SLEEP AND BIOLOGICAL RHYTHMS
THE JAPANESE SOCIETY OF SLEEP RESEARCH

Sleep and Biological Rhythms 2015; **13**: 76–84 doi:10.1111/sbr.12087

ORIGINAL ARTICLE

Sleep disturbances and excessive daytime sleepiness in migraine: A comparison between comorbidities and disability

Yıldızhan SENGUL,[1] Hakan S SENGUL,[2] Bahadir BAKIM,[3] Sevda K YUCEKAYA,[4] Selma YUCEL[5] and Mucella AKGUN[6]

Departments of [1]Neurology and [2]Psychology; Erzurum Regional Training and Research Hospital, Erzurum, [3]Department of Psychiatry, 18 March University, Canakkale, [4]Lutfiye Nuri Burat State Hospital, [5]D.P.U. Kutahya Evliya Celebi Training and Research Hospital, Kutahya, Turkey and [6]Sisli Etfal Hamidiye Training and Research Hospital, Istanbul

Abstract

Many studies have investigated the association between headache and sleep disorders, but few have focused on migraine. The goal of this study was to evaluate sleep disturbance and excessive daytime sleepiness (EDS) in relation to migraine disability. 120 migraine patients who were diagnosed according to The International Classification of Headache Disorders-II and 45 healthy controls were recruited for the study. All participants completed the Pittsburg Sleep Quality Index (PSQI), the Epworth Sleepiness Scale, Beck Depression Inventory and Beck Anxiety Scale. Migraineurs completed Migraine Disability Assessment Scale (MIDAS) and Visual Analog Scale. The prevalence of poor sleep was 83.3% in the patients and 22.2% in the controls. All PSQI subgroup scores were higher for the patients than the controls except "Hours asleep". EDS was more prominent in the patient group (19.2% vs 2.2%). In conclusion, sleep disturbance, EDS, anxiety, and depressive symptoms were detected more commonly in migraine patients and were correlated with the migraine-related disability. The results of multivariate regression analysis indicated that EDS and sleep disturbance were the most effective factors on disability.

Key words: daytime sleepiness, migraine, migraine disability, mood disorder, sleep disturbances.

INTRODUCTION

Migraine is one of the most common neurological diseases[1] and can cause considerable social and domestic problems[2,3] as well as socioeconomic decline and financial loss.[4–6] In a nationwide epidemiological study in Turkey, the 1-year prevalence of migraine was estimated to be 16.4%.[7] Migraine prevalence is the highest in women, between the ages of 25 and 55.[8] Approximately 90% of migraineurs have moderate or severe pain, and three quarters have a reduced ability to function normally during the headache attacks.[9] It is worth noting that these years are the most productive years in a person's life.

Migraine is frequently associated with other pathologies.[10] The most common comorbidities are psychiatric disorders, especially mood disorders like depression.[11–13] Many studies suggest that mood disorders are two to 10 times more prevalent among those who suffer from

Correspondence: Dr Yıldızhan Sengul, Department of Neurology; Erzurum Regional Training and Research Hospital, Cat Yolu, Palandoken, Erzurum, Turkey.
Email: yysengul@gmail.com

The Authors declare that there is no conflict of interest. There was no funding source in this study.

Accepted 30 July 2014.

migraine than in the general population.[14] These comorbidities have been found to increase migraine disability.[15,16]

The relationship between headache and sleep disorders has been known for more than a century.[17] They are both common among the general population.[18] Sleep has long been recognized to both provoke and relieve headache.[19] Sleep and headache disorders overlap epidemiologically and share elements of anatomy and physiology.[20,21] There is a higher prevalence of sleep disorders among patients with headache, and its frequency is related with headache frequency.[22] Among different types of headaches, migraine is especially related with sleep disturbance. However, the relationship between sleep and migraine is complex. Changes in sleep patterns like excess sleep and lack of sleep or bad quality of sleep may trigger migraine attacks.[23,24] The physiology of sleep itself may somehow be related to the underlying mechanism of headache,[17,25] and sleep disturbances may be associated with increased migraine frequency.[18]

