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Review Article

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Updates on the Association between Obesity and Migraine: Systematic Review of Observational Studies

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ABSTRACT

There are conflicting results from several studies that assessed the risk of migraine headaches in obese people. This systematic review aimed to investigate the most recent research on the relationship between migraine and obesity as well as potential mechanisms. A search was performed in PubMed, Science Direct, SCOPUS, EBSCO, Web of Science, and Cochrane Library. The Rayyan QCRI was employed to screen the articles before a full-text assessment was implemented. A total of fifteen studies with 28128 patients were included in this review. All of the reviewed studies showed that obesity increased the frequency of migraine attacks, the sensitivity to pain, the severity of migraines, and the self-efficacy in headache management. According to two studies, individuals under the age of 50 are more likely to exhibit these certain clinical traits. Recent evidence confirms the association between obesity and more frequent and severe migraine attacks. Some studies also reported that this is more common among obese people aged 50 years and below.

Key words: *Total hip arthroplasty, Quality of life, Osteoarthritis, Systematic review*

INTRODUCTION

Obesity is an illness that impacts health-related quality of life very negatively and increases the chance of developing conditions such as hypertension, metabolic syndrome, diabetes, myocardial infarction, and stroke [1]. In the United States, where 64% of adults are either overweight or obese [1], it has reached epidemic levels on a global scale [2]. With 9.1% of all US medical spending in 1998 and as high as $92.6 billion in 2002, obesity and the health issues it causes have had a significant financial impact on the healthcare system [3].

Globally, migraine is a prevalent and frequently serious condition [4, 5]. Migraine sufferers, their families, and society as a whole are all affected [6]. In addition, CM is a condition brought on by the advancement of migraine sickness. The best way to understand migraine is as a main brain illness with implications on the body as a whole [7]. There is much proof that migraine is a genetically based, familial condition [8]. Trigeminovascular system activation may result from peripheral neurovascular events that are caused by primary brain dysfunction [9].

A corresponding rise in the prevalence of CM over time could be anticipated, given the rise in overweight prevalence over the past few decades [10]. Studies on the frequency of CM, however, are recent [11]. Obesity appears to be a risk factor for frequent migraine attacks rather than a comorbidity of migraine [12]. Furthermore, the proportion of migraineurs who experience frequent episodes was not evaluated as a separate category in any of the big prevalence studies carried out in the United States. Although the number of people who experience frequent attacks may be rising as a result of the rise in the prevalence of obesity, the influence on the overall

frequency of attacks should be minimal because the majority of migraineurs in the population have few migraine episodes [13, 14].

The fact that both illnesses have comorbidities that are also established risk factors for migraine transformation may help to explain at least some of the association between chronic migraine and obesity [15]. There has been literature published on the association between obesity and migraine of late. This systematic review aims to study the possible mechanisms and investigate the matter.

MATERIALS AND METHODS

Preferred Reporting Items for Systematic Reviews and Meta-Analyses, (PRISMA) standards were used as the basis of this systematic review.

Study design

This was a systematic Review.

Search strategy

PubMed, Web of Science, Science Direct, EBSCO, Scopus, and Cochrane Library were exhaustively searched to find the relevant literature. The search was restricted to English and considerations were made regarding the unique requirements of each database. The following keywords were converted into PubMed Mesh terms and used to find the relevant studies; "Obesity," "obese people," and "migraine." The Boolean operators "OR" and "AND" were used to match the required keywords. The results yielded publications with full English text, available free articles, and ones with results on human trials.

Selection criteria

Inclusion in this review was based on the fulfillment of these criteria:

- Observational study articles; cross-sectional, case-control, and cohort studies.
- Obesity is defined by the standard World Health Organization (WHO) classification as $30 \leq BMI \leq 35$.
- Adult patients older than 18 years.
- Recent study articles published between 2010 to 2022.
- English language.
- Free accessible articles.

Data extraction

We applied Rayyan (QCRI) to detect duplicates in the output of the search strategy [16]. The researchers used a set of inclusion/exclusion criteria to refine the combined search results to evaluate the title and abstract relevance. The reviewers carefully read each paper that met the criteria for inclusion. The authors talked about ways to resolve conflicts. A data extraction form was utilized to upload the authorized study information. The authors extracted data about the study authors, titles, study designs, country, study year, total participants, mean age, gender, mean BMI, and main outcomes.

