

# Children with Migraine: Three Years of Clinical Experience

## Migren Tanılı Çocukların Değerlendirilmesi: Üç Yıllık Klinik Tecrübe

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### Abstract

**Objective:** Headache in the pediatric patients is a common cause of presentation to both general pediatrics and pediatric neurology outpatient clinics. This study aimed to retrospectively evaluate the clinical and laboratory findings in pediatric patients diagnosed with migraine.

**Material and Methods:** The study included pediatric patients diagnosed with migraine at Dr. Sami Ulus Pediatrics Training and Research Hospital, Pediatric Neurology Outpatient Clinic between 2013 and 2016. Comparisons were made between the patients that had migraine with aura and migraine without aura.

**Results:** In all, 11.6% of the pediatric patients that presented with headache were diagnosed with migraine. Among the patients with migraine, 18.8% (n=27) were aged <10 years and 81.3% (n=117) were aged >10 years. In total, 44 (48.4%) of the migraine patients were female and 13 (24.5%) were male; the difference was significant (p=0.008). In addition, mean age and gender of the migraine with aura patients and migraine without aura patients differed significantly (p=0.017).

**Conclusions:** Migraine is a chronic disease that is more common in children than generally thought. The present study identified the clinical findings indicative of the diagnosis of migraine, and highlighted the characteristics of migraine with and without aura in pediatric patients that present with headache.

**Keywords:** Headache; Migraine; Pediatrics

### Özet

**Amaç:** Pediatrik yaş grubundaki baş ağrısı hem genel pediatri hem de pediatrik nöroloji polikliniklerine sık başvuru nedenlerinden biridir. Bu çalışmada amaç, migren tanısı alan olgularımızın klinik ve laboratuvar bulgularını retrospektif olarak değerlendirmektir.

**Gereç ve Yöntem:** 2013-2016 yılları arasında Dr. Sami Ulus Çocuk Sağlığı ve Hastalıkları Eğitim ve Araştırma Hastanesi Çocuk Nöroloji Polikliniği'ne başvuran ve migren tanısı alan hastalar çalışmaya dahil edildi. Auralı migren ve aurasız migren alt grupları arasında istatistiksel karşılaştırma yapıldı.

**Bulgular:** Bu çalışmada, baş ağrısı şikayeti ile başvuran hastaların %11,6'sı migren tanısı almıştır. Migren hastalarının %18,8'inin (n:27) 10 yaş altında, %81,3'ünün (n:117) 10 yaş üzerinde olduğu belirlendi. Kırk dört (%48,4) kız ve 13 (%24,5) erkek hastada auralı migren vardı ve cinsiyet açısından istatistiksel olarak anlamlı fark saptandı (p=0,008). Auralı ve aurasız migren hastalarının yaş ortalamaları arasında ayrıca istatistiksel olarak anlamlı fark olduğu görüldü (p<0,05).

**Sonuç:** Migren, çocukluk döneminde tahmin edilenden daha sık görülen kronik bir hastalıktır. Bu çalışmada baş ağrısı şikayeti ile başvuran hastalarda migren tanısını düşündürebilecek ve auralı migren özelliklerini gösterebilecek bulguların sonuçlarını paylaşmak istedik.

**Anahtar Sözcükler:** Baş ağrısı; Migren; Çocuk hastalıkları

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## Introduction

Headache is a major cause of presentation to neurology outpatient clinics (1). It is a disease that originates from pain-sensitive structures in the head, varies greatly in terms of type, has complex symptoms, and is difficult to explain with a single simple mechanism. Nonetheless, migraine is a primary episodic headache disorder characterized by asymptomatic periods as well as recurrent episodes accompanied by various neurological, gastrointestinal, and autonomous symptoms and changes. As migraine is a chronic disease that is observed more frequently than commonly thought in children, its burden on patients and society must be acknowledged. In order to diagnose migraine headache it is very important to evaluate all causes of headache a common cause of presentation to pediatric outpatient clinics via thorough anamnesis and physical examination. Migraine can be diagnosed based on patient history and clinical observation. The present study aimed to determine the frequency of migraine in children that present with headache and to retrospectively evaluate the clinical characteristics of migraine based on 3 years of clinical experience.

## Materials and Methods

Pediatric patients that presented to University of Health Sciences Turkey, Dr. Sami Ulus Obstetrics and Gynecology, Child Health and Diseases Training and Research Hospital, Pediatric Neurology Outpatient Clinic, Ankara, Turkey, between January 2013 and January 2016 due to headache and were diagnosed with migraine were retrospectively evaluated. The study is a thesis study that received the approval of the education planning board from the education and research hospital. Among the 1231 pediatric patients that presented with headache, 144 (11.9%) were diagnosed with migraine. All migraine with aura and migraine without aura patients were included in the study. The patients' headache symptoms and accompanying clinical signs were retrospectively evaluated.

