



Association between attention deficit hyperactivity disorder (ADHD) and migraine: a review of observational studies

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Edited by:
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Keywords:

ADHD
Attention deficit disorder with hyperactivity
Migraine disorders
Headache
Neurodevelopmental disorders

Abstract

Introduction

Attention deficit hyperactivity disorder (ADHD) has been related to the presence of primary headaches. Among them, migraine presents a wide range of comorbidities shared with ADHD, both from other psychiatric disorders and somatic conditions.

Objective

This review proposes to describe the association between ADHD and migraine.

Methods

Based on literature research in the major medical databases and using as descriptors “Migraine Disorders” and “Attention Deficit Disorder with Hyperactivity”. Observational studies that addressed the relationship between migraine and ADHD and written only in English were included. Of the 49 articles found, only 6 met the inclusion criteria and were analyzed.

Results

A total of 35,684 patients were included, 22.36% were children. Of these, 1,829 (5.12%) had ADHD. The association between ADHD and migraine was identified in 528 patients (1.47%), representing 28.86% of patients with ADHD. A bilateral relationship was observed between the two diagnoses, having in the presence of ADHD, an almost 3 times greater risk of the presence of migraine. Furthermore, individuals with isolated migraine had significantly higher symptoms of hyperactivity/impulsivity and inattention than healthy individuals.

Conclusion

This review shows a possible sharing of symptoms between migraine and ADHD, requiring further studies to investigate this relationship.

Submitted: March 1, 2023
Accepted: March 27, 2023
Published Online: March 31, 2023



Introduction

Attention deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders, characterized by a persistent pattern of inattention and/or hyperactivity/impulsivity that interferes with the individual's functionality and development.¹ Despite being more observed in children, the symptoms of the disorder may persist or be identified only in adult life.^{2,3}

Other psychiatric disorders such as anxiety and depression, and somatic conditions such as obesity and asthma have also been associated with ADHD comorbidities.⁴ A 2018 meta-analysis found a significant association between the presence of ADHD and primary headaches. In this study, unlike other primary headaches, migraine was associated with the presence of the disorder.⁵

ADHD has an estimated prevalence of between 3% and 7% of the population, being more observed in males, while migraine has a wide spectrum of prevalence, increasing with age and affecting more females, reaching up to 22% of adults.^{6,7} In this sense, the present review aims to analyze the studies that assessed the relationship between these two diagnoses, characterizing the clinical and demographic characteristics of each population.

Methods

This study was an integrative and retrospective review of articles that assessed the relationship between ADHD and migraine. The research was carried out in the Pubmed and SciELO online databases from January to February 2023, using the descriptors "Migraine Disorders" AND "Attention Deficit Disorder with Hyperactivity". The data extraction process was carried out simultaneously by both authors, using a pre-established data extraction form.

Observational studies that addressed the relationship between migraine and ADHD, written in English and without date limitation criteria were included. Editorials, comments, letters to the editor, and articles that were not fully available or that lacked accurate information were excluded. To ensure the validity of these articles, selected studies were analyzed in detail for demographic and clinical characteristics, and instruments used to assess migraine and ADHD symptoms.

Of the 49 articles found in the initial search, those that were repeated or that did not address the relationship between migraine and ADHD (n=16) were eliminated and

only 33 remained and were analyzed. After reading the titles and abstracts, 24 articles were excluded. Of the 9 articles selected, 6 articles met the inclusion criteria.

Results

Table 1 presents the studies included in the review, characterizing them according to design and demographics. A total of 35,684 patients were included, 22.36% children. Of these, 1,829 (5.12%) had ADHD. The association between ADHD and migraine was identified in 528 patients (1.47%), representing 28.86% of patients with ADHD.

Tables 2 and 3 present the instruments used to assess ADHD and migraine. To assess ADHD, all studies used the Diagnostic and Statistical Manual of Mental Disorders (DSM), a diagnostic guide of the American Psychiatric Association, in its current version (DSM-5), past version (DSM-4), or validated questionnaires based on it. To assess migraine, 5 studies used the International Classification of Headache Disorders, in its current version (ICHD-3), past version (ICHD-2), or validated questionnaire. Only a single study, Fasmer et al.¹², accessed migraine in a qualitative way.

