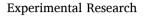


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The clinical characteristics of primary headache and associated factors in children: A retrospective descriptive study



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ARTICLE INFO	A B S T R A C T		
Keywords: Primary headache Children Vitamin D Family history Jordan Incidence	<i>Background:</i> Headache is the most encountered manifestation of pain in childhood. The purpose of this study was to investigate the incidence and clinical characteristics of primary headaches. Further, the factors associated with primary headache were examined. <i>Materials and methods:</i> A retrospective study was conducted among young children and adolescents over 3 years at a tertiary referral teaching hospital in North Jordan. Relevant patient information was obtained by reviewing patients' medical records. <i>Results:</i> This study included 194 children (95 males, 99 females). The incidence rate of primary headache in the current study was 2.815 per 1000 children visited pediatric clinic. The mean age of patients at the time of headache onset was 10 years, and about half of them were males (95/194; 49%). Approximately 30% (56/194) had a family history of headache. Migraine headaches were the most commonly reported types (87/194; 44.8%) and only 17/194; 8.7% suffered from tension type headaches. Approximately, 40% (84/194) of patients reported severe headache and a third of them (67/194; 34.5%) complained of daily headaches. Pain location was reported as bilateral in most patients (153/194; 78.9%). About one fifth (41/194; 21.1%) stated that their headache were significantly associated with primary headache ($p < 0.001$). <i>Conclusions:</i> These findings highlight the importance of early detection and management of headaches among pediatric population. In addition, screening vitamin D status should be encouraged for children presented with primary headaches.		

1. Introduction

Headache is the most frequent neurological symptom and the most common manifestation of pain in childhood [1]. Headaches occur frequently in the pediatric population and negatively affect the patients and their family [2]. It has been shown that headache decreases the quality of life and increases the cost of health care consumption [3–5].

It is essentially important for the healthcare providers to differentiate the characteristics of primary and secondary headaches to provide each patient with the best possible care and thus improving their quality of life and minimizing disability [6]. The frequency of reported headache increases with increasing age and the underlying etiologies range from simple tension to life-threatening infections and brain tumors [7]. The vast majority of childhood headaches are due to a primary headache disorder, such as migraine, or an acute benign process, such as viral infection [7,8]. However, other serious causes of headache should be considered [7,8]. Migraine, the most common headache disorder for which patients see a physician, remains underdiagnosed and under-treated. A thorough evaluation of headache in pediatric population is necessary for the proper diagnosis and management [7,9–11]. Our understanding of pediatric headache is improving with increased recognition of the characteristics and associated symptomology. This has the potential to guide patients' therapy for improving outcome and reducing the progression into adulthood [12].

A study from Turkey by Karli et al., 2006. reported that the prevalence of recurrent headache in adolescents)12–17 years) was 52.2% and

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tension-type headache was the most common (25.9%), followed by migraine (14.5%) [13]. In Jordan, Al Bashtawy et al., 2017 conducted cross sectional study among high school students (16–18 years) and found that nearly two thirds of the students reported having headache (19.0% tension-type headache, 8.8% migraine, and 39.0% unknown type) [14]. Previous studies were limited by small sample size and inclusion of school children only [13–16]. In addition, none of the available studies have examined the incidence and factors associated with primary headache among children in Middle East. The present study aimed to investigate the incidence and clinical characteristics of primary headaches among young children and adolescents (3–16 years) in Jordan. The secondary aim was to explore potential risk factors for primary headache in children.

2. Method

2.1. Study design

A retrospective, observational study was conducted at King Abdullah University Hospital from January 1, 2015 to December 31, 2019. This center is the main tertiary referral teaching hospital in North of Jordan with 543-bed and an annual average admission rate of 40,350 patients. This study included pediatric patients aged 3–16 years with primary headache. The ethical approval to conduct this research was granted by the Institutional Review Board in Jordan University of Science and Technology. Informed consent was waived for this retrospective study. The work has been reported in line with the STROCSS criteria [17], and the study is registered on Research registry under the unique identify number Researchregistry6700 [18].