Excessive daytime sleepiness (EDS) is another aspect of sleep disorders that may also be associated with migraine.[26] It can cause accidents, low school or work performance, impaired psychological functioning etc. There are several studies that investigate the relationship between migraine and EDS. EDS may be an accompanying symptom of migraine and increased EDS may be a result of having migraine, and frequency of migraine may also affect EDS.[27–29]

Migraine is a common disabling disorder. In the *Global Burden of Disease Survey 2010*, it was ranked as the third most prevalent disorder and the seventh-highest specific cause of disability worldwide.[30] Taking into account all of these facts, it is important to understand the factors that can increase the disability of the illness.

The aim of this study is evaluate the frequency and grades of comorbidities like sleep disturbance, EDS, depressive symptoms and anxiety; and to determine types of sleep disturbance differences between migraine patients and normal population and their effects on disability.

METHODS

Patients

Four hundred and fifty six patients with headache (aged between 15–60 years old) who applied to the outpatient unit of the Neurology Department of Erzurum Regional Training and Research Hospital in Erzurum, Turkey between September 2012 and August 2013 were interviewed. Our outpatient clinic is a specialist clinic that reviews difficult neurological cases dispatched from three regions of the country (East Anatolia, Eastern Black Sea, Southeastern Anatolia). Consequently, our patients mostly consisted of patients who had severe headache. Three hundred and thirty six patients were excluded for not meeting inclusion criteria (n = 224) (migraine criteria according to The International Classification of Headache Disorders-II, psychiatric disease history, known sleep disorders, medication that could affect sleep quality except prophylactic treatment), declined to participate (n = 32), and other reasons (n = 80) (such as being illiterate and mental retardation). The control group was selected among healthy, migraine-free people who had similar age, sex and marital status with the patient group. One hundred and twenty patients and 45 migraine-free controls were recruited for the study. None of the participants had known physical causes that could affect sleep quality such as asthma, lung disease, thyroid dysfunctions, etc. All patients had migraine without aura (MwoA) or migraine with aura (MA). Patients with medication overuse, patients who were on anti-migraine medication (prophylactic anti-migraine treatment and/or attack treatment such as triptans) were not excluded. The migraine diagnoses were established by a neurologist. The patient group was divided into two groups: Chronic Migraine (CM) and Episodic Migraine (EM) according to headache days per month. CM was defined as reporting an average of 15 or more headache days per month over the past 3 months, and EM as reporting an average of 14 or fewer headache days per month over the past 3 months.

The study protocol was conducted in accordance with ethical principles stated in the "Declaration of Helsinki" and approved by the Ethical Committee of Erzurum Regional Training and Research Hospital.

Methods

The patients were asked to fill a form in order to record sociodemographic characteristics such as age, sex, education level, occupational and marital status, medical history, headache history, clinical characteristics of headache, medication or analgesic overuse, and number of emergency room visits over the past 6 months.

All subjects underwent a semi-structured interview and completed the Pittsburg Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Beck Depression Inventory (BDI) and Beck Anxiety Scale (BAS); and

the patients group also filled in the Migraine Disability Assessment Scale (MIDAS) and the Visual Analog Scale (VAS).

Pittsburg Sleep Quality Index (PSQI) is a self-rate questionnaire, which assesses sleep quality and disturbances over the last 4 weeks. Nineteen individual items generate seven "component" scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction.[31–34] The test is based on a 0–3 Likert scale whereby 3 reflects the negative extreme. A total score of ≥5 indicates a "poor" sleeper.[35]

Epworth Sleepiness Scale (ESS) is a method for measuring daytime sleepiness in adults. Excessive daytime sleepiness is defined as an ESS score of 10 or more. It consists of eight items. Reponses to each item are ranked from 0–3 according to probability for dozing off during a task.[36–38]

Beck Depression Inventory (BDI) consists of a list of descriptive statements related to 21 aspects of depression. For each category there are four to five statements of increasing severity. The patient reads the scale and marks statement the most suitable for him/her self. The score for each item ranges from 0–3; and total score falls between 0–63. Like the BDI, the BDI-II also contains 21 questions, each answer being scored on a scale value of 0 to 3. The cutoffs used differ from the original: 0–13: minimal depression; 14–19: mild depression; 20–28: moderate depression and 29–63: severe depression. Higher total scores indicate more severe depressive symptoms.[39–41] We used the BDI-II test in our study.