Table 1. Studies included in the review

Study	Design	Country	Study demographics
Attygalle et al. ⁸	Comparative cross-sectional study	Sri Lanka	Children Mean age = 10 (5-14) years N = 226 Males 50.2% Females 49.8%
Hansen et al. ⁹	Cross-sectional study	Denmark	Voluntary blood donors Mean age = 42 (30-52) years N = 26,456 Males 53.7% Females 46.3%
Kutuk et al. ¹⁰	Cross-sectional, case control, multi-center study	Turkey	Children N = 228
Arruda et al. ¹¹	Cross-sectional study	Brazil	Children Age = 5-12 years N = 5,671 Males 50.7% Females 49.3%
Fasmer et al. ¹²	Cross-sectional study	Norway	Adults N = 1,247 Males 44.98% Females 55.02%
Arruda et al. ¹³	Cross-sectional epidemiological study	Brazil	Children Mean age = 8-10 years N = 1,856 Males 51.7% Females 48.3%



Table 2. ADHD assessment tools

ADHD assessment tools	Studies	Description
DSM-4 or DSM-5	Hansen et al. ¹⁴ Kutuk et al. ¹⁰ Fasmer et al. ¹⁵	Diagnostic and Statistical Manual of Mental Disorders (DSM), diagnostic guide of the American Psychiatric Association
SNAP-IV	Attygalle et al. ⁸ Arruda et al. ¹¹ Arruda et al. ¹³	Swanson, Nolan and Pelham Questionnaire.
ASRS	Fasmer et al. ¹⁵	Adult ADHD Self-Report Scale.
WURS	Fasmer et al. ¹⁵	Wender Utah Rating Scale.

Table 3. Migraine assessment tools

Migraine assessment tools	Studies	Description
ICHD-2 or ICHD-3	Attygalle et al. ⁸ Kutuk et al. ¹⁰ Arruda et al. ¹¹ Arruda et al. ¹³	International Classification of Headache Disorders
SQM	Hansen et al. ¹⁴	Screening Questionnaire for Migraine

Table 4 presents the results of the main outcomes of the studies, divided according to the study design into (a) Studies that assessed the presence of migraine in ADHD and (b) Studies that assessed the presence of ADHD in migraine.

Kutuk et al.¹⁰ studied the presence of migraine in children with ADHD and healthy children. The results of the study showed a prevalence of migraine approximately 3 times higher in children with ADHD compared to the control group (26.5% vs. 9.9%). The OR for migraine was 3.3 (95% Confidence interval = [1.6–6.9]; $p=0.002$). In this study, the presence of both conditions was also assessed in the parents of the included children. Mothers of children with ADHD had a higher prevalence of migraine than mothers of children in the control group (68.9% vs. 40.9%, $p=0.049$).¹⁰

In the adult population, Fasmer et al.¹² assessed the presence of migraine in individuals with ADHD and in a control group through a self-report questionnaire. Fasmer and coworkers¹² also found a significantly higher prevalence of migraine in the ADHD group compared to the control group (28.3% vs. 19.2%, $p<0.001$). When analyzed by sex, ADHD proved to be a stronger predictor of migraine in men (OR = 2.43; 95% Confidence interval = [1.51–3.90]; $p<0.001$) than in women (OR = 1.58; 95% confidence interval = [1.13–2.21]; $p = 0.008$).¹²

