

Research article

Cutaneous allodynia association with migraine and their predictors among primary healthcare visitors

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Abstract: **Background:** Migraine, affecting over 1.04 billion people globally, is a severe, recurrent headache disorder with significant impacts on life quality. Despite extensive research on risk factors, the association with cutaneous allodynia (CA) is underexplored. **Objective:** This study aims to assess the predictors contributing to both cutaneous allodynia (CA) and migraine and their prevalence among primary healthcare (PHC) visitors in Madinah City, Saudi Arabia. **Methods:** A total of 403 participants agreed to participate in our cross-sectional study between September 1, 2023, and November 1, 2023. Migraine screening questionnaire (MS-Q) was used to screen for migraine. To assess allodynia symptoms, we used Allodynia Symptoms Checklist-12 (ASC-12). Participants aged 15 and older who attended one of the major PHC centers in Madinah City were included in the study. **Results:** The prevalence of migraine among the participants was found to be 16.4%, with 57.6% of migraine patients exhibiting CA symptoms. Family history of migraine and high BMI were identified as significant predictors of migraine ($P < 0.05$), with odds ratio (OR) of 5.7 and 1.1, respectively. Additionally, female sex and high BMI were significant ($P < 0.05$) risk factors for CA among migraine patients, with ORs of 4.3 and 1.1, respectively. **Conclusions:** The prevalence of migraine in Madinah City was higher than the global average but lower than the national average. A significant proportion of migraine patients also experienced CA. Further research is warranted to elucidate the underlying mechanisms

of migraine and CA, which could aid the development of targeted treatments and improve patient outcomes.

Keywords: cutaneous allodynia; headache disorders; migraine disorders; predictors; prevalence; primary health care

Abbreviations: CA: Cutaneous allodynia; PHC: Primary healthcare; YLDs: Years lived with disability; MS-Q: Migraine screening questionnaire; ASC-12: Allodynia Symptoms Checklist-12

1. Introduction

Migraine is a neurological condition globally prevalent across diverse demographics. Characterized as a primary headache disorder, migraine commonly manifests as recurring episodes of severe, often one-sided, throbbing headache lasting 4–72 h. Such episodes are often accompanied by additional symptoms such as sensitivity to light (photophobia) and sound (phonophobia), as well as nausea and vomiting [1].

Migraine is one of the most prevalent neurological disabilities encountered in primary healthcare (PHC) settings [2]. This condition represents a key health challenge that can considerably impair an individual's quality of life, affecting both professional engagements and social interactions [3]. Worldwide, approximately 1.04 billion people suffer from migraine, accounting for 45 million years lived with disability (YLDs) and positioning it as the second highest contributor to YLDs on a global scale [4].

Migraine encompasses a spectrum of risk factors that exhibit variability across different populations, and its repercussions extend beyond individual suffering to broader societal contexts. Various factors such as anxiety, depression, familial predisposition, hormonal fluctuations, and sex have been extensively investigated in relation to migraine. Nonetheless, few studies have been directed toward cutaneous allodynia (CA) symptoms and their correlation with migraine. CA is characterized by the experience of pain resulting from stimuli to the skin that would typically not evoke pain [5]. Studies have reported that individuals afflicted by migraine in conjunction with CA exhibit diminished responsiveness to acute therapeutic interventions and an increased propensity for transitioning to chronic migraine. In addition, they experience more pronounced disability than those affected solely by migraine [6,7].

The global prevalence of migraine is estimated to exceed 10% [8]. Two extensive cross-sectional studies conducted in Saudi Arabia have reported prevalence rates of 25% and 27% [9,10], which markedly surpass the global average.

Studies conducted in a clinical setting have indicated that approximately 33% of individuals suffering from migraine eventually develop CA, a phenomenon linked to enhanced susceptibility to severe migraine symptoms [11,12]. Despite this significant correlation, the association between migraine and CA has not been adequately explored. Studies on the Saudi Arabian population are particularly lacking.