Beck Anxiety Scale (BAS) is a 21-question multiple-choice self-report inventory that is used for measuring the severity of an individual's anxiety.[42] The BAS has a maximum score of 63. A total score between 0–7 indicates minimal level of anxiety, 8–15: mild anxiety, 16–25: moderate anxiety and 26–63 points to a severe anxiety. The score for each item ranges from 0–3 (Not at all – 0 points; Mildly: It did not bother me much – 1 point; Moderately: It was very unpleasant, but I could stand it – 2 points; Severely: I could barely stand it – 3 points).

Migraine Disability Assessment Scale (MIDAS) was used to assess migraine-related disability.[43] We used the Turkish version of this scale.[44] Patients answered five questions, stating the number of days in which various activity limitations occurred due to migraine in the past 3 months. The total days are summed and categorized into four grades of severity. The four point grading system for the MIDAS questionnaire is as follows: MIDAS 0 to 5 (Grade I) – Little or no disability; MIDAS 6 to 10 (Grade II) – Mild disability; MIDAS 11 to 20 (Grade III) – Moderate disability; MIDAS ≥21 (Grade IV) – Severe disability.[45]

Visual Analog Scale (VAS) is a measurement for assessing pain degree. A 10-cm baseline was used for VAS scale. The numbers from 0 to 10 that represent level of pain.[46,47] '0' represents no pain and '10' represents worst pain. We asked the patients to put a mark on the line that represents their level of pain in relation to the two extremes.

The definitive statistics in the study were summarized by the use of arithmetic means, mean standard deviation, etc. Numbers and percentages were used in the representation of categorical variables. The Mann–Whitney *U*-tests were used in representation of numeric data regarding the comparison of control and patient groups, under the assumption that the data were not distributed normally. The comparisons that include the numeric variables of more than two groups were analyzed by the Kruskal–Wallis test. The comparisons for categorical variables were represented and analyzed by cross tabulation (χ^2). The correlations between the scales were tested using Pearson's correlation analysis. Multivariate regression analysis was performed to investigate clinical determinants for MIDAS. Logistic regression analysis was performed to evaluate the factors associated with EDS; sleep disturbance, depression, MIDAS were entered in the model. A statistical significance limit of $P < 0.05$ was used in all comparisons. SPSS 17.0 was used for the analysis.

RESULTS

Sociodemographic and clinical characteristics

One hundred and twenty patients (mean age ± SD 28.8 ± 8.8 years; range 16–52 years old) and 45 control subjects (mean age ± SD 30.3 ± 7.7 years; range 19–52 years old) were enrolled for the study. There were 91 women (75.8%) and 29 men (24.2%) in the patient group, 34 women (75.6%) and 11 men (24.4%) in the control group. There were no statistically significant differences between the patient and the control group regarding age, sex and marital status. Table 1 shows sociodemographic characteristics of participants.

Forty-seven patients had CM, 73 patients had EM and four patients had MA. The mean duration of migraine was 5.4 ± 4.7 years, while the mean number of attacks was 2.9 ± 1.7. The percentage of patients who had less than four attacks per month was 70.0% and the patients

