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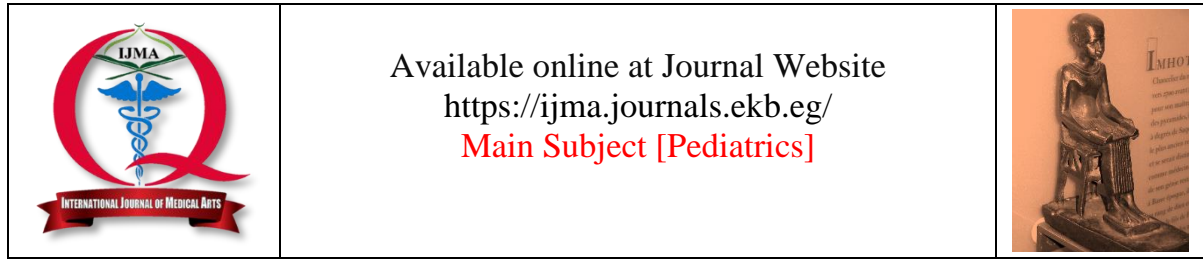


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## Original Article

# Sex-Based Differences in Pediatric Migraine: A Clinico-Epidemiological Study

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## ABSTRACT

### Article information

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**Background:** Despite being a frequent complaint among children and adolescents, there is still a considerable lack of comprehension regarding the distinctive characteristics of migraine in these age groups. One of these aspects is the influence of sex on the prevalence and characteristics of migraine.

**Aim of the work:** To evaluate the clinical characteristics of migraine headaches in children and adolescents in relation to sex of studied cases.

**Patients and Methods:** This Prospective Observational Study included 96 females and 82 males aged 6-18 years with migraine. Detailed history and physical examination were conducted. ICHD-3 criteria were used for diagnosis and migraine features were compared between sexes.

**Results:** Girls had a higher mean age than boys [ $12.5 \pm 3.7$  years vs.  $11.4 \pm 3.5$  years,  $P = 0.044$ ]. Males were more common in the <12 years age group, while females predominated in the 12-16 years group. Migraine onset was earlier in males [ $8.9 \pm 2.7$  vs.  $9.4 \pm 2.6$  years;  $P = 0.21$ ]. Girls experienced higher intensity migraines [ $P = 0.01$ ]. Vomiting was significantly more prevalent in boys compared to girls [39% vs. 24%;  $P = 0.03$ ]. Family history, migraine types and triggers did not differ.

**Conclusion:** This study demonstrated notable sex-based differences in the clinical profiles of pediatric migraine. Females tended to experience higher migraine severity and burden, while males presented with certain gastrointestinal symptoms more commonly. Earlier identification of distinct characteristics according to biological sex may assist clinicians in optimizing evaluation and management strategies tailored for individual patients. Further research should explore potential pathophysiological underpinnings driving these observed clinical disparities between boys and girls with migraine.

**Keywords:** Migraine Disorders; Sex; Child; Adolescent.



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## INTRODUCTION

Headache is one of the most frequent complaints evaluated by pediatricians and neurologists in their office practices [1]. Migraine, a prevalent neurological disorder, has gained increasing recognition for its impact on the quality of life in both children and adults [2-4]. Migraine is the most common type of recurrent headache in children that parents and primary care providers are most frequently alerted to [5].

Migraine is a type of primary headache condition marked by recurring, moderate to intense headache episodes along with symptoms like nausea and vomiting, photophobia, and phonophobia, often leading to significant functional impairment in pediatric populations [6]. It affects approximately 10% of school-aged children and adolescents worldwide [7-9]. While the understanding of migraine in adult populations continues to expand, there remains a significant knowledge gap concerning the clinico-epidemiological characteristics of migraine specifically in children and adolescents [10].

Migraine headaches in children can present with some variations between sexes. Research suggests that migraines are more prevalent in boys during early childhood, but as children reach adolescence, the prevalence becomes higher in girls. The exact reasons for this shift are not yet fully understood [11, 12]. Additionally, girls may experience a greater frequency and duration of migraine attacks compared to boys [13]. Understanding the sex-based differences in migraine characteristics during childhood and adolescence is crucial to optimize diagnosis and management.

While several studies have characterized the clinical features and epidemiology of pediatric migraine in developed countries, limited data exists from developing regions like Egypt. This study aimed to characterize the clinical features and epidemiology of migraine among Egyptian children and adolescents, with specific focus on analyzing sex-based differences. Our goals were to add to the limited local knowledge base and identify novel insights that could guide tailored migraine care approaches for this vulnerable group in Egypt.

## PATIENTS AND METHODS

**Study Design:** This prospective study was conducted at the pediatric neurology outpatient clinic of Al-Azhar University Hospital at New Damietta from January 2021 to December 2022.

