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**ORIGINAL ARTICLE**

# Insomnia and its Correlates in Migraine Patients with or without Aura

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## ABSTRACT

**Purpose:** Few studies have investigated the correlates of insomnia severity level in a clinically diagnosed sample of migraine patients. This study explored associated factors of insomnia severity in a sample of Saudi Arabian patients with migraine headaches with/without aura (MA/MWA).

**Methods:** This observational study used a cross-section design, and conveniently selected MA and MWA patients visiting outpatient department at general hospitals, Madinah, Saudi Arabia. The patients completed the Athens Insomnia Scale and an inventory to record sociodemographics and clinical data.

**Results:** Insomnia was highly prevalent (50.6%) in both the MA/MWA patients. Being female ($\beta$ = .25, p = .01), and overweight-obese ($\beta$ = .19, p = .05) were associated with increasing insomnia severity. Most MA, and MWA patients were female (70.2%), were undergoing treatment for comorbid conditions (58.3%), and reported no habitual exercise or sports activities (57.1%).

**Discussion:** A high prevalence of insomnia in the MA and MWA patients reinforces insomnia-migraine comorbidity. It may be useful to screen females and migraine patients who are obese for insomnia to better manage this comorbid epidemic.

**Keywords**: migraine; headache; exercise; sleep; insomnia; obesity

## INTRODUCTION

Migraine, the second leading cause of disability, is a primary headache disease prevalent throughout the world, causing malaise, loss of quality of life, and a substantial cost in medical care [1-2]. Migraine with aura (MA), and migraine without aura (MWA) are two major types of these headaches. Both forms have distinct clinical features. In the case of MA, the defining feature is the presence of temporary neurologic indications occurring before or with the headache [3]. In MWA patients report repeat episodes of headache persisting for hours up to three days. Pain is on one side of the head, throbbing in nature, and varying in intensity. Such headaches deteriorate with usual physical work, have a tendency to cause vomiting, and/or sensitivity to light and sound [4]. However, it is worth noting that patients with MA may have headache episodes that may be classified as MWA and vice versa [5-6]. The difference between MA and MWA with respect to response to treatment, most effective treatment, neuroanatomical structure, and function does necessitate further exploration of these two subtypes [7-8]. Also comparative studies with different designs including epidemiological research investigating associated factors and correlates of MA and MWA may further help understand migraine pathophysiology to develop management strategies [9 -10] . Therefore, in this study we assessed association between insomnia and migraine, specifically MA and MWA subtypes and correlates of this probable relationship.

Migraine and sleep disturbances are widely prevalent, and usually bidirectional [11-12]. Similarly, insomnia and migraine have been found to be closely associated even in large population-based studies, and bidirectional in nature ; established in both cross-sectional and longitudinal studies [13-15]. Migraine patients were at higher risk of insomnia, and vice-versa, patients with insomnia were more likely to have migraines, in different cross-sectional studies [13,16,17]. Further adding strength to this relationship, in longitudinal studies migraine increased the risk of developing insomnia after 11 years; vice-versa, insomnia increased the risk of developing migraine at 11-year follow-up [13,18,19]. However, to the best of this researcher's knowledge, no studies have explored the relationship between insomnia, MA or MWA. Furthermore, these aspects of the insomnia-MA/MWA relationship, and their correlates in Middle East and in the Saudi population are not known. Therefore, this study investigates the relationship between two types of migraine, MA and MWA, and insomnia. Further, the study attempted to explore the determinant of this relationship.

## MATERIAL AND METHODS

**Participants and procedure:** The target population for this study was patients with migraines with orwithout aura, visiting the outpatient department of Ministry of Health hospitals in Madinah, Saudi Arabia. Patients visiting the outpatient department between January 2018 and June 2019, who fit the inclusion criteria, were included in this study, who were eligible and gave written consent to participate and educated about the research study: its aim, methods, what is expected from them, voluntary nature of participation, right to withdraw at any time, non-involvement of individual benefits or risks, etc. All adult patients with clinically diagnosed MA/MWA were included. Exclusion criteria were secondary headache, and self-account of headache/migraine that has not been established as a clinical diagnosis.