Table 1 Socio-demographic characteristics for 165 study participants

	Migraineurs (n = 120)	Controls (n = 45)
Age (years)	28.8 ± 8.8	30.3 ± 7.7
Gender		
Male	24.2%	24.4%
Female	75.8%	75.6%
Marital status		
Single, divorced or widowed	52.5%	35.6%
Married	47.5%	64.4%

who had more than four attacks per month accounted for 30.0%. 56.7% of patients had all accompanying symptoms such as pulsating quality, unilateral location, moderate or severe pain intensity, aggravation by or avoidance from routine physical activity, nausea, vomiting, photophobia, and phonophobia. 35% of the patients had at least one emergency room visit over the last 6 months. The mean number of emergency room visits was 1.3 ± 3.1. The percentage of patients who also had headache due to analgesic overuse was 23.3%, and 29.1% of the patients were taking prophylactic or attack treatment. The mean VAS score was 7.9 ± 1.9. The mean headache days over the last 3 months was 22.5 ± 21.2. The mean MIDAS score was 43.1 ± 41.9. The number of patients who had Grade I disability according to MIDAS was 12 (10%), Grade II: 12 (10%), Grade III: 22 (18.3%) and Grade IV: 74 (61.7%).

Comparison between migraine disability and sleep disturbance, excessive daytime sleepiness, depressive symptoms, and anxiety

The percentage of probands who had poor sleep quality defined by PSQI was 83.3% in the patient group and 22.2% in the control group ($P < 0.01$), while the mean PSQI score was 8.4 ± 3.1 in the patient group and 3.8 ± 2.8 in the control group ($P < 0.01$). When PSQI scores were compared with the number of migraine attacks, headache days, the VAS scores, the MIDAS scores, emergency room visits, analgesic overuse, there was statically positive correlation between PSQI scores and number of migraine attacks (r = 0.28, $P < 0.01$), MIDAS scores (r = 0.35, $P < 0.01$), headache days (r = 0.28, $P < 0.01$). Mean PSQI score was 8.1 ± 3.1 in episodic migraine (EM) patients and 8.8 ± 3.1 in chronic migraine (CM) patients ($P = 0.32$). There was no correlation between chronicity of the disease and PSQI scores, on the other hand there was statistically significant positive correlation between PSQI scores and ESS (r = 0.32, $P < 0.01$), BDI scores (r = 0.41, $P < 0.01$), BAS scores (r = 0.48, $P < 0.01$).

All subgroup scores were higher in the patient group than the control group except "Hours asleep". Table 2 shows the comparison between patients' and control group's PSQI subgroup scores. Correlation analysis showed that there was significantly positive correlation between "Cannot get to sleep within 30 minutes"(r = 0.22, $P = 0.02$), "Trouble breathing" (r = 0.22, $P = 0.02$), "Feeling cold" (r = 0.23, $P = 0.01$), "Pain" (r = 0.20, $P = 0.03$), "Decreased sleep quality" (r = 0.38, $P < 0.01$), "Difficulties staying awake" (r = 0.20, $P = 0.03$), and "Lack of enthusiasm" (r = 0.47, $P < 0.01$) subgroups scores and MIDAS scores.

No statistical difference was observed between the PSQI ($P = 0.66$) and ESS scores ($P = 0.20$) between the patients who were on prophylaxis and the controls.

Excessive daytime sleepiness was more prominent in the patient group than the controls, and the difference was found to be statistically significant (19.2% vs 2.2%). The mean ESS score was higher in the patient group than those in the control group (6.2 ± 4.1 vs. 4.5 ± 2.5, $P = 0.03$). Table 3 shows a comparison of test scores between migraineurs and controls. In addition to this, the patients with EDS had higher BDI scores ($P = 0.03$), BAS scores ($P < 0.01$), MIDAS scores ($P < 0.01$), and headache days ($P = 0.01$) but there was no statistically significant difference between PSQI scores ($P = 0.06$) and VAS scores ($P = 0.88$). ESS scores were higher in the patients with CM, but it was not statistically significant when compared with EM (6.4 ± 4.4 vs. 6.1 ± 3.9, $P = 0.81$). However, the patients with EM had higher ESS scores than the controls (6.1 vs. 4.5, $P = 0.05$). Analgesic overuse ($P = 0.73$) and number of attacks ($P = 0.96$) did not have any effect on EDS.

Forty-three patients were examined after we excluded patients who had moderate and severe depression or anxiety levels, as these conditions are known to have negative effects on sleep quality. PSQI mean score was 6.8 ± 2.9, ESS mean score was 4.4 ± 3.6 in this group. When these scores were compared with the control group, statistical significance was found between PSQI scores ($P < 0.01$); and while ESS mean scores were higher in this group than controls', the difference was not big enough to be statistically significant ($P = 0.86$).