**Participants:** The study included a total of 178 participants, consisting of 96 females and 82 males, between the ages of 6 to 17 years old.

**Inclusion criteria:** Children and teenagers between 6 and 18 years old diagnosed with migraine as per the third edition of the International Classification of Headache Disorders [ICHD-3] guidelines were considered for the study.

**Exclusion criteria:** Patients with other types of headaches, other neurological conditions, or any comorbidities affecting the interpretation of migraine symptoms.

**Ethical consideration:** Participants gave informed consent by himself or their parents after explaining of study aims and approval of local ethical committee of Damietta Faculty of Medicine, Al-Azhar University.

### Data collection

A detailed history was obtained from each participant, encompassing information on age, sex, family history, and age of onset of migraine. The clinical assessment encompassed the classification of migraine subtypes, identification of trigger factors by requesting patients to report all possible triggers of their episodes, and a detailed examination of headache characteristics including location, severity, duration, and frequency of migraine attacks in both female and male groups. The severity of headaches was evaluated using the Verbal Rating Scale [VRS], whereby children verbally indicated their pain level as mild, moderate, or severe. The impact of migraine on daily activities, such as school and play, was assessed utilizing the PedIMMPACT questionnaire. Furthermore, all patients underwent a thorough general physical and neurological examination, and relevant investigations such as MRI brain scans were conducted where indicated.

### Sample size calculation

The sample size was calculated using statistical software [OpenEpi]. With a significance level [ $\alpha$ ] set at 0.05 and a desired power [ $1-\beta$ ] of 0.80, the effect size was estimated based on findings from Slater *et al.* [14] at 1.37, indicating the expected difference in migraine characteristics between males and females. Additionally, considering the prevalence of migraine in children and adolescents at 9.1% as reported by Wöber-Bingöl [11], the sample size calculation accounted for these factors to detect clinically significant sex-specific differences in migraine presentation. After inputting these

parameters into the software, the analysis indicated that a total sample size of 175 participants.

### Statistical analysis

Data was entered into a pre-designed proforma and analyzed using SPSS 23.0. Descriptive statistical analysis was performed. Numeric data were examined using Student's t-test, while categorical data were assessed using the Chi-square test. A P value of less than 0.05 was deemed to be statistically significant.

## RESULTS

In the present study, the mean age of girls [ $12.5 \pm 3.7$  years] was higher than that of boys [ $11.4 \pm 3.5$  years] with a statistically significant difference [ $P = 0.044$ ]. Males were more frequent than females among the age group  $< 12$  years, while females were more frequent in the age group of 12-16 years. The majority of children had a positive family history, with no difference between boys and girls [Table 1].

Average onset was earlier in males [ $8.9 \pm 2.7$  years vs.  $9.4 \pm 2.6$  years,  $p=0.21$ ]. Most of cases

had migraine without aura [70.7% in boys and 67.7% in girls]. No significant difference between males and females regarding headache duration or location. Girls showed significant higher intensity than boys [ $P = 0.01$ ] [Table 2].

The most frequent associated symptom in males and females was photophobia [80.5% in boys vs. 83.3% in girls] followed by phonophobia [74.7% in boys vs. 81.25% in girls]. There were no significant differences between boys and girls regarding associated symptoms except for vomiting, which was significantly higher among boys [39% in boys vs. 23.9% in girls;  $P = 0.03$ ] [Table 3].

Regarding triggers of migraine, the most frequent factor was stress followed by lack of sleep. There were no significant differences between boys and girls regarding trigger factors [Table 4].

In the present study, migraine attacks did not interfere with daily activity in boys and girls. Most of attacks were during the day with no significant difference between both sexes. Most participants reported no difference [65.9% in boys and 75% in girls] between seasonal variation [Table 5].

**Table [1]:** Personal character of study participants

Parameter	Boys [n = 82]	Girls [n = 96]	P value	
Age [yr.]	Mean $\pm$ SD	$11.4 \pm 3.5$	$12.5 \pm 3.7$	<b>0.044*</b>
	< 12 years	42 [51.2%]	36 [37.5%]	0.065
	12-16	40 [48.8%]	60 [62.5%]	
Family history	No Family history	16 [19.5%]	19 [19.8%]	0.8
	Paternal only	20 [24.4%]	29 [30.2%]	
	Maternal only	38 [46.3%]	41 [42.7%]	
	Both parents	8 [9.8%]	7 [7.3%]	

