000; 23: 1556-1562.

- [18] Ali S, Stone M, Peters JL, Davies MJ, Khunti K. The prevalence of co-morbid depression in adults with type 2 diabetes: a systematic review and meta-analysis. Diabetic Medicine 2006; 23(11):1165-1173.
- [19] Nichols GA, Brown JB. Unadjusted and adjusted prevalence of diagnosed depression in type 2 diabetes. Diabetes Care 2003; 26:744-749.
- [20] A. Al-Ghamdi, A high prevalence of depression among diabetic patients at a teaching hospital in western Saudi Arabia. Neurosciences 2004; 9:108-112.
- [21] Keita GP. Psychosocial and cultural contributions to depression in women: considerations for women midlife and beyond. J Manag Care Pharm. 2007; 13(9 Suppl A):S12-5.

- [22] Type 2 Diabetes: Practical Targets and Treatments. 4 ed. International Diabetes Institute (IDI); 2005.
- [23] Bjelland I, Krokstad S, Mykletun A, Dahl AA, Tell GS, Tambs K. Does a higher educational level protect against anxiety and depression? The HUNT study. Soc Sci Med. 2008; 66(6):1334-45.
- [24] Steele LS, Dewa CS, Lin E, Lee KL. Education level, income level and mental health services use in Canada: associations and policy implications. Healthc. Policy. 2007; 3(1):96-106.
- [25] Maryam Palizgir, Maryam Bakhtiari, Alireza Esteghamati Iranian Red Crescent Medical Journal. 2013 August; 15(8): 644-8.
- [26] Zhao W, Chen Y, Lin M, Sigal RJ. Association between diabetes and depression: Sex and age differences. Pub health. 2006; 120(8):696-704.

Original Article

The Effect of Smoking on Health-Related Quality of Life (HRQoL) in Adult Patients of Arthritis

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Abstract

Background & Aims: Arthritis is an inflammation infects any joint of the body or tissues around that joint. As any disease, arthritis has an effect on health-related quality of life (HRQoL) in adult patients. Although many researches showed how smoking can worse the condition of arthritis as a disease, there is not a specific study investigated the effect of smoking on HRQoL in adult patients of arthritis, which is the goal of this study.

Methods: This study used a publicly open data source from the 2017-Behavioral Risk Factor Surveillance System (BRFSS) in the United States. It is a health survey using the telephone in order to collect data from the United States residents. There were 450,013 participants in this survey. Different descriptive, inferential, and predictive analysis methods were used by the Statistical Analysis System (9.4 version) to achieve the goal of this study. Results: There were 450,013 participants in 2017-BRFSS, 147,288 of them were adult patients of arthritis. 63,466 of these participants in BRFSS-2017 were current smokers. 13,542 of these smokers were adults patients of arthritis.

Results: this study showed a statistically significant effect of the association between arthritis and smoking on activity limitations, physical health problems, and mental health problems.

Conclusion: Smoking has a great effect on health-related quality of life (HRQOL) in adult patients of arthritis. Smoking increased each of the activity limitations in adult patients of arthritis by 164%, physical health problems by 34.75%, mental health problems by 20.58% in adult patients of arthritis.

Keywords: Arthritis; Smoking; HRQoL; BRFSS; SAS Analysis.

Introduction

Arthritis, in general, is an inflammation infects any joint of the body or tissues around that joint. More than 100 kinds of

الملخص:

الخلفية والأهداف: التهاب المفاصل هو التهاب يصيب أي مفصل في الجسم أو الأنسجة حول هذا المفصل. مثل أي مرض، التهاب المفاصل له تأثير على جودة الحياة الصحية للمرضى البالغين. بالرغم ان بعض الدراسات أظهرت كيفية تأثير التدخين على زيادة سوء التهاب المفاصل كمرض، فإنه لا توجد دراسة محددة حققت في تأثير التدخين على جودة الحياة الصحية للمرضى البالغين المصابين بالتهاب المفاصل وهذا هو الهدف من هذه الدراسة

طريقة البحث: استخدمت هذه الدراسة مصدر بيانات متوفر للعامة من نظام مر اقبة عوامل الخطر السلوكية لعام ٢٠١٧ في الولايات المتحدة الأمريكية والتي هي عباره عن استبيان صحى باستخدام الهاتف من أجل جمع البيانات من سكان الولايات المتحدة. كان هناك ١٣٠ . ٥٠٠ مشارك في هذا الاستبيان. تم استخدام طرق التحليل الوصفي والاستدلالي والتتبئي المختلفة بواسطة نظام التحليل الإحصائي (الإصدار ٩٠٤) لتحقيق هدف هذه الدراسة. النتائج: كان هناك ١٣٠٠، ٤٥٠ مشارك في هذا الاستبيان ١٤٧,٢٨٨ منهم مرضى بالغين يعانون من التهاب المفاصل ٢٦٦ . ٦٣ من هؤ لاء المشار كين في الاستبيان كانوا مدخنين حاليين. وكان ١٣٠٥٤٢ من هؤلاء المدخنين مرضى بالغين يعانون من التهاب المفاصل أظهرت نتائج هذه الدر اسة وجود تأثير ذو دلالة إحصائية للعلاقة بين التهاب المفاصل والتدخين على قصور النشاط، ومشاكل الصحة البدنية، ومشاكل الصحة العقلية لهؤلاء المرضى. الخلاصة: التدخين له تأثير كبير على جودة الحياة الصحية لمرضى التهاب المفاصل البالغين. زاد التدخين من قصور النشاط لدى مرضى التهاب المفاصل البالغين بنسبة ١٦٤٪، ومشاكل الصحة البدنية بنسبة ٣٤.٧٥ ٪، ومشاكل الصحة العقلية بنسبة ٢٠.٥٨ ٪ في المرضي البالغين المصابين بالتهاب المفاصل

arthritis can infect the human body. Some of these kinds infect only joints while other kinds can infect the immune system or other internal organs of the human body. [1,2]

However, the most common types of arthri-

tis in the United States include osteoarthritis, rheumatoid arthritis, fibromyalgia, and gout. Common symptoms of arthritis may include pain, reduction in motion, stiffness, redness, and swelling. [1,2]

According to the Centers for Disease Control and Prevention (CDC) and Johns Hopkins Arthritis Center, there were around 42.7 million adult patients of arthritis in the United States in 1995. [3] In 2015, this number increased to be around 54.4 million adult patients of arthritis in the United States. [1] By 2020, the expected number of adult patients of arthritis in the United States would raise to be 59.4 million. [3] Thus, the total of adult patients of arthritis in the United States increased by around 16.7 million in 25 years.

Although many physicians and scientists believe certain genetics and environmental factors may lead or worsen several types of arthritis, specific causes to cause or worsen a specific type of arthritis remain unknown. ^[1,2]

One of these environmental factors is smoking. ^[4] According to the World Health Organization (WHO) in 2017, smoking is accountable for the death of more than 7 million individuals per year. ^[5] In addition, WHO stated that if the manner of smoking in the world continues the same, by 2030 more than 8 million people would die per year. ^[6]

Smoking can cause many diseases including; heart diseases and lung cancer. Moreover, it has the ability to damage many organs of the human body. [7,8] While some researchers stat-

ed that smoking is a fundamental risk factor for certain types of arthritis, there are many researchers found that smoking can worsen arthritis conditions in many ways. [9,10]

Since that arthritis is an inflammation infects any joint of the body or tissues around that joint. According to Hosseinzadeh and his team in 2016, smoking has the ability to increase inflammation in the body by activating neutrophils (white blood cells) leading to increased inflammation and then worsen the condition of arthritis [11].

Health-related quality of life (HRQoL), in general, means measuring the effect of a specific disease, condition, or any other factors on the functions and health of the human body. The goal of measuring HRQoL is to assess patient's health and life from the patient's perspective. [3] Although there are many researches showed how smoking can worse the condition of arthritis as a disease, [3,9,10,12] there is not a specific study yet investigated the effect of smoking on HRQoL in adult patients of arthritis including activity limitations, physical health problems, and mental health problems, which is the purpose of this study.

Materials and Methods

Data source: This study used publicly open data source from the 2017 Behavioral Risk Factor Surveillance System (BRFSS) from Centers for Disease Control and Prevention (CDC) in order to investigate the effect of smoking on health-related quality of life (HRQoL) in adult patients of arthritis for both genders.

BRFSS data is the first national approach of health surveys in using the telephone in order to collect data from the United States residents in relation to their health and behaviors. Population of this data used for this study include adult patients of arthritis (18 – 65 years old), both genders as well as different races form all the states of the United states. ^[13] BRFSS is a source data that collects data about different types of diseases as well as behavioral, and social factors that can affect the quality of life in different patients.

Variables: This study based on two questions as predictor variables and three questions as indicator variables. Predictor variable questions include; 1) having arthritis (HAVARTH3), and 2) currently a smoker (SMOKDAY2). In contrast, HRQoL indicator variables questions include; 1) self-assessment of having activity limitations (LMTJOIN3), 2) self-assessment of having physical health problems (PHYSHLTH) and, 3) self-assessment of having mental health problems (MENTHLTH).

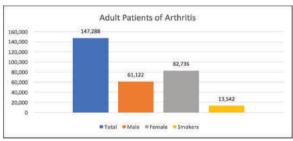
Statistical Analysis: Various descriptive, inferential, and predictive analysis methods were used by the Statistical Analysis System (SAS-9.4 version) to achieve the goal of this study. After cleaning the data, different methods of frequency distributions were used to describe the variables of the study. Then, by choosing the significance level to be ($P \le 0.05$), conducting inferential analysis, by using Chi-Square test, to check the association between these variables is the most important step. Finally, by using a meth-

od of predictive analysis, logistic regressions, relation among the variables of this study can be confirmed and the differences percentage can be calculated.

Results

There were 450,013 participants in 2017-Behavioral Risk Factor Surveillance System (BRFSS), 147,288 of these participants were adult patients of arthritis (18 years and older). 61,122 these patients are males and 82,736 are females. 63,466 of these participants in BRFSS-2017 were current smokers. 13,542 of these smokers were adults patients of arthritis (figure 1).

Figure 1: Distribution of adult patients of arthritis



Moreover, there were 69,913 non-smokers adult patients of arthritis with activity limitation while smokers' adult patients of arthritis with activity limitation were 11,461 (table 1). Also, there were 120,235 non-smokers adult patients of arthritis with physical health problems while smokers' adult patients of arthritis with physical health problems were 12,931 (table 1). However, for mental health problems, there were 32,660 non-smokers adult patients of arthritis with mental health problems while smokers' adult patients of arthritis with mental health problems while smokers' adult patients of arthritis with mental health problems were 8,231 (table 1).

Table 1: Distribution of adult patients of arthritis by activity limitations, physical health problems, and mental health problems

Distribution of adult patients of arthritis						
Variables		Non-smokers with arthritis	Smokers with arthritis			
	Male	31,371	6,612			
Activity limitations	Female	38,542	4,849			
	Total	69,913	11,461			
	Male	57,361	7,538			
Physical health problems	Female	62,874	5393			
	Total	120,235	12,931			
	Male	11,724	4,821			
Mental health problems	Female	20,936	3,410			
	Total	32,660	8,231			

Chi-Square test was used in this study to variables including arthritis and smoking and examine the association between predictor indicator variables of HRQoL (table 2).

Table 2: P-value of Chi-Square test to examine the association between predictor variables indicator variables

P-values of Chi-Square test							
Indicator variables of HRQoL		Predictor variables					
		Arthritis	Arthritis and Smoking				
A ativity limitations	Male	< .0001	< .0001				
Activity limitations	Female	< .0001	< .0001				
Dhygiaal haalth problems	Male	< .0001	< .0001				
Physical health problems	Female	< .0001	< .0001				
Mental health problems	Male	< .0001	< .0001				
	Female	< .0001	< .0001				

Logistic regression was used in this study variables including arthritis and smoking and to confirm the relation between predictor indicator variables of HRQoL (table 3)

Table 3: P-value and odds ratio of logistic regression to confirm the relation between predictor variables and indicator variables and to calculate the differences percentage.

P-values and odds ratio of logistic regression							
	Predictor variable						
Indicator variables of HRQoL		tis Alone nd Female)	Arthritis and Smoking (Male and Female)				
	Pr > chi-Sq	OR	Pr > chi-Sq	OR			
Activity limitations	0001.>	0.350	0001. >	0.924			
Physical health problems	0001.>	0.823	0001. >	1.109			
Mental health problems	0001.>	0.996	0001. >	1.201			

Also, by using logistic regression, odds ratio (OR) can be taken to calculate the differences percentage of the effect of arthritis alone and arthritis with smoking on health-related quality of life (HRQoL) including activity limitations, physical health problems, and mental health problems. Differences percentage of the effect can be calculated by the following equation. [13]

Percentage differences = (VI-V2) / ((V1+V2)/2)*100

While:

V1= Number of exposed cases.

V2 = Number of exposed non-cases.

Discussion

Measuring health-related quality of life (HRQoL) for a specific population of a specific disease, factor, or even association among these several conditions and factors can give significant, reliable, sensitive, and interpretable results as well as an overview of these population life. Since there are many researches showed how smoking can worse the condition of arthritis as a disease and none one of them have investigated the effect of smoking on HRQoL in adult patients of arthritis, the overall goal of this study is to investigate that effect_based on measuring activity limitations, physical health problems, and mental health problems as HRQoL for adult patients of arthritis.

In the survey of 2017-Behavioral Risk Factor Surveillance System (BRFSS), there were

450,013 participants. This survey was used in this study as a source of data to accomplish the goal of this study. In order to confirm the effect of smoking on health-related quality of life (HRQoL) on adult patients of arthritis, this study performed different descriptive, inferential, and predictive analysis methods by the Statistical Analysis System (SAS-9.4 version).

In the descriptive analysis, there were 450,013 participants and 147,288 of these participants were adult patients of arthritis (18 years and older). 61,122 of patients of arthritis are males and 82,736 are females. 63,466 of these participants in BRFSS-2017 were current smokers. 13.542 of these smokers were adults patients of arthritis (figure 1). These 13,542 smokers with arthritis are the main sample of this study to examine the differences between them and non-smokers with arthritis. Moreover, there were 11,461 smokers' adult patients of arthritis with activity limitation, 12,931 smokers' adult patients of arthritis with physical health problems, and 8,231 smokers' adult patients of arthritis with mental health problems (table 1).

To examine the associations between arthritis and smoking on health-related quality of life (HRQOL) including activity limitations, physical health problems, and mental health problems in adult patients of arthritis, inferential analysis by using Chi-Square test with a significance level of $P \le 0.05$ were conducted. Results of inferential analysis showed all of p-values are < 0.0001 (table 2) concluding

that there are significant associations between arthritis and smoking with activity limitations, physical health problems, and mental health problems.

To confirm the hypothesis of this study, the relationship between variables of the study must be examined by predictive analysis. Logistic regression was used as a predictive analysis method to confirm the relation and extracting the odds ratio (OR) in order to calculate the differences percentage of the effect of arthritis alone on HRQoL as well as the effect of the association between arthritis and smoking on HRQoL of adult patients of arthritis.

Results of predictive analysis showed all of Pr > chi-Sq. is < 0.0001 (table 3) concluding that there are significant relations between arthritis and smoking with activity limitations, physical health problems, and mental health problems.

However, to measure the differences percentage between the effect of arthritis alone on HRQoL and the effect of the association between arthritis and smoking on HRQoL in adult patients of arthritis, odds ratio (OR) must be extracted (table 3). Differences percentage of the effect can be calculated by the following equation. [14]

Percentage differences = (VI-V2) / ((V1+V2)/2)*100

While:

V1= Number of exposed cases.

V2 = Number of exposed non-cases.

Odds ratio (OR) of the activity limitations for non-smokers adult patients of arthritis is 0.350 while in the activity limitations for smokers' adult patients of arthritis is 0.924 (table 3). Meaning that smokers' adult patients of arthritis have increased the activity limitations by 164% more than non-smokers adult patients of arthritis. Odds ratio (OR) of physical health problems for non-smokers adult patients of arthritis is 0.823 while in physical health problems for smokers' adult patients of arthritis is 1.109 (table 3). Meaning that smokers' adult patients of arthritis have increased physical health problems by 34.75% more than non-smokers adult patients of arthritis. Odds ratio (OR) of mental health problems for non-smokers adult patients of arthritis is 0.996 while in mental health problems for smokers' adult patients of arthritis is 1.201 (table 3). Meaning that smokers' adult patients of arthritis have increased mental health problems by 20.58% more than nonsmokers adult patients of arthritis.

Conclusions

The overall goal of this study is to investigate the effect of the effect smoking on health-related quality of life (HRQOL) including activity limitations, physical health problems, and mental health problems in adult patients of arthritis. Data source of this study is 2017 Behavioral Risk Factor Surveillance System (BRFSS) from Centers for Disease Control and Prevention (CDC) in the United States. The results of this study based on 147,288 adult patients of arthritis (18 years and older).

13,542 of these patients were smokers. The results of this study used different descriptive, inferential, and predictive analysis methods by the Statistical Analysis System (SAS-9.4 version). This study showed that smoking can increase each of the activity limitations in adult patients of arthritis by 164%, physical health problems by 34.75%, mental health problems by 20.58%. Therefore, based on these finding, smoking has a great ability to worse health-related quality of life in adult patients of arthritis. However, even if this study showed the effect of smoking on HRQoL in adult patients of arthritis for both genders, as a limitation of this study, the reason behind that arthritis is more prevalent in female more than males remains unknown

References:

- [1] Centers for Disease Control and Prevention (CDC). Arthritis. 2019. Available at: https://www.cdc.gov/arthritis Retrieved from the internet on May 05, 2019.
- [2] Arthritis Foundation. Arthritis by the Numbers / Book of Trusted Facts & Figures. 2018; v2; 4100.17.10445.
- [3] F, Kevin. Arthritis and Health-related Quality of Life. 2019 Available at: https://www.hopkinsarthritis.org/patient-corner/disease-management/quality-of-life-and-arthritis/#ref1 Retrieved from the internet on May 05, 2019.
- [4] Hutchinson D, Shepstone L, Moots R, et al Heavy cigarette smoking is strongly as-

- sociated with rheumatoid arthritis (RA), particularly in patients without a family history of RA Annals of the Rheumatic Diseases 2001;60:223-227.
- [5] World Health Organization (WHO). WHO Report on the Global Tobacco Epidemic. 2017. Geneva: Switzerland. World Health Organization.
- [6] World Health Organization (WHO). WHO Report on the Global Tobacco Epidemic. 2011. Geneva: Switzerland. World Health Organization.
- [7] Howard G, Wagenknecht LE, Burke GL, Diez-Roux A, Evans GW, McGovern P, et al. Cigarette smoking and progression of atherosclerosis: The Atherosclerosis Risk in Communities (ARIC) Study. JAMA. 1998 Jan 14;279(2):119-24.
- [8] Doll R, Peto R, Wheatley K, Gray R, Sutherland I. Mortality in relation to smoking: 40 years' observations on male British doctors BMJ 1994; 309:901
- [9] Chang K, Yang S, Kim S, Han K, Park S, Shin J. Smoking and Rheumatoid Arthritis. International Journal of Molecular Sciences. 2014;15(12):22279-22295.
- [10] Dunkin MA. 5 Reasons Smoking Makes Arthritis Worse. Arthritis Foundation. 2019. Available at: http://blog.arthritis.org/living-with-arthritis/smoking-risks-ra-oa/ Retrieved from the internet on May 10, 2019.

- [11] A. Hosseinzadeh, P. R. Thompson, B. H. Segal, C. F. Urban. Nicotine induces neutrophil extracellular traps. Journal of Leukocyte Biology, 2016; 100 (5): 1105
- [12] Dominick K, Ahern F, Gold C, Heller D. Health and Quality of Life Outcomes. 2004;2(1):5.
- [13] The Behavioral Risk Factor Surveillance System (BRFSS). 2017 BRFSS Survey Data and Documentation. 2018. Available at: https://www.cdc.gov/brfss/annual_data/annual_2017.html Retrieved from internet on April 1, 2019.
- [14] Clemson University.2006.Physics Tutorial: % Error & % Difference. Available at http://www.clemson.edu/ces/phoenix/tutorials/error/ Retrieved from internet on May 16, 2019.

Original Article

Self-Medication Among Saudi Children by Parents in Al-Qassim Region, Saudi Arabia

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Abstract

Background and Aims: Use of over the counter (OTC) medications in children is a common practice by parents in developing countries. Specific doses for OTC medications are required, according to a child's age and weight. Parents' awareness about the risk of OTC is essential, and it needs to be raised to minimize OTC risk. This study aims to explore Saudi parents' knowledge, attitude and practice toward self-medicating their children.

Methods: A cross-sectional survey was conducted among Saudi parents aged 18–50 years, for over a period of 3 months, from May 2018 to August 2018. The total Saudi parents participated in this study 481 from multiple cities in Qassim region, Saudi Arabia.

Results: Synthetic medicines were predominantly administered by the parents to their children (86.1%), meanwhile 29.3% of the participants self-medicated their children more than four times a year. The most common symptoms for taking OTC medication were fever (64.7%), and flu (50.3%). With respect to parents' actions, in cases where the child did not improve with self-medication, 59.3 % of them attended a hospital. The primary sources of medicine were administered by the hospital (48.6%), and pharmacy (27.4%), with paracetamol being the most frequently used (82.5%). Top sources of information regarding medication for the parents were the doctor (81.6%), pharmacist (45.9%) and internet (26.4%).

Conclusion: There is generous use for OTC medication for children by their parents in Qassim region, Saudi Arabia. Most of the respondents were educated but their knowledge about OTC is insufficient.

Keywords

Knowledge, Saudi, Medicine, Parents, Children

الملخص

خلفية: يعتبر استخدام الأدوية غير الموصوفة للأطفال من قبل والديهم من الممارسات الشائعة في الدول النامية. جرعات الأدوية غير الموصوفة لتكون بالاعتماد على عمر ووزن الطفل. ويعتبر وعي الوالدين حول مخاطر الإفراط في إعطاء هذه الأدوية غير الموصوفة لأطفالهم أمراً ضرورياً ويجب تحسين استخدامهم لها لتقليل مخاطر هذه الأدوية. تهدف الدراسة لتقييم معرفة الآباء وسلوكهم وممارساتهم اتجاه العلاج الذاتي لأطفالهم.

طريقة البحث: أجربت هذه الدراسة المقطعية على الآباء السعوديون الذين تتراوح أعمارهم بين ١٨-٥٠ سنة على مدى ثلاث أشهر من شهر مايو ٢٠١٨ الى أغسطس ٢٠١٨ وشارك فيها ٤٨١ من الآباء السعو دبين من مدن مختلفة بمنطقة القصيم بالمملكة العربية السعو دية النتائج: فيما يتعلق بالمعرفة والممارسات من الآباء تجاه الدواء كانت الأدوية الصناعية تستخدم في الغالب من قبل الوالدين لأطفالهم بنسبة ١ ٨٦ ٪ ما يقار ب ثلث المشاركين (٣ ٢٩٪) يقومون بالعلاج الذاتي لأطفالهم أكثر من أربع مرات في السنة. فيما يتعلق بفعل الآباء، إذا كان الطفل لم يتحسن في العلاج الذاتي، معظمهم يذهب إلى المستشفى بنسبة ٣. ٥٩ ٪ المصادر الرئيسية للأدوية هي المستشفى (٤٨.٦ ٪) و الصيدلية (٤٠٢٤ ٪)، في حين كانت الأعراض الأكثر شيوعاً هي الحمي (٢٤٤) /) والانفلونز ا (٣٠٠٠ /). الأدوية الأكثر استخداما كانت البار اسيتامول (١/ ٨٢) أهم مصادر المعلومات للآياء عن الدواء كان الطبيب (١ ٨١) ٪)، الصيدلي (٥٩٩ ٪) والإنترنت (٢٦٠٪). يقدم الممارس الطبي دورًا محوريًا في تغيير نظرة الآباء في استخدام الأدوية غير الموصوفة. هناك حاجة إلى المزيد من التعليم للآباء و الأمهات لضمان إعطاء الأدوية لأطفالهم بشكل سليم. والأهم من ذلك، المشاركة المستمرة بالنصائح حول تحسن صحة الطفل

الكلمات المفتاحية: المعرفة، سعودي، دواء، آباء، أطفال

Introduction

Children represent a large proportion of the community in developing countries, and they are prone to various diseases [1]. Minor ailments are the most frequent episode during childhood [2]. The first response by most parents when children have any disease is self-medication [3]. Moreover, the parents prefer to treat common illnesses such as fever, cough and diarrhea without consulting a physician either in developed or developing countries [4]. Antipyretic, cough syrups and decongestants are common to be used by parents to treat their children [5].