Of the studies that assessed the presence of ADHD in migraine, 3 were carried out in the pediatric population. Attygalle et al.⁸ studied this relationship in children from Sri Lanka, where a higher percentage of ADHD was observed

in children with migraine compared to children without migraine (5% vs. 3.5%), but there was no statistical significance. However, despite not meeting diagnostic criteria, children with migraine had a significantly higher mean score on the SNAP-IV scale ($p=0.014$), indicating a possible relationship between the primary headache and symptoms of hyperactivity/impulsivity and inattention.⁸ This finding is corroborated by Arruda et al.¹³, who has also observed an increased prevalence of hyperactivity/impulsivity symptoms in the pediatric population due to the presence of migraine (8.1% vs. 19.9%; RR = 2.2; 95% confidence interval = [1.5–3.3]; $p<0.001$).¹³ In a second study, Arruda et al.¹¹ reinforced the presence of these symptoms in migraine children. The prevalence of hyperactive/impulsive symptoms was 5.6% in controls and 10.6% in children with migraine (RR = 1.9; 95% confidence interval = [1.4, 2.7]). As for inattention symptoms, the prevalence was 4.8% in controls and 10.3% in children with migraine (RR = 2.1; 95% confidence interval = [1.5, 3.1]).¹¹

Hansen et al.⁹ studied a sample of 26,456 adult individuals, where a significant association between the presence of migraine and ADHD symptoms was observed ($p<0.001$). When adjusting for covariates, migraine with aura had a higher risk of presenting ADHD symptoms (OR = 2.05; 95% confidence interval = [1.55–2.68]; $p < 0.001$). Both ADHD phenotypes were associated with migraine.⁹

Table 4. Sample groups of included studies

Studies that assess the presence of migraine in ADHD			
Study	Control Group	ADHD Group	Migraine and ADHD Group
Kutuk et al. ¹⁰	N = 111	N = 117	N=31
Fasmer et al. ¹⁵	N = 675	N = 572	N=162
Studies that assessed the presence of ADHD in migraine			
Study	Migraine Group	ADHD Group	Migraine and ADHD Group
Attygalle et al. ⁸	N = 141	N = 10	N = 7
Hansen et al. ¹⁴	N = 6.390	N = 690	N = 238
Arruda et al. ¹¹	N = 546	N = 303	N=59
Arruda et al. ¹³	N = 427	N = 137	N = 31

Discussion

In the present review, the prevalence of migraine among individuals with ADHD was 28.86%, while the prevalence of ADHD among individuals with migraine was 4.46%,



with only the first ratio being increased in relation to the general population. In this sense, the studies included in the review point to ADHD as a predictor for the presence of migraine. However, individuals with migraine had significantly more symptoms related to ADHD than the control population, raising the hypothesis of some mechanism in the pathophysiology of the disease that mimics ADHD characteristics, such as hyperactivity/impulsivity and inattention.

Villa et al.¹⁶ compared the visual attention of children with and without migraine, where children with headache had lower levels of attention on the test, showing difficulty with selective and alternating attention tasks. Therefore, it was proposed that attention was dependent on neurotransmitters such as dopamine and noradrenaline, which are also involved in the pathophysiology of migraine and which, when deregulated, could lead to symptoms of inattention.¹⁶ In addition to these, the deregulation of other neurotransmitters such as GABA are also present in both disorders.¹⁷

Furthermore, Kutuk et al.¹⁰ observed a higher prevalence of migraine among mothers of children with ADHD than mothers of children without ADHD ($p=0.049$). This outcome reinforces the possible pathophysiological and genetic link between the two disorders. William et al.¹⁸ in genetic mapping of individuals with ADHD, observed a significantly increased amount of large and rare deletions and chromosomal duplications, introducing genetic evidence for the symptoms of hyperactivity/impulsivity and inattention. Migraine, in turn, also has a broad genetic component. Recent studies have identified more than 180 polymorphisms involved in the disease's genome.¹⁹ In addition, both ADHD and migraine have comorbidities with a known genetic factor in common, such as epilepsy and vasovagal syncope.⁵

Conclusion

Studies included in this review suggested an increased prevalence of migraine in individuals with ADHD, as well as ADHD-like symptoms in the migraine clinic. Therefore, new studies must be carried out to elucidate the pathophysiological and genetic mechanisms of both conditions and their interactions.

Funding

The authors have no competing interests to declare.

Conflict of interests

The authors report no conflict of interest

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HMSF, Conceptualization, Investigation, Writing - Original Draft, Writing - Review & Editing; CLA, Conceptualization, Investigation, Writing - Original Draft, Writing - Review & Editing.

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