Strategy for data synthesis

To provide a qualitative analysis of the results and study components, summary tables were created from the data extrapolated from the studies. The best strategy for utilizing the data extracted from the systematic review of the included articles was chosen. Studies meeting the full-text inclusion criteria but missing data on the association between obesity and migraine were excluded.

Risk of bias assessment

The ROBINS-I risk of bias assessment method for non-randomized trials of treatments was used to assess the quality of the included studies [17]. The seven topics that were assessed included confounding, participant selection for the study, classification of interventions, deviations from intended interventions, missing data, assessment of outcomes, and selection of the reported result.

RESULTS AND DISCUSSION

Search results

The systematic search yielded 560 study papers, of which 58 duplicates were removed. A total of 502 papers were screened for title and abstract, with 398 being eliminated. One hundred and ten reports were requested for recovery, with just ten items not being found. Eventually, 100 papers were screened for full-text evaluation; 47 were removed due to incorrect research results, 28 due to insufficient data on obesity and migraine, and 10 due to the incorrect population type. This systematic review contained fifteen eligible study papers. **Figure 1** depicts an overview of the study selection procedure.

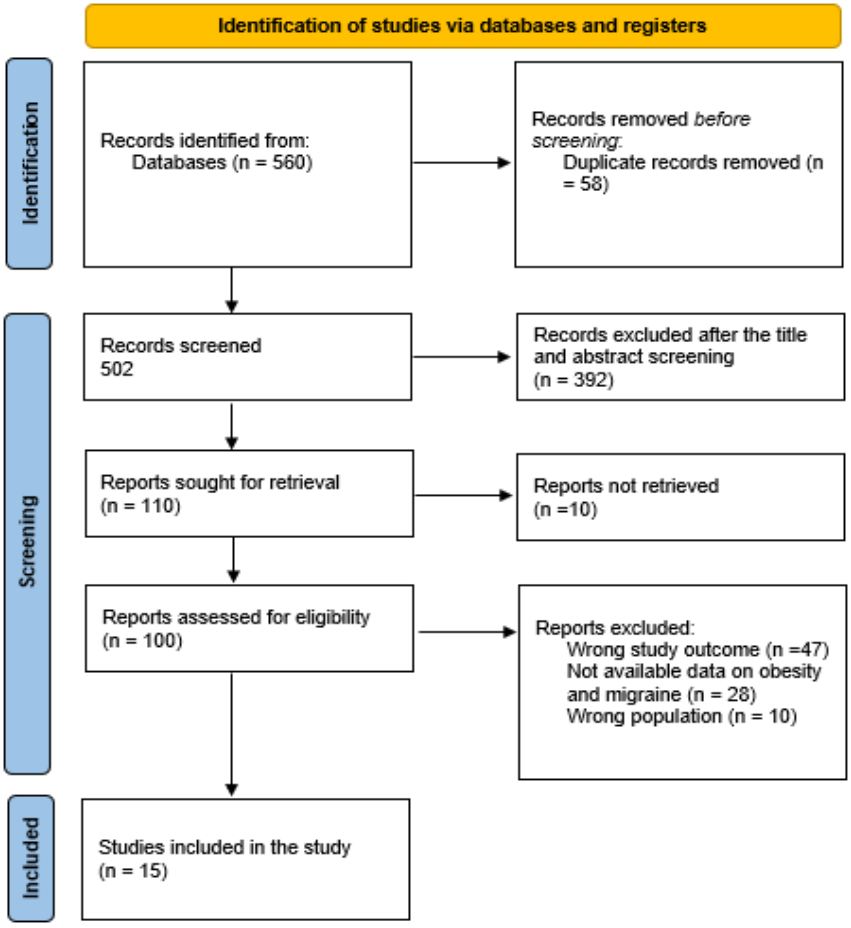

Figure 1. PRISMA flowchart summarizes the study selection process.

Characteristics of the included studies

Table 1 includes the sociodemographic characteristics. A total of fifteen studies with 28128 patients were included. Three studies were conducted in the USA [18-20], two in Iran [21, 22], two in India [23, 24], two in Iraq [25, 26], one in Norway [27], one in Brazil [28], one in Turkey [29], one in Benin [30], and one in Pakistan [31]. Eleven studies were cross-sectional studies [18-20, 22-25, 27, 28, 31, 32], and four were case-control studies [21, 26, 29, 30]. **Table 2** presents the characteristics of the included studies. All of the included studies demonstrated that obese people experienced more frequent migraine attacks, higher pain sensitivity, more severe headaches, and decreased self-efficacy in managing headaches. Two studies reported that these clinical characteristics are more common among people under 50 years [18, 27].