The attitudes of parents towards some illnesses might directing them to use OTC medicine. Many studies showed that knowledge of parents about fever is still inaccurate. In addition, a large percentage of parents are unaware about which medication can be given to their child to control the pain or fever associated with minor conditions. Some minor symptoms could be treated with OTC medications, such as antipyretic, or with some herbal medication, without seeking pediatrician consultation [6].

The World Health Organization (WHO) has defined self-medication as 'the selection and use of medicines by individuals to treat self-recognized illnesses or symptoms' [7]. Several regulatory agencies carefully select OTC medicines to promote safe and effective use of medication for pediatric patients without physician's care. However, OTC medicines may cause harm to child's life, because some

interact with other medicines, supplements, food and drinks, and others cause comorbidities in people with certain medical conditions [8]. Parents might get advice by family member, media, friends or other sources which affect their responses toward the illness [6]. Most of the parents consider an illness of mild nature when it that does not require physician's care [9]. There are some advantages for self-medication, such as convenience, saving time for parents and cost effective, if it is used in appropriate way for minor illnesses [10].

Parents may be unaware of indications, doses, contraindications, and medication interactions when they use OTC medicines for their children [11]. Many studies have evaluated the administration of OTC medicines by parents to their children and have shown various problems because parents do not have adequate and proper knowledge about self-medication [12, 13]. Also, several studies have evidenced that the use of self-medication is influenced by personal, organizational and environmental factors [14, 15]. The objective of this study is to explore the parents' knowledge, attitudes and practice toward self-medicating their children.

Methods:

Study Design: A cross-sectional survey was conducted among Saudi parents of 18–50 years of age over a period of 3 months, from May 2018 to August 2018. The questionnaire was previously designed, and validated to assess parents' knowledge, , attitudes and awareness about OTC medication (12). We used Google

forms for the questionnaire, and it was sent via WhatsApp application. The questionnaire was sent through twelve volunteers living in different cities at Qassim region, to all their phone contacts. The aim of this study beside the importance of the data and its confidentiality were explained to participants, who subsequently provided informed consents in Arabic language, prior to answering the questionnaire. The ethical approval for this study was obtained from Prince Nourah Bint Abdulrahman University (IRB registration Number is H -01-R-059).

The population Qassim region is approximately one million, of whom 81 % are Saudis, and 19 % are non-Saudis. The capital city of Qassim region is Buraidah and it comprises about 50% of the total population of the region. the sample size calculated with an estimated absolute error to be 5% and a 95 % confidence interval. The required sample size is 384 using n=z2pq\d2. However, to guarantee accuracy, and considering minor data loss and non-response rates, the sample size was increased to 481.

The questionnaire included three main sections. The first part asked for the parents' demographics data, such as age, gender, level of education, the city of living in Qassim region, and children number. The second part evaluated the parents' knowledge and practice toward administration of OTC medicines to their children, which consisted of nine questions. Moreover, it assessed the most frequent used medicines, and the parents' action if the

child's health did not improve with self-medication. The third part explore the parents' attitude, and the reasons behind self-medication. All questions were recorded, according to the 3 Likert 3-point scale, and "agree", "neutral", and "disagree" were the answer options. There are eight questions included for the practice of self-medicating and the scale of 1 =Always to 3 = Never has been used. Total KAP scores were calculated by summing up the Likert scale responses for each category.

We used chi-square test on table to measure the association between level of attitude and socio demographic characteristics of participants with p-values which indicates whether the association is statistically significant. We used p-≤0.05 as a cutoff point of significant level for all statistical tests.

Ethical approval

The ethical approval for this study was obtained from Prince Nourah Bint Abdulrahman University (IRB registration Number is H-01-R-059). Informed consent was obtained from parents before completing the questionnaire

Results:

A total of four-hundred eighty-one participants were recruited in this study, of which 280 (58.2%) were females, and 201 (41.8%) were males. Among them, the age distribution was as follows: 18-20 years old (2.3%), 21-25 years old (7.9%), 26-30 years old (15.6%), 31-35 years old (18.7%), 36-40 years old

21.4%, 41 – 45 years old 16.0%, 46 – 50 years old 8.5%, and more than 50 years old 9.6%. Furthermore, 56.1% were non-healthcare employees, 15.6% were healthcare employees, and 28.3% were unemployed. Three-fourth (75.7%) of the participants graduated from

the University, of which 6.7% had postgraduate education, while 12.9% finished tertiary school, and (4.8%) finished less than tertiary school. The description of socio-demographic characteristics of participants is in Table 1.

Table 1: Socio-demographic characteristics

	N (%)		
Study variables	(n=481)		
Gender			
Male	201 (41.8%)		
Female	280 (58.2%)		
Age group in years			
18 – 20 years old	11 (2.3%)		
21 – 25 years old	38 (7.9%)		
26 – 30 years old	75 (15.6%)		
31 – 35 years old	90 (18.7%)		
36 – 40 years old	103 (21.4%)		
41 – 45 years old	77 (16.0%)		
46 – 50 years old	41 (8.5%)		
> 50 years old	46 (9.6%)		
Resident location			
Buraidah	80 (16.6%)		
Unayzah	184 (38.3%)		
Arras	86 (17.9%)		
Albadaya	62 (12.9%)		
Al Khabra	38 (7.9%)		
Others	31 (6.4%)		
Occupation			
Healthcare employee	75 (15.6%)		
Non-healthcare employee	270 (56.1%)		
Unemployed	136 (28.3%)		
Educational level			
Less than tertiary school	23 (4.8%)		

Tertiary school	62 (12.9%)
Graduate	364 (75.7%)
Postgraduate	32 (6.7%)
Number of children	
One	85 (17.7%)
Two	98 (20.4%)
Three	73 (15.2%)
Four	89 (18.5%)
More than four	136 (28.3%)

Number (N), percentage (%)

Knowledge and practices of parents toward OTC were summarized in Table 2. Most of the participants (86.1%) predominantly used synthetic medicines, while 13.9% used herbal medication. Importantly, parents self-medicated their children at different frequencies during one-year period (29.3% of them more than 4 times, 6% four times, 12.1% three times, 15.8% twice, 10% one time, and 26.8% never did). Regarding parents' actions, if the child's health did not improve with self-

medication, 59.3% of them attended the hospital, 30.4% private clinic, 6.9% consulted the community pharmacist, 2.5% searched medication online, 0.6% cases sought advice from friends and/or relatives, and 0.4% cases continued with self-medication. Majority of the parents (86.1%) used OTC medication when child's symptoms were mild, 13.9% in the presence of moderate symptoms, and no participant chose to use self-medication in severe or critical conditions.

Table 2: Knowledge and practices of parents toward OTC

Study variables	N (%)
	(n=481)
Type of treatment	
Synthetic Medicine	414 (86.1%)
herbal treatment	67 (13.9%)
The frequency of self-medication by parents to their	
children in 1 year.	
Never	129 (26.8%)
One time	48 (10.0%)
Two times	76 (15.8%)
Three times	58 (12.1%)
Four times	29 (6.0%)
More than four times	141 (29.3%)

Parent action if the child did not improve with self-medication	
Go to hospital	285 (59.3%)
Go to a private clinic	146 (30.4%)
Consult community pharmacist	33 (6.9%)
Search internet	12 (2.5%)
Seek advice from friends and/or relatives	03 (0.6%)
Continue self-medication	02 (0.4%)
Parents usually used the medication in the following cases.	
mild symptoms	414 (86.1%)
moderate symptoms	67 (13.9%)

Number (N), percentage (%)

The medicine providers varied as well, 48.6% were provided by a hospital, 27.4% by a pharmacy, 18.5% by a private clinic, while 3.3% were received from friends and relatives. The sources of medical information were the doctor (84.6%), followed by the pharmacist (45.9%), internet (26.4%), relatives (10.4%), newspaper (9.6%), and friends (7.1%). The most frequent OTC used by the parent were antipyretics (82.5%), cough syrups (35.3%),

anti-allergy medication (27%), antiemetic (12.9%), and antibiotics (12.3%) as revealed in figure1. However, fever (64.7%) was most common symptoms in children treated with OTC followed by flu (50.3%), diarrhea (35.8%), vomiting (26.4%), and skin rash (4.4%) as shown in figure 2. Moreover, Reasons for parental self-medication to their children stated in Table 3.

Table 3: Reasons for parental self-medication to their children

Statement	Disagree N (%)	Neutral N (%)	Agree N (%)
1. Waiting time on the clinic is too long	64 (13.3%)	97 (20.2%)	320 (66.5%)
2. Consultation fees are too expensive	115 (23.9%)	128 (26.6%)	238 (49.5%)
3. The nearest clinic is too far away	185 (38.5%)	151 (31.4%)	145 (30.1%)
4.Bad attitude of healthcare workers	177 (36.8%)	154 (32.0%)	150 (31.2%)
5. Lack of sufficient health information from the medical provider	173 (36.0%)	155 (32.2%)	153 (31.8%)
6.I am expert enough	119 (24.7%)	185 (38.5%)	177 (36.8%)
7. Awareness of side effect medication	44 (9.1%)	116 (24.1%)	321 (66.7%)
8. Awareness about my children disease from the symptoms	67 (13.9%)	102 (21.2%)	312 (64.9%)

(%) Number (N), percentage

The level of attitude toward medicine has been calculated by adding all responses from attitude questionnaires, "Reasons of parental self-medication to their children" (Table 3). For the ease of analysis, strongly disagree and disagree has been merged and coded as 1, neutral has been coded as 2 and agree and strongly agree has been merged and coded as 3. Based on the analysis, the mean score was 17.8, the minimum score was 8 and the maximum score was 24. This result has been recoded into two categories such as; 8 – 12 as negative attitude with 32 (06.7%) and 13 - 24 as positive attitude with 449 (93.3%).

We used chi-square test on table to measure the association between level of attitude and socio demographic characteristics of participants with p-values which indicates whether the association is statistically significant. We used p-≤0.05 as a cutoff point of significant level for all statistical tests. Based on analysis, among socio demographic characteristics that we included in the table, only resident location found to be statistically significant (p-0.044). Other demographical variables included in the table shows negative association in the level of attitude as shown in Table 4.

Table 4: Association between attitude toward medicine and socio demographic characteristics of participants (n=481)

Study variables	Positive (n=449)	Negative (n=32)	P-value §	
	N (%)	N (%)		
Gender				
Male	325 (72.4%)	30 (62.5%)	0.230	
Female	124 (27.6%)	12 (37.5%)		
Age group in years				
≤35 years old	200 (44.5%)	14 (43.8%)	0.930	
> 35 years old	249 (55.5%)	18 (56.2%)	0.930	
Resident location				
Buraidah	80 (17.8%)	0		
Unayzah	172 (38.3%)	12 (37.5%)		
Arras	79 (17.6%)	07 (21.9%)	0.044 **	
Albadaya	54 (12.0%)	08 (25.0%)]	
Al Khabra	34 (07.6%)	04 (12.5%)		
Others	30 (06.7%)	01 (03.1%)		
Occupation				
Employed	325 (72.4%)	20 (62.5%)	0.230	
Unemployed	124 (27.6%)	12 (37.5%)	0.230	

Educational level			
Tertiary and below	79 (17.6%)	06 (18.8%)	0.869
Graduate and above	370 (82.4%)	26 (81.2%)	
Number of children			
• 1 – 3	240 (53.5%)	16 (50.0%)	0.705
• >3	209 (46.5%)	16 (50.0%)	

.P-value has been calculated using chi-square test. ** Significant at $p \le 0.05$ level§

Discussion

This study measured the parents' knowledge, attitude, and practices of administering OCT medicines to their children, in Al-Qassim, Kingdom of Saudi Arabia. Various published articles unveiled that OTC medication has been widely practiced by parents for their children regardless of the side effect it might cause. This practice should be carefully assessed due to some contradiction that might be encountered during the course such as; child allergy to medicine, improper dosage, wrong medicine, expired medicine and other related drug complications [16].

Our study results show that most of the participants were mothers with more than eighty percent of the parents were college graduate or above. Regarding knowledge and practices of parents toward medication, synthetic medicine was predominantly used by the parents to their children with 86.1 %, and (29.3%) using self-medication for their children more than four times per year. The parents' action, if the child not improved in self-medication, more than half of them will go to a hospital with 59.3 percent.

In Saudi Arabia, Eldalo et al. reported that more than 95% of the parents used self-medication to treat minor illness, of which 86.7% used synthetic medicines. The most common medicines used were paracetamol and antibiotics to treat symptoms like fever. The primary sources of medications were community pharmacist, followed by the hospital, and private clinics. He also reported that the health information generally derived from the doctors, pharmacist, and relatives. These findings were congruent with our study results where we also exemplified the same frequencies for the following occasions such as the used of medicine to treat children, most common disease as fever, paracetamol as frequently used of medicine and doctor as the primary sources of information. We only observed a difference in the medicine provider, as our study indicated hospital as the primary source, whereas the Eldalo et al. identified pharmacy [12].

In Madinah, Saudi Arabia, it was reported that 63% of parents used medicine without medical prescription for common indications, such as fever [17]. They also conveyed that antipyretic and cough medicines were the most commonly used medicines the parents used to

treat their children's symptoms. When comparing this report with our study, our results showed a higher prevalence for self-medication, while it showed similar on common diseases with a minor difference in most common diseases. A group of researchers from Central, Saudi Arabia, evidenced that 51% of the OTC consumables were antibiotics and analgesics/antipyretics, the most sold medicine to treat minor illness [18]. They also indicated that physicians and pharmacists were the most common sources of health information. Furthermore, their study of knowledge, perception, and attitude characteristics toward self-medication revealed that the majority of the consumers had poor knowledge, while more than 60% had a positive attitude, and more than half of them had a negative perception. In contrast to this study, our results only illustrated parents' knowledge, attitude, and perception, whereas Central Region study focused more on the consumers' perspectives, which could distinctively influence the study outcome. In general, both studies exhibited the same pattern of OTC consumption by both consumers and parents.

Albsoul et al. reported that more than 90% of the parents in Jordan believed OTC medication was effective and safe, and most of them indicated that pharmacists were the source of information. Albsoul et al. survey was deemed the closest project results, as both indicated more than 85 percent of the parents practiced self-medication, and the most commonly used of medicine and most common symptoms of kids [19].

Eldalo et al. conducted a study on Sudanese parents, which showed that 84% of them used western medicine from private pharmacies and public hospitals for self-medication [13]. They provided further details, such as that 72.4% of the children did not have any drug-related allergy, the most frequently used medicines were antibiotics and paracetamol to treat the most common symptoms, and that doctor and pharmacist were the primary sources of health information. Additionally, they confirmed that parents tended to go to the hospital if self-medication did not improve the children's condition. It also showed a positive association between attitude and parents' education and occupation. International surveys indicated different points of views about OTC and self-medication. For example, in Spain, only 8.2% of the parents administered OTC drugs for colds, analgesic and antipyretics, the most commonly used medications [20].

Just like any other study, this study has also subjected to some limitations. First, the plurality of the participants in this study were mothers. Achievement of a 50:50 gender distribution of parents might not be possible as the mothers usually taking care of children. Second, we could not determine if parents' economic status was contributing to self-medication because the income data were not collected. Lastly, adding more important variables would be more beneficial especially when studying the knowledge and practices of parents toward self-medication.

Conclusion

There is generous use for OTC medication for children by their parents in Al Qassim region, Saudi Arabia. Most of the respondents were educated but their knowledge about OTC is insufficient. the long waiting time in the hospital is the main reason for parents to practice self-medication for their children. Further education to parents is required to ensure proper administration of medicine to their child, principally emphasizing that the mishandling of medication can aggravate child condition. More importantly, continuous tips and advice sharing about health improvement could improve child health. Future studies should investigate this topic in more depth by conducting a study at the national level, and recruiting parents from all over the country, where the general population would determine the substantiality of the study outcome.

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Competing interest

The author declared no conflict of interests.

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References

- [1] Lee D, Balasubramaniam K, Ali HM. Drug utilization studies: Their transferability between industrialized and developing countries. WHO REGIONAL PUBLICATIONS EUROPEAN SERIES. 1993:193-.
- [2] ESKERUD JR, LAERUM E, FAGER-THUN H, LUNDE PK, NAESS A. Fever in general practice I. Frequency and diagnoses. Family practice. 1992 Sep 1;9(3):263-9.
- [3] Zaki A, Abdel-Fattah M, Bassili A, Arafa M, Bedwani R. The use of medication in infants in Alexandria, Egypt. Eastern Mediterranean health journal= La revue de sante de la Mediterranee orientale= al-Majallah al-sihhiyah li-sharq al-mutawassit. 1999 Mar;5(2):320-7.
- [4] Alele PM. Self-Medication Practices by Caretakers for Children. International Invention Journal of Medicine and Medical Sciences. 2015;2(11):165-71.
- [5] Maison P, Guillemot D, Vauzelle-Kervroedan F, Balkau B, Sermet C, Thibult N, Eschwege E. Trends in aspirin, paracetamol and non-steroidal anti-inflammatory drug use in children between 1981 and 1992 in France. European journal of clinical pharmacology. 1998 Nov 1;54(8):659-64.
- [6] Kai J. Parents and their child's fever: do as I say, not as I do?. Family practice.

- 1998 Dec 1;15(6):505-6.
- [7] World Health Organization. The role of pharmacist in self-care and self-medication. Report of the 4th WHO Consultative Group on the role of pharmacist. Geneva (CH): WHO; 1998.
- [8] Qato DM, Alexander GC, Conti RM, Johnson M, Schumm P, Lindau ST. Use of prescription and over-the-counter medications and dietary supplements among older adults in the United States. Jama. 2008 Dec 24;300(24):2867-78.
- [9] Garofalo L, Di Giuseppe G, Angelillo IF. Self-medication practices among parents in Italy. BioMed Research International. 2015;2015.
- [10] Du Y, Knopf H. Self-medication among children and adolescents in Germany: results of the National Health Survey for Children and Adolescents (KiGGS). British journal of clinical pharmacology. 2009 Oct 1;68(4):599-608.
- [11] Lokker N, Sanders L, Perrin EM, Kumar D, Finkle J, Franco V, Choi L, Johnston PE, Rothman RL. Parental misinterpretations of over-the-counter pediatric cough and cold medication labels. Pediatrics. 2009 Jun 1;123(6):1464-71.
- [12] Eldalo AS. Saudi parent's attitude and practice about self-medicating their children. Archives of Pharmacy Practice. 2013 Apr 1;4(2):57-63.

- [13] Eldalo AS, El-Hadiyah TM, Yousif MA. Sudanese parents' knowledge, attitudes and practice about self-medication to their children: Qualitative study.
- [14] Sawalha AF. A descriptive study of self-medication practices among Palestinian medical and nonmedical university students. Research in Social and Administrative Pharmacy. 2008 Jun 1;4(2):164-72.
- [15] Tibdewal S, Gupta M. Mother's use of medication in their children of preschool age. Indian journal of public health. 2005 Jan 1;49(1):27.
- [16] Hughes L, Whittlesea C, Luscombe D. Patients' knowledge and perceptions of the side-effects of OTC medication. Journal of clinical pharmacy and therapeutics. 2002 Aug;27(4):243-8.
- [17] Alkhayat M, Albouq N, Osailan A, Alharbi H, Alharbi H, Alharbi R. Prevalence of Parental Self Medication And Its Possible Effect To Their Children In Al-Madinah, Kingdom Of Saudi Arabia. Int. J. Adv. Res. 2017 Jan;5(1), 1699-1707.
- [18] Aljadhey H, Assiri GA, Mahmoud MA, Al-Aqeel S, Murray M. Self-medication in Central Saudi Arabia: Community pharmacy consumers' perspectives. Saudi medical journal. 2015;36(3):328.
- [19] Albsoul-Younes A, Tahaineh L, Moumani B. Parents' knowledge, perception, and practices of over-the-counter medi-

cines used for their children. Jordan Journal of Pharmaceutical Sciences. 2011 Sep;4(3):181-9.

[20] Martín-Pérez M, Lopez De Andres A, Barcenilla Gonzalez MA, Jiménez-García R, Hernández-Barrera V, Jiménez-Trujillo I, Palacios-Ceña D, Carrasco-Garrido P. Parental administration of over-the-counter medication to Spanish children: A population-based national study. Journal for Specialists in Pediatric Nursing. 2016 Apr;21(2):64-73.

Review Article

The Mighty Role Of Platelets In Immunity, Inflammation, Cancer And Angiogenesis

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Abstract

Platelets are the smallest anucleated cells, in the circulation. Platelets are produced from the megakaryocytes in the bone marrow. Platelets participates in maintaining vascular integrity and hemostasis. However, their role extends beyond hemostasis to thrombosis, inflammation, immunity, wound healing, cancer, and angiogenesis. The multifunctional roles of platelets are achieved through the expression of diverse adhesive and immune receptors, a wide array of bioactive proteins stored in their granules, and the elaboration of membrane lipid mediators upon activation. There is an obvious involvement of platelets in inflammation, immunity, cancer, and angiogenesis. Thus, the concept arises that platelets, at the intersection of these conditions, are multifunctional cells. A better understanding of the exact, as well as the diverse roles and mechanisms of platelets in pathologic conditions is a promising research area and may open a window for new strategies and prevention methods of diseases.

Key words: Platelets, hemostasis, thrombosis, angiogenesis, immunity, inflammation, cancer

Introduction

Platelets were first identified and observed by Schultze in 1865 and Osler in 1874, and Bizzozero discovered their role in hemostasis in 1882 (1–3). However, the nature and other functions of these small cells have been important areas for research and discussion for the past several decades (3–6)Platelets are small (2-4 μm in diameter) anucleated discoid cells in the circulation. Their production from the cytoplasm of megakaryocytes in the bone marrow (7), involves the role of thrombopoi-

الملخص

الصفائح الدموية تعتبر أصغر الخلايا الدموية بدون نواة في الدورة الدموية ويتم إنتاجها من الخلايا الكبيرة «الميجاكاريوسايت» (إحدى سلالات الصفائح الدموية) في النخاع العظمي. الصفائح الدموية تشارك في الحفاظ على سلامة الأوعية الدموية والإرقاء. ومع ذلك، فإن دور الصفائح الدموية يمتد إلى ما وراء الارقاء إلى تجلط الدم والالتهابات والمناعة واستشفاء الجروح والسرطان وتولد الأوعية. يتم تحقيق الأدوار متعددة الوظائف للصفائح الدموية من خلال مستقبلات متعددة منها المناعية، ومجموعة واسعة من البروتينات النشطة بيولوجيا المخزنة في حبيباتها. مما يعطي الصفائح الدموية صفة خلايا متعددة الوظائف. ويعد الفهم الأفضل للوظائف الدقيقة، بالإضافة إلى الأدوار والآليات المتنوعة للصفائح الدموية في الحالات المرضية، مجال بحث واعد، وقد يقتح نافذة لاستراتيجيات جديدة وأساليب الوقاية من الأمراض.

etin (a hormone produced by the liver and kidneys) (5,6,8)James Homer Wright described how platelets formed from megakaryocytes and entered the circulation. Subsequent clinical and animal studies have enumerated a number of principles of platelet physiology: the platelet count is constant in any one individual but varies greatly between individuals; an inverse relationship exists between the platelet count and platelet size; the body conserves the mass, not the number, of platelets; and megakaryocyte number, size and ploidy vary in

response to changing demands for platelets. With the discovery of thrombopoietin (TPO and lineage-specific transcription factors (9). The lifespan of a platelet is 7–10 days. Platelets normally circulate in their inactive state with no interaction with the endothelium or other cells. Platelets become activated if they encounter vascular injury (damage, or at the site of inflammation) to maintain hemostasis and vascular integrity. Otherwise, they undergo apoptosis at the end of their life cycle and are removed by the spleen (6,7)a systematic review of published randomized clinical trials was conducted through extensive searches in Medline, Embase and Current Contents from 1966 till 1996 as well as manual reviews of 28 journals. The methodological quality of all trials was assessed by guidelines of the Cochrane Collaboration. Thirty-one trials were included, only one of which had no serious methodological flaws. The mean score of parasitological examination was 4.8 out of a possible 15. There was a considerable effect in cure rate of treatment versus placebo (odds 9.3, 95% CI 4.69-18.4.

The main role of platelets is associated with hemostasis, primarily to form a platelet plug to stop bleeding and to support blood coagulation (10–12). However, this is not their sole function as platelets are involved in, and contribute to, wound healing, (13)inflammation,(14)(15)immunity,(16,17) angiogenesis,(18) and cancer.(16,19)Platelets are the cellular elements that are general to these interrelated processes, indicating their role in the pathophysiology of these conditions (11–

19). While the role of platelets in the pathophysiology of thrombosis is well-established, their contribution to the immune system, inflammatory pathways, angiogenesis, and cancer are yet to be clearly defined (17,20–25). A better understanding of the exact, as well as the diverse roles and mechanisms of platelet involvement in these conditions, will open new strategies and prevention methods of diseases. This short review summarizes the role of platelets in inflammation, immunity, angiogenesis, and cancer.