Primary healthcare centers serve as the initial interface for individuals accessing healthcare services in Saudi Arabia and play an important role in identifying and treating migraines. Investigating the prevalence of migraine, its associated risk factors, and CA symptoms in PHC centers within

Madina City, Saudi Arabia, is of considerable importance since it is associated with a variety of psychological comorbidities [13]. Such studies are expected to aid in understanding the disease burden, identifying high-risk demographics, and formulating effective prevention and management strategies.

2. Methodology

This study adopted an analytical approach and employed a multicenter, cross-sectional design. Eligible participants were individuals aged 15 or older, of both sexes, who visited one of the major PHC between September 1, 2023, and November 1, 2023.

Participants who fulfilled any of the following conditions were excluded from the study: history of head trauma or concussions; diagnosis of neurological conditions such as epilepsy, stroke, or intracranial hemorrhage; use of medications known to impact migraine symptoms (e.g., antidepressants, anti-seizure medications, beta-blockers, triptans, or other migraine-specific treatments); women who were on oral contraceptive pills; women who were either pregnant or breastfeeding at the time of the study (owing to potential hormonal influences on migraine frequency and severity); and having other confirmed secondary causes of headaches, such as sinusitis or elevated intraocular pressure. In addition, participants who were incapable of completing the questionnaire or did not provide informed consent were excluded from the study.

The study included 403 participants. The sample size was calculated using the following formula: $n = Z^2\alpha P (1-P)/d^2$. Assuming a 95% confidence level, a 5% margin of error, an 80% power, and an estimated prevalence of migraine of 25% according to previous studies [9,10], a sample size of 289 participants was considered adequate.

The questionnaire for screening migraine (MS-Q) was utilized to evaluate individuals seeking care at PHC centers for symptoms indicative of migraine headaches. The MS-Q is a questionnaire that individuals complete on their own, designed to identify migraine. The questionnaire consists of five questions that focus on how often headaches occur, their features, and whether migraine-related symptoms are present. The responses are scored as 0 points for negative answers (no) and 1 point for positive answers (yes). A cutoff value of ≥ 4 points indicates suspicion of migraine, whereas a rating below 4 indicates an absence of suspicion of migraine [14]. The validation research of the Arabic adaptation of the MS-Q demonstrated a high degree of accuracy, producing an area under the curve (AUC) of 0.97, with a confidence interval (CI) spanning from 0.94 to 0.99, and robust sensitivity and specificity rates of 95% and 99%, respectively [15].

To determine the presence of CA, the Allodynia Symptoms Checklist-12 (ASC-12) was utilized. This checklist was used to evaluate the presence of CA symptoms and to determine its prevalence and intensity among migraine sufferers. The ASC-12 comprises 12 items designed to gauge various manifestations of CA [16]. Each item is assigned a score of 0 (indicating never, rarely, or not applicable), 1 (less than half the time), or 2 (half the time or more). The scores are then categorized as follows: no allodynia (0–2), mild (3–5), moderate (6–8), and severe (≥ 9) [17]. The ASC-12 was developed and validated in a substantial migraine population. The findings demonstrated a strong correlation with headache frequency, intensity, and migraine-related disability [18].

A separate questionnaire was used to collect sociodemographic data, encompassing factors like age, sex, educational background, income, marital status, presence of chronic diseases, family history of migraine, habits related to coffee consumption and smoking, and body mass index (BMI). This comprehensive approach was intended to capture a diverse array of sociodemographic factors related

to the objectives of the study and provide a holistic understanding of the participant characteristics within the research context.

2.1. Statistical analysis

Data management and analysis were conducted using SPSS version 21.0 (IBM, Armonk, New York). The responses from the questionnaire were coded and entered into an electronic spreadsheet for additional analysis. The level of significance chosen was 0.05. The study utilized multiple logistic regression analysis techniques to examine the correlation between different factors and the outcomes under investigation. The logistic regression was conducted using a step-back technique starting with all the sociodemographic variables reported in Table 1. In the last step, only significant variables ($P < 0.05$) were reported.