Table 1. Sociodemographic characteristics of the included participants.

Study	Country	Study design	Participants (n)	Mean age	Males (%)
Peterlin *et al.*, 2013 [18]	USA	Cross-sectional	3862	46.6 ± 0.63	49.7%
Bond *et al.*, 2015 [19]	USA	Cross-sectional	105	38.1 ± 8	0%
Kristoffersen *et al.*, 2020 [27]	Norway	Cross-sectional	4290	46.2 ± 12.9	24.6%
Miri *et al.*, 2018 [21]	Iran	Case-control	102	34.9 ± 8.4	21.6%
Santos *et al.*, 2015 [28]	Brazil	Cross-sectional	14566	34-74 (range)	46%
Sadeghi *et al.*, 2016 [22]	Iran	Cross-sectional	129	34.07 ± 10.68	21.7%

Özcan & Özmen 2019 [29]	Turkey	Case-control	141	33.6 ± 9.3	0%
Thierry *et al*., 2018 [30]	Benin	Case-control	66	31.87 ± 8.37	30.3%
de Oliveira *et al*., 2013 [32]	Brazil	Cross-sectional	166	45 ± 14	0%
Ojha *et al*., 2018 [23]	India	Cross-sectional	50	28.7 ± 6.8	42%
Saeed & Shukr 2020 [25]	Iraq	Cross-sectional	300	28.2 ± 7.5	55%
Nuaman & Sadik 2019 [26]	Iraq	Case-control	50	35.8 ± 8.8	51.4%
Faruqi *et al*., 2019 [31]	Pakistan	Cross-sectional	400	30.7 ± 6.9	39.8%
Bond *et al*., 2018 [24]	India	Cross-sectional	168	32.7 ± 9.9	0%
Vo *et al*., 2011 [20]	USA	Cross-sectional	3733	32.6 ± 4.5	0%

Table 2. Characteristics and outcomes of the included studies.

Study	Mean BMI	Key findings and implications	ROBIN-I
Peterlin *et al*., 2013 [18]	-	Obesity increases a person's risk of developing episodic migraine, with the highest associations seen in those under 50, white people, and women.	Moderate
Bond *et al*., 2015 [19]	35.3 ± 6.4	Participants who had migraines and were obese reported clinical catastrophizing in a quarter of cases. These people experienced longer-lasting attacks, more frequent attacks, higher pain sensitivity, more severe headaches, and decreased self-efficacy in managing headaches.	Moderate
Kristoffersen *et al*., 2020 [27]	27.3 ± 5	The prevalence and frequency of migraine attacks were both correlated with total body obesity (TBO) and abdominal obesity (AO). People under 50 years old made up the majority of this association.	Moderate
Miri *et al*., 2018 [21]	25.9 ± 4.6	The risk of migraines with aura was positively correlated with obesity. In addition, people with obesity experienced more headaches daily than subjects with normal weight.	Moderate
Santos *et al*., 2015 [28]	-	Higher BMI levels, but not AO, are linked to daily migraine frequency.	Moderate
Sadeghi *et al*., 2016 [22]	-	The severity and frequency of migraine attacks and the headache diary results were all strongly correlated with central obesity indicators but not the length of attacks.	Moderate
Özcan & Özmen 2019 [29]	26.9 ± 5.1	The association between central obesity and migraine was inverse.	High
Thierry *et al*., 2018 [30]	27.72 ± 4.94	Since obesity and migraines have been linked, managing migraines must consider this.	Moderate
de Oliveira *et al*., 2013 [32]	27.8 ± 6.0	There is only a weak correlation between anthropometric measurements and the frequency of migraine attacks, which does not account for how long they last, how severe they are, or how disabled they make the patient feel.	Moderate
Ojha *et al*., 2018 [23]	30.4 ± 6.4	Obese individuals experience migraines more frequently and with greater severity. Losing weight may help reduce the frequency and severity of migraines.	Moderate
Saeed & Shukr 2020 [25]	-	Obese people experience migraines more frequently than non-obese people, and this difference was statistically significant.	Moderate
Nuaman & Sadik 2019 [26]	-	Patients with central obesity have double the risk of migraines as patients with general obesity.	High
Faruqi *et al*., 2019 [31]	-	Both obesity and migraine are extremely common disorders that are influenced by both genetic and environmental risk factors in the general population.	Moderate
Bond *et al*., 2018 [24]	23.7±4.3	Generalized obesity has an impact on the clinical aspects of migraine in female sufferers. The frequency and severity of migraines are among these characteristics.	Moderate
Vo *et al*., 2011 [20]	-	There is a correlation between high BMI and frequent migraines.	Moderate