Structure of platelets

Circulating platelet is considered a featureless cell from the outside; with the open canalicular system (OCS) connecting the platelet's membrane with the internal membrane system. The OCS is a pathway to transport platelets' contents upon activation to their surface. In activated platelets, the content of the platelets' granules fuse with the OCS, and are released into the surrounding environment (26,27). Platelets have other components such as glycogen and organelles (like endoplasmic reticulum, lysosomes, mitochondria, and dense tubular system) (26,28). The structure of platelets is organized into three distinct zones: the platelet plasma membrane, cytoskeleton, and granular structure (27,29,30).

Platelet plasma membrane

The membrane structure of any cell, including platelets, is a standard bilayer composed of proteins (glycoproteins [GPs]) and lipids

(phospholipids and cholesterol). Phospholipids form the basic structure, while cholesterol is distributed asymmetrically and arranged throughout the phospholipids. Negatively charged phospholipids (phosphatidylserine and phosphatidylinositol) are retained in the inner layer, and neutrally charged phospholipids (phosphatidylcholine) in the outer layer thus maintaining polar heads on both sides of the membrane (i.e., towards the plasma side and towards the cytoplasm). In addition, various GPs are found on the surface of the platelet including GPIb-IX-V complex, GPI-IB-IIIa, and/or GPIa-IIa, which are essential for their appropriate and normal functioning (7,31). The platelet membrane also contains glycocalyx that provides a dock to transfer proteins (such as fibrinogen) from blood to platelets (7). Overall, the membrane structure serves diverse functions in platelets, including agonist stimulation, permeability, adhesion, secretion, and aggregation (7,31).

Cytoskeletal zone

The cytoskeletal system supports the discoid shape of platelets. It consists of spectrin protein (2000 molecules per platelet), actin filaments (2 million molecules per platelet) and microtubules. In resting platelets, spectrin is an elongated protein strand interconnected by actin filaments. Spectrin and actin filaments support the platelet membrane, while microtubules located under the spectrin protein, and actin filaments, maintain platelet shape (7,29).

Granular zone

Platelets have three distinct cytoplasmic granules (alpha granules, dense granules, and lysosomal granules) that store bioactive molecules (32,33). Alpha $[\alpha-]$ granules (50–80 per platelet) contain high molecular weight factors (i.e., soluble and membrane-bound proteins including adhesion molecules, coagulation factor V, P-selectin, integrins, von Willebrand factor (vWF), platelet factor 4 (PF4: CXCL4), fibrinogen, fibronectin, vitronectin, protein S, plasminogen activator inhibitor-1, β-thromboglobulin, thrombospondin (TSP), proteoglycans, multimerin, α2-plasmin inhibitor, α1-protease inhibitor, C-1 inhibitor, chemokines such as CXCL7, CXCL1, and CXCL1 (GROa), CCL5 (regulated upon activation, normal T cell expressed and secreted [RANTES]), CCL3 (MIP1a), platelet-derived growth factor (PDGF), and transforming growth factor beta (TGF- β).(7,33) Dense [δ -] granules (3-8 per platelet) contain low molecular weight factors such as serotonin, ADP, ATP, Ca^{2+} , and histamine. Lysosomal [λ] granules contain glycohydrolases and proteases such as cathepsin, acid phosphatase, collagenase, and elastase (7,17,30,33,34).

Platelets and immunity

The main function of platelets is to limit blood loss at the site of injured endothelium. However, platelets also rapidly respond to the invasion of microbial pathogens in the bloodstream (34). The rapid response of platelets to infections at the site of colonization and inflammation not only maintains blood hemostasis and vascular integrity, but also releases chemokines to fight microbes; and trap and engulf them, indicating an important role for platelets in the immune response (35,36). This role is achieved with the help of inflammatory mediators released by activated platelets (14,37,38). Platelets store and release bioactive molecules (mediators and chemokines) and express functional immunoreceptors that modulate the immune system (17,24). Furthermore, platelets communicate with and modulate other cells to participate in innate as well as adaptive immunity by expressing receptors (36).

Innate immunity

Platelets exhibit diverse immunoreceptor attributes and have antimicrobial properties by interacting with viruses, bacteria, and fungi (14,39,40). Platelets are activated when bound to certain bacteria; this is mediated via direct and indirect interactions between bacteria and platelets. These interactions induce full responses of platelets (adhesion, degranulation, shape change, and aggregation). Platelets also participate in defense against microbial products and the products of inflamed tissues. The platelet-bacteria interaction is a complex process mediated through diverse receptors including complement receptors, such as Fc gamma receptor type 2, pattern recognition receptors, toll-like receptors (TLRs), and GPIIb-IIIa and GPIb on platelets (41).

Platelets express TLRs that modulate the re-

lease of different cytokines from platelets upon engaging with bacterial lipopolysaccharide (42–44). The presence of TLRs on platelets suggests direct engulfment of pathogens similar to leukocytes. TLRs also recognize pathogen-associated molecular patterns (PAMPs; i.e., lipids, lipoproteins, proteins, or nucleic acids) that are derived primarily from bacteria, viruses, fungi, or parasites (45,46). PAMPs in various cellular compartments, such as plasma membrane, endosomes, endolysosomes, and lysosomes, can be recognized by TLRs expressed by platelets (47).

TLRs initiate inflammation against microbial products or the products of inflamed tissues. TLRs are the primary sensors of infection because they recognize conserved structures in PAMPs. TLR2, TLR4, TLR6, TLR7, and TLR9 are shown to be expressed in human platelets. TLR activation on platelets triggers different biological responses,(43) leading to the release of acute phase reactant tumor necrosis factor- α (48) and interleukin-1 (49,50). Furthermore, platelets recognize different isoforms of lipopolysaccharide, eliciting a distinct response and release of specific chemokine and cytokine types (51).

Platelets also express various chemokine (CC and CXC) and kinocidin receptors. These have the ability to recognize signals from all types of chemokines and kinocidins in the infected area, eliciting a specific host defense response. This ensures the rapid recruitment and accumulation of platelets at the site of infection (52,53). Furthermore, platelets not

only have receptors to recognize chemokines and kinocidins, but also release platelet microbicidal proteins such as kinocidins (CXCL4, CXCL7, and CCL5), defensins (human β defensin 2), thymosin β 4, and some derivatives (thrombocidins and fibrinopeptide A or B) (52,54). Moreover, platelets can modulate and coordinate the actions of other cells; i.e., immune cells to release chemokines and kinocidins including PF4 (CXCL4) and RANTES (CCL5) (52).

RANTES, derived from activated platelets, has an immune-modulator function and enhances the cytotoxic ability of T cells, as well as the production of cytokines. The expression of RANTES mRNA increases immunoglobulin synthesis from cells upon the platelet-B cell interaction. Other platelet products, such as PF4, kill erythrocytes infected with parasites, suggesting that PF4 is anti-parasitic. In addition, thrombocidins (chemokine-derived peptides) have antibacterial and antifungal properties, making platelets a player in innate immunity. The contents of lysosomal granules in platelets, such as cathepsin, also break down microbes, though non-specifically (55) (56).

Platelets not only internalize pathogens (microbes and viruses), but also kill various internalized pathogens including bacterial species (e.g., *Escherichia coli* and *Staphylococcus aureus*) and viruses (e.g., human immunodeficiency virus) to promote their clearance from the bloodstream and tissues (57,58). The exact mechanism of the phagocytic role

of platelets in pathogen defense requires further investigations. Platelets are also known to fight microbes by generating and releasing reactive oxygen species as part of their antimicrobial role (59,60).

Platelets, as mentioned previously, modulate other immune cells. Specifically, they regulate the maturation and activation of cells that play crucial roles in innate immunity, such as macrophages, neutrophils, and dendritic cells (61,62). Indeed, platelets can interact with neutrophils to form a neutrophil extracellular trap (NET) (63,64). A NET can also be formed by platelet-derived β-defensin, which has a novel antibacterial activity. Activated platelets surround and trap S. aureus and use β-defensin 1 to force them into clusters, thereby diminishing their growth. Neutrophils trap bacteria using a NET comprised of the neutrophil nucleus and other intracellular contents that ensnare and kill bacteria. NET formation (NETosis) is an important mechanism of neutrophil killing, and inhibition of NETosis can increase the development of infections (64).

Adaptive immunity

Mobilization of the adaptive immune response is chiefly mediated by CD154. CD154 is a member of the tumor necrosis factor superfamily, which significantly enhances the presentation of antigens as well as the innate immune response. Platelets express CD154 and, thereby, have a role in adaptive immunity. This is achieved by platelets communicating with B- and T-cells (65,66). Elzey *et al.*

(2005) showed enhancement of B- and T-cells in CD154^{-/-} mice mediated by CD154-derived from platelets. Furthermore, platelet-derived CD154 includes CD8+ T-cell responses and is essential for IgG production in a murine model. These emerging data suggest a role of platelets in adaptive immunity (66). However, their exact role and mechanism in adaptive immunity is not well-established and needs more research.

Platelets and inflammation

Platelets are highly responsive to agonists, tissue injuries, and inflammation. It is suggested that platelets initiate and propagate the inflammatory response (35,67,68). The involvement of platelet in inflammation is proposed in inflammation; with data from literature suggest the effectiveness of antiplatelet drugs in inflammatory conditions (69–72). This role was recognized long ago, as demonstrated by platelets' involvement in atherosclerosis (73–75). Atherosclerosis is a chronic inflammatory process involving a well-observed interaction of platelets with leukocytes and endothelium. This leads platelets to secrete inflammatory molecules that can alter the proteolytic properties of endothelial cells. Such a sequence promotes the migration and adhesion of monocytes to the site, facilitating the formation of atherosclerotic plaque (76). This illustrates an important association between inflammation and atherogenesis.

Platelets contain, express, and release various inflammatory mediators, mostly stored

in granules, mainly α -granules (33,77). Examples of these mediators include arachidonic acid metabolites, serotonin, adhesive proteins (fibrinogen, vWF), cell growth factors (PDGF, TGF- α and - β , platelet-derived angiogenesis factor, and basic fibroblast growth factor), and other plasma proteins and protease inhibitors. These mediators facilitate the role of platelets in inflammation either by adhesion to other cells via immunoreceptors, or the release of chemokines. In addition, platelets interact with many cells, including leukocytes (lymphocytes, neutrophils, and monocytes) dendritic cells, endothelial cells, erythrocytes, and tumor cells (23,78).

The most abundant protein secreted from activated platelet α-granules is PF4, a member of the CXC chemokine family. PF4 is chemotactic for neutrophils. In addition, PF4 contributes to atherosclerosis by accelerating atherogenesis, resulting in vascular inflammation. Even though, the retention of lipoproteins in the vascular wall is promoted by PF4 and prevents the catabolism of low-density lipoproteins by hindering the interaction between low-density lipoproteins and their receptor, increasing the retention of low-density lipoproteins on the cell surface; (79,80) PF4 also increases the release of neutrophil granules and adhesion to endothelial cells. This adhesion is facilitated by L-selectin receptor and leukocyte function-associated molecule-1 (81). In addition, PF4 influences monocytes, where it inhibits monocyte apoptosis, increases monocyte differentiation into macrophages, and induces reactive oxygen species generation (54)

Platelets and cancer

Armand Trousseau observed an increased risk of thrombotic "hypercoagulability" in certain cancer patients that was accompanied with hemostatic and platelet abnormalities (82,83). He also identified a coagulant state in his own blood before his death from pancreatic cancer, leading to the term "Trousseau's syndrome". The molecular mechanism of Trousseau's syndrome was established in the 20th century following studies on tumor cellinduced platelet activation, mainly platelet aggregation (82,83).

The role of platelets in tumor cell proliferation has been demonstrated in animal studies (84–86). Their contribution to metastasis and angiogenesis in various types of tumors, such as colon, breast, lung, ovarian carcinomas, and melanoma, is well-recognized (87,88). The obvious connection between platelets and tumor angiogenesis and growth predicts their potential impact on malignancies (89). Platelets form complex bidirectional interactions with tumor cells, leading to the pathogenesis of malignancies (84). In addition, surface molecules, proteins, and platelet lipids contribute to the progression of inflammation in cancer, and cancer itself (90-92). Indeed, tumor cells express a variety of membrane receptors that bind directly to platelets (85,86).

Platelets contribute to the pathophysiology of cancer in terms of the increase and progression of tumor growth, and offer physical and mechanical support for tumor cells to escape the immune system and move to secondary organs (84). This is achieved by platelet-tumor cell aggregates that mask cancer cells and allow cancer metastasis. Research in this area led to the identification of a wide range of platelet receptors from the α -granules that are involved in malignancy, including cancer cells binding to P-selectin on platelet surface. P- selectin is transported from the α -granule to the surface of activated platelets (93). In P-selectin-deficient mice, tumor growth was reduced in colon carcinoma and melanoma cells (94,95).

Other platelet membrane receptors are involved in cancer metastasis, further supporting the importance of platelets in cancer development (84). This is clearly demonstrated with GPIb-IX-V that has a role in platelet adhesion with injured endothelium. GPIb-IX-V-deficient mice have a 15-fold reduction in melanoma cell metastasis (96). Other membrane receptors, such as GPVI(97) and GPI-Ib-IIIa,(98–100) are also involved in cancer pathophysiology.

PDGF have been shown to be rich and play a role in tumor environment, this role is achieved by autocrine stimulation of the cancer cell, and by the effect on the tumor's interstitial pressure (101,102). PDGF is also expressed by tumor and stromal cells, and drives their carcinogenesis and tumor progression. Targeting PDGF had shown effectiveness on tumors' environment interstitial pressure and augments the effect of chemotherapy in ex-

perimental models (103). In addition, promising results have been found when PDGF signaling was blocked in inhibiting tumor growth in ovarian cancer (104,105), prostate cancer (106), and gliomas cell lines (107).

As platelets contribute to tumor growth and environment, antiplatelet drugs have shown a potential therapeutic strategy as anticancer drugs. Antiplatelet drugs reduce tumor growth, cancer metastasis and angiogenesis in many conditions (108).

Platelets and angiogenesis

Angiogenesis broadly refers to the formation of new blood vessels. This process occurs in physiological (e.g., wound healing, menstrual cycle, and embryonic development) and pathological (e.g., diabetic retinopathy, rheumatoid arthritis, and all types of malignancies) condition (109). Angiogenesis is essential for vascular development and organ growth,(110) and has been linked to tumor formation and prognosis because the newly formed vessels feed the tumor mass by providing it with oxygen and nutrition.

Tumor growth is an angiogenesis-dependent process (109), where platelets contribute to the regulation, modulation, and control of angiogenesis through several pathways, (111) as well as in atherosclerotic plaque formation (79). Activated platelets, at the site of an atherosclerotic lesion, release modulators to recruit endothelial progenitors and monocytes to promote angiogenesis (79). Platelets are rich sources of angiogenesis modulators, but

their exact role is not fully elucidated (111). The wide array of pro- and anti-angiogenic factors stored in platelets participate directly and indirectly in physiological and pathological angiogenesis, and tumor growth (109,111).

Platelets are involved in promoting angiogenesis in diverse conditions (80,112,113) including cancer (96,114). Platelets contain pro-angiogenic (activators including vascular endothelial growth factor (VEGF), PDGF, and fibroblast growth factor-2, and matrix metallopeptidase-9) and anti-angiogenic (inhibitors such as endostatin, TSP-1, PF4, plasminogen activation inhibitor-1, and TGF-β) proteins (111). These factors are organized in platelets and megakaryocytes in distinct α-granule populations. These pro- and anti-angiogenic factors are released selectively from platelets in response to different stimuli. This suggests potential clinical implications to target the release of specific factors. Therefore, the role of platelets in controlling angiogenic switches may be defined by the activation of specific cell surface receptors (109).

The role of platelets in regulating angiogenesis has been clearly shown from studies of tumor angiogenesis. VEGF is found abundantly in platelet α -granules. It plays a role in endothelial cell proliferation, migration, and tube formation. VEGF released from platelets is increased in the serum of cancer patients and has been associated with the prognosis of several cancers. Importantly, inhibition of VEGF is associated with a reduction in tumor growth (90).

Another example of a pro-angiogenic factor in platelets is platelet-derived endothelial cell growth factor (PD-ECGF). PD-ECGF is an important angiogenic growth factor and its presence indicates a poor prognosis (91). Both VEGF and PD-ECGF have shown to augment neovascularization in diabetic retinopathy (91,92,115). The release of angiogenic molecules from platelets is agonist dependent. A study of the angiogenic effect of platelets on human umbilical vein endothelial cells showed that ADP activated platelet stimulate the release of VEGF but not endostatin, and this promoted the migration of human umbilical vein endothelial cells and the formation of capillary structures. In contrast, TxA2 stimulated the release of endostatin but not VEGF from platelets, which inhibited cell migration and capillary-like tube formation (111).

Conclusions

Platelets exert a role not only in hemostasis and thrombosis, but also in other conditions. There is an obvious involvement of platelets in inflammation, immunity, cancer, and angiogenesis. Thus, the concept that platelets are at the intersection of these conditions makes them a multifunction cell. Achieving a better understanding of the exact as well as diverse roles and mechanisms of platelet involvement in these conditions is a promising research area and will open a window for new strategies and prevention methods of diseases.

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References

- [1] Cooper B. Osler's role in defining the third corpuscle, or "blood plates". Proc (Bayl Univ Med Cent). 2005;18(4):376–8.
- [2] Brewer DB. Max Schultze (1865), G. Bizzozero (1882) and the discovery of the platelet. Br J Haematol. 2006;133(3):251–8.
- [3] Ribatti D, Crivellato E. Giulio Bizzozero and the discovery of platelets. Leuk Res. 2007;31(10):1339–41.
- [4] Hou Y, Carrim N, Wang Y, Gallant RC, Marshall A. Platelets in hemostasis and thrombosis: Novel mechanisms of fibrinogen-independent platelet aggregation and fibronectinmediated protein wave of hemostasis. J Biomed Res [Internet].2015;29 (October):437–44. Available from: http://www.jbr-pub.org/ch/reader/view_abstract.aspx?file no=JBR150602&flag=1
- [5] Kaushansky K. Thrombopoietin and the physiology of platelet production. Leuk Res. 1996;20(9):705–7.
- [6] Kuter DJ. The Physiology of Platelet Production. Stem Cells [Internet]. 1996;14(S1):88–101. Available from:http://doi.wiley.com/10.1002/ stem.5530140711
- [7] Fritsma GA. Platelet Structure and Function. Clin Lab Sci. 2015;28(2):125–31.
- [8] Wendling F. Thrombopoietin: its role from

- early hematopoiesis to platelet production. Haematologica. 1999;84(2):158-66.
- [9] Italiano JE. Unraveling Mechanisms that Control Platelet Production. Semin Thromb Hemost. 2013;39:15–24.
- [10] Ghoshal K, Bhattacharyya M. Overview of platelet physiology: Its hemostatic and nonhemostatic role in disease pathogenesis. Sci World J. 2014;2014.
- [11] Wagner DD, Burger PC. Platelets in Inflammation and Thrombosis. Arterioscler Thromb Vasc Biol. 2003;23(12):2131–7.
- [12] Gresele P, Lopez JA, Kleiman NS, Page CP. Platelets in thrombotic and non-thrombotic disorders: Pathophysiology, pharmacology and therapeutics: An update. Platelets Thromb Non-Thrombotic Disord Pathophysiol Pharmacol Ther an Updat. 2017;1–1445.
- [13] Golebiewska EM, Poole AW. Platelet secretion: From haemostasis to wound healing and beyond. Blood Rev [Internet]. 2015;29(3):153–62. Available from: http://dx.doi.org/10.1016/j. blre.2014.10.003
- [14] Klinger MHF, Jelkmann W. Review: Role of Blood Platelets in Infection and Inflammation. J Interf Cytokine Res [Internet]. 2002;22(9):913–22. Available from: http://www.liebertonline.com/doi/abs/10.1089/10799900260286623
- [15] Collins CE, Rampton DS. Platelets in inflammatory bowel disease Pathogenetic role and therapeutic implications. Aliment Pharmacol Ther. 1997;11(2):237–

47.

- [16] Sabrkhany S, Griffioen AW, oude Egbrink MGA. The role of blood platelets in tumor angiogenesis. Biochim Biophys Acta Rev Cancer. 2011;1815(2):189–96.
- [17] Ali RA, Wuescher LM, Worth RG. Platelets: Essential components of the immune system. Curr Trends Immunol. 2015;16:65–78.
- [18] Repsold L, Pool R, Karodia M, Tintinger G, Joubert AM. An overview of the role of platelets in angiogenesis, apoptosis and autophagy in chronic myeloid leukaemia. Cancer Cell Int. 2017;17(1):1–12.
- [19] Cui MM, Li N, Liu X, Yun ZY, Niu Y, Zhang Y, et al. Platelet distribution width correlates with prognosis of non-small cell lung cancer. Sci Rep. 2017;7(1):1–6.
- [20] Cerletti C, Tamburrelli C, Izzi B, Gianfagna F, De Gaetano G. Platelet-leukocyte interactions in thrombosis. Thromb Res. 2012;129(3):263–6.
- [21] Cerletti C, de Gaetano G, Lorenzet R. Platelet leukocyte interactions: multiple links between inflammation, blood coagulation and vascular risk. Mediterr J Hematol Infect Dis. 2010;2(3):e2010023.
- [22] ZG F, RA C, AS W, MT. R. Platelet-leukocyte interactions link inflammatory and thromboembolic events in ischemic stroke. Ann N Y Acad Sci. 2010;1207:11–7.
- [23] Ghasemzadeh M, Hosseini E. Platelet-leukocyte crosstalk: Linking proin-

- flammatory responses to procoagulant state. Thromb Res. 2013;131(3):191–7.
- [24] Herter JM, Rossaint J, Zarbock A. Platelets in inflammation and immunity. J Thromb Haemost. 2014;12(11):1764–75.
- [25] Morrell CN, Aggrey AA, Chapman LM, Modjeski KL. Emerging roles for platelets as immune and inflammatory cells. Blood. 2014;123(18):2759–67.
- [26] Michelson A. Platelets. Academic Press; 2012. 1398 p.
- [27] White JG. Platelets Structure. 2007. Academic Press.
- [28] White JG. The Dense Bodies of Human Platelets: Inherent Electron Opacity of the Serotonin Storage Particles. Blood. 1969;33(4).
- [29] Saboor M, Chotani R, Ilyas S, Usman MM. Anatomy and physiology of platelets. J Public Heal Biol Sci 2013;2(2)201-6. 2013;2(2):201-6.
- [30] Zelen JSJ. The role of the platelet cytoskeleton in platelet function. Thesis-Universitat Utr. 2012;1–25.
- [31] Lhermusier T, Chap H, Payrastre B. Platelet membrane phospholipid asymmetry: from the characterization of a scramblase activity to the identification of an essential protein mutated in Scott syndrome. J Thromb Haemost. 2011;9:1883–91.
- [32] Smyth S, McEver R, Weyrich A, Morrell C, Hoffman M, Arepally G, et al. Platelet functions beyond hemostasis. J Thromb Haemost. 2009;7(11):1759–66.

- [33] Blair P, Flaumenhaft R. Platelet Alpha–granules: Basic biology and clinical correlates Price. Blood Rev [Internet]. 2009;23(4):177–89. Available from: http://www.sciencedirect.com/science/article/pii/S0268960X09000290
- [34] Semple J, Italiano J, Freedman J. Platelets and the immune continuum. Nat Rev Immunol. 2011;11(4):264–74.
- [35] Mezger M, Nording H, Sauter R, Graf T, Heim C, von Bubnoff N, et al. Platelets and Immune Responses During Thromboinflammation. Front Immunol [Internet]. 2019;10:1371. Available from: doi: 10.3389/fimmu.2019.01731
- [36] Caudrillier A, Kessenbrock K, Gilliss B, Nguyen J, Marques M, Monestier M, et al. Platelets induce neutrophil extracellular traps in transfusion-related acute lung injury. J Clin Invest. 2012;122(7):2661–71.
- [37] McDonald B, Urrutia R, Yipp BG, Jenne CN, Kubes P. Intravascular neutrophil extracellular traps capture bacteria from the bloodstream during sepsis. Cell Host Microbe. 2012;12(3):324–33.
- [38] Stocker TJ, Ishikawa-Ankerhold H, Massberg S, Schulz C. Small but mighty: Platelets as central effectors of host defense. Thromb Haemost. 2017;117(4):651–61.
- [39] Yeaman M. The Role of Platelets in Antimicrobial Host Defense. Clin Infect Dis [Internet]. 1997;25(5):951–68. Available from: https://academic.oup.com/cid/

article-lookup/doi/10.1086/516120

- [40] Yeaman M, Yount N, Waring A, Gank K, Kupferwasser D, Wiese R, et al. Modular determinants of antimicrobial activity in platelet factor-4 family kinocidins. Biochim Biophys Acta Biomembr. 2007;1768(3):609–19.
- [41] Hamzeh-Cognasse, H. Damien P, Chabert A, Pozzetto B, Cognasse F, Garraud O. Platelets and infections - complex interactions with bacteria. Front Immunol 2015 Feb 26;682. 2015;6(28).
- [42] Shiraki R, Inoue N, Kawasaki S, Takei A, Kadotani M, Ohnishi Y, et al. Expression of Toll-like receptors on human platelets. Thromb Res. 2004;113(6):379–85.
- [43] Cognasse F, Nguyen K, Damien P, McNicol A, Pozzetto B, Hamzeh-Cognasse H, et al. The inflammatory role of platelets via their TLRs and Siglec receptors. Front Immunol [Internet]. 2015;6(83). Available from: doi: 10.3389/fimmu.2015.00083
- [44] Cognasse F, Hamzeh H, Chavarin P, Acquart S, Genin C, Garraud O. Evidence of Toll-like receptor molecules on human platelets. Immunol Cell Biol. 2005;83(2):196–8.
- [45] Zhang G, Han J, Welch E, Ye R, Voyno-Yasenetskaya T, Malik A, et al. Lipopolysaccharide stimulates platelet secretion and potentiates platelet aggregation via TLR4/MyD88 and the cGMP-dependent protein kinase pathway. J Immunol. 2009;182(12):7997–8004.