3. Results

This study involved 403 individuals who visited PHC centers in Madinah City. The study population displayed a balanced sex distribution. The largest age group was 26–35 years. The marital status was also evenly distributed between single and married. In addition, the majority had a monthly income of <4000 SAR. A considerable proportion of the participants (143 individuals, 35.4%) disclosed having been diagnosed with at least one chronic disease, which is aligned with the expected prevalence among those seeking care at PHC Centers. A total of 49 participants, amounting to 12% of the total sample, reported having at least one family member who suffered from migraine (refer to Table 1).

Table 1. Participants' sociodemographic composition.

Characteristics	Frequency (N)	Percentage (%)
Sex		
Male	207	51.3
Female	196	48.7
Age		
15–25	91	22.6
26–35	121	30.1
36–45	73	18.1
46–55	46	11.4
>55	72	17.8
Marital status		
Single	181	44.9
Married	182	45.2
Divorced	27	6.2
Widowed	13	3.7

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Characteristics	Frequency (N)	Percentage (%)
Income per month		
<4000 SAR	218	56.1
4001–9999 SAR	79	18.9
10000–14999 SAR	72	16.7
>14999 SAR	34	7.9
Level of education		
Elementary education	69	17.1
Intermediate education	54	13.4
Secondary education	126	31.2
University level or higher	154	38.2
Presence of comorbidities		
Yes	143	35.4
No	260	64.6
Daily coffee intake		
No	114	28.3
1 cup	107	26.5
2 cups	70	17.4
3 cups	41	10.1
>3 cups	71	17.6
Smoking status		
Smoker	148	36.7
Non-smoker	238	58.9
Ex-smoker	17	4.3
Family history of migraine		
Yes	49	12.1
No	354	87.8

Note: SAR: Saudi Riyal.

Table 2 displays the MS-Q, which aided in identifying potential migraine sufferers among the participants. With regard to the screening questions, 119 individuals (29.5%) reported experiencing frequent or intense headaches, prompting further assessment. In this subgroup, a significant proportion, i.e., 56 individuals (46.2%), answered that the headache duration exceeded 4 h. Additionally, 58 participants (48.7%) experienced nausea during their headache, and an even larger proportion were sensitive to light, noise, or both 98 (82.3%). Moreover, 76 participants (63.8%) had their physical or cognitive activities limited because of their headaches. The MS-Q results revealed that among individuals with recurrent or severe headaches, 66 individuals (55.5%) fulfilled the criteria for suspected migraine. Further classification based on self-reported migraine intensity showed that 21 participants (17%) experienced mild migraine, 54 (45.5%) had moderate-intensity migraine, and 44 (37%) described their pain level as severe to unbearable.

Table 2. Migraine screening questionnaire (MS-Q) results among the participants.

Characteristics	Frequency (n)	Percentage (%)
Are you prone to frequent or intense headaches?		
Yes	119	29.5
No	284	70.5
Do your headaches typically persist for more than 4 hours?		
Yes	56	46.2
No	63	53.8
Do you often experience nausea when you have a headache?		
Yes	58	48.7
No	61	51.3
Are you sensitive to light or noise or both during a headache attack?		
Yes	98	82.3
No	21	17.7
Have your physical or intellectual activities ever been limited by a headache?		
Yes	76	63.8
No	43	37.2
Migraine screen questionnaire (MS-Q)		
Migraine excluded	53	44.5
Migraine suspected	66	55.5
Migraine intensity (self-reported)		
Mild	21	17.4
Moderate	54	45.5
Severe	23	19.8
Very severe	14	11.6
Unbearable	7	5.8

Table 3 presents the sociodemographic characteristics of the 119 participants who reported experiencing frequent or intense headaches and subsequently completed the MS-Q questionnaire, allowing for their classification into either the suspected migraine or excluded migraine groups.

According to the data in Table 4, of the 66 participants who screened positive for migraine, subsequent investigations regarding allodynia symptoms using ASC-12 revealed that 23 individuals (34%) had mild CA and 12 (18%) had moderate CA. A small yet noteworthy proportion of participants (3 individuals, 4.5%) exhibited severe CA symptoms. Thus, the prevalence of CA among participants who screened positive for migraine was 57.6%.

Table 3. Demographic characteristics of participants with frequent or intense headaches.