**Table [2]:** Migraine characters of study participants

Characteristic	Boys [n = 82]	Girls [n = 96]	P value	
Migraine age onset [yrs.]	$8.9 \pm 2.7$	$9.4 \pm 2.6$	0.21	
Type of migraine	Migraine without aura	58 [70.7%]	65 [67.7%]	0.58
	Migraine with aura	21 [25.6%]	24 [25%]	
	Probable migraine	3 [3.7%]	7 [7.3%]	
Headache duration	< 30 min	28 [34.1%]	36 [37.5%]	0.52
	About 1 h	21 [26.6%]	29 [30.2%]	
	About 2 h	15 [18.3%]	18 [18.75%]	
	> 2 h	18 [22%]	13 [13.55%]	
Intensity	Mild	40 [48.8%]	29 [30.2%]	<b>0.01*</b>
	Moderate	35 [42.7%]	46 [47.9%]	
	Severe	7 [8.5%]	21 [21.9%]	
Pain Localization	Localized at fixed points	36 [43.9%]	47 [48.9%]	0.18
	Different localizations	34 [41.5%]	28 [29.2%]	
	I do not know	12 [14.6%]	21 [21.9%]	

**Table [3]:** Associated symptoms

Characteristic	Boys [n = 82]	Girls [n = 96]	P value
Photophobia	66 [80.5%]	80 [83.3%]	0.62
Phonophobia	61 [74.4%]	78 [81.25%]	0.27
Nausea	56 [68.3%]	70 [72.9%]	0.49
Awakening pain	36 [43.9%]	41 [42.7%]	0.87
Vomiting	32 [39.0%]	23 [23.9%]	<b>0.03*</b>
Vertigo	25 [30.5%]	37 [38.5%]	0.21

**Table [4]:** Common trigger factors

Characteristic	Boys [n = 82]	Girls [n = 96]	P value
Stressful home/school	58 [70.7%]	75 [78.1%]	0.26
Lack of sleep	36 [43.9%]	46 [47.9%]	0.59
Video games	28 [34.1%]	20 [20.8%]	0.046
Intense noise or light	13 [15.9%]	25 [26%]	0.098
Fasting	10 [12.2%]	15 [15.6%]	0.51

**Table [5]:** Periodicity and effect on daily activities of migraine

Characteristic	Boys [n = 82]	Girls [n = 96]	P value
Need to stop daily activities	No	33 [40.3%]	0.19
	Sometimes	27 [32.9%]	
	Always	12 [14.6%]	
	Always, and I need to rest in bed	10 [12.2%]	
Moment of the day	During the day	34 [41.5%]	0.45
	At night	7 [8.5%]	
	Both during the day and at night	14 [17.1%]	
	At fixed hours	6 [7.3%]	
Seasonality	I cannot identify a specific timing	21 [26.6%]	0.166
	Spring	4 [4.9%]	
	Winter	11 [13.4%]	
	Fall	5 [6.1%]	
	Summer	8 [9.8%]	
No differences	54 [65.9%]	72 [75%]	

## DISCUSSION

Children and adolescents represent a unique population, as their physiological, psychological, and social development differs from adults [15]. Migraine, with its potential to disrupt daily activities and impair emotional well-being, warrants special attention in this age group. Understanding the distinct clinical and epidemiological aspects of pediatric migraine is essential for accurate diagnosis, effective treatment, and improved management strategies [16].

Egypt, with its diverse population and unique environmental factors, poses an intriguing context to study migraine in children and adolescents. Despite the high prevalence and clinical significance of migraine, the current knowledge regarding its characteristics in the Egyptian pediatric population is limited. By exploring these factors, we aim to enhance our understanding of the prevalence,

clinical presentation, comorbidities, and potential risk factors associated with pediatric migraine in this region.

In the present study, 178 children and adolescents are diagnosed with migraine disorder. Among them, 96 were females and 82 were males with female: male ratio of 1.17: 1. However, Males were more frequent than females among the age group < 12 years, while females were more frequent in the age group of 12-16 years. Furthermore, the mean age of females was significantly higher than males.

These findings align with numerous studies in the existing literature. For instance, **Akyol et al.** [17] reported a female-to-male ratio of 1.5:1, with migraine being significantly more prevalent in girls compared to boys [P < 0.001]. The highest prevalence of migraine among girls was observed at the age of 13 years, and migraine prevalence

increased with age in both genders [ $P < 0.05$ ]. Similarly, **Philipp et al.** <sup>[8]</sup> corroborated our results in their research, indicating that headache prevalence rises with age and is greater in girls than in boys.

Migraine stands out as the most prevalent primary headache type in childhood. Its occurrence increases with age and is notably impacted by puberty, typically occurring between 8–14 years in girls and 9–15 years in boys <sup>[18]</sup>.

Among pre-pubertal children, the relatively low prevalence of migraine [3–10%], with no discernible gender difference, may be attributed to more developed brainstem mechanisms <sup>[19]</sup>. In contrast, during post-puberty adolescence, the hypothalamus resumes its functionalities, including hormone release and autonomic system regulation, potentially rendering females more prone to experiencing migraines <sup>[20]</sup>.