- [46] Scott T, Owens MD. Thrombocytes respond to lipopolysaccharide through Toll-like receptor-4, and MAP kinase and NF-κB pathways leading to expression of interleukin-6 and cyclooxygenase-2 with production of prostaglandin E2. Mol Immunol. 2008;45(4):1001–8.
- [47] Czapiga M, Kirk A, Lekstrom-Himes J. Platelets deliver costimulatory signals to antigen-presenting cells: a potential bridge between injury and immuneactivation. Exp Hematol. 2004;32(2):135–9.
- [48] Aslam R, Speck ER, Kim M, Crow AR, Bang KWA, Nestel FP, et al. Platelet Toll-like receptor expression modulates lipopolysaccharide-induced thrombocytopenia and tumor necrosis factor-α production in vivo. Blood. 2006;107(2):637–41.
- [49] Pancré V, Monte D, Delanoye A, Capron A, Aurialt C. Interleukin-6, the main mediator of interaction between monocytes and platelets in killing of Schistosoma mansoni. Eur Cytokine Net (1990). 1990;1(1):15–9.
- [50] Blair P, Rex S, Vitseva O, Beaulieu L, Tanriverdi K, Chakrabarti S, et al. Stimulation of Toll-like receptor 2 in human platelets induces a thromboinflammatory response through activation of phosphoinositide 3-kinase. Circ Res. 2009;104(3):346–54.
- [51] Berthet J, Damien P, Hamzeh-Cognasse H, Arthaud C, Eyraud M, Zéni F, et al. Human platelets can discriminate between various bacterial LPS iso-

- forms via TLR4 signaling and differential cytokine secretion. Clin Immunol. 2012;145(3):189–200.
- [52] Yeaman M. Platelets: at the nexus of antimicrobial defence. Nat Rev Microbiol. 2014;12(6):426–37.
- [53] Clemetson K, Clemetson J, Proudfoot A, Power C, Baggiolini M, Wells T. Functional expression of CCR1, CCR3, CCR4, and CXCR4 chemokine receptors on human platelets. Blood. 2000;96(13):4046–4054.
- [54] Scheuerer B, Ernst M, Dürrbaum-Landmann I, Fleischer J, Grage-Griebenow E, Brandt E, et al. The CXC-chemokine platelet factor 4 promotes monocyte survival and induces monocyte differentiation into macrophages. Blood [Internet]. 2000;95(4):1158–66. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10666185
- [55] Sonmez O, Sonmez M. Role of platelets in immune system and inflammation [Internet]. Porto Biomedical Journal. 2017. Available from: http://linkinghub.elsevier.com/retrieve/pii/S2444866417300107
- [56] Hundelshausen P, Weber C. Platelets as Immune Cells Bridging Inflammation and Cardiovascular Disease. Circ Res. 2007;100(1):27–40.
- [57] Yeaman M. Bacterial—platelet interactions: virulence meets host defense. Futur Microbiol. 2010;5:471–506.
- [58] Youssefian T, Drouin A, Masse JM,

- Guichard J, Cramer EM. Host defense role of platelets: engulfment of HIV and Staphylococcus aureus occurs in a specific subcellular compartment and is enhanced by platelet activation. Blood. 2002;99:4021–9.
- [59] Zielinski T, Wachowicz B, Saluk-Juszczak J, Kaca W. The generation of superoxide anion in blood platelets in response to different forms of Proteus mirabilis lipopolysaccharide: effects of staurosporin, wortmannin, and indomethacin. Thromb Res. 2001;103:149–55.
- [60] Lopes-Pires M, Casarin A, Pereira-Cunha F, Lorand-Metze I, Antunes E, Marcondes S. Lipopolysaccharide treatment reduces rat platelet aggregation independent of intracellular reactiveoxygen species generation. Platelets. 2012;23(3):195–201.
- [61] Banchereau J, Briere F, Caux C, Davoust J, Lebecque S, Liu Y, et al. Immunobiology of dendritic cells. Annu Rev Immunol. 2000;18:767-811.
- [62] Hagihara M, Higuchi A, Tamura N, Ueda Y, Hirabayashi K, Ikeda Y, et al. Platelets, after Exposure to a High Shear Stress, Induce IL-10-Producing, Mature Dendritic Cells In Vitro. J Immunol [Internet]. 2004;172(9):5297–303. Available from: http://www.jimmunol.org/cgi/doi/10.4049/jimmunol.172.9.5297
- [63] Clark S, Ma A, Tavener S, McDonald B, Goodarzi Z, Kelly M, et al. Platelet TLR4 activates neutrophil extracellular traps to ensnare bacteria in septic blood.

- Nat Med. 2007;13(4):463-9.
- [64] Kraemer B, Campbell R, Schwertz H, Cody M, Franks Z, Tolley N, et al. Novel Anti-bacterial Activities of β-defensin 1 in Human Platelets: Suppression of Pathogen Growth and Signaling of Neutrophil Extracellular Trap Formation. PLoS Pathog. 2011;7(11):e1002355.
- [65] Elzey B, Grant J, Sinn H, Nieswandt B, Waldschmidt T, Ratliff T. Cooperation between platelet-derived CD154 and CD4+ T cells for enhanced germinal center formation. J Leukoc Biol. 2005;78(1):80–4.
- [66] Elzey B, Tian J, Jensen R, Swanson A, Lees J, Lentz S, et al. Platelet-mediated modulation ofadaptive immunity. A communication link between innate and adaptive immunecompartments. Immunity. 2003;19(1):9–19.
- [67] Bombeli T, Schwartz BR, Harlan JM. Adhesion of Activated Platelets to Endothelial Cells: Evidence for a GPIIbIIIa-dependent Bridging Mechanism and Novel Roles for Endothelial Intercellular Adhesion Molecule 1 (ICAM-1), α v β 3 Integrin, and GPIbα. J Exp Med [Internet]. 1998;187(3):329–39. Available from: http://www.jem.org/lookup/doi/10.1084/jem.187.3.329
- [68] Mezger M, Göbel K, Kraft P, Meuth S, Kleinschnitz C, Langer H. Platelets and vascular inflammation of the brain. Hamostaseologie. 2015;35(3):244–51.
- [69] Winning J, Neumann J, Kohl M, Claus R, Reinhart K, Bauer M, et al. Antiplatelet

- drugs and outcome in mixed admissions to an intensive care unit. Crit Care Med. 2010;38(1):32–7.
- [70] Erlich J, Talmor D, Cartin-Ceba R, Gajic O, Kor D. Prehospitalization Acute, antiplatelet therapy is associated with a reduced incidence of Study., lung injury: a population-based cohort. Chest. 2011;139(2):289–95.
- [71] Pitchford S. Novel uses for anti-platelet agents as anti-inflammatory drugs. Br J Pharmacol. 2007;152(7):987–1002.
- [72] Müller K, Chatterjee M, Rath D, Geisler T. Platelets, inflammation and anti-inflammatory effects of antiplatelet drugs in ACS and CAD. Thromb Haemost. 2015;114(3):498–518.
- [73] Hundelshausen P, Schmitt M. Platelets and their chemokines in atherosclerosis—clinical applications. Front Physiol. 2014;5:294.
- [74] Ross R, Glomset J. The pathogenesis of atherosclerosis (first of two parts). N Engl J Med. 1976;295:369–77.
- [75] Ross R, Glomset J. The pathogenesis of atherosclerosis (second of two parts). N Engl J Med. 1976;295:420–5.
- [76] Herbin O, Regelmann A, Ramkhelawon B, Weinstein E, Moore K, Alexandropoulos K. Monocyte Adhesion and Plaque Recruitment During Atherosclerosis Development Is Regulated by the Adapter Protein Chat-H/SHEP1. Arter Thromb Vasc Biol. 2016;36(9):1791–801.
- [77] Heijnen H, van der Sluijs P. Platelet

- secretory behaviour: As diverse as the granules... or not? J Thromb Haemost. 2015;13(12):2141–51.
- [78] Franco AT, Corken A, Ware J. Platelets at the interface of thrombosis, in fl ammation, and cancer. Blood [Internet]. 2015;126(5):582–8. Available from: http://www.bloodjournal.org/content/126/5/582
- [79] Gawaz M, Stellos K, Langer H. Platelets modulate atherogenesis and progression of atherosclerotic plaques via interaction with progenitor and dendritic cells. J Thromb Haemost. 2008;6(2):235–42.
- [80] Gawaz M, Langer H, May A. Platelets in inflammation and atherogenesis. J Clin Invest. 2005;115:3378–84.
- [81] Petersen F, Bock L, Flad HD, Brandt E. A chondroitin sulfate proteoglycan on human neutrophils specifically binds platelet factor 4 and is involved in cell activation. J Immunol [Internet]. 1998;161(8):4347–55. Available from: http://www.ncbi.nlm.nih.gov/pubmed/9780212
- [82] Varki A. Trousseau's syndrome: multiple definitions and multiple mechanisms. Blood. 2007;110(6):1723–9.
- [83] Gasic G, Gasic T, Galanti N, Johnson T, Murphy S. Platelet-tumor-cellinteractions in mice. The role of platelets in the spread of malignant disease. Int J Cancer. 1973;11(3):704–18.
- [84] Jain S, Harris J, Ware J. Platelets: linking hemostasis and cancer. Arter Thromb Vasc Biol. 2010;30(12):2362–7.

- [85] Nieswandt B, Hafner M, Echtenacher B, Mannel D. Lysis of tumor cells by natural killer cells in mice is impeded by platelets. Cancer Res. 1999;59:1295–300.
- [86] Palumbo J, Talmage K, Massari J, La Jeunesse C, Flick M, Kombrinck K, et al. Platelets and fibrin(ogen) increase metastatic potential by impeding natural killer cell mediated elimination of tumor cells. Blood. 2005;105:178–85.
- [87] Elaskalani O, Berndt M, Falasca M, Metharom P. Targeting Platelets for the Treatment of Cancer. Cancers (Basel). 2017;22(9).
- [88] Rachidi S, Kaur M, Lautenschlaeger T, Li Z. Platelet count correlates with stage and predicts survival in melanoma. Platelets. 2019;13:1–5.
- [89] Pinedo H, Verheul H, D'Amato R, Folkman J. Involvement of platelets in tumour angiogenesis? Lancet. 1998;352(9142):1775–7.
- [90] Verheul H, Hoekman K, Luykx-de B, Eekman C, Folman C, Broxterman H, et al. Platelet: transporter of vascular endothelial growth factor. Clin Cancer Res. 1997;3(12):2187–90.
- [91] Dobbs S, Brown L, Ireland D, Abrams K, Murray J, Gatter K, et al. Platelet-derived endothelial cell growth factor expression and angiogenesis in cervical intraepithelial neoplasia and squamous cell carcinoma of the cervix. Ann Diagn Pathol. 2000;4(5):286–92.
- [92] Aiello L, Avery R, Arrigg P, Keyt B,

- Jampel H, Shah S, et al. Vascular endothelial growth factor in ocular fluid of patients with diabetic retinopathy and other retinal disorders. N Engl J Med. 1994;331(22):480–1487.
- [93] Monzavi-Karbassi B, Stanley J, Hennings, L. Jousheghany F, Artaud C, Shaaf S, Kieber-Emmons T. Chondroitin sulfate glycosaminoglycans as major P-selectin ligands on metastatic breast cancer cell lines. Int J Cancer. 2007;120:1179–91.
- [94] Kim Y, Borsig L, Varki N, Varki A. P-selectin deficiency attenuates tumor growth and metastasis. Proc Natl Acad Sci U S A. 1998;95:9325–9330.
- [95] Borsig L, Wong R, Hynes R, Varki N, Varki A. Synergistic effects of L- and P-selectin in facilitating tumor metastasis can involve non-mucin ligands and implicate leukocytes as enhancers of metastasis. Proc Natl Acad Sci U S A. 2002;99:2193–2198.
- [96] Jain S, Zuka M, Liu J, Russell S, Dent J, Guerrero J, et al. Platelet glycoprotein Iba supports experimental lung metastasis. Proc Natl Acad Sci U S A. 2007;104:9024–9.
- [97] Jain S, Russell S, Ware J. Platelet gly-coprotein VI facilitates experimental lung metastasis in syngenic mouse models. J. Thromb Haemost. 2009;7:1713–7.
- [98] Varon D, Dardik R, Shenkman B, Kotev-Emeth S, Farzame N, Tamarin I, et al. A new method for quantitative analysis of whole blood platelet interaction with

- extracellular matrix under flow conditions. Throm Res. 1997;85:283–94.
- [99] Trikha M, Zhou Z, Timar J, Raso E, Kennel M, Emmell E, et al. Multiple roles for platelet GPIIb/IIIa and alphavbeta3 integrins in tumor growth, angiogenesis, and metastasis. Cancer Res. 2002;62:2824–33.
- [100] Amirkhosravi A, Amaya M, Siddiqui F, Biggerstaff J, Meyer T, JL. F. Blockade of GpIIb/ IIIa inhibits the release of vascular endothelial growth factor (VEGF) from tumor cell-activated platelets and experimental metastasis. Platelets. 1999;10:285–92.
- [101] Pietras K, Ostman A, Sjöquist M, Buchdunger E, Reed R, Heldin C, et al. Inhibition of platelet-derived growth factor receptors reduces interstitial hypertension and increases transcapillary transport in tumors. Cancer Res. 2001;61(7):2929–34.
- [102] Heuchel R, Berg A, Tallquist, Ahlén M, Reed R, Rubin K, et al. Platelet-derived growth factor β receptor regulates interstitial fluid homeostasis through phosphatidylinositol-3′ kinase signaling. Proc Natl Acad Sci U S A. 1999;96(20):11410–5.
- [103] Cairns R, Papandreou I, Denko N. Overcoming Physiologic Barriers to Cancer Treatment by Molecularly Targeting the Tumor Microenvironment. Mol Cancer Res. 2006;4(2):61–70.
- [104] Alsina-Sanchís E, Figueras A, Lahiguera A, Gil-Martín M, Pardo B, Piulats J, et al. TGFβ Controls Ovarian

- Cancer Cell Proliferation. Int J Mol Sci. 2017;18(8):1658.
- [105] Apte S, Fan D, Killion J, Fidler I. Targeting the Platelet-Derived Growth Factor Receptor in Antivascular Therapy for Human Ovarian Carcinoma. Clin Cancer Res. 2004;10(3):897–908.
- [106] Liu C, Jernigan D, Zhang Y, Fatatis A. Implication of platelet-derived growth factor receptor alpha in prostate cancer skeletal metastasis. Chin J Cancer. 2011;30(9):612–9.
- [107] Lindberg N, Holland E. PDGF in gliomas: more than just a growth factor? Ups J Med Sci. 2012;117(2):92–8.
- [108] Wojtukiewicz M, Hempel D, Sierko E, Tucker S, Honn K. Antiplatelet agents for cancer treatment: a real perspective or just an echo from the past? Cancer Metastasis Rev. 2017;36(2):305–29.
- [109] Walsh T, Metharom P, Berndt M. The functional role of platelets in the regulation of angiogenesis. Platelets. 2015;26(3):199–211.
- [110] Carmeliet P. Angiogenesis in life, disease and medicine. Nat 2005. 2005;438:932–936.
- [111] Battinelli EM, Markens BA, Italiano JE, Dc W, Jr JEI. Release of angiogenesis regulatory proteins from platelet alpha granules: modulation of physiologic and pathologic angiogenesis Release of angiogenesis regulatory proteins from platelet alpha granules: modulation of physiologic and pathologic angiogenes.

- 2013;118(5):1359-69.
- [112] Milovanovic M, Nilsson E, Jaremo P. Relationships between platelets and inflammatory markers in rheumatoid arthritis. Clin Chim Acta. 2004;343:237–40.
- [113] Berrettini M, Parise P, Constantini V, Grasselli S, Nenci G. Platelet activation in psoriasis. Thromb Haemost. 1985;53:195–7.
- [114] Ho-Tin-Noe B, Goerge T, Cifuni S, Duerschmied D, Wagner D. Platelet granule secretion continuously prevents intratumor hem- orrhage. Cancer Res. 2008;68:6851–8.
- [115] Yamashiro K, Tsujikawa A, Ishida S, Usui T, Kaji Y, Honda Y, et al. Platelets accumulate in the diabetic retinal vasculature following endothelial death and suppress blood-retinal barrier breakdown. Am J Pathol. 2003;163:253–9.

Review Article

Psychosocial Aspects of Thalassemia and Patient's Quality of Life: A Narrative Review

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> Phone Number :00966594239596 E-mail: Dr_Alsaad@hotmail.com Abbreviations:

WHO: World Health Organization. QOL: Quality of Life. CBT: Cognitive Behavioral Therapy CBFT: Cognitive-Behavioral Family Therapy ACT: Acceptance and Commitment Therapy EFFT: Emotion-Focused Family Therapy

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Abstract

Background & Aims: Mental health and quality of life are commonly affected in patients with thalassemia and their caregivers. This review aims to synthesize the available evidence and to assess the prevalence of depression and anxiety in patients with thalassemia and their caregivers. This review also examines the bidirectional relationship between thalassemia and depression and anxiety and its impact on the quality of life of patients and their caregivers.

Methods: Five electronic databases were searched [PsychInfo, PubMed, Medline, Google Scholar, and EMBASE] and also other sources. This search combined different terms of mental health and quality of life of patients with thalassemia and caregivers. The search went up until January 2019

Results: Forty articles are included in this review. The studies showed a high prevalence of mental illnesses, particularly depression and anxiety, among patients with thalassemia and their caregivers. Many factors have been found that impacts the quality of life of patients with thalassemia and their caregivers, including thalassemia, its related-complications, medical treatment and, psychological distress, and comorbid mental illness. Although all the studies that looked at comorbid mental illness and thalassemia recommended adding a psychological treatment, only three studies did investigate this and had shown some benefits

Conclusion: Thalassemia should be addressed as an illness with biopsychosocial components and should be treated as such. More studies are needed to assess the effectiveness of different psychological interventions for patients with thalassemia and their caregivers. Also, two new psychotherapies are mentioned and discussed as they address the psychological needs of patients and their caregivers.

Keywords:

Thalassemia, Depression, Anxiety, Therapy, Quality of life Caregivers

الملخص

الخلفية والأهداف: من الشائع أن تتأثر الصحة النفسية وجودة الحياة لدى مرضى الثلاسيميا ومقدمي الرعاية لهم. تهدف هذه المراجعة إلى تجميع الأدلة المتاحة وتقييم مدى انتشار اضطراب الاكتئاب والقلق لدى مرضى الثلاسيميا ومقدمي الرعاية لهم. أيضًا تتناول هذه المراجعة العلاقة ثنائية الاتجاه بين مرض الثلاسيميا والاكتئاب والقلق وتأثير ها على جودة حياة المرضى ومقدمي الرعاية لهم

طريقة البحث: تم البحث في خمس قواعد بيانات إلكترونية PsychInfo و EMBASE و Google Scholar و PubMed و وأيضًا مصادر أخرى. جمع هذا البحث بين المصطلحات المختلفة للصحة النفسية و جودة حياة مرضى الثلاسيميا ومقدمي الرعاية. استمر البحث حتى شهر يناير ٢٠١٩.

النتائج: أربعون مقالة مدرجة في هذه المراجعة. أظهرت الدراسات ارتفاع معدل انتشار الأضطرابات النفسية، وخاصة اضطرابي الاكتئاب والقلق ، بين مرضى الثلاسيميا ومقدمي الرعاية لهم. تم العثور على العديد من العوامل التي تؤثر على جودة حياة مرضى الثلاسيميا ومقدمي الرعاية لهم ، بما في ذلك مرض الثلاسيميا والمضاعفات المرتبطة الرعاية لهم ، بما في ذلك مرض الثلاسيميا والمضاعفات المرتبطة المصاحبه لمرض الثلاسيميا. وعلى الرغم من أن جميع الدراسات التي نظرت وبحثت في الأضطرابات النفسية المصاحبه لمرض الثلاسيميا أوصت بإضافة العلاج النفسي لمرضى الثلاسيميا ، إلا أنه فقط ثلاث دراسات حققت في إضافة العلاج النفسي وأظهرت بعض الفوائد له. الخلاصة : يجب معالجة الثلاسيميا كمرض يحتوي على مكونات نفسية اجتماعية ويجب علاجها على هذا النحو. هناك حاجة إلى مزيد من الدراسات لتقييم فعالية العلاجات النفسية المختلفة لمرضى الثلاسيميا ومقدمي الرعاية لهم. أيضا، تم ذكر ومناقشة اثنين من العلاجات النفسية المرضى ومقدمي الرعاية لهم. أيضا، تم ذكر ومناقشة اثنين من العلاجات النفسية المجتمى الرعاية لهم.

Introduction

Thalassemia is an Inherited hemoglobin disorder, and it is common in the Middle East, Mediterranean regions, and South and Southeast Asia [1]. According to the WHO, hemoglobin disorders are common in 71% of countries and affecting around 89% of births. 50,000-100,000 children with thalassemia major die each year in low and middle-income countries [2].

Thalassemia is a chronic medical disorder that impacts not only the patient but also the whole family. It impacts their mental health and their quality of life [3,4]

A new study that came out on Nov 2018 again showed that psychosocial issues are common among children with thalassemia [5]. The prevalence of psychological problems in patients with thalassemia is around 43% [6]. Mental illness, particularly depression, is the leading cause of disability worldwide [2]. In low-middle income countries, around 76-85% and around 35-50% in high-income countries of people with mental disorders receive no treatment for their disorder [2].

Different guidelines and reviews have been written on the management and treatment of Thalassemia. However, they tend to cover the biological aspects of this disorder.

Not until 2014 that the Thalassemia International Federation (TIF) did add a chapter on psychological support on the 3rd edition of guidelines for the management of transfusion-

dependent thalassemia 2014. Psychological support is important for patients with thalassemia, regardless of it being transfusion-dependent or transfusion independent.

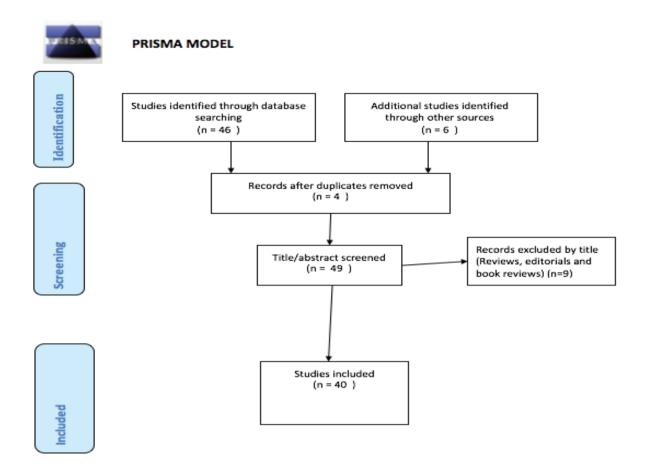
In this article, we will review the prevalence and impact of comorbidity between thalassemia and depression and anxiety and also the quality of life of patients with thalassemia and their caregivers and how to improve the care provided to them. Finally, it will propose methods for addressing areas of uncertainty.

Methods

Five electronic databases were searched [PsychInfo, PubMed, Medline, Google Scholar, and EMBASE] and also other sources. This search combined different terms of mental health and quality of life of patients with thalassemia and caregivers.

The search went up until January 2019 using the following terms "mental illness", "psychiatric disorder", psychosocial impact or aspect", "depression," "anxiety," "psychotherapy," "psychological," "quality of life", "caregivers," or "parents" AND "thalassemia".