Characteristics	Frequency (N)	Percentage (%)
Sex		
Male	47	39.5
Female	72	60.5
Presence of comorbidities		
Yes	91	76.5
No	28	23.5
Daily coffee intake		
No	47	39.5
1 cup	32	26.9
2 cups	29	24.4
3 cups	7	5.8
>3 cups	4	3.3
Smoking status		
Smoker	35	29.4
Non-smoker	79	66.4
Ex-smoker	5	4.2
Family history of migraine		
Yes	71	59.7
No	48	40.3
BMI		
BMI \leq 30	55	46.2
BMI $>$ 30	64	53.8

Note: BMI: Body Mass Index.

Table 4. The CA severity among participants with suspected migraine.

CA severity	Frequency (N)	Percent (%)
No allodynia	28	43.3
Mild	23	34.3
Moderate	12	17.9
Severe	3	4.5
Total	66	100

The results of logistic regression analysis, as illustrated in Table 5, offered valuable insights into potential predictors of migraine among participants who screened positive for the condition. A family history of migraine emerged as the most significant predictor, with participants having a familial background exhibiting 5.72 times higher odds of experiencing migraine than those without such a history (95% CI: 2.039–16.024). Furthermore, a high BMI (>30) showed a positive association with migraine, with an odds ratio of 1.1 (95% CI: 1.013–1.307). Although the variables outlined in Table 1

were incorporated into the regression analysis model, they did not demonstrate statistically significant associations. Hence, these predictors were subsequently removed from the logistic regression model via step-back regression analysis.

Table 5. Potential predictors of migraine (logistic regression model).

Variables	Groups	Comparative group	P value	OR	Lower CI (95%)	Upper CI (95%)
Family history of migraine	Yes	No	0.001	5.716	2.039	16.024
BMI	A higher BMI	A lower BMI	0.047	1.1	1.013	1.307

Note: BMI: Body Mass Index; OR: Odds ratio; CI: Confidence interval.

Table 6 provides potential predictors of CA symptoms among participants who screened positive for migraine. Women exhibited significantly higher odds of experiencing CA than men, with a prominent 4.3-fold increase (95% CI: 1.57–11.91), which highlights the sex-based variation in CA prevalence. Moreover, a high BMI (>30) was found to be a significant predictor of CA symptoms among individuals who screened positive for migraine, with an OR of 1.09 (95% CI: 1.001–1.194). Although the variables outlined in Table 1 were incorporated into the regression analysis model, they also did not demonstrate statistically significant associations and were hence eliminated from the model via step-back regression analysis.

Table 6. Potential predictors of allodynia symptoms among migraine suspected participants (logistic regression model).

Variables	Groups	Comparative group	P value	OR	Lower CI (95%)	Upper CI (95%)
Sex	Female	Male	0.005	4.32	1.57	11.91
BMI	A higher BMI	A lower BMI	0.048	1.093	1.001	1.194

Note: BMI: Body Mass Index; OR: Odds ratio; CI: Confidence interval.

4. Discussion

Migraine is a neurological condition that is highly prevalent among diverse demographic groups on a global scale. Therefore, estimating its prevalence and assessing the related factors are crucial. CA is an important, underestimated predictor of the severity of migraine that has not been adequately investigated, especially in our region. In Madinah City, migraine prevalence among primary healthcare center visitors was 16.4%, which exceeded the global average of 10% [8]. In the Saudi Arabian general population, migraine prevalence is estimated to be 25%, which significantly surpasses the global average [9,10]. A study in Taif City observed a comparable migraine prevalence of 14.1%, probably because the sample composition was similar to that in our study [19].

Our logistic regression model identified a family history of migraine and high BMI as significant migraine predictors, having ORs of 5.7 and 1.1, respectively. This agrees with findings linking higher BMI to increased migraine attack frequency [20]. However, contrary to expectations, our study could

not reveal a statistically significant link between migraine and low education level, low socioeconomic status, or caffeine consumption, which is contrary to the observations of earlier studies [21–23]. Similarly, despite evidence linking smoking with migraine, our study did not discern such an association, which could potentially be attributed to population differences.