In all a sample of 168 migraine patients with/without aura (n: 168, and age: 27.05 ± 6.42 years) participated. A cross-section design with convenient sampling method was used. In this study, the Athens Insomnia Scale (AIS) a semi-structured tool to record self-reported clinical history and sociodemographic data were used. The researcher contacted patients when they visited the outpatient department and carried out data collection.

**Athens Insomnia Scale (AIS):** Insomnia is reliably assessed by standardized questionnaire tools such as the Insomnia Severity Index, AIS, Pittsburgh Sleep Quality Index, etc. [20-25]. The psychometric validity of the AIS, a

commonly used structured questionnaire to assess insomnia, has been established in many types of demographics including Asians [24]. AIS has eight questions: five assess insomnia-related nighttime problems, while three take account of daytime problems. All questions are scored on a similar ordinal scale of 0-3, where higher scores indicate increasing severity of insomnia-related complaints. There are no reverse-scored questions, and the total score is the sum of all eight items. For individual item scores, higher AIS total scores imply more severe symptoms related to insomnia [25-26].

**Semi-structured questionnaire for recording clinical history and sociodemographics:** A questionnaire with seven items was used to record participants' clinical history and sociodemographics. All questions except for age, were close-ended; weight, and height were recorded to determine body mass index(BMI).

**Statistical analysis:** Data analysis was done using SPSS version 26.0. Descriptive statistics and a multiple linear test for association were used. Cronbach's alpha test was used to determine reliability of the standard questionnaire, i.e., AIS. For performing multiple regression analysis, the AIS total score was the dependent variable, while sociodemographics and clinical history variables were independent variables. A p-value of 0.05 was taken to indicate significance level.

## RESULTS

**Participants' characteristics:** The mean ± SD of age, and BMI were 27.05 ± 6.42 years and 24.93 ± 3.12 kg/m$^2$, respectively in study participants (Table 1). The majority of participants (70.2%) were female. Most reported not participating in regular exercise or sports activities (57.1%). More than two-fifths of participating MA/MWA patients had a history of head-neck injury (41.1%).The majority of participating patients were under treatment for comorbid medical conditions (58.3%) at the time of the study. Almost half (48.2%) frequently used migraine medications, and most (50.6%) had insomnia symptoms (Table 1).

Table 1. Characteristics of participating migraine patients with/without aura.

| Characteristics | Mean ± SD/ Frequency (percentage) |
|---|---|
| Gender | |
| Male | 50 (29.8) |
| Female | 118 (70.2) |
| Age (yr.) | 27.05 ± 6.42 |
| BMI (kg/m$^2$) | 24.93 ± 3.12 |
| Sports activity | |
| Yes | 71 (42.3) |
| No | 96 (57.1) |
| Did not report | 1 (0.6) |
| History of Head-neck injury | |
| No | 95 (56.5) |
| Yes | 69 (41.1) |
| Did not report | 4 (2.4) |
| Currently under treatment for medical conditions | |
| Yes | 98 (58.3) |
| No | 68 (40.5) |
| Did not report | 2 (1.2) |
| Use of migraine medication | |
| Sometime | 86 (51.5) |
| Often | 74 (44.0) |
| Very often | 7 (4.2) |
| Did not report | 1 (0.6) |
| Insomnia symptoms | |
| No | 81 (48.2) |
| Yes | 85 (50.6) |
| Did not report | 2 (1.2) |

SD: standard deviation; BMI: body mass index; Presence of insomnia symptoms was determined by Athens Insomnia Scale score ≥6.