Initially, 52 studies have been identified, and after screening 40 studies have been included in this review. Twelve studies were excluded because of duplications and meeting exclusion criteria. Figure 1



Inclusion criteria:

All thalassemia subtypes are included Articles included are those written in English only.

Exclusion Criteria:

- · Non-English written articles.
- · Studies that did not address the search keywords.
- · Review articles, editorials, and book chapters.

1-Thalassemia and Depression:

The relationship between thalassemia and depression had been proven in many studies [7-25]. Different scales have been used to assess depression. See Table 1

Depression is the most common psychologi-

cal health disorder among patient with thalassemia and their caregivers. [11,18,26], Prevalence of depression in children with thalassemia ranges from 19.8% to 62% and around 10.3-35% in adults with thalassemia [16, 17,18, 20,21,26,27]

This wide range in prevalence depends on different factors, for example, the power of the study; the time and place it was conducted. The relationship between depression and thalassemia is bidirectional [26]. Depression did affect the physical and mental health of the children with Beta-thalassemia Major. Depressed children with thalassemia had more fatigue, pain, discomfort, and more sleep disturbance. [26,28]

Table 1

Author	Number	Thalassmia	Scale used	Country
Ahmad Ghanizadeh et al (2006)	110 children	Thalassemia Major	Kiddie-SADS - Life- time Version (K- SADS-PL)	Iran
Burcu Cakaloz, et al (2009)	20 children	Thalassemia major	The child behavior check-list (CBCL) Semi-structured interview with a clinician according to DSMIV	Turkey
Brigitte Khoury et al (2012)	80 Adults	Beta-Thalas- semia Major and Intermedia	The Beck Depression Inventory (BDI)	Lebanon
Akbar Shafiee et al (2014)	56 children	Beta-Thalas- semia Major	Beck's Depression Inventory (BDI)	Iran
Aghbabak Maheri et al (2018)	389 Adults	Beta-Thalas- semia Major	The hospital anxiety and depression scale The Multidimensional Scale of Perceived Social Support	Iran
Krupa Patel et al (2018)	10,046 Adults	Beta-Thalas- semia Major	USED Clinical Classifications Software (CCS) to utilized the discharge data from the National Inpatient Sample (NIS).	United States

Risk factors

Different factors could lead patients with thalassemia to develop depression, either in their childhood and /or adulthood. These factors include: hospitalization and blood transfusion frequency, the separation from the parents and peers, and disease-related complications, such as facial dysmorphisms, skeletal anomalies, gallstones, delayed puberty, hepatosplenomegaly, and heart failure [14,18].

Hypercholesterolemia

Hypercholesterolemia is an independent risk factor for depression [29]. Patients with thal-assemia trait have low levels of total cholesterol and LDL-cholesterol [30]. This is one possible mechanism to understand their increased risk of developing depression.

Ferritin level and type of iron chelation therapy

Although the serum ferritin level and type of iron chelation therapy had been thought of as possible factors affecting psychological disorders in patients with beta-thalassemia major. Two studies [17,22] had shown that the type of iron chelation therapy, blood transfusion interval, and ferritin levels had no significant impact on the patient's level of depression or anxiety.

Level of education

Depressed adults with beta-thalassemia major were less likely to have a university degree compared to non-depressed adults with beta-thalassemia [17]. The opposite was also correct, meaning that adults with beta-thalassemia without a high school diploma had higher depressive scores in comparison to those with a high school diploma [17]. This could be because of different factors, for example, people with higher education tend to have a better socioeconomic status, they are more likely to understand their illness, thalassemia, and thus cope better with it. They also might be more resourceful, socially, and financially. All of these factors could be protective against depression.

Age

Three studies [7,32,33] found that adolescents with thalassemia experience fewer depressive symptoms compared to younger children and thus had higher health-related quality of life

scores than younger children. This could be a reflection of their ability to adjust and cope with the demands of the disease

Gender

Six studies [11, 18,19,21,25,34] have looked at the relationship between the gender of the patient with thalassemia and mental illness. Even though there is no difference in the overall prevalence of mental disorders among males and females. Different mental disorders, however, affects females more than males and vice versa. Females are more likely to have depression and anxiety disorders. Males, on the other hand, are more likely to have a comorbid substance use disorder and disruptive behavioral disorders.

Maladaptive cognitive styles

Adults with thalassemia major use verity of maladaptive coping styles. They tend to use escape-avoidance thinking and behavior, and their self-image was found to be low [31]. These coping styles led patients with thalassemia to feel helplessness and hopelessness and eventually depressed.

Factors to help cope with depression

Different factors have been found of help to patients with thalassemia to better cope with mental illnesses.

- 1. Gender: girls cope better than boys [7]
- 2. Older Age: adolescents seem to adjust to the demands of thalassemia better as they grow up [33].

- 3. Level of education also helps patients cope with the disease and to continue treatment [33].
- 4. Family and social support [33].
- 5. Negative affect differentiation: Adults who were able to regulate their negative, sad emotions were more able to adapt to their illness (Thalassemia) and were more compliant to treatment [36].

6. Thalassemia and Anxiety

Ten studies reported that the prevalence of anxiety disorder in children with thalassemia is 34%- 64% and 23.7% in adults with thalassemia [6,10,14,17,18,19,20,21,22,27, 37].

Children with thalassemia are more vulnerable to have a specific phobia (blood and injections), separation anxiety disorder, illness anxiety disorder, and generalized anxiety disorder [10,20, 38].

3. Thalassemia and Hospital outcome

Having a comorbid depression or anxiety did not increase the all-cause mortality in adults with beta-thalassemia in comparison to those without a comorbid depression or anxiety [18]. However, the length of stay and total hospital charges are higher in patients with beta-thalassemia and comorbid depression or anxiety. Comorbidity increased the length of stay by 44.6% and total costs by 23.4%. The all-cause mortality rate was reported at 1.9% in overall beta-thalassemia patients [18].

4. Parents of children with Thalassemia

Depression and generalized anxiety are common among parent of children with thalassemia. Out of 100 parents of children with thalassemia, 29% had depression, and 41.3% had generalized anxiety [3,26]. Depression and anxiety are more common among mothers. Mothers also tend to have more severe depressive symptoms compared to fathers [3]. Rates of anxiety were also higher among mothers [26]

Parents' depression and anxiety could be for various reasons. Their uncertainty about their child's future and health, poor support from relatives and society, social isolation, and their low level of education. Also, it had been found that spousal conflicts are more among parents of children with thalassemia. In Greece, for example, [35] fathers tend to blame mothers for the child's illness, thus causing an ongoing conflict.

A study was done in Thailand [39] that involved 15 mothers of children with thalassemia found that the mother's lack of knowledge about thalassemia and its related-complications did impact their mood and quality of life.

One study [40] looked at protective factors that helped parents cope better with their child's illness. They found that higher educational level, high socioeconomic status, social support, and being more informed about their child's illness and its complications did help parents cope better. Also, self-discipline was a positive character relating to the parents' ability to cope with their responsibilities

and the burden of their child's illness.

5. Thalassemia and Quality of life

Different studies used different Quality of life questioners like EQ5D [6], Pediatric Quality of Life (PedsQLTM) [19,31,32,41, 42] Health-Related Quality of Life (HRQoL) measurement [31,32,41] and WHOQOL-BREF questionnaire [38,40]. While one study used a subjective measure [21, 43].

The quality of life of children with thalassemia is affected for several reasons, such as complications related to thalassemia and treatment side effects, poor academic achievements, comorbid mental illness, and low family income. Parents tend to assess their children's quality of life significantly lower than the children themselves [6,19,47].

In two studies, higher levels of depression and anxiety caused children with thalassemia to have lower scores on their psychosocial health in comparison to their physical health [32,33].

One study [44] did compare the quality of life of patients with Transfusion independent thalassemia with Transfusion dependent thalassemia patients. They found that both groups had a poor quality of life because of having pain, emotional difficulties, and inadequate social support. Transfused thalassemia patients did, however, have higher scores in term of daily activities and Physical fitness.

Education level and QOL

Seven studies looked at the impact of thalassemia on children's education. Children and adults with thalassemia tend to have a lower educational level compared to those without thalassemia [14,17,21,22,31,30,39,43]. In these articles, many factors have been reported explaining the poor academic achievements in patients with thalassemia. These factors include; frequent school absenteeism, peer relationship disruption, their present mental illness, and their lower for emotional or social functioning, the negative effect of chronic anemia, and disease-related complications. Parent's poverty, parenting style, and level of education are also important factors that impact the patient's academic achievements [32].

Education level does impact the quality of life of patients with thalassemia [21,44].

One study did use a full, standard neuropsychological testing for 23 children and nine young adults [45]. They found that none of the patients with beta-thalassemia demonstrated any abnormal neurophysiological that resulted in any relevant signs or symptoms. They, however, found that patients with beta-thalassemia demonstrated subclinical involvement of the central and peripheral neural pathways and may require a regular IQ testing using (WISC-III) to detect relevant abnormalities and apply appropriate management.

Interestingly, one study showed that when all patients with thalassemia have equal access to a comprehensive treatment program, their educational achievement would be comparable to those without thalassemia [46].

Blood Transfusion and QOL

Children with thalassemia with a pre-transfusion hemoglobin level higher than 9 g/dL had a significantly higher health-related quality of life than patients whose pre-transfusion hemoglobin level was below 9 g/dL [33].

6. Ferritin level, chelation therapy, and OOL

One study found that the delayed start of iron chelation had a negative impact on the quality of life in children with thalassemia. This is possibly a complications caused by excessive accumulation of iron in body organs, especially heart, liver, or pancreas [41].

Serum ferritin level and disease-related complications significantly affected the quality of life of adults with thalassemia [40, 42].

7. Therapeutic interventions, depression, and QOL

Only three studies have been identified that focused on therapeutic interventions for patients with thalassemia.

Cognitive Behavioral Therapy (CBT)

In 2015 a Cochrane review concluded that Randomized Controlled Trial (RCT) have not been done to assessing the effectiveness of specific psychological interventions for thal-assemia [47]. In 2018 an RCT was done to evaluate the effects of CBT on comorbid depression and anxiety among 76 adult patients

with thalassemia [48].

This study did show that CBT is an effective intervention to treat depression and anxiety among patients with thalassemia. This RCT was done in one center, and the power of this study is low. It needs to be replicated with adequate-powered, and preferably as a multicenter study.

Cognitive-Behavioral Family Therapy (CBFT)

One study did CBFT for children with betathalassemia major and their mothers [49]. They found that children with beta-thalassemia major who underwent CBFT had proper compliance with their medical treatment plan. However, they were still struggling emotionally and physically. Targeting mothers in the therapy did help in improving the relationship with the child and medical staff. This, however, did not improve the mother's quality of life

Partnership Care Model

One study had been done to investigate a model based on collaboration between patients with thalassemia major, their caregivers, and treating team [13]. The model is called partnership care model (developed first by Wiggins 2006 [50]). After implementing this model, patients with thalassemia had a significant improvement in their mental health, particularly in the level of symptoms of depression, anxiety, social dysfunction, and physical complaints compared to the control group [13].

The partnership care model had been shown to be effective in improving mental health of patients with chronic medical illnesses like patients with cardiovascular disease (e.g hypertension [51] and coronary artery disease [52]), chronic bronchitis [53], and patients undergoing hemodialysis [54]).

Discussion

As it had been shown through this review, patients with thalassemia and their caregivers are at an increased risk of mental illness and also have a decreased quality of life. Also, Patient with thalassemia with undiagnosed comorbid mental illnesses have an increased hospital stay and total treatment cost.

Three studies, however, have been done on the treatment of comorbid mental illness and on improving the quality of life of patients with thalassemia. Only the one that looked at the effectiveness of CBT was an RCT and had a significant outcome in term of alleviating comorbid anxiety and depression.

Cognitive-Behavioral Family Therapy (CBFT) showed some benefits to children with thalassemia and their mothers in term of improving quality of life and thus could be used in combination with additional psychological support. The Third treatment model is the partnership care model, which is useful in improving depressive and anxiety symptoms in patients with thalassemia and their caregivers.

Many thalassemia treatment centers through-

out the world, especially in countries where thalassemia is common, unfortunately, did not implement such support. This lack of translation of research and guidelines has an impact on the health and quality of life of patients with thalassemia.

Limitation

This is a narrative review done by one reviewer, and this could lead to unintentional bias in the data collection.

Recommendations

Enhancing Healthcare Team Outcomes

- Quality of life and disease burden of patients with thalassemia is predicted by physical activity, good interpersonal relationships, social/ family support, and good social integration and the accessibility of medical treatment for thalassemia [17,46]. These protective factors could be a target of therapy for patients.
- Patients with thalassemia and their caregivers should be screened for comorbid mental illnesses.
- A team consists of the pediatrician (or family physician), a hematologist, a nurse, a social worker, and a psychologist should be involved in treating patients with thalassemia. If required, psychiatric consultation should be made.
- Medical and psychological education should be provided to caregivers of patients with thalassemia. Caregiver psy-

chological support.

Mental health support should be considered as part of the individualized treating plan provided by treating team. It is of a significant benefit to having a clinical psychologist and a social worker as part of the treating team

Suggested Psychotherapy Treatments for Future Studies

Different kinds of therapy might be of help, such as Acceptance and Commitment Therapy (ACT) and Emotion-Focused Family Therapy (EFFT) could be of help to patients with thalassemia and their caregivers.

Acceptance and Commitment Therapy (ACT)

ACT is considered a third-wave behavior therapy [55]. ACT is a trans-diagnostic approach, a diagnosis-specific intervention aiming for improving the function and quality of life of the individual regardless of the cause of stress or difficulties.

This intervention encourages values-consistent living teaches the willingness to experience difficult and unavoidable internal experiences (like pain, anxiety, fatigue, and depression) as they are without defense.

Acceptance and Commitment Therapy's effectiveness has been proven across many long-term conditions including, Sickle cell disease, epilepsy, multiple sclerosis, cancer, chronic pain, cardiac disease, and diabetes [56-60].

2. Emotion-Focused Family Therapy (EFFT)

Patients with thalassemia and their caregivers struggle with emotional distress. Caregivers also are highly involved in the care of patients with thalassemia. For these two reasons, EFFT could be of help to them as it helps to manage emotions and helps caregivers to be more effective, to be the main coach for the patient.

EFFT is an emotion-processing skills-based approach that helps parents to identify their emotional blocks and how to overcome them [61,62]. Also, through this therapy, parents learn skills on how to support their child in processing his or her emotions and increase his/ her emotional self-efficacy. All of that also improves the parent-child relationship, and this could improve the patient and caregiver's quality of life. In this recent study [61] that involved 124 parents of children with a wide range of mental health issues, EFFT lead to significant improvement in the total clinical symptoms of Children's. Also, parental stress decreased.

The effectiveness of Acceptance and Commitment Therapy and Emotion-Focused Family Therapy for patients with thalassemia and their caregivers with comorbid mental illness need to be studied

Conclusion

Much research has been done and proved that depression and anxiety are highly comorbid with thalassemia. However, few studies targeting the treatment of comorbid mental illness have been done. Further, many patients with thalassemia and their caregivers do not receive psychosocial support. Treating team should focus on treating patients with thalassemia in a bio-psycho-social approach as this will help improve their physical and mental health and improve their quality of life.

Declaration

No conflict of interest.

References

- [1] Weatherall DJ. Thalassemia as a global health problem: recent progress toward its control in the developing countries. Ann N Y Acad Sci 2010;1202:17-23.
- [2] Modell B, Darlison M. Global epidemiology of haemoglobin disorders and derived service indicators. Bull World Health Organ. 2008;86(6):480-487.
- [3] Aziz K, Sadaf B, Kanwal S. Psychosocial problems of Pakistani parents of Thalassemic children: a cross sectional study done in Bahawalpur, Pakistan. Biopsychosoc Med 2012;6:15.
- [4] Anum J, Dasti R. Caregiver Burden, Spirituality, and Psychological Well-Being of Parents Having Children with Thalassemia. J Relig Health 2016;55:941-955.
- [5] Raman V, Prakash A, D'Souza F. Psychosocial Issues in Children With Thalassemia: From Identification to a Model for Management in a Developing Country. J Pediatr Hematol Oncol 2018.

- [6] Shaligram D, Girimaji SC, Chaturvedi SK. Psychological problems and quality of life in children with thalassemia. Indian J Pediatr 2007;74:727-730.
- [7] Mikelli A, Tsiantis J. Brief report: Depressive symptoms and quality of life in adolescents with b-thalassaemia. J Adolesc 2004;27:213-216.
- [8] Hajibeigi B, Azarkeyvan A, Alavian SM, Lankarani MM, Assari S. Anxiety and depression affects life and sleep quality in adults with beta-thalassemia. Indian J Hematol Blood Transfus 2009;25:59-65.
- [9] Naderi M, Hormozi MR, Ashrafi M, Emamdadi A. Evaluation of Mental Health and Related Factors among Patients with Beta-thalassemia Major in South East of Iran. Iran J Psychiatry 2012;7:47-51.
- [10] Moorjani JD, Issac C. Neurotic manifestations in adolescents with thalassemia major. Indian J Pediatr 2006;73:603-607.
- [11] Naderi M, Hormozi MR, Ashrafi M, Emamdadi A. Evaluation of Mental Health and Related Factors among Patients with Beta-thalassemia Major in South East of Iran. Iran J Psychiatry 2012;7:47-51.
- [12] Yengil E, Acipayam C, Kokacya MH, Kurhan F, Oktay G, Ozer C. Anxiety, depression and quality of life in patients with beta thalassemia major and their caregivers. Int J Clin Exp Med 2014;7:2165-2172.
- [13] Shamsi A, Amiri F, Ebadi A, Gha-

- deri M. The Effect of Partnership Care Model on Mental Health of Patients with Thalassemia Major. Depress Res Treat 2017;2017:3685402.
- [14] Yahia S, El-Hadidy MA, El-Gilany AH, Anwar R, Darwish A, Mansour AK. Predictors of anxiety and depression in Egyptian thalassemic patients: a single center study. Int J Hematol 2013;97:604-609.
- [15] Keşkek SO, Kirim S, Turhan A, Turhan FG. Depression in subjects with beta-thalassemia minor. Ann Hematol 2013;92:1611-1615.
- [16] Shafiee A, Nazari S, Jorjani S, Bahraminia E, Sadeghi-Koupaei M. Prevalence of depression in patients with β-thalassemia as assessed by the Beck's Depression Inventory. Hemoglobin 2014;38:289-291.
- [17] Maheri A, Sadeghi R, Shojaeizadeh D, Tol A, Yaseri M, Rohban A. Depression, Anxiety, and Perceived Social Support among Adults with Beta-Thalassemia Major: Cross-Sectional Study. Korean J Fam Med 2018;39:101-107.
- [18] Patel K, Bhivandkar S, Desai R, Antin T. The burden of psychiatric illnesses in adult patients with beta-thalassemia: a 5-year nationwide inpatient evaluation in the United States. Ann Hematol 2018.
- [19] Behdani F, Badiee Z, Hebrani P, Moharreri F, Badiee AH, Hajivosugh N, et al. Psychological Aspects in Children and

- Adolescents With Major Thalassemia: A Case-Control Study. Iran J Pediatr 2015;25:e322.
- [20] Ghanizadeh A, Khajavian S, Ashkani H. Prevalence of psychiatric disorders, depression, and suicidal behavior in child and adolescent with thalassemia major. J Pediatr Hematol Oncol 2006;28:781-784.
- [21] Gharaibeh H, Amarneh BH, Zamzam SZ. The psychological burden of patients with beta thalassemia major in Syria. Pediatr Int 2009;51:630-636.
- [22] Cakaloz B, Cakaloz I, Polat A, Inan M, Oguzhanoglu NK. Psychopathology in thalassemia major. Pediatr Int 2009;51:825-828.
- [23] Sharghi A, Karbakhsh M, Nabaei B, Meysamie A, Farrokhi A. Depression in mothers of children with thalassemia or blood malignancies: a study from Iran. Clin Pract Epidemiol Ment Health 2006;2:27.
- [24] Saini A, Chandra J, Goswami U, Singh V, Dutta AK. Case control study of psychosocial morbidity in beta thalassemia major. J Pediatr 2007;150:516-520.
- [25] Shaligram D, Girimaji SC, Chaturvedi SK. Quality of life issues in caregivers of youngsters with thalassemia. Indian J Pediatr 2007;74:275-278.
- [26] Yengil E, Acipayam C, Kokacya MH, Kurhan F, Oktay G, Ozer C. Anxiety, depression and quality of life in patients with

- beta thalassemia major and their caregivers. Int J Clin Exp Med 2014;7:2165-2172.
- [27] Khoury B, Musallam KM, Abi-Habib R, Bazzi L, Ward ZA, Succar J, et al. Prevalence of depression and anxiety in adult patients with β-thalassemia major and intermedia. Int J Psychiatry Med 2012;44:291-303.
- [28] Örengül AC, Ucuz L, Battaloglu NO, Ozek G, Gormez V. Prevalence of psychiatric disorders and suicidality among children and adolescents with thalassemia major—A Turkish sample, Children's Health Care, 48:1, 120-129, DOI: 10.1080/02739615.2018.1500290.
- [29] Segoviano-Mendoza M, Cardenas-de la Cruz M, Salas-Pacheco J, Vazquez-Alaniz F, La Llave-Leon O, Castellanos-Juarez F, et al. Hypocholesterolemia is an independent risk factor for depression disorder and suicide attempt in Northern Mexican population. BMC Psychiatry 2018;18:7.
- [30] Maioli M, Pettinato S, Cherchi GM, Giraudi D, Pacifico A, Pupita G, et al. Plasma lipids in beta-thalassemia minor. Atherosclerosis 1989;75:245-248.
- [31] Messina G, Colombo E, Cassinerio E, Ferri F, Curti R, Altamura C, et al. Psychosocial aspects and psychiatric disorders in young adult with thalassemia major. Intern Emerg Med 2008;3:339-343.
- [32] Hakeem GLA, Mousa SO, Moustafa

- AN, Mahgoob MH, Hassan EE. Health-related quality of life in pediatric and adolescent patients with transfusion-dependent β-thalassemia in upper Egypt (single center study). Health Qual Life Outcomes 2018;16:59.
- [33] Thavorncharoensap M, Torcharus K, Nuchprayoon I, Riewpaiboon A, Indaratna K, Ubol BO. Factors affecting health-related quality of life in Thai children with thalassemia. BMC Blood Disord 2010;10:1.
- [34] Gupta V, Singh A, Upadhyay S, Bhatia B. Psychopathology in Children with Thalassemia Major. Psychol Stud 2012) 57(1):55–57
- [35] Tsiantis J, Dragonas T, Richardson C, Anastasopoulos D, Masera G, Spinetta J. Psychosocial problems and adjustment of children with beta-thalassemia and their families. Eur Child Adolesc Psychiatry 1996;5:193-203.
- [36] Coifman KG, Ross GS, Kleinert D, Giardina P. Negative affect differentiation and adherence during treatment for thalassemia. Int J Behav Med. 2014;21(1):160-168.
- [37] Aydin B, Yaprak I, Akarsu D, Okten N, Ulgen M. Psychosocial aspects and psychiatric disorders in children with thalassemia major. Acta Paediatr Jpn. 1997;39(3):354-357.
- [38] Aydinok Y, Erermis S, Bukusoglu N, Yilmaz D, Solak U. Psychosocial impli-

- cations of Thalassemia Major. Pediatr Int. 2005;47(1):84-89.
- [39] Prasomsuk S, Jetsrisuparp A, Ratanasiri T, Ratanasiri A. Lived experiences of mothers caring for children with thalassemia major in Thailand. J Spec Pediatr Nurs 2007;12:13-23.
- [40] Jawaria Anum, Rabia Dasti. Caregiver Burden, Spirituality, and Psychological Well-Being of Parents Having Children with Thalassemia. J Relig Health (2016) 55:941–955.
- [41] Caocci G, Efficace F, Ciotti F, Roncarolo MG, Vacca A, Piras E, et al. Health related quality of life in Middle Eastern children with beta-thalassemia. BMC Blood Disord 2012;12:6.
- [42] Boonchooduang N, Louthrenoo O, Choeyprasert W, Charoenkwan P. Health-Related Quality of Life in Adolescents with Thalassemia. Pediatr Hematol Oncol. 2015;32(5):341-348.
- [43] Khurana A, Katyal S, Marwaha RK. Psychosocial burden in thalassemia. Indian J Pediatr. 2006;73(10):877-880.
- [44] Ansari S, Baghersalimi A, Azarkeivan A, Nojomi M, Hassanzadeh Rad A. Quality of life in patients with thalassemia major. Iran J Ped Hematol Oncol 2014;4:57-63.
- [45] Economou M, Zafeiriou DI, Kontopoulos E, Gompakis N, Koussi A, Perifanis V, et al. Neurophysiologic and in-

- tellectual evaluation of beta-thalassemia patients. Brain Dev 2006;28:14-18.
- [46] Floris F, Comitini F, Leoni G, Moi P, Morittu M, Orecchia V, et al. Quality of life in Sardinian patients with transfusion-dependent Thalassemia: a cross-sectional study. Qual Life Res 2018.
- [47] Anie KA, Massaglia P. Psychological therapies for thalassaemia. Cochrane Database Syst Rev 2014:CD002890.
- [48] Mohamadian F, Bagheri M, Hashemi MS, Komeili Sani H. The Effects of Cognitive Behavioral Therapy on Depression and Anxiety among Patients with Thalassemia: a Randomized Controlled Trial. J Caring Sci 2018;7:219-224.
- [49] Mazzone L, Battaglia L, Andreozzi F, Romeo MA, Mazzone D. Emotional impact in beta-thalassaemia major children following cognitive-behavioural family therapy and quality of life of caregiving mothers. Clin Pract Epidemiol Ment Health 2009;5:5.
- [50] Splaine Wiggins M. The partnership care delivery model: an examination of the core concept and the need for a new model of care. J Nurs Manag 2008;16:629-638.
- [51] Mohammadi E, Abedi HA, Jalali F, Gofranipour F, Kazemnejad A. Evaluation of 'partnership care model' in the control of hypertension. Int J Nurs Pract 2006;12:153-159.