The study group was established based on R51, G43, and G44 ICD codes from the hospital medical database, and the relevant data were included. Migraine was diagnosed based on International Headache Society 2013 criteria (ICHD-3 beta) (2). Accordingly, the patients were divided into the migraine with aura group and migraine without aura group. Patient age, gender, duration of headache complaint, type and localization of pain, frequency, duration, and intensity of pain, factors triggering pain, presence of phonophobia-photophobia, the effect of daily activities, type of accompanying aura (visual, sensory, brain stem), signs accompanying an episode, prescribed treatment, response to treatment (decrease in episode frequency and severity, and decrease in episode duration in patients that received acute attack treatment were verbally ascertained) were analyzed. The severity of pain was evaluated using a visual analog scale (VAS) (3); an intense headache score was determined to be 4-5/5. Response to treatment was defined as a decrease in the frequency of pain, spontaneous relief of pain, and duration of pain <2h. Data were compared between the 2 groups. Data were collected via patient headache diaries and telephone follow-up every 3 months. This manuscript was prepared in accordance with Research and Publication Ethics.

Data were analyzed using IBM SPSS Statistics for Windows v.22.0 (IBM Corp., Armonk, NY). Numerical variables are presented as mean±SD or median (range) values. Categorical variables are presented as number and percentage. Differences in categorical variables between the groups were evaluated using the chi-square test or Fisher's exact test. The normality of the distribution of numerical variables was evaluated using the Kolmogorov-Smirnov test and homogeneity of variance was analyzed using Levene's test. Differences in numerical variables between the 2 groups were evaluated using the t-test if parametric test assumptions were met; if parametric test assumptions were not met, the Mann-Whitney U test was used. The level of statistical significance was set at  $p<0.05$ .

## Results

In total, 11.6% of the patients that presented with the complaint of headache were diagnosed with migraine, of which 18.8% (n=27) were aged <10 years and 81.3% (n=117) aged >10 years. Mean age at the time of presentation was 12.3±2.76 years. There was a significant difference in mean age between the patients that had migraine with and without aura ( $p=0.017$ ). In all, 59% (n=84) of the patients had migraine without aura, 39.6% (n=57) had migraine with aura, and 1.4% (n=3) had episodic syndromes that might have been associated with migraine. Among the patients that had migraine with aura, 25 had migraine with brainstem aura, 3 had hemiplegic migraine, and 2 had ocular migraine.

Among the patients, 44 (48.4%) of the females and 13 (24.5%) of the males had migraine with aura, and the difference was significant ( $p=0.008$ ). There wasn't a significant difference in the duration of pain between the patients that had migraine with and without aura ( $P=0.965$ ). The most common type of pain was throbbing pain and the most common pain location was the forehead. Pain was unilateral in 40.7% (n=48) of the patients and was bilateral in 59.3% (n=77). Intense pain was observed in 94.1% (n=16) of patients in the migraine with aura group, versus 64.8% (n=24) in the migraine without aura group. Headache intensity did not differ significantly between the migraine with aura and migraine without aura groups. Moreover, signs accompanying migraine did not differ significantly between the 2 groups, although the most common accompanying sign was nausea in the migraine with aura group (90% [n=51]) and migraine without aura group (90.5% [n=78]). Among the patients, visual aura was the most common type of aura (54.3% [n=30]). Migraine pain negatively affected daily activities in 73.6% (n=42) of the patients in the migraine with aura group, versus 80.5% (n=70) of the patients in the migraine without aura group, but the difference was not significant ( $p=0.452$ ). The frequency of accompanying diseases did not differ significantly between the migraine with aura and migraine without aura groups ( $P=0.742$ ). Additionally, the presence of migraine-triggering factors did not differ between the 2 groups ( $p=0.609$ ), although stress and sorrow were overall the most common (22.2%).

There weren't any significant differences between the 2 groups in terms of duration of complaint ( $p=0.32$ ) or episode frequency ( $p=0.643$ ). The maximum episode duration was 48 h and the mean episode duration was 4.0±10.09h. The signs

accompanying migraine were as follows: nausea: 58.3%; vomiting: 31.2%; phonophobia: 71.5%; photophobia: 68%. Moreover, 13 patients had blurry vision, 2 had sweating, 1 had pallor, 1 had abdominal pain, and 1 had listlessness accompanying migraine. Overall, a family history of headache was noted in 57.6% of the patients, as follows: 56.8% (n=29) in the migraine with aura group and 58.1% (n=43) in the migraine without aura group, but the difference was not significant ( $p=0.733$ ). Clinical characteristics of migraine with and without aura given in Table 1.