Table 2: Multiple Regression Predictors of the insomnia symptoms severity level in migraine patients with/without aura

| Independent variable | Beta Coefficient | Standard error | T values | P values | Model unadjusted R2; adjusted R2; P value |
|---|---|---|---|---|---|
| BMI | 0.19 | 0.11 | 1.97 | 0.05 | 0.17, 0.13, <0.01 |
| Age | 0.11 | 0.05 | 1.28 | 0.20 | |
| Gender | 0.25 | 0.70 | 2.81 | 0.01 | |
| Migraine with-without aura | 0.00 | 0.62 | 0.04 | 0.97 | |
| Sports activity | -0.06 | 0.58 | -0.77 | 0.44 | |
| History of head-neck injury | 0.05 | 0.58 | 0.62 | 0.54 | |
| Currently under treatment for other medical conditions | 0.16 | 0.61 | 1.91 | 0.06 | |
| Frequency of migraine medicine intake | 0.08 | 0.48 | 0.99 | 0.32 | |
| Intercept | -3.43 | 2.91 | -1.18 | 0.24 | |

* Unstandardized beta coefficient for intercept, for all other independent variables standardized beta coefficient are shown.

insomnia severity was assessed by AIS: Athens insomnia scale

Multivariate analysis: Multiple linear regression-predictors of the insomnia symptoms in migraine patients with/without aura

A multiple linear regression model assessed the prediction of changes in insomnia symptoms severity level in MA and MWA patients from BMI, age, gender, type of migraine (i.e., MA/MWA), regular sports activity (Yes/No), history of head-neck injury (Yes/No), presently under treatment for comorbid medical conditions (Yes/No), and frequency of migraine medication intake (i.e., sometime, often, and very often). This regression model significantly predicted changes in insomnia symptoms severity level in the participating MA and MWA patients, $F(8, 153) = 3.90$, $p < .001$, $R2 = .17$ (Table 2). BMI ($p = .05$) and gender ($p = .01$) significantly predicted insomnia symptoms severity level in the participating patients (Table 2). Female MA and MWA patients had more severe insomnia

symptoms (Figure 1), as did overweight-obese MA and MWA patients (Figure 2).

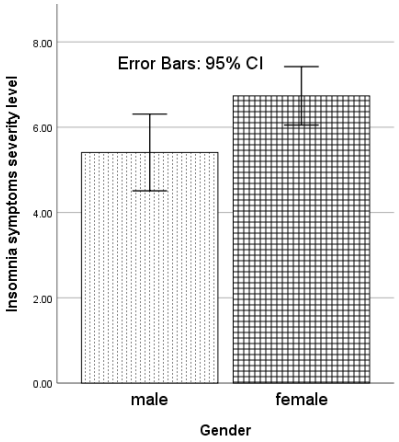


Figure 1: Gender-related variation in insomnia symptoms severity level (Athens Insomnia Scale score) in migraine patients with/without aura.

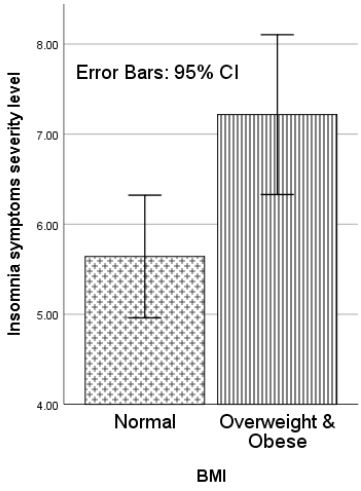


Figure 2: BMI-related variation in insomnia symptoms severity level (Athens Insomnia Scale score) in migraine patients with/without aura

## DISCUSSION

To the best of the author's knowledge, this is the first study showing correlates of insomnia symptoms severity level in a sample of clinically diagnosed patients of migraine with/without aura. In this study being female and overweight-obese was associated with an increase in insomnia symptoms. Further, this study found a majority of the MA and MWA patients were females, did not participate in regular sports activity, were undergoing treatment for comorbid conditions, and had insomnia symptoms.