- [52] Sadeghi S, Razmjooei N, Ebadi A, Najafi M, Asadi Lari , Bozorgzad P. Effect of applying continuous care model on patients' quality of life after Coronary Artery Bypass Graft Iranian Journal of Critical Care Nursing Spring 2009, Volume 2, Issue 1; 1-6
- [53] Khoshnevis M, Javadinasab M, Ghanei M, Hoseini S, Karimi Z, Ebadi A, Babatabar D. Effect of using collaborative care model on life quality of chemical injured patients suffering from chronic bronchiolitis. Iranian Journal of Critical Care Nursing Summer 2009, Volume 2, Issue 2; 47-50
- [54] Ghavidel F., Mohammadzadeh S., Pirasteh H., Alavi Majd H. Effect assessment of applyin the partnership care model on quality of life in hemodialysis patients referring to Be'sat Hospital of IRI Air Force. Journal of IRIAF Health Administration. 2009;12(2):22–27.
- [55] Hayes SC1, Luoma JB, Bond FW, Masuda A, Lillis J. Acceptance and commitment therapy: model, processes and outcomes. Behav Res Ther. 2006 Jan;44(1):1-25.
- [56] Masuda A, Cohen LL, Wicksell RK, Kemani MK, Johnson A. A case study: Acceptance and commitment therapy for pediatric sickle cell disease. J Pediatr Psychol 2011;36:398-408.
- [57] Lundgren T, Dahl J, Melin L, Kies B. Evaluation of acceptance and com-

- mitment therapy for drug refractory epilepsy: a randomized controlled trial in South Africa--a pilot study. Epilepsia 2006;47:2173-2179.
- [58] Feros DL, Lane L, Ciarrochi J, Blackledge JT. Acceptance and Commitment Therapy (ACT) for improving the lives of cancer patients: a preliminary study. Psychooncology 2013;22:459-464.
- [59] Goodwin CL, Forman EM, Herbert JD, Butryn ML, Ledley GS. A pilot study examining the initial effectiveness of a brief acceptance-based behavior therapy for modifying diet and physical activity among cardiac patients. Behav Modif 2012;36:199-217.
- [60] Gregg JA, Callaghan GM, Hayes SC, Glenn-Lawson JL. Improving diabetes self-management through acceptance, mindfulness, and values: a randomized controlled trial. J Consult Clin Psychol 2007;75:336-343.
- [61] Foroughe M, Stillar A, Goldstein L, Dolhanty J, Goodcase ET, Lafrance A. Brief Emotion Focused Family Therapy: An Intervention for Parents of Children and Adolescents with Mental Health Issues. J Marital Fam Ther 2018.
- [62] Robinson AL, Dolhanty J, Greenberg L. Emotion-focused family therapy for eating disorders in children and adolescents. Clin Psychol Psychother 2015;22:75-82.

Review Article

Physical Assessment Competence of Nursing Students: A Literature Review

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Abstract

Background: Physical assessment is an integral part of nursing and a key learning outcome in nurse education programs. Some nursing students, however, feel inadequately trained to perform physical assessment effectively.

Objectives: This literature review surveys and evaluates current research findings on the training of nursing students in physical assessment and their confidence and competence in performing this skill.

Methods: In four electronic databases—CINAHL (1), Medline (2), ProQuest-Nursing and Allied Health Database (3), and PubMed (4)—Boolean operators and nested key terms were used to craft strings for database searches. Broad search criteria were employed to ensure that all relevant articles were included. Titles were hand-searched based on the reference lists of the full texts of reviewed literature. The data was extracted from January 2019 to March 2019.

Results: Three major topics were derived from a synthesis of the findings: (a) barriers in performing physical assessment, (b) assessment tools, (c) approaches towards the improvement of physical assessment competence.

Conclusion: Physical assessment competence is fundamental to the delivery of nursing care. Evaluation and measurement of physical assessment competence is essential to determine and foster the skills of nurses in training, and evaluation and feedback are necessary to take proper corrective action for improvement. Assessment includes identifying barriers to arrive at action plans to eliminate them. Action plans can focus on good practice environments, improvement of curriculum, trainings and simulations, mentoring, emphasis on safety, and improving non-technical skills.

Keywords: assessment tools; barriers; competence; nursing student; physical assessment

Introduction

Physical Assessment (PA) is an essential part of the nursing process and a key learning outcome in nursing education [1]. It comprises a set of skills that nurses and future

الملخص

الخلفية: التقييم الصحي هو جزء لا يتجزأ من التمريض ونتائج التعلم الرئيسية في برامج تعليم التمريض. ومع ذلك ، يشعر بعض طلاب التمريض بعدم كفاية التدريب على إجراء التقييم الصحي بفعالية. الأهداف: توفير مراجعة أدبية لتقديم فهمًا دقيقًا لكفاءة التقييم الصحي لطلاب التمريض.

الأساليب: في أربع قواعد بيانات إلكترونية - CINAHL (١) ProQuest-Nursing and Allied Health (٢) Medline ProQuest-Nursing and Allied Health (٤) Database والمصطلحات الأساسية المتداخلة لصياغة سلاسل لعمليات البحث في قواعد البيانات. تم استخدام معايير البحث على نطاق واسع لضمان إدراج جميع المقالات ذات الصلة. تم البحث البدوي في العناوين ذات الصلة بناءً على قوائم مراجع النصوص الكاملة. تم استخراج البيانات من يناير بناءً على مارس ٢٠١٩.

النتائج: تم استخلاص ثلاثة مواضيع رئيسية: (أ) الصعوبات في إجراء التقييم التقييم الدوات التقييم ، (ج) النهج نحو تحسين كفاءة التقييم الصحى.

الخلاصة: كفاءة التقييم الصحي أمر أساسي لتقديم الرعاية التمريضية. تقييم وقياس كفاءة التقييم الصحي ضروري لتحديد وتعزيز مهارات الطلاب في التدريب ، والتقييم والتغذية الراجعة ضروريان لاتخاذ الإجراءات التصحيحية المناسبة للتحسين. يشمل التقييم تحديد الحواجز من أجل التوصل إلى خطط عمل للقضاء عليها. يمكن أن تركز خطط العمل على بيئات الممارسة الجيدة ، وتحسين المناهج الدراسية ، والترييات والمحاكاة ، والتوجيه ، والتركيز على السلامة ، وتحسين المهارات غير الفنية.

nurses learn from academic preparation and actual practice in clinical settings to provide patients with quality care [1]. Competence is the ability to accomplish a task, and clinical instructors evaluate their students' competence and readiness for clinical exposure [1]

when they demonstrate knowledge, attitude, and skills in relevant situations [3]. Rather than attempt to define levels of competence in this paper, we accumulate available evidence regarding competence regardless of the level adopted in particular studies. According to Alamri and Almazan [2], PA consists of system assessment (e.g. cardiovascular, respiratory, gastrointestinal, genitourinary, neuromuscular, and integument).

There are several tools for assessing students' PA competence. They include Objective-Summative (a) **Examinations** (e.g. structured observation and assessment of practice [SOAP]) [3], (b) Objective Structured Clinical Examinations (OSCEs) [4], (c) patient observation [5,6], (d) the use of case scenarios [5,6], and (e) clinical skills readiness checklists [5,6]. Knowledge and skills are measured through PA competence in nursing education [7]. It contains six important domains: (a) responsibility, (b) performancebased evaluation, (c) circumstantial significance, (d) evidence-based evaluation, (e) tool validity and reliability, (f) and participation and collaboration [8]. Students are expected to demonstrate mastery in each of domains. PA evaluation relies upon the head-to-toe assessment principle [9]. Evaluating a student's competence can be extremely challenging, as nursing requires multidimensional skills and areas of knowledge including interpersonal indications, clinical decision methods (i.e. interpreting, responding and reflecting), and psychomotor programs. However, the ability to render a precise assessment of a student's practice competence is critical in the nursing profession [10], especially given the complexity of the clinical practice environments in which future nurses are challenged to acquire a comprehensive range of PA skills in order to provide safe and effective patient care across different health care settings [11].

Healthcare institutions and nursing schools face numerous challenges pertaining to PA competence. A study conducted in Saudi Arabia identified dependence on others and technology, the culture in the ward, and the lack of patient care as barriers to PA competence in both the classroom and clinical settings [2]. A study in Sweden found that patient's congestion as perceived by 83 students (45%) was a barrier in performing PA [12]. In Ireland, PA obstacles and complexity of the language were reported to be hindrances in PA performance [13]. Addressing these hindrances is the first step to improving patient assessment by student nurses. Hospitals are expected to equip their nurses with the PA skills necessary to provide safe nursing care [14]. Academia can also play a significant role in better equipping nursing students to effectively perform PA [15]. However, several health care institutions are worried that current nursing graduates are not knowledgeable or capable enough to do basic PA and their work competencies are misaligned [16].

Empirical studies showed that nursing student's PA competence was vague ^[2,16]. Further, some nursing students reported that they felt inadequately trained ^[15] and con-

fused [2]. PA competencies are introduced in a classroom setting [2], and the gap between the orientation in the classroom and the actual demand in a clinical setting contributes to this confusion. What is not yet clear is the impact on the PA competence of nursing student worldwide. PA is very essential to the delivery of nursing care. Through PA, future nurses should be aware of the health problems affecting a patient and how to manage it.

Currently, no synthesis of available empirical reports has been conducted, suggesting the need for this type of literature review. A review of present studies is necessary to collect and synthesize evidence necessary to reach accurate and consistent judgments about PA among nursing students. Deliberate scrutiny and analysis of the mined data regarding PA competence can help improve current practices in the classroom and clinical settings, which will eventually improve the quality of nursing care [17].

Methods

Aims

This literature review aims to provide an understanding of PA competence among nursing students based on information that is accurate and documented appropriately. The researcher wants to explore the current available evidence to arrive at recommendations for students to improve their PA skills.

Search strategy

Strategies using relevant search terms

in electronic databases to identify relevant literature were implemented [18]. The following four electronic databases were utilized: (a) CINAHL, (b) Medline, (c) ProQuest-Nursing and Allied Health Database, and (d) PubMed. The following keywords were used for literature search: ("physical assessment" OR "health examination") AND (competence OR competency) AND ("nursing student" OR "future nurses" OR "student nurses"). Keywords were identified using a thesaurus of the searched databases and MeSH terms. The author utilized broad search criteria to ensure that all relevant articles were included. Titles were hand-searched based on the reference lists of the full texts of reviewed literature. The data was extracted from to March January 2019.

Inclusion and exclusion criteria of articles

Inclusion criteria: (a) no restriction of year, (b) peer-reviewed journal articles, (c) original research, and (d) English language. Exclusion criteria: conference proceedings abstracts, articles in press; irrelevant to research keywords, letters to the editor, unpublished manuscripts (abstracts or dissertations), and non-English languages. Only studies in which nursing students were enrolled as research participants were included in the review, regardless of the venue in which PA competence was measured (classroom, laboratory or clinical). The PA competence of nurses was not considered in this paper, since nursing students have different level of knowledge, skills, experience and training.

Search outcomes

A comprehensive search review on PA

competence of nursing students was conducted resulting in the following:

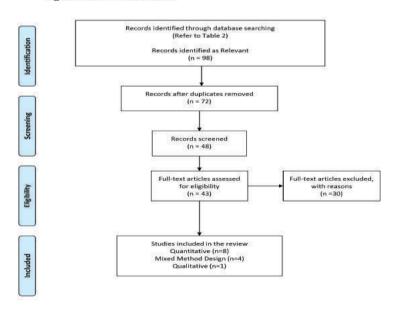
Table 1. Number of hits per Database

Database	String	Hits
CINAHL	((physical assessment) OR (health examination)) AND (com-	57
	petence OR competency) AND ((nursing student) OR (future	
	nurses) OR (student nurses))	
Medline	((physical assessment) OR (health examination)) AND (com-	114
	petence OR competency) AND ((nursing student) OR (future	
	nurses) OR (student nurses))	
ProQuest-Nursing	("physical assessment" OR "health examination") AND (com-	191
and Allied Health	petence OR competency) AND ("nursing student" OR "future	
Database	nurses" OR "student nurses")	
PubMed	((physical assessment) OR (health examination)) AND (com-	458
	petence OR competency) AND ((nursing student) OR (future	
	nurses) OR (student nurses))	

After title review, a total of 98 articles were identified as relevant. After reading the abstracts, 43 were selected. After reading the complete article texts, 13 articles were judged to meet the criteria. One utilized qualitative

method; eight used quantitative methods; and four used a combination of methods. The flow diagram illustrating the process of identifying relevant articles is presented in Figure 1.

Figure 1. Search Flow Process



From: Moher D, Liberati A, Tetzleff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000997. doi:10.1371/journal.pmed1000097

Quality appraisal and data synthesis

Each article was appraised for methodological validity using the instrument authored by Kmet et al. [19]. The instrument has standard quality assessment criteria for evaluating primary research papers. The checklist contains two scoring systems for assessing the quality of the research articles to identify articles suitable for review inclusion. The checklist for quantitative research reports contains 14 questions regarding the objective, study design, methods, respondents, sample size, measurements, main results and conclusion. For qualitative research reports, the checklist contains 10 questions concerning the study objectives, study design, connection to a theoretical framework, sampling strategy, data collection methods, data analysis, results, conclusions, and reflexivity. The scale was coded with "Yes" (score of 2), "Partial" (score of 1), and "No" (score of 0) response options. The total for 'Yes' responses served as the quality score index. In this review,

the quality score ranged from 75% to 95 % out of a possible score of 100%. More than one checklist was developed by Kmet et al. [19] to assess different research methodologies. Studies employing quantitative methods were appraised using the system for quantitative studies, while qualitative studies (such as focus groups, semi-structured interviews) were appraised using the system for qualitative studies. Articles using mix method design utilized both instruments

The checklists were used to assess the methodological quality of the research articles [19]. The results were organized in a tabular manner that demonstrated the features of the studies (author/country, design, study aim, sample population, data collection and analysis, and key findings). The research articles were then synthesized based on the following: (a) barriers to performing effective PA, (b) assessment tools, (c) approaches towards improvement of PA competence.

Results

Table 2. Reviewed of studies included

Author, country	Design	Aim of the study	Sample population	Data collection and analysis	Key findings
Alamri et al. (Saudi Arabia)	Quantitative	To examine the PA bar- riers among Saudi nurs- ing students	Convenience sampling, nursing stu- dents (n=206)	Question- naire, Independent Samples t-test	• Subscale "reliance on others and technology," ward culture, "lack of influence on patient care" are considered barriers in PA.

Bisholt et al. (Sweden)	Quantitative	To illustrate the learning environment in different clinical settings as perceived by nursing students	Nursing students (n=185)	Question- naire, Kruskal- Wallis Test, Qualita- tive content analysis	Learning environment affects students PA regardless of the students exposed to primary health care, psychiatric care, and community health care Leadership skills contribute to the PA competence
Burke et al. (Ireland)	Mixed methods	To identify the nursing student's clinical com- petence with the used of competence tool	Preceptor nurse (n=170)	Question- naire, Focus group interviews, Qualitative analysis, Descriptive statistics	 The key themes identified as an assessment tool, recognizing competence and valuing adult learners. Complex language affects students PA performance.
Clemens et al. (US)	Quantitative	To determine the perception of nursing students about oral health assessment.	Convenience sampling, nursing student (n=163)	Question- naire, Descriptive statistics	• Majority of respondents have a good understanding of oral health assessment.
Duygulu et al. (Turkey)	Quantitative	To determine the effect of service users in clinical practice assessments as perceived by nursing students	convenience sampling, baccalaure- ate degree nursing students (N=179)	Question- naire, Content analysis, Chi-square	 Majority of respondents have PA problems in clinical practice. Majority of respondents is using a service user involvement in clinical PA.

Heaslip (United King- dom)	Mixed methods	To evaluate a practice assessment tool using a grading of practice.	Mentors (n=112) Nursing students (n=210)	Question- naire, Chi-square	 The assessment tool enabled to determine the students PA competence. Grading system help to determine the students PA competence.
Hunt et al. (UK)	Qualitative	To identify reason why mentor fail to recognize underperforming students in PA.	Nursing mentor (n=31)	Semi-structured interviews, Theoretical sampling techniques	• Students used guilt and fear towards mentors and coercive actions action in order to pass their PA competence.
Langari et al. (Finland and UK)	Quantitative	To examine and compare the self-assessment of patient safety competence between British and Finnish nursing students.	Nursing students in Finland (n=195) and the UK (n=158)	Question-naire, Mann- Whitney U, Pearson's chi-squared tests	• Over 60% of both British (n = 100, 65.8%) and Finnish (n = 124, 63.9%) pre-registration nursing students highly agreed that their "patient safety competence has continuously improved during their nursing education". • Students high in terms of competence to prevent patient safety incidence (attitude) (mean = 3.48, SD = .40), building patient safety competence (knowledge) (mean = 3.44, SD = .44), and competence to act after an error (skill) (mean = 3.20, SD = .53) respectively.

Leung et al. (Hong Kong)	Mixed method	To examine the PA competence of students enrolled in a mental health nursing course.	Purposive sampling students (n=31)	Focus group interviews, Two-step cluster analysis.	• Multiple- choice tests constructed with case scenarios facilitate students critical thinking skills.
Murray et al. (UK)	Quantitative	To assess the NTS framework towards nursing stu- dents' PA	Purposive sampling, nursing student (N=200)	Question- naire, Content validity analysis	• NTS improved students: communication, decision making, situational awareness, teamwork and task management, initiative and responsiveness to patient.
Pratinidhi et al. (India)	Quantitative	To evaluate the simulation training device as teaching tool used among nursing students	Total sampling, nursing student (N=88)	Question- naire, Descriptive statistic	• Simulation training device improved student's PA competence.
Slater et al. (US)	Mixed method	To evaluate strategies for PA.	Convenience sampling, nursing student (N=117)	Question- naire, Descriptive statistics, Open ended question Content analysis	• Instructional video improved students PA grade performance.
Zolezzi et al. (Qatar)	Quantitative	To assess the perception of students towards performing CVD risk assessments	Total sampling, nursing students (N=207)	Question- naire, Kruskal- Wallis test	• Students have good knowledge and equipped in CVD risk assessment.

Barriers in performing PA

Four studies [2,12,13,20] reported barriers to the effective performance of PA. The study by Alamri et al. [2] of 206 Saudi nursing students conveniently selected found that "reliance on others and technology," "ward culture," and "lack of influence on patient care" were perceived as barriers to their performance of PA. The study by Bisholt et al. [12] of 185 Swedish nursing students found out that a large patient load presents challenges to students in performing PA. The same study found that the learning environment is important in building confidence and competence in performing PA. In a mixed method design conducted by Burke et al. [13] among Irish nursing students, the very complex language employed in the assessment tool was found to create difficulty interpreting the results of students' PA performance. In the same study, time constraints during the PA hindered performance. In terms of tools used to assess PA, Duygulu et al. [20] conducted a quantitative cross-sectional study that conveniently selected 179 Turkish students. They reported that these students lacked confidence in performing PA. These students further expressed their difficulties in discussing this lack of confidence with their nursing instructors (68.2%). Adjustment to the clinical setting environment (17.9%) posed additional difficulties, as did other assessment methods utilized (24.0%). Insufficient time, lack of clarity in assessments, and frequent clinical rotations also acted as barriers to effective PA.

Assessment tools

Three studies highlighted different tools used to assess students' PA competence [13,20,21]. Burke et al. [13] used competence tools to assess nursing students' clinical competence and found that a humanistic approach to learning and the principles of adult learning improved their PA competence. Duygulu et al. [20] discussed in-service users' assessment involvement as a useful factor in assessing students' PA competence. In a two-stage mixed-method study conducted by Heaslip et al. [21] among mentors (n=112) and nursing students (n=210), the tool utilized was a service evaluation of PA integrating the grading of practice. The tool can grade both PA competence and confidence in performing PA. Leung [1] assessed the influence of multiplechoice examinations on the PA learning of nursing students enrolled in a mental health nursing assessment course. The study found that multiple-choice examinations with case scenarios are useful in accelerating students' critical thinking about PA and improving PA skills.

Approaches toward improvement of PA competence

Nine studies highlighted approaches to improving physical assessment competence [1,12,17,22,23,24,25,26,27]. The study conducted in Sweden [12] recommended a good practice environment (e.g. good teamwork and collaboration, adequate patient-student ratio, and good pedagogy) to allow nursing students to become more proficient in performing PA.

Close cooperation and supervision should be required between nursing instructors and nursing staff in order to create and maintain a good environment for learning PA. More with cooperation and supervision, collaboration also play a role in improving PA competence. A study in Qatar [27] measuring medical, nursing, and pharmacy students' performance of cardiovascular disease (CVD) risk assessments suggested that collaboration decreased assessment barriers, while teamwork and team communication led to greater efficiency and higher quality results. The study recommended that collaboration be increased in order to decrease (CVD) assessment barriers.

Simulations and clinical training programs also play a role in developing PA competence. A study in the US [17] cited that simulations and participation in clinical training programs could improve student accuracy in oral PA. A study conducted in India investigated the effect of a simulation training device on nursing students' performance and found out that the cervical dilatation training device improved judgment of cervical dilatation in actual clinical settings [19]. Outcomes of simulations and trainings are always targeted to participants' learning, but the facilitator's role is another factor in the equation. That role may include mentorship. A UK published study [22] investigated why underperforming students fail as perceived by nursing instructors and arrived at a recommendation that mentoring should be employed. The study claimed that a mentoring role when efficiently employed increases students' confidence in performing PA

Simulations and training with mentoring is not adequate; evaluation is necessary to determine the effects of training and to provide feedback for continuous improvement employment. Furthermore, evaluation of nontechnical skills is necessary to determine how they contribute to performance of PA. Murray et al. [24] described a framework for evaluation of non-technical skills (NTS) to assess nursing students' PA skills. The authors suggested that NTS improve nurses' PA skills. A separate study conducted in the United States [26] used evaluation strategy for PA competence among nursing students and found that evaluation strategy encouraged greater learning and PA understanding and created a more realistic clinical experience. Part of the evaluation should also address safety, since it is part of PA competence. A study conducted in UK and Finland [23] assessed the patient safety competence of students. It noted that the competence of students is an important part of improving patient safety, which puts emphasis on integrating student development into the curriculum. Curricula revision was recommended to focus more on patient safety and a safe practice environment.

An interesting empirical report from Hong Kong [1] evaluated the effects of multiple-choice tests on the learning and competence of nursing students enrolled in a mental health nursing course. In this study, a surface learning approach helps students cope with the weighty workload of acquiring various

PA skills within strict time limitations.

Discussion

This literature review provides an expansive understanding of the PA competence of nursing students. The majority of the research studies were conducted in the US and Europe (N=7). Three significant themes were generated from the review.

First, barriers in performing physical assessment affect students' performance and the quality of patient care. Three studies revealed that the complexity of the earning environment hinders students' performance of PA [2,12,13], reinforcing the notion that a proper learning environment is necessary to perform a comprehensive health assessment utilizing the core competencies so that it can develop essential skills and improve PA selfconfidence in assessing patient's health status. It should be noted, however, that two of the studies analyzed are cross-sectional [2,12], and only one utilized a mixed-method design [13], which cannot be used to analyze behavior over a period of time and does not help determine cause and effect. Further studies could be developed, particularly interventional studies, to minimize barriers in performing PA.

Four studies highlighted advantages of different tools for assessing students' PA competence [1,13,20,21]. Two studies focused on service users in clinical practice assessments [20,21], while one study assessed students' PA competence Burke et al. [13] and yet another study evaluated students' PA competence

using multiple-choice tests on the learning approaches [1]. All these studies were self-administered, which can lead to social desirability bias. Another weakness is that all respondents from the above studies were from one geographical area, limiting the generalizability of the studies. Future research could draw from a larger and more diverse population to generalize the findings.