This systematic review included an update on the studies that investigated the association between obesity and migraine. All of the included studies demonstrated that obese people experienced more frequent migraine attacks, higher pain sensitivity, more severe headaches, and decreased self-efficacy in managing headaches. However, our study is limited by its qualitative assessment.

This was consistent with previous reviews, which stated that clinicians and patients must understand the migraine-obesity association because it may be modifiable. Theories regarding the causes of the link between obesity and migraines and treatment options for people who suffer from obesity-related headaches [33]. However, a recent meta-analysis found that, although it was not considered in our meta-analysis, being underweight also increased the likelihood of getting a migraine headache. Some studies attempted to determine whether a decrease in weight and BMI may lessen a migraine course because obesity has been linked to an increase in the rate, frequency, and severity of migraines [34].

Two studies reported that these clinical characteristics are more common among people under 50 years [18, 27]. Peterlin *et al.* conclude that the prevalence of migraines is influenced by age, sex, and adiposity distribution. Obesity increased migraine prevalence in people under the age of 55, and at this age, AO was a major contributing factor. Surprisingly, neither in men nor in women over the age of 55 was obesity a factor in migraine prevalence. After age 55, in the same group, the prevalence of migraines was lower in cases of AO but was unaffected by TBO. Authors advise categorizing the obese population according to age and where the fat is located. They recommend dividing women into premenopausal and postmenopausal groups as well [35].

Numerous theories have been put forth to clarify the connection between migraine and fat. The role of neurotransmitters such as serotonin and pro-inflammatory mediators, the role of the hypothalamus in migraine and obesity, particularly via the orexinergic system, or the potential role of raised intracranial pressure found in a subset of obese patients as well as some migraineurs, are all being investigated [36]. Moreover, some of the pathophysiological factors are implicated in both diseases. Others are based on clinical grounds. We will go over a few of these theories [37].

According to clinical research, one popular theory contends that the common link between migraine and obesity is accidental. The high incidence of both illnesses may be the only reason for this frequent relationship. Additionally, these individuals could tend to see their doctors more frequently, which could cause clinical practitioners to overstate the association. In theory, this concept makes sense [37].

Another explanation is that obesity and migraines directly affect one another as a result of medical interventions, behavioral modifications, or reduced quality of life. The majority of first-line preventive migraine treatments can lead to weight gain. As a result, a rise in the proportion of fat people in the severe headache group is predicted. Frequent migraines are frequently to blame for a large decrease in physical activity and an increase in rest time, both of which contribute to obesity. Obesity itself is frequently linked to inactivity, overeating, anxiety, and depressive symptoms, all of which are well-known migraine triggers [38]. These examples show that there may be a direct correlation between the two situations, but it is still insufficient to account for epidemiological statistics [39].

Another idea contends that similar elements could help both obesity and migraine disorders. The common keys in this approach can be biological. The connection between several biological compounds and migraine and fat. These authors are adamant about the importance of adipose tissue, which serves as an endocrine organ and releases pro-inflammatory cytokines, including interleukin 6 and tumor necrosis factor-alpha. During a migraine attack, the majority of these chemicals are actually observed to be higher. Obesity-related inflammation is linked to pain transmission, has the potential to affect the trigeminal nervous system, and actively contributes to an increase in migraine frequency. For instance, the adipose tissue hormones leptin and adiponectin, which are linked to the pro-inflammatory state, may be significant [40, 41].

CONCLUSION

The recent evidence confirms the association between obesity and more frequent and severe migraine attacks. Some studies also reported that this is more common among obese people aged under 50 years; however, the mechanism that is associated with younger age is still unknown. Obese migraineurs should be monitored and treated with greater care. Additionally, when prescribing preventative medication for migraine, doctors must inform their patients that weight gain may occur and that this may have an impact on the course of their condition. A diet plan must be recommended, and treatment must be reevaluated when weight gain is seen.

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