The majority of our patient group consisted of those who had grade IV disability according to MIDAS. This

Table 2 Comparison between patients and controls Pittsburg Sleep Quality Index (PSQI) subgroup scores

	Migraineurs (n = 120)	Controls (n = 45)	*P
PSQI Score	8.4 ± 3.1	3.8 ± 2.8	<0.01
Sleep latency (min)	35.4 ± 25.9	14.1 ± 11.5	<0.01
Hours asleep	7.2 ± 1.7	7.0 ± 1.2	0.33
Sleep disturbances			
Cannot get to sleep within 30 min	1.9 ± 1.1	0.7 ± 1.0	<0.01
Waking up in the middle of the night or early morning	2.0 ± 1.1	1.2 ± 1.1	<0.01
Getting up to use bathroom	1.0 ± 1.0	0.4 ± 0.9	0.01
Trouble breathing	1.0 ± 1.1	0.2 ± 0.5	<0.01
Snoring	0.7 ± 1.0	0.3 ± 0.7	0.02
Feeling cold	1.5 ± 1.1	0.6 ± 0.9	<0.01
Feeling warm	1.7 ± 1.1	0.6 ± 1.0	<0.01
Bad dreams	1.3 ± 1.1	0.5 ± 0.8	<0.01
Pain	2.1 ± 1.0	0.9 ± 1.0	<0.01
Other reasons	0.6 ± 0.9	0.3 ± 0.7	0.04
Decreased sleep quality	1.7 ± 0.8	0.9 ± 0.7	<0.01
Difficulties staying awake	1.2 ± 1.1	0.4 ± 0.8	<0.01
Lack of enthusiasm	1.8 ± 0.9	0.4 ± 0.8	<0.01

*Mann-Whitney *U*-test.

Table 3 Comparison of scores between migraineurs and controls

Scores	Migraineurs (n = 120) Mean	Controls (n = 45) Mean	*P
PSQİ	8.4 ± 3.1	3.8 ± 2.8	<0.01
ESS	6.2 ± 4.1	4.5 ± 2.5	0.03
BDI	16.7 ± 10.5	8.2 ± 7.9	<0.01
BAS	20.8 ± 11.9	8.15 ± 7.8	<0.01

*Mann–Whitney *U*-test. BAS, Beck Anxiety Scale; BDI, Beck Depression Inventory; ESS, Epworth Sleepiness Scale; PSQI, Pittsburg Sleep Quality Index.

Table 4 Mean test scores distribution according to Migraine Disability Assessment Scale (MIDAS) Grades

	MIDAS	n	Mean	SD	*P
PSQI					*<0.01*
	Grade I	12	6.2	3.4	
	Grade II	12	6.8	1.8	
	Grade III	22	6.8	2.7	
	Grade IV	74	9.5	2.9	
ESS					*0.02*
	Grade I	12	3.4	3.6	
	Grade II	12	5.3	2.5	
	Grade III	22	5.8	4.1	
	Grade IV	74	7.0	4.2	
BDI					*<0.01*
	Grade I	12	11.1	11.1	
	Grade II	12	11.6	5.7	
	Grade III	22	11.5	9.1	
	Grade IV	74	20.0	10.2	
BAS					*<0.01*
	Grade I	12	10.8	9.3	
	Grade II	12	21.3	12.6	
	Grade III	22	14.4	9.0	
	Grade IV	74	24.2	11.5	

*Kruskal–Wallis test. BAS, Beck Anxiety Scale; BDI, Beck Depression Inventory; ESS, Epworth Sleepiness Scale; PSQI, Pittsburg Sleep Quality Index; SD, standard deviation.

group of patients had the highest test scores. Table 4 shows mean test scores distribution according to MIDAS Grades.