Several approaches to improvement of PA competence will clearly improve learning outcomes [1,12,17,22,23,24,25,26,27], including a good clinical practice environment, communication, and teamwork [5,22,24]. with the surface learning approach is useful in coping with the weighty nursing workload of several nursing PA skills within limited time constraints and developed critical PA skills [1]. Case-based scenario simulation has also proven to be a consistent and effective method of PA evaluation [26]. While the above strategies certainly help to improve students' PA competence, the results are complicated by the fact that PA simulation-based and case scenarios requires multiple trainings for nursing instructors [28].

Assessment of PA competence is essential, since the feedback students receive can be the basis for their improvement and for the crafting of strategies by nursing educators. Evaluation and feedback are necessary to the student, teachers, and academic administrators so that proper corrective action can be taken, and improvements made. When the students become aware of their skill deficits, they can retreat to their confi-

dence and adjust their learning strategies to improve those skills. Teachers and academic administrators are guided by identifying the symptom, investigate for the root causes, and employ appropriate interventions. The lists of barriers to and approaches for improving PA competence provide useful information for academic planning to improve PA competence. The barriers can be eliminated with a good plan and proper execution. Action plans can focus on a good practice environment, improved curriculum, trainings and simulations, mentoring, safety training, and instruction in non-technical skills.

Limitations of this review

Only four electronic databases were utilized, so some relevant studies may not have been included. The use of a limited set of keywords and the two-month window for data extraction may also have decreased the strength of the scientific evidence. Combining diverse data sources such as quantitative studies and qualitative studies is complex and challenging. Nevertheless, reviews can play a large role in describing the complexity of PA competence, identifying central issues in PA education, and exploring potentially useful future research methods.

What does the study add to what was already known?

This review reveals that the barriers to PA competence are numerous and may differ based on nursing students' clinical environment and practice. It also highlights the shift in focus from perceived barriers in physical assessment skills, which served as the basis for curriculum development. The use of PA skills is associated with good validated and reliable PA tools. Individualmotivational, professional, environmental, educational, cultural, and communicational factors, as well as the factors related to patients and their cultures, are involved in skilled assessment. Indeed, future nurses themselves express a need for improved training in these areas.

Conclusion

PA competence is fundamental to good nursing care. This review highlights the barriers that prevent nursing students from performing PA effectively, as well as the need for PA assessment tools to be validated and integrated into the grading practices. A valid and reliable PA competence evaluation tool develops critical thinking skills and improved PA skills. Specific approaches to building PA competence (e.g. good teamwork and collaboration, adequate patient-student ratio, simulations and clinical training program participation, and a surface learning approach) led to improved PA skills performance. A review of studies of PA competence should be undertaken to guarantee continuing improvement of nursing education and nursing care. This study provides valuable insights into PA competence and the barriers to its effective performance in order to better prepare student nurses to perform PA in a clinical environment.

Assessment of PA competence is essential to determine a student nurse's skills and preparedness. Evaluation and feedback are necessary so that proper corrective actions and improvement can be taken. This includes identifying barriers to arrive at action plans to eliminate them. Action plans can focus on good practice environment, improvement of curriculum,

Recommendation

Nursing education recommendation. The assessment of competence of students to perform PA is an important part of improving patient safety and patient quality care. PA theory and skills should be taught in all clinical and laboratory nursing courses so that students will be consistent in performing PA. Clinical training programs and case-scenarios simulations could also be included. Clinical instructors will also have more time to focus on the improvement of each competence. They will also conduct debriefing to encourage students to verbalize their concerns and issues. Finally, clinical instructors should be open and identify students' learning needs in order to reduce anxiety and stress in performing PA and increase student self-confidence in the performance of all clinical nursing skills. Finally, in order to maintain high levels of PA competence in healthcare, the researcher recommends that all schools of nursing and faculties revise their curricula so that more patient safety theory is discussed and applied to clinical practice in a safe environment.

Implications for Clinical Practice.
Upholding a positive PA practice environment for nursing students is also the shared respon-

sibility of staff nurses and hospital administrators. A clear line of communication should exist between clinical instructors and students to avoid errors in clinical settings. Clear coordination between nursing universities and hospitals is also important to the support of students' PA practice in clinical setting. Adequate supervision during students' exposure in clinical practice will prevent errors and promote patient safety. Early exposure to clinical practice can foster positive feelings in nursing students toward performing PA.

Future Research. The current review illustrates the value of PA competence among nursing students. This review recommends further research in PA competence among nursing students to validate the findings. It also recommends that barriers affecting PA could be studied utilizing research methods other than the use self-reported data from nursing students. PA assessment tools should also be studied to determine the validity and reliability of specific tools in assessing students' PA competence.

Key Point Box:

- PA competence is fundamental to the delivery of nursing care.
- This review highlighted how assessment tools used to measure PA competence, the barriers to PA competence, and approaches to improving PA competence affect students' PA performance.
- This paper provides valuable insights into

PA competence and the barriers its development when students work in an actual clinical environment

• PA theory and skills should be taught in all clinical and laboratory nursing courses so that student will be consistent in performing PA effectively.

Conflicts of Interest

The author declares that there are no conflicts of interest.

References

- [1] Leung S, Mok E, Wong, D. The impact of assessment methods on the learning of nursing students. Nurse Education Today 2008; 28(6):711-719.
- [2] Alamri M, Almazan J. Barriers of physical assessment skills among nursing students in Arab Peninsula. International Journal of Health Sciences 2018; 12: 1-9
- [3] Ilic D. Assessing competency in evidence-based practice: Strengths and limitations of current tools in practice. BMC Medical Education 2009; 9(53) 1—5.
- [4] Zayyan M. Objective structured clinical examination: the assessment of choice. Oman medical journal 2011; 26(4), 219–222.
- [5] Cant R, McKenna L, Cooper S. Assessing preregistration nursing students' clinical competence: a systematic review of objective measures. International Journal of Nursing Practice. 2013;19(2):162–176.

DOI: 10.1111/ijn.12053

- [6] Oermann MH, Yarbrough SS, Saewert KJ, Ard N, Charasika ME. Clinical evaluation and grading practices in schools of nursing: national survey findings part II. Nursing Education Perspectives. 2009;30(6):352–357.
- [7] Quail, M., Brundage, S. B., Spitalnick, J., Allen, P. J., & Beilby, J. (2016). Student self-reported communication skills, knowledge and confidence across standardised patient, virtual and traditional clinical learning environments. BMC medical education, 16, 73. doi:10.1186/s12909-016-0577-5
- [8] Chiarella M, Thoms D, Lau C, McInnes E. An overview of the competency movement in nursing and midwifery. Collegian 2008; 15: 45–53
- [9] Ličen S, Plazar N. Identification of nursing competency assessment tools as possibility of their use in nursing education in Slovenia A systematic literature review. Nurse Education Today 2015; 35(4): 602-608.
- [10] Franklin N, Melville P. (2015). Competency assessment tools: An exploration of the pedagogical issues facing competency assessment for nurses in the clinical environment. Collegian 2015; 22(1): 25-31.
- [11] Birks M, James A, Chung C, Cant R., & Davis, J. (2014). The teaching of physical assessment skills in pre-registration nurs-

- ing programmes in Australia: Issues for nursing education. Collegian, 21(3), 245-253. doi:10.1016/j.colegn.2013.05.001
- [12] Bisholt B, Ohlsson U, Engström A, Johansson A, Gustafsson M.Nursing students' assessment of the learning environment in different clinical settings. Nurse Education in Practice 2014, 14(3): 304-310.
- [13] Burke E, Kelly M, Byrne E, Ui Chiardha T, Mc Nicholas M, Montgomery A. Preceptors' experiences of using a competence assessment tool to assess undergraduate nursing students. Nurse Education in Practice 2016, 17: 8-14.
- [14] Alquwez N, Cruz J, Alshammari F, Felemban E, Almazan J, Tumala, R., et al. A multi-university assessment of patient safety competence during clinical training among baccalaureate nursing students: A cross-sectional study. Journal of Clinical Nursing 2019; 28(9-10): 1771-1781.
- [15] Blažun H, Kokol P, Vošner J. Research literature production on nursing competences from 1981 till 2012: A bibliometric snapshot. Nurse Educ Today. 2015;35(5):673-9
- [16] Fan J-Y, Wang YH, Chao LF, Jane S-W, Hsu L-L. Performance evaluation of nursing students following competency-based education. Nurse Educ Today 2015;35(1):97-103
- [17] Clemmens D, Rodriguez K. Leef B. Knowledge, Attitudes, and Practices of

- Baccalaureate Nursing Students Regarding Oral Health Assessment. Journal of Nursing Education 2012; 51(9):532-535.
- [18] Whittemore, R. & Knafl, K. The integrative review: updated methodology. Journal of Advanced Nursing 2005; 52: 546–553
- [19] Kmet LM, Lee RC, Cook LS. Standard Quality Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields. Alberta Heritage Foundation for Medical Research, Edmonton AB. 2004.
- [20] Duygulu S, Abaan S.Turkish nursing students' views on practice assessments and service user involvement. Contemp Nurse 2013; 43(2):201-12.
- [21] Heaslip V, Scammell J. Failing underperforming students: The role of grading in practice assessment. Nurse Education in Practice 2012; 12(2):95-100.
- [22] Hunt L, McGee P, Gutteridge R, Hughes, M. (2016). Manipulating mentors' assessment decisions: Do underperforming student nurses use coercive strategies to influence mentors' practical assessment decisions? Nurse Education in Practice 2016; 20154-162.
- [23] Langari M, Tella S, Smith N, Turunen H. Self-Assessment of Patient Safety Competence: A Questionnaire Survey of Final Year British and Finnish Pre-Registration Nursing Students International Journal of Caring Sciences 2017; 10 (3)

1212.

- [24] Murray K, McKenzie K, Kelleher M. (2016). The evaluation of a framework for measuring the non-technical ward round skills of final year nursing students: An observational study. Nurse Education Today 2016;45:87-90.
- [25] Pratinidhi A,Patange R,Patil,S, Salunkhe J,Samson S,Kakade,S Testing of simulation training device for assessment of cervical dilatation among nursing student of Karad, India.Health Science Journal.2014;8 (4):495-501
- [26] Slater L, Bryant K, Ng V. Nursing Student Perceptions of Standardized Patient Use in Health Assessment. Clinical Simulation in Nursing 2016; 12(9);368-376.
- [27] Zolezzi M, Abdallah O, Aden S, Major S, White D, El-Awaisi A. Perceived Preparedness of Health Care Students for Providing Cardiovascular Disease Risk Assessment and Management. Pharmacy (Basel, Switzerland), 2017; 5(1):9.
- [28] Takase M, Teraoka S, Miyakoshi Y, Kawada A. A concept analysis of nursing competence: a review of international literature. Nihon Kango Kenkyu Gakkai Zasshi. 2011;34:103-9.

Case Report

Physical Therapy Management for Child with Generalized Joint Hypermobility

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Abstract

The purpose of this case report is to provide insight regarding the screening and early physical therapy interventions for a child with Generalized joint hypermobility (GJH). The increased mobility in joints than the normal range of movement in one joint is referred to as Hypermobility. The Hypermobility occurring in more than one joint is referred to as Generalized Joint Hypermobility (GJH). GJH is usually benign (asymptomatic) however, over time may lead to joint pain and developmental delay. Identifying the GJH at the school-age would facilitate to monitor early changes and to plan for early rehabilitative intervention. This case report describes the clinical findings of a 7-year-old primary school male student with GJH. This patient scored 9 points in the Beighton score. The preliminary physical therapy sessions were targeted to improve joint protection, joint control, and stability. The long-term goals were injury prevention and physical fitness.

Key words:

Case report, Children, Hypermobility, Physical therapy, Ligament laxity, Joint protection, Joint control, Proprioception.

Introduction

The increased mobility in joints than the normal range of movement in one joint is referred to as Hypermobility. Hypermobility occurring in more than one joint is referred to as Generalized Joint Hypermobility (GJH) [1]. Ligamentous laxity is a major cause of hypermobility of the Joint. The occurrence of GJH in children of age group 6–15 years

الملخص

الغرض من تلك الدراسة هو تقديم نظرة ثاقبة فيما يتعلق بالفرز و التدخلات العلاجية المبكرة للطفل المصاب بفرط الحركة في المفصل (GJH). يشار إلى زيادة الحركة في المفاصل عن المعدل الطبيعي للحركة في مفصل واحد أو أكثر باسم الحركة المفرطة (Hypermobility) ، أما بالنسبة إلى التي تحدث في أكثر من مفصل واحد باسم حركة مفرطة عامة واحد باسم حركة مفرطة عامة (Generalized Joint Hypermobility) عادة ما يكون حميداً (بدون أعراض) ، ومع مرور الوقت قد يؤدي إلى آلام المفاصل وتأخر النمو. تحديد GJH في سن المدرسة من شأنه أن يسهل لرصد التغييرات المبكرة والتخطيط للتدخل التأهيلي المبكر. يصف تقرير الحالة هذا النتائج السريرية لطالب يبلغ من العمر ٧ سنوات في مدرسة ابتدائية مصاب بفرط الحركة في المفصل (GJH). هذا المريض سجل ٩ نقاط في مقياس Beighton استهدفت جلسات العلاج البدني الأولية لتحسين حماية المفاصل ، والسيطرة على المفاصل والاستقرار. وكانت الأهداف طويلة الأجل الوقاية من الإصابة واللياقة البدنية.

الكلمات الدالة:

تقرير حالة ، الأطفال ، فرط الحركة ، العلاج الطبيعي ، تراخي الرباط ، حماية المفاصل ، التحكم في المفصل ، التحسس.

differ between 8.8% and 64.6% ^[2,3]. GJH is more common in females and declines with an increase in age. Earlier researchers demonstrated an influence of ethnic background on GJH. There is a high prevalence of GJH among Asian and African populations compared to the Western population ^[2]. Yet literature is scarce regarding the prevalence of GJH among children in the Gulf region.

Beighton score is a valid and reliable measure to screen the Joint hypermobility and widely used across the globe. Beighton score assesses hypermobility in 9 joints such as right and left thumbs, right and left small fingers, right and left elbows, left and right knees and body trunk. The score ranges from value of 0 to value of 9, one point awarded when the subject can perform each of the 9 tasks. All 9 tasks were easy to perform and provide quantitative data. The common choice of cut off score was ≥ 4 for GJH ^[2]. Juul et al and Smits-Engelsman et al recommended standard protocols to be administered in children ^[1].

GJH is usually benign (asymptomatic) However, over time may lead to joint pain and developmental delay. Identifying the GJH at the school-age would facilitate to monitor early changes [4] and to plan for early rehabilitative intervention. The purpose of this case report is to provide insight regarding the screening and early intervention aiming at joint protection and injury prevention of children with generalized joint hypermobility.

Case Report

The patient was a 7-year old male Grade 1 student at a primary school in the Majmaah region, Saudi Arabia. The patient was evaluated by the Physical therapist during a School Health Screening Program after obtaining consent from the child, parents and school authorities. The anthropometric data like height, weight and arm span were 114 cm, 20.2 kg, and 117 cm respectively. The body mass index was 15.5 (underweight) and the Arm

span / Height ratio was 1.02. The patient was screened for Marfanoid habitus features like Steinberg and Walker–Murdoch sign.

For eliciting Steinberg or the thumb sign, the subject should fold his thumb into a closed fist. And this test is considered positive if the tip of the thumb extends from the palm. The Walker–Murdoch sign or the wrist sign could be obtained by instructing the subject to grip his wrist by using thumb and little finger of the other hand. Overlapping of the thumb and little finger is considered positive for this test [5]. Both Steinberg and Walker–Murdoch sign was found to be negative and Arm span / Height ratio of 1.02 also falls in the normal range.

The child was screened for GJH using the Beighton score. The components and the scoring criteria of the Beighton score are as follows.

- 1. Extension of metacarpophalangeal joint of the little finger. The range of motion (ROM) of $\geq 90^{\circ}$ is considered positive. (Maximum 2 Points 1 point for each side).
- 2. Hyperextension of the elbow. The range of motion (ROM) of $\geq 10^{0}$ is considered positive. (Maximum 2 Points 1 point for each side).
- 3. Hyperextension of the knee. The range of motion (ROM) of $\geq 10^{0}$ is considered positive. (Maximum 2 Points 1 point for each side).

- 4. Passive opposition of the thumb to the flexor aspect of the forearm. The test is positive if the entire lateral border of the thumb touches the anterior surface of the forearm. (Maximum 2 Points 1 point for each side).
- 5. Forward flexion of the trunk with knees in extension. The test is positive if the palmar aspect of the entire hands touches the floor. (1 Point).

The Beighton score ranges from 0 to 9 and the score of \geq 4 is widely used cutoff for classifying as generalized joint hypermobility.

The subject in this case report scored positive bilaterally in the little fingers (2 Points), thumbs (2 Points), elbows (2 Points), knees (2 Points) and trunk (1 Point). Hence, the total score is found to be 9 and classified as a case of generalized joint hypermobility (Figure 1-4). However, he did not exhibit any additional characteristics as specified in Brighton's criteria like arthralgia, back pain, dislocation or subluxation, soft tissue rheumatism (eg: epicondylitis, tenosynovitis, bursitis) marfanoid habitus (arm span / height ratio < 1.03, positive Steinberg / wrist signs) abnormal skin (eg: striae, hyperextensibility, thin skin, papyraceous scarring), eye signs (eg: drooping eyelids, myopia or antimongoloid slant), varicose veins or hernia or rectal prolapse to be diagnosed as Hypermobility syndrome [6].



Figure 1(A) Passive opposition of the Thumb to Flexor aspect of the forearm, (B) Passive dorsiflexion of little finger beyond 10°



Figure 2 Hyperextension of elbow beyond 10°



Figure 3 Hyperextension of Knee beyond 100



Figure 4 Forward flexion of the trunk with knees extended so that the palms of the hand rested on the floor

The interventions focused on patient education, joint protection, enhancing balance, coordination, proprioception, muscle strength, functional stability, and kinetic control of symptomatic joints. The condition was explained as noninflammatory and non-progressive connective tissue disorder to the child in the presence of parents and physical educator. Regarding joint protection, the child was advised to refrain from any contact sports activities and not to stretch the joints beyond the end range of motion during the daily and recreational activities.

The functional stability and kinetic control of symptomatic joints were trained by teaching the child to control neutral joint position. The child was oriented to regarding abnormal resting position and avoids it (Eg: to avoid

knee hyperextension while standing). The postural muscles were retrained to regain optimal joint alignment. Once the neutral joint position was achieved, dynamic control was performed by retraining the spinal muscle to maintain a neutral spine while moving adjacent joints (Eg: hip flexion while maintaining the spine in neutral). Motion control was achieved by enhancing the ability of the specific muscles to control the joint through the entire range both concentrically and eccentrically (Eg: quadriceps working concentrically during standing up and eccentrically while sitting down). Functional stability and kinetic control exercises were performed 20 -30 slow repetitions per session. The patient was trained for 6 weeks (3 sessions per week) supervised by the Physical therapist.

The tight muscles like hamstrings were stretched after adequate postural control was attained. The initial phase of proprioceptive training included exercises like unilateral stance, mini squats, and single-leg knee bend and later progressed to advanced activities like wobble board balance exercises. The patient underwent 12 sessions of proprioceptive and balance activities lasting for 15 minutes each, over a period of 4 weeks. Finally, the child performed standardized general exercises to improve muscle strength and fitness activities like shuttle-run, step-up and sitting to standing. Initially, each fitness exercises were repeated 10 times during each session and progressed with an increment of 5 repetitions. These fitness activities were performed during the physical education period under

the supervision of the physical educator. The child did not develop any musculoskeletal injury at 6 weeks follow up.

Discussion

This case report describes the clinical findings of a primary school male student with GJH. The hypermobility is more common in younger children as seen in this current case scenario. This patient did not exhibit any associated clinical features of hypermobility related genetic disorders such as Ehler- Danlos syndrome or Marfan's syndrome. However, he did not exhibit any symptoms of musculoskeletal disorders or other additional characteristics as specified in Brighton's criteria to be diagnosed as Hypermobility syndrome [6]. This patient is underweight as reflected by BMI of 15.5 Kg/m². Earlier researches did not report any significant association between BMI and GJH [2].

The patient was screened for the presence of joint hypermobility using the Beighton score (BS). The BS was developed in South Africa and was based on 1,083 Tswana Africans (adults and children) and subsequently used globally to identify generalized joint hypermobility in all populations and age groups. The BS is influenced by age, gender, and ethnicity. In adults, the cutoff of $\geq 4/9$ is used to classify hypermobility. But there is no consensus regarding the cutoff for children [2]. The BS score of this patient was 9/9 and classified as Hypermobile.

It is essential to screen the children for issues

related to hypermobility to start the exercise interventions at the earliest to prevent devastating complications. The hypermobile children tend to adopt the end joint range during resting position to gain stability. This faulty resting position along with features like abnormal movement patterns, decreased proprioception causes supporting joint structures to undergo excessive stress and strain resulting in fatigue and pain [7]. Pain reduces the joint mobility and leads to weakness of the surrounding muscles and result in joint injuries and musculoskeletal disorders [7-9]. The hypermobile individual commonly experience ankle sprains and functional ankle instability followed by anterior cruciate ligament (ACL) injury and shoulder instability (subluxation or dislocation) [10]. The healing period for hypermobile individuals was longer compared to the normal population and result in deconditioning [7].

Physical therapy plays an integral role in the management of joint hypermobility. The preliminary physical therapy sessions were targeted to reduce pain and improve joint protection, joint control, and stability. The long-term goals were injury prevention and physical fitness. This patient did not experience any pain and hence focused on other mentioned interventions. This patient was advised to refrain from contact sports as a measure of joint protection because participation in contact sports increases the risk of joint injuries in hypermobile individuals.

The interventions on joint control focused to

maintain the normal range of movement with an emphasis on attaining effective control of the entire range of movement, especially in the hypermobile range as recommended in the literature. The objective of the joint control exercises was to retrain tonic low threshold activation of the local stability system to enhance muscle stiffness and train the functional low load integration of the local and global stabilizer muscles to regulate the neutral position of the joints [11]. In a recent school-based study in UK, Hand physical therapy significantly improved grip strength among Hypermobile children. The grip strength of this patient was found to be in the normal range [12-14]

The ideal amalgamation of proprioception and motor control is essential for normal movement. Proprioception is the ability to sense the position of the joint (position sense) and movement (kinesthesia) for the sake to guarantee the optimal joint position and acquire adequate muscle tone for the specific activity [15]. Earlier researchers reported proprioceptive deficits among hypermobile individuals and the reason for this is still not clear. The proprioceptive exercises performed by this patient effectively improved joint stability in addition to proprioception and were highly recommended in the literature [7].

Once effective joint control is accomplished, hypermobile individuals are motivated to create a lifelong dedication to physical activity to preserve excellent health and well-being. It is imperative to identify safe and entertaining activities and sports which could maintain adequate cardiopulmonary fitness [7]. We plan to advise him to take part in swimming activities during the next follow-up.

Conclusion

This case report discusses a pediatric patient with GJH. The screening and early rehabilitation strategies for joint hypermobility were discussed to start the exercise interventions at the earliest to prevent devastating complications. The preliminary physical therapy sessions were targeted to improve joint protection, joint control, and stability. The long-term goals were injury prevention and physical fitness. There is a scarcity of research focusing on the effectiveness of Physical therapy in the management of GJH. Hence, further studies are essential to agree or contradict the treatment strategies mentioned in this case report.