In this study a regression model significantly predicted changes in insomnia severity based on changes in the level of seven independent predictors. This model demonstrated a variance of about 17 %. No previous work explores the dynamics of a direct comparison on the relationship of insomnia severity in a sample of MA/MWA patients. However, a recent study involving a small sample of 50 participants identified three predictors of sleep quality in chronic migraine patients [26,27] . Garrigós-Pedrón et al. identified depression, disability related to headache, and feeling of associating worse fallouts explained about 33% of variances in the sleep quality [27]. The model by Garrigós-Pedrón et al. was able to explain more variances compared to that in the present study. However, there are important differences to keep in mind: 1) differences in the sleep measures in the two studies, Garrigós-Pedrón et al. assessed sleep quality, while this study measured insomnia severity; 2) the sample size in Garrigós-Pedrón et al. was smaller than in this study, (50 compared to 168 in this study); and 3) Garrigós-Pedrón et al. worked on chronic migraine patients, while, in this study, episodic and chronic migraine patients were involved [27]. Future studies should expand on these outcomes to further explore this insomnia-migraine relationship so that more prospective predictors and correlates can be identified. Indeed, the level of explained variance in both the studies, i.e., 33% in the Garrigós-Pedrón et al. study, and 17% in the present study do indicate that both studies failed to consider other correlates/predictors that might have provided more robust models [27]. Evidence from functional neuroimaging studies provides support for this migraine-insomnia relationship [28,29]. Chou et al. found that functional changes associated with motor and somatosensory areas in some cortical regions such as the dorsomedial prefrontal and posteromedial cortex were regularly found in comorbid patients of insomnia and migraine [28,30].

In this study, females comprised the majority of patients, indicating a relationship between migraine and gender. This is similar to previous results. Moreover, previous studies have shown that a higher prevalence of migraine among females is related to their reproductive cycles and milestones, and associated hormonal changes. [31-33]. Notably, this is the first study to show female-related higher prevalence of MA and MWA in a sample of clinically diagnosed migraine patients. Additionally, the findings of this study also revealed that being female predicted more severe insomnia symptoms in these patients. In this study, being overweight-obese was associated with increasing severity of insomnia in MA/MWA patients. Interestingly, another important and related finding of this study was that the majority of participating patients did not report active exercise participation. These two finding may be related, for many the lack of physical activity might result in being obese-overweight, leading to this relationship between obesity and insomnia severity. Similarly, a recent review based on a meta-analysis of 16 articles found there is a 1.29 times increased risk of migraine in obese people compared to those of normal weight [34-35]. However, analysis of the su-group found this increased risk was observed in Asian and European populations but not in Americans [36-37].

A majority of the MA and MWA patients in this study were also undergoing treatment for other health conditions. Previous studies reported this same trend. A recent review on the mechanistic approach of migraine comorbidity outlined some of the pathophysiological changes that may help understand this relationship [38-40]. Therefore, future studies should try to unravel the mechanisms behind this

relationship. To begin with, as this group (i.e., those under treatment for comorbidities) seem to be heterogeneous, that may suggest pathophysiological mechanisms or states behind this relationship. Moreover, Altamura et al. summarized in a recent review that alterations in excitations of neurons in thalamocortical network, increased pro-inflammatory mechanisms, and imbalanced energy kinetics may further activate neuronal and endocrinal systems that may underlie this migraine comorbidity relation [41-43]. At this point, the findings support the existence of a migraine comorbidity association. [44,45]

It is worth keeping some of the limitations in mind to comprehend the implications of the study. Though the sample size was small, it is important to bear in mind this study enrolled a clinically diagnosed sample of patients with MA and MWA. A longitudinal approach would have been better in exploring the insomnia-migraine relationship. The amount of variance explained by the regression model of insomnia-migraine relationship was 17%. Therefore, future studies may better employ a more elaborate list of prospective independent variables to understand this insomnia-migraine relationship.

In summary, prevalence of insomnia was significantly high (50.6%) in MA and MWA patients. Female gender and being overweight-obese were associated with increases in insomnia severity in this group. A majority of the MA and MWA patients were females, did not participate regularly in sports or exercise activity, and were undergoing treatment for comorbid conditions.

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