Logistic regression analysis was performed for evaluation of EDS predictors. The following values were entered as covariates: PSQI, BDI, MIDAS scores. Migraine disability (OR = 1.02, %95 CI: 1.004–1.026, $P < 0.01$) and depression (OR = 1.05, %95 CI: 1.001–1.102, $P < 0.05$) contributed to EDS in migraine but sleep disturbance (OR = 1.00, %95 CI: 0.840–1.193, $P = 0.99$) did not have a significant effect on EDS. Multivariate regression analysis was performed to evaluate clinical determinants of MIDAS. Migraine related disability was significantly associated with high scores of the ESS (OR = 0.21, %95 CI: 0.48–4.29, $P = 0.30$) and PSQI (OR = 0.24, %95 CI: 0.28–5.45, $P = 0.01$). However, depression (OR = 0.19, %95 CI: –0.76–0.90, $P = 0.86$) and anxiety (OR = 0.11, %95 CI: –0.38–1.16, $P = 0.32$) did not have same affect on disability.

Table 5 Beck Depression Inventory (BDI) and Beck Anxiety Scale (BAS) subgroup distribution

		Migraineurs		Controls	
		n	%	*n*	%
BDI	Minimum	50	41.7	37	82.2
	Mild	25	20.8	4	8.9
	Moderate	27	22.5	1	2.2
	Severe	18	15.0	3	6.7
BAS	Minimal	15	12.5	26	57.8
	Mild	29	24.2	9	20.0
	Moderate	36	30.0	8	17.8
	Severe	40	33.3	2	4.4
		120	100.0	45	100.0

The prevalence of depressive symptoms and anxiety was significantly higher in the patients group than the controls. Table 5 shows BDI and BAS subgroup distribution. BDI and BAS score means were significantly higher in migraineurs (BDI: 16.7 ± 10.5 vs. 8.2 ± 7.9, $P < 0.01$; BAS: 20.8 ± 11.9 vs. 8.15 ± 7.8, $P < 0.01$) and these were correlated with MIDAS scores (BDI and MIDAS correlation r = 0.26, $P < 0.01$; BAS and MIDAS correlation r = 0.32, $P < 0.01$). Patients who had CM were found to have significantly higher mean BAS scores (18.3 ± 11.2 vs 23.7 ± 12.3, $P = 0.02$) than those with EM. There was no statistically important difference between EM and CM regarding BDI scores.

Percentage of patients who had at least one of these comorbid situations was 93.3%.

DISCUSSION

The goal of this study was to point out comorbidities of migraine, such as sleep disturbances, EDS, depressive symptoms and anxiety, to determine frequency of comorbidities, to compare sleep disturbance between each group, to expose their differences, and to investigate the associations between comorbidities of migraine and their role of migraine disability.

The relation was evident. The mean scores of PSQI, ESS, BAS, and BDI were higher in migraineurs than the controls. These scores were correlated with MIDAS scores. The most effective factors on migraine-related disability were EDS and sleep disturbance. Poor sleep quality was correlated with EDS, depressive symptoms and anxiety levels. Higher BAS and MIDAS scores were indicative of the chronicity of the disease. Analgesic overuse was correlated with depressive symptoms and anxiety. Percentage of patients who had at least one of the comorbidities was a prominent 93.3%.

The present study showed that the prevalence of poor sleep quality in migraine patients is even more frequent than our predictions. The percentage of patients who had poor sleep quality was 83.3%, while it was 22.2% in the patient group. Karthik and colleagues found that 66.7% of the patients had a poor sleep quality.[48] Seidel and colleagues found that the prevalence of poor sleepers was 64.9%, 64.0%, 57.4% and 34.9% in patients with eight or more, five to seven and one to four migraine days per month and controls, respectively. They also found differences of sleep disturbances related to pain and sleep quality subscores between each migraine groups and controls.[49] All subgroup scores were higher in patients than the controls except "Hours asleep", while the abovementioned studies did not find significant differences in "Hours asleep" subscores. The fact that there was no significant difference in "Hours asleep" between the patient and the control group, despite the major difference in sleep quality, may indicate migraine's effect on physiology, biochemistry and phases of sleep; and therefore its negative effect on sleep quality.[23] "Difficulties staying awake" and "Lack of enthusiasm for activities" subgroup scores were correlated with MIDAS scores. This result is evidence that decreased sleep quality may affect daytime performance and this may have a role in increased disability. Walters and colleagues found that poor sleep quality was significantly associated with headache frequency and headache-related disability in EM patients.[50] Similarly we found evident association between poor sleep quality and headache days, and migraine disability.