References

- [1] Smits-Engelsman B, Klerks M, Kirby A. Beighton score: a valid measure for generalized hypermobility in children. J Pediatr 2011;158:119-123.
- [2] Clinch J, Deere K, Sayers A, Palmer S, Riddoch C, Tobias JH et al. Epidemiology of Generalized Joint Laxity (Hypermobility) in Fourteen-Year-Old Children From the UK: A Population-Based Evaluation. Arthritis and Rheumatism. 2011;63(9):2819-2827.
- [3] Vougiouka O, Moustaki M, Tsanaktsi M. Benign hypermobility syndrome in Greek schoolchildren. Eur J Pediatr

- 2000;159:628.
- [4] Lamari NM, Chueire AG, Cordeiro JA. Analysis of joint mobility patterns among preschool children. Sao Paulo Med J 2005;123:119-123.
- [5] Gupta S, Gupta N. Wrist (Walker–Murdoch) and Thumb (Steinberg) Signs. MAMC Journal of Medical Sciences. 2017;3(2):111-112.
- [6] Simpson MR. Benign joint hypermobility syndrome: evaluation, diagnosis, and management. The Journal of the American Osteopathic Association. 2006;106(9):531-536.
- [7] Keer R, Simmonds J. Joint protection and physical rehabilitation of the adult with hypermobility syndrome. Current opinion in rheumatology. 2011;23(2):131-136.
- [8] Sirajudeen MS, Alaidarous M, Waly M, Alqahtani M. Work-related musculoskeletal disorders among faculty members of college of Applied Medical Sciences, Majmaah University, Saudi Arabia: A cross-sectional study. International journal of health sciences. 2018;12(4):18-25.
- [9] Manhal S, Sirajudeen MS, Pillai PS, Nair HR, Marla J. Occurrence of Shoulder disorders among Post coronary Artery Bypass Surgery Patients in India. Archives of Medicine and Health Sciences. 2015; 3(1):34-39.
- [10] Wolf JM, Cameron KL, Owens BD. Impact of joint laxity and hypermobility on the musculoskeletal system. JAAOS-

- Journal of the American Academy of Orthopaedic Surgeons. 2011;19(8):463-471.
- [11] Kemp S, Roberts I, Gamble C, Wilkinson S, Davidson JE, Baildam EM, Cleary AG, McCann LJ, Beresford MW. A randomized comparative trial of generalized vs targeted physiotherapy in the management of childhood hypermobility. Rheumatology. 2009;49(2):315-325.
- [12] Sirajudeen MS, Shah UN, Pillai PS, Mohasin N, Shantaram M. Correlation between Grip Strength and Physical Factors in Men. Int J Health Rehabil Sci. 2012; 1(2): 58-63.
- [13] Shah UN, Sirajudeen MS, Somasekharan P, Mohasin N, Shantaram M. The Association between Hand grip Strength and Hand dimensions in Healthy Indian Females. International Journal of Current Research and Review. 2012; 4(2):36-42.
- [14] Bale P, Easton V, Bacon H, Jerman E, Watts L, Barton G, Clark A, Armon K, MacGregor AJ. The effectiveness of a multidisciplinary intervention strategy for the treatment of symptomatic joint hypermobility in childhood: a randomised, single Centre parallel group trial (The Bendy Study). Pediatric Rheumatology. 2019; 17:2.
- [15] Kumar CGS, Syed N, Sirajudeen MS, Karthikbabu S. Position Sense acuity across Shoulder Rotational range of motion. Journal of Musculoskeletal Research. 2012;15(3).

Case Report

Psychosis in a Young Patient with a Left Temporal Arachnoid Cyst: A Case Report

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Abstract

Background:

Psychiatric disorders can be caused by organic conditions. Arachnoid cysts are suggested to be related to psychiatric disorders since many case reports have be published presenting coexistence of arachnoid cyst and psychosis.

Case report:

An 18-year-old single male was admitted to the psychiatry hospital with severe fearfulness, disorganized behavior, decreased sleep, and refusal of oral intake. He had delusions of guilt, persecution and misidentification. He also showed periods of incoherent and very poor speech, perplexity, disorientation, and some catatonic features. There was no history of substance use or significant medical problem. Physical, including neurological, examination and laboratory investigations were normal. A brain CT revealed the presence of an arachnoid cyst in the left temporal lobe. He was treated pharmacologically with partial and slow response.

Conclusion:

Causal relationship between arachnoid cyst and psychosis is difficult to be concluded in this case, but the possibility should not be ignored. This case is reported from Arab region where there is lack of such publications. More in depth research is needed.

Key words: Psychosis; Temporal lobe; Arachnoid Cyst; Arab; Case report.

Introduction:

Intracranial lesions are among possible organic causes of psychotic disorders, although the relation between arachnoid cysts and psychiatric disorders is not confirmed [1]. Arachnoid cysts are uncommon benign neurological tumors and they represent only 1% of all intra-

الملخص

خلفية: الاضطرابات النفسية قد تكون ناتجة عن امراض عضوية، وهناك علاقة محتملة بين الكيسات العنكبوتية والاضطرابات النفسية بناء على عدد من تقارير الحالات المنشورة لكيسات عنكبوتية مصحوبة بالذهان

تقرير الحالة: تم تنويم شاب أعزب عمره ١٨ عاماً بالمستشفى النفسي يعاني من خوف شديد وسلوك غريب مع قلة النوم ورفض تناول الطعام، وجد لديه ضلالات الذنب والاضطهاد وضلالة التعرف الخاطئ، كما كان كلامه قليلا جدا وغير مفهوم، وكان يبدو متحيرا ومشوشا مع بعض المظاهر التخشيية. لم يكن لديه تاريخ سابق لتعاطي المؤثرات العقلية ولا لأمراض عضوية مؤثرة كانت نتائج الفحص الجسدي، بما في ذلك فحص الجهاز العصبي، طبيعية وكذلك التحاليل المختبرية. بينما أظهرت صورة الأشعة المقطعية للدماغ وجود كيسة عنكبوتية في الفص الصدغي الأيسر. تمت معالجة المريض دوائيا لكن استجابته كانت بطيئة وجزئية. الخلاصة: من الصعب الجزم بالعلاقة السببية بين الكيسة العنكبوتية والذهان من خلال هذه الحالة ومع ذلك لا يمكننا تجاهل هذا الاحتمال. هذه الحالة سجلت في المنطقة العربية حيث تكاد لا توجد أوراق منشورة مشابهة. ولا يزال الموضوع بحاجة إلى مزيد من البحث العميق.

كلمات مفتاحية:

ذهان، الفص الصدغي، كيسة عنكبو تية، المنطقة العربية، تقرير حالة.

cranial space-occupying lesions ^[2, 3]. Arachnoid cysts are mostly congenital, and they are formed by an arachnoid membrane containing cerebrospinal fluid (CSF) ^[4, 5]. Most cases of arachnoid cysts are asymptomatic and are accidentally diagnosed by neuroimaging ^[6, 7]. Despite that, many articles have reported cases with intracranial arachnoid cysts present-

ing with psychotic features [1, 2, 4-7]. Although it is usually hard to prove the causal relationship in most of those cases, the increasing number of cases described in literature cannot be simply justified by the coincidence [7]. More studies on such cases is needed to add to the knowledge regarding both etiological and management aspects of this condition.

Case report:

An 18-year-old Saudi male, single was admitted to the Mental Health Hospital because of severe fearfulness, behavioral change, decreased sleep, and refusal of oral intake associated with marked weight loss.

According to his parents, the condition started 8 months ago with behavioral change; patient started to isolate himself, to ask his father to forgive him inappropriately, and he asked his mother to bring him a little brother to play with. Few months later, He became enclosed in his room, with poor sleep, fearful and behaving in a strange way (dancing and getting anger outbursts without obvious reason), he thought that his friends took pictures to him while he was nude in the bathroom and threatened him to diffuse them on internet. He started to think that his mother is not his real mother.

Patient had no history of mental illnesses, no history of psychoactive substance use, no forensic history, and no significant family history of mental illnesses. His medical history was insignificant. He had been graduated from secondary school few months ago with a

very good performance, just before the onset of his illness.

On Mental status examination, patient was conscious, having good self-care and self-hygiene, but uncooperative, restless, and having some disorganized behavior. He was anxious and fearful, but his affect was restricted. He had delusions of guilt, persecution and misidentification. There were no suicidal or homicidal ideas and no hallucinations. He had lack of insight and impaired judgment. During his hospital stay, patient showed periods of incoherent and very poor speech, perplexity, disorientation, and some catatonic features (mutism and negativism). He refused oral food intake during first few days in hospital which necessitated parenteral feeding.

Patient's physical examination were normal and there were no focal neurological deficits. All laboratory investigations were within normal, including complete blood picture, thyroid, liver and renal function test, and blood glucose. Urine toxicology were negative. Electroencephalograph (EEG) did not reveal any abnormality. Brain Computed tomography (CT) Scan with contrast was done and has revealed an extra-axial left temporal arachnoid cyst. The lesion was about 3.6 × 1.6 cm in size (Fig. 1).



Figure 1: Brain CT showing an extra-axial left temporal arachnoid cyst

The neurosurgeon was consulted; however, due to the lack of neurological symptoms; he recommended against any neurosurgical intervention and he proposed the medical management.

Patient received injectable antipsychotics; Haloperidol 5 mg bid, in the beginning, because he was uncooperative and refusing oral medications. Then it was replaced by olanzapine, because of the appearance of extrapyramidal side effects, started with 5 mg/day and increased gradually to reach 20 mg/day. Six weeks after starting olanzapine, a small dose of flupenthixol was added as an augmentation because of limited response. During the following three weeks, patient showed remarkable improvement. On discharge, after 9 weeks of hospitalization, patient was calm and cooperative, with no problem in sleep or appetite. He was no longer deluded, anxious or fearful, although he was still socially isolated and having little speech.

Discussion:

This patient presented with prominent psychotic features characterized by delusions and disorganized behavior, as well as some catatonic features and negative symptoms, for a duration of about 8 months. There were few affective symptoms which were not enough to make a diagnosis of a mood disorder. Depending on this presentation and considering the neurosurgeon's report that the arachnoid cyst had no any mass effect, our patient received a provisional diagnosis of schizophrenia.

Despite this diagnosis, there are some reasons to suggest possible association, not just a simple coincidence, between this psychotic illness and the arachnoid cyst. In our patient, the arachnoid cyst was in the left temporal lobe, and there is a relation between dysfunction in this area and the presence of schizophrenia [8] and psychological symptoms were found in 76% of patients whose temporal lobes were affected [9]. Other factors supporting this suggestion include the absence of past or family history of psychiatric disorders in our patient and the absence of clear precipitating factors. According to previous studies [10, 11], psychiatric symptoms of the cyst may include: paranoid delusions, alexithymia, attention deficit and hyperactivity disorder, and guilt feeling which were present among our patient's features.

Regarding treatment response, our patient responded partially and slowly to the medications he received which was similar to results achieved in several patients presented with an arachnoid cyst with psychosis who were treated pharmacologically without any surgical intervention and complete remission of the psychotic symptoms was not achieved [5, 12]. On the other hand, rapid improvement reported when surgical intervention was performed [13, 14] in form of craniotomy, excision, or drainage [1,15]. In a case series published by Kohn et al, eight patients presented with both arachnoid cysts and psychiatric features, cyst was surgically removed in one of them and he was the only one to show complete remission of symptoms [1].

Conclusion:

It is difficult to confirm whether the arachnoid cyst was responsible for the psychotic features in our current patient, but its possible role in the etiology should be considered. This case reported a rare presentation especially in the Arab region where there is lack of published similar case reports. Further studies of more cases with coexistence of arachnoid cyst and psychosis are recommended for more exploration and confirmation of the causal relationship and then deciding the optimum plan of management.

Ethical Considerations:

Ethical approval was obtained from the ethical committee of Ministry of Health and informed consent for publication was signed by the patient's father.

Conflict of Interests:

The authors declare that there is no conflict

of interests regarding the publication of thispaper.

References

- [1] Kohn R, Lilly RB, Sokol MS, Malloy PF. Psychiatric presentations of intracranial cysts. The Journal of neuropsychiatry and clinical neurosciences. 1989, 1: 60-66.
- [2] Khan AH, Ahmed SE. Arachnoid Cyst and Psychosis. Cureus. 2017 Sep;9(9).
- [3] Gosalakkal JA. Intracranial arachnoid cysts in children: a review of pathogenesis, clinical features, and management. Pediatric neurology. 2002 Feb 1;26(2): 93-8.
- [4] Guliani GS. Association of episodic psychotic behaviour with an arachnoid cyst of the brain "A rare case report". Journal of Child and Adolescent Psychiatry. 2018 Oct 3;2(3).
- [5] da Silva JA, Alves A, Talina M, Carreiro S, Guimarães J, Xavier M. Arachnoid cyst in a patient with psychosis: Case report. Annals of General Psychiatry. 2007 Dec;6(1):16.
- [6] Akar H, Yazar S, Özmen E, Keskinkiliç C, Eradamlar N, ET AL. An arachnoid cycst case presented with neuropsychiatric symptoms. Düsünen Adam 2006, 17: 238-243.
- [7] Maner F, Babalioglu M, Cetinkaya O, Ipekcioglu D, Ergen N, Yesil R, Üstün I, Bas O, Ulukaya S, Yerebakan M, Alici S. The coexistence of arachnoid cyst with first episode psychosis: Four cases. Jour-

- nal of Neurological Disorders. 2014 Oct 30, 2: 186.
- [8] Shenton ME, Kikinis R, Jolesz FA, Pollak SD, LeMay M, Wible CG, Hokama H, Martin J, Metcalf D, Coleman M, McCarley RW. Abnormalities of the left temporal lobe and thought disorder in schizophrenia: a quantitative magnetic resonance imaging study. New England Journal of Medicine. 1992 Aug 27;327(9):604-12.
- [9] Soniat TL. Psychiatric symptoms associated with intracranial neoplasms. American journal of psychiatry. 1951 Jul;108(1):19-22.
- [10] Wester K. Intracranial arachnoid cysts—do they impair mental functions?. Journal of neurology. 2008 Aug 1;255(8):1113.
- [11] Gelabert-Gonzalez M. Intracranial arachnoid cysts. Revista de neurologia. 2004;39(12):1161-6.
- [12] Kuloglu M, Caykoylu A, Yilmaz E, Ekinci O. A left temporal lobe arachnoid cyst in a patient with schizophrenia-like psychosis: a case report. Progress in neuro-psychopharmacology & biological psychiatry. 2008 Jul 1;32(5):1353.
- [13] Colameco S, DiTomasso RA. Arachnoid cyst associated with psychological disturbance. The Journal of the Medical Society of New Jersey. 1982 Mar;79(3):209.
- [14] Baquero GA, Molero P, Pla J, Ortuño F. A schizophrenia-like psychotic disorder

- secondary to an arachnoid cyst remitted with neurosurgical treatment of the cyst. The open neuroimaging journal. 2014;8:1.
- [15] Kuhnley EJ, White DH, Granoff AL. Psychiatric presentation of an arachnoid cyst. The Journal of clinical psychiatry. 1981 Apr;42(4):167-8.

E

Guidelines for Manuscript Preparation



A. TYPES OF MANUSCRIPTS

I. ORIGINAL MANUSCRIPTS

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.

- The structured abstract must not exceed 250 words.
- The title must not exceed 130 characters.
- A maximum of 4 tables and 4 figures is allowed.
- 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.
- Three to ten key words at the end of the abstract must be provided.

The manuscript must be arranged as follows:

- Title page
- Abstract
- Introduction
- · Materials and methods (or Patients and methods)
- Results
- Discussion
- Acknowledgements
- References
- Tables
- Figure legends
- Figures

Acceptance of original manuscripts will be based upon originality and importance of the investigation. These manuscripts are reviewed by the Editors and, in the majority of cases, by two experts in the field. Manuscripts requiring extensive revision will be at a disadvantage for publication and will be rejected. Authors shall be responsible for the quality of language and style and are strongly advised against submitting a manuscript which is not written in grammatically correct English. The Editors reserve the right to reject poorly written manuscripts even if their scientific content is qualitatively suitable for publication. Manuscripts are submitted with the understanding that they are original contributions and do not contain data that have been published elsewhere or are under consideration by another journal.

II. REVIEW ARTICLES

Review articles on selected clinical and basic topics of interest for the readers of the Majmaah Journal of Health Science will be solicited by the Editors. Review articles are expected to be clear, concise and updated.

- The maximum length is 5000 words, excluding the summary, references, tables, and figures.
- References should not exceed a maximum of 150.
- The inclusion of a maximum of 4 high-quality tables and 4 colored figures to summarize critical points is highly desirable.
- Review articles must be accompanied by a title page and a summary.

25 Publication Guidelines

Reviews should include at least one Key Point Box, with a maximum of 5 bullet points, that briefly summarizes the
content of the review.

Review articles are reviewed by the Editors and may be sent to outside expert reviewers before a final decision for publication is made. Revisions may be required.

III. EDITORIALS

This section consists of invited brief editorial comments on articles published in the Majmaah Journal of Health Science

The length of an editorial should not exceed 1500 words, excluding references.

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- · A title page must be provided.

IV. CASE REPORTS

Case reports would be only accepted if they represent an outstanding contribution to the Etiology, pathogenesis or treatment of a specific condition.

- The maximum length is 3000 words, including the summary and references.
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V. LETTERS TO THE EDITOR

Letters to the Editor will be considered for publication if they are related to articles published in recent issues of Majmaah Journal of Health Science. Occasionally, Letters to the Editor that refer to articles not published in Majmaah Journal of Health Science will be considered.

The length of a Letter to the Editor should not exceed 800 words.

- A maximum of 1 table or 1 figure is allowed.
- References should not exceed a maximum of 10.
- No more than 4 Authors may appear in the author list.

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International commentaries will be solicited by the Editors only.

- · Commentary articles should not exceed a maximum of 800 words, excluding tables or figures.
- A maximum of 1 table or 1 figure is allowed.
- References should not exceed a maximum of 10.
- A title page must be provided.

B. MANUSCRIPT SUBMISSION

ORGANIZATION OF THE MANUSCRIPT

- The submitted manuscript must be typed double-spaced throughout and numbered (including references, tables
 and figure legends). Preferably using a "standard" font (we prefer Times/Arial 12).
- 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.
- Full gene names are generally not in italics and Greek symbols are not used. Proteins should not be italicized.
- Improperly prepared manuscripts will not be entered into the peer review process and will be sent back to the author for correction.

TITLE PAGE MUST CONTAIN:

A title of no more than 130 characters.

- Running title (not to exceed 60 characters)
- Names of the Authors as it should be published (first name, middle initial, last name)
- Affiliations of all authors and their institutions, departments, or organizations (use the following symbols in this
 order to designate authors' affiliations: *, †, ‡, \$, ¶, ||, #, **, ††, ‡‡, §§, ¶¶, || ||, ##).
- Name, address, telephone and fax numbers, and electronic mail address of the corresponding Author.
- Electronic word count.
- Number of figures and tables.
- List of abbreviations in the order of appearance.
- · Conflict of interest.
- Financial support.

Animal trials: Manuscripts reporting experiments using animals must include a statement giving assurance that all animals received human care and that study protocols comply with the institution's guidelines. Statistical methods used should be outlined.

Human trials: Manuscripts reporting data from research conducted on humans must include a statement of assurance in the methods section of the manuscript reading that:

- 1. Informed consent was obtained from each patient included in the study and
- The study protocol conforms to the ethical guidelines of the 1975 declaration of helsinki as reflected in a priori approval by the institution's human research committee.

Randomized controlled trials: Any paper that is a randomized control trial should adhere to the guidelines that can be found at the following web-site: www.consort-statement.org. The checklist should be printed out and faxed to the Editorial office at the time of submission. The trial registration number must be included on the title page of the manuscript reporting a registered clinical trial. Failure to do so will prevent entry to the peer review process.

Drugs and chemicals: Drugs and chemicals should be used by generic name. If trademarks are mentioned, the manufacturer's name and city should be given. All funding sources supporting the work, either public or private, especially those from pharmaceutical companies, must be provided.

Genetic Sequence data: In papers reporting a novel DNA or amino sequence, verification that the data have been or will be submitted either to Gen-Bank or EMBL is required. Please provide this verification and the accession number in the covering letter.

REFERENCES

References must be in accordance with the Journal of Hepatology reference style. References are ordered as they appear in the text and citation numbers for references are placed between "brackets" ("[]") in the text as well as in the reference list.

Authors should be listed surname first, followed by the initials of given names (e.g. Bolognesi M). If there are more than six authors, the names of the first six authors followed by et al. should appear.

Titles of all cited articles are required. Titles of articles cited in reference list should be in upright, not italic text; the first word of the title is capitalized, the title written exactly as it appears in the work cited, ending with a full stop. Journal titles are abbreviated according to common usage, followed by Journal years, semicolon (;) before volume and colon (:) before full page range (see examples below).

All articles in the list of references should be cited in the text and, conversely, all references cited in the text must be included in the list.

Personal communications and unpublished data should be cited directly in the text by the first Author, without being numbered. Please make sure you have the latest, updated version of your reference management software to make sure you have the correct reference format for Majmaah Journal of Health Science.

An example of how references should look within the text:

"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]."

An example of how the reference list should look:

[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.

[15] Groszmann RJ, Wongcharatrawee S. The hepatic venous pressure gradient: anything worth doing should be done right. Hepatology 2004;39:280-282.

FIGURES

A maximum of 4 figures is allowed

(This can be modified if needed by Editorial board).

- Figures will be often, but not always, re-designed by graphic designers. By signing and transferring the Copyright
 Agreement to MJHS, the author gives permission to the graphic designers to alter the visual aspect of any figures,
 tables, or graphs. The scientific content of figures will not be altered. Please provide this information with your
 covering letter.
- All graphics submitted to Majmaah Journal of Health Science should be sent at their actual size, which is 100% of their print dimension and in portrait orientation.
- Two standard widths are used and figures should fit in one (8.5 x 23.5 cm) or two (17.5 x 23.5 cm) columns
- Figures should be supplied in the following preferred file formats: PDF (*.pdf), Power Point (*.ppt), Adobe Illustrator (*.ai, *.eps), Photoshop (*.psd) files in grayscales or in RGB color mode. It is highly recommended that figures not be sent in JPG (*.jpg) format.
- Photographs (scans, immunofluorescences, EM, and histology images) should be submitted as: 1. TIFF (*.tif) with
 a resolution of at least 300 pixels per inch, or
- Illustrator compatible EPS files with RGB color management (*.eps),
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- 1. 300 dpi for color figures
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- For all photomicrographs, where possible, a scale should appear on the photograph. Photographs of identifiable patients should be accompanied by written permission to publish from patient(s).
- Furthermore, panel lettering should be in Arial bold 14 pt, capitalized and no full stop (A, B) while lettering in figures (axes, conditions), should be in Arial 8 pt, lower case type with the first letter capitalized and no full stop.
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TABLES

A maximum of 4 tables is allowed

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- Tables should be provided as Word files (*.doc) or Illustrator/InDesign (*.ai, *.eps, *.indd) compatible files. No TIFF
 and JPG files are acceptable for table submission.
- When submitting tables in Microsoft Word table function, no tab, space or colors should be used. Tables should contain a maximum of 10 columns.
- Tables submitted in landscape orientation will not be accepted. Tables should include a title, table legend, and if necessary footnotes.
- Include tables in the submitted manuscript as a separate section.

FIGURE LEGENDS

- Figure legends should be listed one after the other, as part of the text document, separate from the figure files.
- Please do not write a legend below each figure. Each figure legend should have a brief title that describes the entire
 figure without citing specific panels, followed by a description of each panel, and the symbols used.
- Enough information should be provided in the figure legend text to permit interpretation of figures without reference to the text; but should not contain any details of methods, or exceed 100 words.
- The abbreviated word for figure "Fig." should be typed and bolded, followed by the figure number and a period

(i.e. "Fig. 1."). Every figure legend should have a Title written in bold.

- If a figure contains multiple sections (i.e. A, B, C, D) the letter for these subsections should be in capital letters. Within the figure legend text the capital letters should be surrounded by parenthesis [i.e. (A)(B)(C)(D)].
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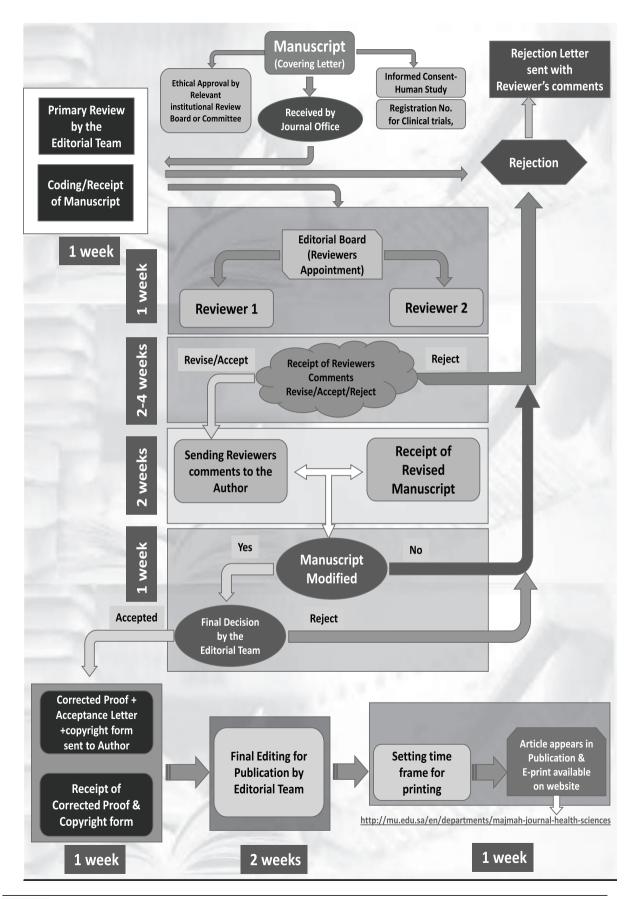
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