**Table 1.** Clinical characteristics of migraine with and without aura

	With aura (N=57)	Without aura (N=87)	p value
Patient age, years, mean $\pm$ SD	12.99 $\pm$ 2.68	11.87 $\pm$ 2.75	0.017
Gender (M/F), n	13/44	40/47	0.008
Family history of headache, n (%)	29(56.8%)	43(58.1%)	0.73
Triggering factors, n (%)	30(52.6%)	42(48.3%)	0.60
Duration of complaint, m, mean $\pm$ SD	20.78 $\pm$ 23.21	24.56 $\pm$ 25.36	0.32
Episode frequency/year, mean $\pm$ SD	12.16 $\pm$ 10.29	9.93 $\pm$ 7.56	0.64
Duration of the attack, hour, mean $\pm$ SD	9.35 $\pm$ 11.4	8.12 $\pm$ 9.18	0.96
Intence headache, n (%)	16 (94%)	24(64.8)	0.71
Pain affected everyday activities, n (%)	42(73.6%)	70(80.5%)	0.45
Accompanying diseases, n (%)	26(45.6%)	36(41.4%)	0.58
Acute treatment of the episode, n (%)	15(26.3%)	16(18.4%)	0.35

The symptoms of migraine improved with the use of analgesics in 45.1% of the patients, with quiet-dark environment/sleep in 45.7%, and spontaneously in 9%. In total, 56.8% (n=25) of the patients in the migraine with aura group used analgesics for pain, versus 69.4% (n=50) in the migraine without aura group. In all, 81.2% (n=117) of the patients received treatment for migraine. Prophylaxis treatment was recommended for 101 (86.3%) of the patients in whom treatment was initiated. Episodic treatment was added to prophylaxis during migraine episodes in 15 (14.8%) of the patients that received prophylaxis treatment. In all, 16 (13.6%) of the patients were followed-up with acute episode treatment only and 27 patients (18.8%) were followed-up without treatment. Treatment response was achieved in 56 (74.6%) of the patients that received treatment. Response to treatment did not differ significantly between the 2 groups.

For neuroimaging, brain MRI was performed in 112 (77.8%) of the 144 patients. Based on brain MRI, the most commonly observed non-specific change was in the perivascular space (n=9). There wasn't a significant difference in brain MRI findings between the patients with aura (19.3%) and without aura (19.5%) ( $p=0.890$ ). In addition, abnormal findings were noted in only 4 (5%) of the 80 patients (55.6%) that underwent EEG. The mean duration of follow-up was 3.25  $\pm$  15.12 months (range:3-148 months).

## Discussion

Headache, particularly migraine, has negative effects on children physically, emotionally, and socially, and negatively affects their academic performance and quality of life. The high incidence and prevalence, and the economic burden of headache in children and adults have resulted in an increase in the number of studies on childhood headache. The present study was conducted in an effort to add high-quality data on the demographic and clinical features of childhood migraine to the literature. The present findings show that there are significant differences in age and gender between pediatric patients that have migraine with and without aura.

One of the largest series on migraine is a 2004 study by Zwart et al. (4) that included 8255 students aged 13-15 years. They reported that the 1-year prevalence of migraine was 7%, whereas it was 8.8%-10.4% in studies that were conducted in Turkey (4-6). The reported prevalence of migraine varies between 3% and 23% (7-10). In the present study 11.6% of the patients that presented to the pediatric neurology clinic due to headache were diagnosed with migraine. The frequency of migraine with aura was reported to be 15%-30% (4). Other studies reported that the frequency of migraine with aura is 26.4%-45.2% (11-13). The frequency of migraine with aura in the present study was 36.9%.

Monthly episode frequency is among the diagnostic criteria for migraine. According to diagnostic criteria for migraine,  $\geq 2$  episodes per month is considered as migraine. Mavromichalis et al. (14) compared children that had migraine with and without aura in terms of episode frequency of 1 week-1, >1 week-1, 1 two weeks-1, and 1 month-1, and did not find any significant differences. Similarly, Markus et al. (15) did not observe a significant difference in the monthly episode frequency between children that had migraine with and without aura. In the present study episode frequency in the migraine with aura group was 12.16  $\pm$  10.29 year<sup>-1</sup>, versus 9.93  $\pm$  7.56 year<sup>-1</sup> in the migraine without aura group, and the difference was not significant.