2.2. Case selection

The list of patients (3-16 years) with any type of headache who visited pediatric clinic in the hospital between Jan 1, 2015 to Dec 31, 2019 was identified using the hospital database. Medical records of all these patients were reviewed, and patient with primary headache type was included in the current study. Children suffered from diseases that could potentially be associated with secondary headache such as brain tumors, paranasal sinus diseases, febrile illness, other systemic diseases, and vision problems were excluded. Patients' data was evaluated on the basis of the medical records from the first visit. The diagnosis and classification of headache was according to the ICHD-3 or ICHD-2 criteria applied to children and adolescents. We divided headaches into three groups: migraine, tension type headaches (TTH), and unclassified headache. In the analysis, definite migraine and probable migraine were grouped as migraine, and definite TTH and probable TTH as TTH. Patients with headache who fell into none of these categories were categorized as "unclassified headache". The documented patient's data regarding demographics (such as age, gender, comorbidity) and clinical as well as medical information (such as family history of headache, characteristic of headache, blood investigations such as vitamin D level and complete blood count) were collected for each patient. Blood investigations including complete blood count, vitamin D level, liver function test, kidney function test and thyroid function test were used to be performed in our practice to all pediatric patients who presented to the neurology clinic with headache.

Based on previous studies and reports of the Institute of Medicine, anemia in children is defined according to the age and gender. The normal hemoglobin level for children aged 3–5 years is 10.9-15.0 g/dL and 11.9-15.0 g/dL for children aged 5–11 years for both gender. While children aged 11–16 years, the female range from 11.9 to 15.0 g/dL and the male range is 12.7-17.7 g/d. Serum 25-hydroxy vitamin D was considered to be the most reliable indicator for assessment of vitamin D status. Results of serum 25-hydroxy vitamin D levels >29 ng/ml were considered normal, 21-29 ng/ml were insufficient, and <20 ng/ml were deficient.

Data from control group was collected to investigate the factors that were associated with primary headache. Patients with corresponding age and gender who presented to pediatric respiratory clinics in the hospital were included in control group. The mean age of controls was 10.66 years (standard deviation = 3.055) and the mean age of cases was 10.40 years (standard deviation = 3.056]. In addition, about half of both control and case groups were females; control (47.9%, n = 93) Vs cases (51%, n = 99). The patients in control group had mainly respiratory infections (except sinusitis) and with no personal history of headache. Those patients with any neurological condition were excluded to avoid any confounding effect. Controls were selected from hospital system database using a random sequence number generator and from the same years of the included cases of primary headache.

2.3. Statistical analysis

Collected data was analyzed utilizing Statistical Package for Social Sciences (SPSS Inc., Chicago, IL) version 23. Descriptive statistics were used to summarize the samples' data. Categorical variables were presented as number and percentage while continuous variables were presented as mean and standard deviation. Chi square test (χ^2) test was used to assess the association of categorical variables with primary headache. Factors that associated with primary headache were evaluated such presence of family history of headache, anemic status, and abnormal level of vitamin D. Odds ratio (OR) and 95% confidence (95% CI) were calculated. P value < 0.05 was considered statistical significant.

3. Results

During the study period, a total of 490 patients with headache were identified. Of those, 296 cases were excluded because they had secondary headache leaving 194 (39.5%) cases with primary headache. The incidence rate of primary headache in the current study was 2.815 per 1000 children visited the general pediatric clinics.

Table 1 outlines the demographic and clinical characteristics of all included cases. The mean age of patients at time of onset of headache was 10 years, and males and females were equally affected. Approximately 30% (56/194, 28.9%) of patients had a family history of headache. Migraine headaches were the most commonly reported type (44.8%; 87/194) and only 8.7% (17/194) suffered from tension type headaches. Less than half of patients (46.4%; 90/194) were of unclassified type of headache. Approximately 40% of patients (84/194) reported severe headache and a third of them (34.5%; 67/194) complained of daily headache. A quarter (49/194; 25.2%) complained of an attack which lasted from 30 min to 4 h and a half (101/194; 52.1%) of the patients could not clearly explain the duration. Pain location was reported as bilateral in the majority of patients (153/194; 78.9%). Sleep deprivation precipitated headache was reported by a quarter of patients (41/194; 21.1%).

There was significant association between reported severity of primary headache and use of analgesia (p = 0.001). Patients who reported severe headache used analgesia (57.7%; 45/84) more significantly compared to patients with mild-moderate headache (42.3%; 33/110) (P = 0.001). Regarding laboratory findings (Table 2), only 11.7% (22/194) of patients with primary headaches were anemic at presentation. Of those patients who carried out vitamin D serum level (n = 77), majority (96.1%; 74/77) had low vitamin D serum levels (deficient or insufficient). In addition, neuroimaging studies (CT or MRI) were performed in third of patients (36%; 71/194), and the results were abnormal in 18.3% (13/71) of cases as shown in Table 2.