Regarding CA symptoms, 57.6% of the identified patients with migraine exhibited allodynia symptoms of varying severity. A rigorous narrative review reported similar results, with 60% of migraine sufferers experiencing CA symptoms [24]. However, the specific mechanisms underlying CA in migraine are yet to be elucidated. This similarity in the prevalence of CA compared with other studies might be due to similarities in the underlying mechanisms. Female sex and high BMI were significant predictors of CA in patients with migraine, with ORs of 4.3 and 1.1, respectively, which is aligned with a previous finding [25].

The proposed mechanism of allodynia in migraine could be explained by the nociceptive pathways. These include sensory neurons that detect pain and temperature, which can become sensitized, resulting in an exaggerated response to normally non-painful stimuli [26]. Central and peripheral sensitization is marked by widespread hyperalgesia, which results in a larger area of pain and a lower pressure pain threshold (PPT) [27]. Migraine can also be seen as a genetic predisposition where the brain struggles to effectively regulate sensory inputs [28].

The high migraine prevalence highlights the need to allocate public resources and devise strategic plans. In clinical practice, healthcare providers should be attentive to migraine prevalence and the associated CA symptoms, which emphasizes the need for thorough assessment and management. Future studies should attempt to investigate the underlying molecular and genetic factors of migraine and CA to develop targeted therapies for enhancing patient outcomes.

Although this study has provided valuable insights, limitations such as the reliance on self-declared information and the cross-sectional nature of the study may have introduced biases related to recall and sampling. Therefore, caution should be exercised in establishing causal relationships and the generalizability of the findings. Additional studies are required to compare the sociodemographic factors of different populations and to compare our results with other similar populations.

5. Conclusions

In summary, migraine prevalence in Madinah City exceeds the global average but falls below the national average, with a significant proportion of patients experiencing CA. Key predictors of migraine include a family history of the condition and a high BMI. Moreover, the female sex and a high BMI are significant predictors of CA among migraine sufferers. The high prevalence of migraine and CA emphasizes the importance of allocating public health resources and formulating strategic plans to enhance early detection, access to care, and the development of targeted interventions. These approaches can ultimately aid in alleviating the burden of migraine and CA on patients and the healthcare system. Healthcare providers should be aware of these findings so that they can deliver comprehensive care to the patients. Future investigations in the field should delve into the underlying mechanisms of migraine and CA to develop targeted therapies that can enhance patient outcomes.

Author contributions

Mohammed Qarah: Led the study design and conceptualization, conducted the primary data collection and comprehensive data analysis, and drafted the Introduction and Results sections. Also coordinated manuscript preparation and revisions. Noura Alshammari: Acted as the primary supervisor, providing oversight on the study's design and methodology. Reviewed and critically revised the Introduction and Results sections, and contributed to the Discussion section, ensuring alignment with the study objectives. Ali Alsolami: Focused on writing the Methods section, detailing data collection and analysis procedures. Assisted in data organization and preparation of tables and the Results section. Ahmed Abualkhair: Contributed to data collection efforts, particularly in gathering demographic and specific data points. Drafted the initial Discussion section, interpreting study results and connecting them to existing literature. Abdulaziz Aloufi: Assisted with data analysis and contributed to the Results section by summarizing key findings. Participated in writing the Conclusion section, emphasizing study significance and implications. Anas Alzhrani: Supported data collection and organization. Provided additional input for the Methods section, describing sampling techniques and study protocols. Also reviewed the Discussion section for coherence and relevance. Shatha Almuyidi: Conducted the initial literature review and drafted the Introduction, highlighting background and rationale for the study. Provided feedback on the Discussion and Conclusion sections to enhance the clarity of study findings. Mayada Almohandes: Contributed to the manuscript revision process, focusing on technical accuracy and grammar. Reviewed the entire manuscript for consistency and assisted in finalizing the Abstract and Conclusion sections to ensure key points were effectively communicated.

Use of AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

Ethics approval of research and informed consent

The ethical approval is obtained from Institutional Review Board (IRB), General Directorate of Health Affairs in Madinah, and the informed consent has been received prior to study.

Conflict of interest

The authors declare no conflict of interest.

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