The prevalence of EDS was higher in the patient group than the controls (19.2% vs 3.3%). EDS was correlated with poor sleep quality, migraine disability, depressive symptoms, anxiety and headache days. After exclusion of patients with moderate and severe depression or anxiety levels; ESS mean scores were still higher in the patient group than the control group but the difference was not big enough to be statistically significant. Barbanti *et al*. found that EDS was more frequent in EM than in the controls and EDS was correlated with migraine disability, sleep problems and anxiety.[26] They also found similar findings for patients with CM.[51] We found that ESS scores were higher in the patients with CM, but it was not statistically significant when we compared them with the patients with EM. But Siedel and Morten Engstrom observed no differences between migraineurs and controls.[49,52] Gori *et al*. found that habitual excessive daily sleepiness, evaluated by means

of ESS, was not more frequent in patients with episodic migraine than in controls (12% migraineurs vs. 8% controls). They found sleepiness increased before the attack onset, starting 12 h before, a peak of Stanford Sleepiness Scale values seen at the onset of the migraine attack and then a gradual decrease that reaches baseline values only 12–24 h later.[28] Hence, it still can be theorized that EDS is part of a migraine attack and also a prodromal sign. In addition, we found that EDS had the strongest association with the migraine-related disability.

In our study 58.8% of migraineurs had depressive symptoms and 15.0% of patients had severe depression levels according to BDI. In controls 17.8% had depression while 8.9% of the controls had severe depression levels. Depression levels were correlated with MIDAS scores. The percentage of patients who had high anxiety levels (moderate and severe.) was 63.3% and it was 22.2% in the controls. BAS levels also had positive correlation with MIDAS scores. Lantéri-Minet and colleagues detected a depressive episode in 59.9% of patients with migraine and anxiety in 18.4% of patients with migraine.[15] Depression levels are similar but we found higher anxiety levels in our study. In Yavuz's study 38.2% of the migraineurs suffered from depressive symptoms. 62% of the patients with migraine had anxiety symptoms.[53] Pareja-Angel and colleagues found 70.0% presented anxiety and 52.7% depression.[11] The latter study has more similar findings with ours. Migraine and depression are highly comorbid and each exerts a significant and independent influence on quality of life.[16] It has been indicated that migraine comorbid with depression or anxiety causes higher medical costs than migraine does alone.[15] According to Jelinski's study, migraine-related disability was significantly correlated with the level of depressive symptoms.[54] Depression scores were significantly higher in migraineurs with moderate and severe disability than in the patients with minimal and mild disability.[12] Our study confirms these previous studies.

Number of patients and the controlled study design are the strength of this study, but we had some limitations, as all the tests we used were filled by subjects and there was no psychiatric interview with the participants beforehand. Ours is a countryside area where people have a low level of education and are occupied with agriculture and breeding livestock. Consequently our population had low education status. The majority of subjects were women. We did not question subjects about caffeine use and menstrual cycle. The control group was selected from among hospital workers, university students, and patients' relatives. Most of our patients had severe headache and most of them had Grade III–IV disability according to MIDAS.

In conclusion, sleep disturbance, anxiety, and depressive symptoms are detected more commonly in migraine than we predicted. EDS was also more prevalent in the migraine group. After excluding the patients with moderate and severe depressive symptom levels there was no statistically significant difference, but still the mean scores were higher in the patient group. There is a strong correlation between these comorbidities with disability. Almost all patients were found to have one or more of these conditions. We tried to clarify the role of sleep dysfunction as a causal cofactor regarding migraine disability. We found that EDS and sleep disturbance had an important role on migraine-related disability. The strong part of the present study is that MIDAS and PSQI (as well as BDI and BAS) data have been collected in a sample of 120 migraine patients free from psychiatric/sleep disorder history. This paper shows the role of sleep disturbances on disability, and this particular issue was not mentioned in the past studies about sleep disturbance in migraine.