The results of univariate analysis identified that both abnormal level of vitamin D and presence of family history of headache were significantly associated with primary headache (p < 0.001) (Table 3). On the other hand, presence of anemia was not associated with primary headache (p = 0.078).

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Table 1

Demographic and clinical characteristics of primary headache.

Characteristics ^a	N = 194 (%)		
Gender			
•Male	95 (49)		
•Female	99 (51)		
Age at time of onset of headache ^b	10.40 ± 3.056		
Type of headache			
 Migraine 	87 (44.8)		
 Tension-type headache 	17 (8.7)		
 Unclassified 	90 (46.4)		
Family history of headache			
 Positive 	56 (28.9)		
 Negative 	138 (71.1)		
Intensity (reported)			
•Mild	38 (19.6)		
•Moderate	72 (37.1)		
•Severe	84 (43.3)		
Frequency			
•Daily	67 (34.5)		
•2–3/week	32 (16.5)		
•1–3/month	40 (20.6)		
 Unexplained 	55 (28.4)		
Duration of the pain			
•Few seconds	7 (3.6)		
●<5 min	9 (4.6)		
•5–30 min	12 (6.2)		
•0.5–4 h	49 (25.2)		
●>4 h	16 (8.2)		
 Unexplained 	101 (52.1)		
Pain location			
•Unilateral	41 (21.1)		
•Bilateral	153 (78.9)		
Precipitating factors			
•None	131 (67.5)		
•Sun exposure	12 (6.2)		
•Sleep deprivation	41 (21.1)		
•Stress	10 (5.2)		
Associated factors			
•Nausea/Vomiting	50 (43.1)		
•Dizziness	36 (31)		
 Photophobia 	48 (41.4)		
•Others	45 (38.8)		
Use of analgesia			
•No	116 (59.8)		
•Yes	78 (40.2)		

^cvalues were calculated based on the number of patients whom their data were available.

^a Data were presented as number (percentage) otherwise indicated.

 $^{\rm b}$ Data were presented as mean \pm standard deviation.

Table 2

Laboratory findings and patients' brain imaging results.

Variable ^a	N (%)
Presence of anemia	
•No	172 (88.7)
•Yes	22 (11.7)
Vitamin D level ^b	
•Normal	3 (3.9)
 Abnormal (Deficient/insufficient) 	74 (96.1)
Brain scan (either CT or MRI) ^a	
•Not done	123 (63.4)
•Done	71 (36.6)
Normal	58 (81.7)
Positive finding (abnormal)	13 (18.3)

^a Data were presented as number (percentage) otherwise indicated.

^b Values were calculated based on the number of patients whom their data were available.

4. Discussion

Headaches are a common complaint in childhood and adolescence and cause serious distress and disability [19]. A relatively low incidence

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Table 3

Factors associated with primary headaches.

Factors	$\begin{array}{l} \text{Control} \\ N=194 \end{array}$	Primary headache $N = 194$	P-value	ORs (95%CI)
Vitamin D ^a			< 0.001	25.98
•Normal	99 (51.3%)	3 (3.9%)		(7.92–85.25)
 Abnormal 	94	74 (96.1%)		
(Deficient/ insufficient)	(48.7%)			
Presence of anemia			0.078	1.92
•No	180 (93.8%)	172 (88.7%)		(0.92–3.99)
•Yes	12 (6.3%)	22 (11.3%)		
Family history of headache ^a			< 0.001	3.68 (2.01–6.72)
•No	145 (90.1%)	138 (71.1%)		
•Yes	16 (9.9%)	56 (28.9%)		

OR: odds ratio, CI: confidence interval.

^a Values were calculated based on the number of patients whom their data were available.

of primary headache was reported in the current study as 2.815 cases per 1000 children visited the pediatric clinic. There was no previous estimated incidence in the literatures to compare the results with. Previous studies in Jordan and Austria reported high prevalence of primary headache among school students (67.2% and 75.7% respectively) [14, 15]. The current study showed most children suffered from migraine headache (44.8%) followed by tension type headaches (8.7%). This was similarly documented by other studies [19,20]. In contrast, previous studies from South Korea [16]and Jordan [14] among school children reported that tension type headache was the most frequent type followed by migraine headache [14,16]. Many factors could contribute to variations in the reported results among different studies, including biological, environmental, cultural, geographical, methodological or diagnostic criteria.