Headache intensity and triggering by sunlight and certain foods are the most important factors in the differential diagnosis of migraine (16). Şenbil et al. (3) reported that the frequency of initiation of headache without any triggers was high in children with migraine. In the present study triggers for migrain episode were stress, sorrow, infection, hunger, smells, sleeplessness/fatigue, bright light/watching TV, noise, crowds, irregular eating habits, temperature (heat or cold), exercise, and travel. The presence of migraine-triggering factors in the present study was noted in 30 (52.6%) of the patients in the migraine with aura group and 42 (48.3%) of the patients in the migraine without aura group. One study reported that stress was the triggering factor for migraine in 41.6% of children (6). Similarly, in the present study stress and sorrow were the most common triggering factors (22.2%).

Many studies reported that the duration of migraine episodes in children is <2 h (9,17,18). Mavromichalis et al. (14) evaluated school-age children in terms of migraine episode duration of 2-3 h versus >3 h and did not observe a difference between the 2 groups. Markus et al. (15) did not observe a difference in the duration of migraine episodes between children that had migraine with and without aura.

Similarly, in the present study the mean duration of migraine episodes was  $9.35 \pm 11.49$  h in the migraine with aura group and  $8.12 \pm 9.18$  h in the migraine without aura group, and the difference was not significant.

Unilateral localization of migraine pain is considered predictive of migraine headache. The frequency of unilateral localization of migraine pain in children was reported to be 20%-67% (19). Hershey et al. (19) reported that migraine episodes in pediatric patients were bilateral in 83% of cases (19). In the present study migraine pain was unilateral in 40.7% of the patients and bilateral in 59.3%.

Studies have shown that the pain intensity is moderate to severe in 46.8%-71.6% of migraine patients (20). Mavromichalis et al. (14) compared children that had migraine with and without aura in terms of headache intensity and reported that there wasn't a difference in terms of moderate intensity (preventing daily activities) and severe intensity (requiring bed rest and sleep) headache episodes (14). In the present study 94.1% of patients in the migraine with aura group had severe migraine pain, versus 64.8% in the migraine without aura group. There wasn't a significant difference in headache intensity between the migraine with aura and migraine without aura groups. These findings indicate that migraine headache intensity in children is not affected by aura. One study on childhood migraine reported that 86.6% had phonophobia, 75% had photophobia, 43.2% had nausea, and 36.6% had vomiting (20). Similarly, in the present study 58.3% of the patients had nausea, 31.2% had vomiting, 71.5% had phonophobia, and 68% had photophobia.

It was reported that migraine pain was ameliorated with the use of analgesics in 45.1% of patients, with a quiet-dark environment/sleep in 45.7%, and spontaneously in 9%. In the present study the use of analgesics for pain was observed in 25 (56.8%) of the patients in the migraine with aura group and in 50 (69.4%) of the patients in the migraine without aura group. Although the literature does include studies on analgesic use for acute migraine episodes in adults, to the best of our knowledge the present study is the first to make such a comparison between pediatric patients with migraine and without aura (21).

It was reported that 72%-89% of migraine patients have a family history of headache (14). Numerous studies recommend a family history of headache as a diagnostic criterion for migraine (12,21,22). A study that included 220 children with migraine reported that 56.5% had a family history of headache (5). In the present study a family history of headache was noted in 57.6% of the migraine patients; 56.8% of the patients in the migraine with aura group and 58.1% of those in the migraine without aura group had a family history of headache, but the difference was not significant ( $P=0.733$ ).

In cases of migraine, which is a paroxysmal disease, it is known that there can be EEG (a neurophysiological test) abnormalities, but the findings are inconsistent (23,24) While there are many internal and external factors associated with migraine, positive spikes of 14 Hz and 6 Hz were once considered pathological, but have not been considered so since the 1970s (25). EEG was performed in 80 (55.6%) of the present study's patients; the findings were normal in 76 (95%) of these patients and abnormal in 4 (5%).

The primary limitation of the present study is its retrospective design, which limited our ability to obtain sufficient data on the patients' clinical observation parameters, although we attempted to obtain as much relevant data as possible from the medical records database.

## Conclusion

The present study is important as it identified the clinical characteristics of pediatric migraine patients a patient population that frequently presents to general pediatrics and pediatric neurology outpatient clinics. Detailed anamnesis, physical examination, clinical and radiological evaluation, continuous multidisciplinary observation of symptoms, accurate diagnosis, treatment planning, and increasing patient quality of life are important for preventing workforce loss.

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