Furthermore, environmental influences, often termed epigenetic factors, could significantly contribute to gender disparities in pediatric migraine. Some research indicates that childhood adversity and early stress can be imprinted in the genome, forming an epigenetic memory that can later impact health <sup>[21, 22]</sup>.

In the present work, the majority of children had positive family history, with no difference between males and females. Consistent with our results, **Tarasco et al.** <sup>[23]</sup>'s research showed that over 88% of children had a family history of migraines. Similarly, **Wilcox et al.** <sup>[24]</sup> found that a large portion of migraine patients, 87.1% of the total sample, reported a family history of migraines. When comparing boys and girls, there was no statistically significant difference in terms of gender [ $P = 0.77$ ]. It is established that migraines have a strong genetic foundation, supported by studies involving families and twins <sup>[25]</sup>.

In this study, the average age at which migraines began was slightly higher in females compared to males, although this difference was not found to be statistically significant. In a retrospective analysis involving 468 children and teenagers with an average age of  $11.3 \pm 3.6$  years, comprising 215 males [45.9%] and 253 females [54.1%], female patients exhibited notably higher values for the age of migraine onset compared to male patients, with a statistically significant difference noted [ $p = 0.021$ ] <sup>[26]</sup>.

Regarding migraine characteristics, most of studied cases in both sexes had migraine without aura, of short duration [ $< 30$  min.] and localized. Females experienced more severe episodes than boys. No significant difference between sexes.

Migraine represents a major contributor to disability across various age brackets, imposing a considerable yearly economic strain through both direct healthcare costs and reduced work efficiency. Within the pediatric population, migraine can substantially influence a child's quality of life, impacting their education, social interactions, and family dynamics. Achieving optimal migraine management for children and adolescents necessitates a profound understanding of migraine symptoms, while also taking into account potential variations influenced by sex <sup>[20]</sup>.

Research studies have examined gender variances in additional clinical aspects of migraine. A retrospective study involving 4121 migraine patients aged 1–21 years explored gender distinctions related to age of onset, pain localization, accompanying symptoms, and consequent impairment. Prior to puberty [before 13 years], a higher percentage of males than females sought medical attention for treatment initiation; however, this pattern reversed post-puberty, with a shift towards more females than males being referred to specialized care facilities. Additionally, girls more frequently reported frontal, temporal, or occipital pain locations, whereas boys tended to experience pain at the crown of the head. Concerning associated symptoms, photophobia, nausea, and feelings of dizziness were more prevalent in females, while males exhibited higher occurrences of nausea, vomiting, confusion, and difficulty concentrating <sup>[14]</sup>.

**Wilcox et al.** <sup>[24]</sup> found a greater occurrence of vomiting in boys than in girls with migraine, while there was no discrepancy in terms of sensitivity to light, sound, or nausea. Similarly, **Eidlitz-Markus and Zeharia** <sup>[26]</sup> noted substantially elevated rates of vomiting in boys compared to girls, which could be attributed to a relatively more pronounced autonomic dysfunction in boys as a factor influencing this distinction.

The results of our study help advance understanding of migraine in the developing population by highlighting clinically meaningful sex-based variations. Recognizing differences in presentation according to biological attributes like gender allows for more tailored diagnosis and management approaches in pediatric headache

care. With earlier identification of at-risk subgroups, clinicians may be better positioned to deliver targeted therapies shown to improve outcomes.

A strength of this research lies in its prospective design enhancing reliability of comparisons. We employed widely used diagnostic criteria and standardized assessment methods, adding validity to findings. By analyzing an array of demographic, clinical and headache-related factors between sexes, our study furnishes a comprehensive glimpse into heterogeneous migraine profiles in boys versus girls. These insights offer valuable guidance for individualizing treatment strategies to each patient's unique needs.

While multicenter studies on broader populations could augment generalizability, we hope our analysis stimulates further mechanistic explorations aimed at personalized pediatric migraine solutions. With additional high-quality epidemiological data and rigorous clinical trials, providers may ultimately deliver precision medicine tailored according to factors like age, gender and symptoms for improved quality of life in developing patients.

Several limitations should be noted. Firstly, the relatively small sample size may limit the generalizability of the findings. The reliance on self-reported data for migraine features and potential recall bias could also affect the accuracy of the results. Furthermore, the study's restriction to a specific age range of 6-18 years may not fully capture the spectrum of migraine characteristics across all pediatric age groups. Future research with larger sample sizes, longitudinal designs, and diverse age ranges could address these limitations and provide a more comprehensive understanding of sex differences in pediatric migraine.

In conclusion, girls had a higher mean age compared to boys, with notable variations in migraine prevalence across different age groups. Family history of migraine was common among children, irrespective of gender. Migraine onset tended to occur earlier in males, with most cases being migraine without aura. These findings contribute to a better understanding of sex-related differences in pediatric migraine and may have implications for clinical management and further research in this area.

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**Conflicts of interest:** None.

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