In the current study, headaches of severe intensity, that occurred on daily basis, bilaterally with duration less than 4 h, were considered the major characteristics of the study population. Approximately, a third of the included cases had moderate pain which is inconsistent with a previous Jordanian study where moderate headache was the most prevalent in 51.9% [14]. Moreover, around 40% of patients in the current study reported pain with a duration of less than 4 h and half of them complained of headache either daily or two to three times per week. On contrary, AlBashtawy and colleagues found that the majority of the school students had pain with duration of more than 4 h and occurred at least once per month [14]. This discrepancy can be explained by differences of study designs, participants with different sociodemographic characteristics and high subjectivity of measurement of pain between individuals.

It is important to explore family history of headache, including first degree relatives such as parents and siblings, or other family members. The present study revealed that more than quarter (28.9%) had family history of headache and this was found to be significantly associated with primary headache. In parallel with this finding, Seon Kang et al. found that 28.1% of children younger than 7 years in Korea had family history of headache [20]. Additionally, Cavestro et al. (2014) reported that primary headache was significantly associated with the family history of headache amongst other comorbidities in Italy [21]. On the other hand, a previous study in Jordan reported that nearly 60% of school children indicated that they have a family history of headache [14] which is about double the figure reported in the present study. Jeong et al. reported a significant association between parental headaches and childhood headaches, especially in preschool patients [19]. Kröner-Herwig et al. also found a strong association in the prevalence of headache between parents and their children [22].

The current study showed that patients with severe headache used analgesia more often than patients with mild-moderate symptoms. This could be explained by medication overuse headache which occurs when analgesics are taken frequently to relieve the pain. However, it was difficult to confirm such conclusion due to the nature of the current retrospective study.

Vitamin D deficiency is widely prevalent and found to be associated with various disorders [23-25]. Low serum vitamin D levels causes chronic pain and headaches disorders, especially tension-type headache and migraine [26]. In the present study, abnormal vitamin D levels was found to be significantly associated with primary headache (P < 0.001). Current literature regarding vitamin D levels and headache in pediatrics is limited and conflicting. O'Brien et al. documented a high prevalence of vitamin D deficiency among 300 pediatric patients with migraine [27]. Moreover, they stated that the prevalence of vitamin deficiency was considerably higher among children with recurrent headaches compared to those without [27]. Supporting this, Cayir et al. reported that vitamin D therapy with amitriptyline reduced the recurrence of migraine attacks in pediatric patients with migraine compared to patients who received amitriptyline alone [28]. Similarly, Kilic and Kilic (2019) found that vitamin D therapy was beneficial in decreasing the frequency and duration of migraine in the pediatric population (p < p0.001) [29]. On the contrary, other studies among pediatric population found no association between headache and vitamin D levels [30,31]. Further randomized clinical trials need to be conducted with a larger sample size to test the correlation between vitamin D level and primary headache.

There are a few limitations to the current study. Firstly, this is a retrospective study in which the information was limited to the data found in each patient's file. For example, no data about the patients' lifestyle, geographical location and socioeconomic status were available. Secondly, this was a single center study which might not represent the general pediatric population.

5. Conclusion

This study is the first of its kind in Jordan and the Middle Eastern Arab countries that investigated the incidence of the primary headaches among children and adolescents and explored factors affecting primary headache. The current study revealed that the incidence of primary headache in Jordan was relatively low and that both low vitamin D level and presence of family history of headache were significantly associated with primary headache in children. This highlights the need for screening vitamin D status on routinely basis for children presented with primary headaches. Identifying incidence and clinical characteristics of primary headaches among the pediatric population is important in the early detection and management of headaches in children. As such, further studies should be conducted with a larger sample size to validate the current findings.

Declaration of competing interest

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.102374.

Provenance and peer review

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Ethics approval and consent to participate

This study was approved by the Institution Review Board (IRB) of King Abdullah University Hospital (KAUH), Jordan University of Science and Technology (JUST). Reference number 10/111/2017.

Consent for publication

Not applicable.

Availability of data and materials

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

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Authors' contributions

Miral Almomani is the principle investigator of this manuscript. MA, BAA and ATM participated in the design, analysis and interpretation. MA, BAA and ATM performed literature review and drafted and edited the manuscript. All the authors have approved submission of the manuscript.

Guarantor

Dr Miral Al Momani

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