An understanding of the anatomy and physiology of both conditions allows for a clearer explanation of this complex relationship and a more rational clinical and therapeutic approach.[17] Recently some research has suggested that comorbidities such as sleep disturbances, daytime sleepiness, depression and anxiety may share similar mechanisms with migraine.[55] There are some theories about this such as serotonergic dysfunction, and dysregulation of the hypothalamic pituitary adrenal (HPA) axis.[56–58] There is growing evidence to suggest that these comorbidities can be part of the disease. This theory leads to the thought that sleep disturbance is a part of the disease and can cause migraine-related disability. Our study contributes some new evidence to this concept. It is very helpful to ask the patients about these comorbid situations to map out the treatment options and the efforts required to decrease the disability of the disease. In order to manage the disability of patients, it is therefore crucial to understand the relationship between migraine and sleep disturbances. Further studies, which may clarify the role of sleep dysfunction as a causal cofactor regarding migraine disability, are needed.

ACKNOWLEDGMENTS

We thank to Dr Hulki Forta and Dr Gamze Can for their valuable contribution.

REFERENCES

1 World Health Organization. *Country Resources for Neurological Disorders 2004. World Federation of Neurology Atlas*. World Health Organization: Geneva, 2004.
2 Leonardi M, Raggi A. Burden of migraine: international perspectives. *Neurol. Sci.* 2013; **34**: S117–18.
3 Igarashi H. Societal impact of migraine chronification. *Rinsho Shinkeigaku* 2013; **53**: 1225–7.
4 Bloudek LM, Stokes M, Martelletti P. Cost of healthcare for patients with migraine in five European countries: results from the International Burden of Migraine Study. (IBMS). *J. Headache Pain* 2012; **13**: 361–78.
5 D'Amico D, Grazzi L, Usai S, Leonardi M, Raggi A. Disability and quality of life in headache: where we are now and where we are heading. *Neurol. Sci.* 2013; **34**: S-5.
6 Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF. Migraine prevalence, disease burden, and the need for preventive therapy. AMPP Advisory Group. *Neurology* 2007; **68**: 343–9.
7 Ertas M, Baykan B, Orhan EK *et al*. One-year prevalence and the impact of migraine and tension-type headache in Turkey: a nationwide home-based study in adults. *J. Headache Pain* 2012; **13**: 147–57.
8 Bigal ME, Lipton RB. The epidemiology, burden, andcomorbidities of migraine. *Neurol. Clin.* 2009; **27**: 321–34.
9 Lipton RB, Stewart WF. Migraine in the United States: a review of epidemiology and health care use. *Neurology* 1993; **43**: S6–S10.
10 Baskin SM, Smitherman TA. Migraine and psychiatric disorders: comorbidities, mechanisms, and clinical applications. *Neurol. Sci.* 2009; **14**: 61–5.
11 Pareja-Angel J, Campo-Arias A. The prevalence of symptoms of anxiety and depression in female migraine sufferers. *Rev. Neurol.* 2004; **39**: 711–14.
12 Sevillano-García MD, Manso-Calderón R, Cacabelos-Pérez P. Comorbidity in the migraine: depression, anxiety, stress and insomnia. *Rev. Neurol.* 2007; **45**: 400–5.
13 Nguyen TV, Low NC. Comorbidity of migraine and mood episodes in a nationally representative population-based sample. *Headache* 2013; **53**: 498–506.
14 Hamelsky SW, Lipton RB. Psychiatric comorbidity of migraine. *Headache* 2006; **46**: 1327–33.
15 Lantéri-Minet M, Radat F, Chautard MH, Lucas C. Anxiety and depression associated with migraine: influence on migraine subjects' disability and quality of life, and acute migraine management. *Pain* 2005; **118**: 319–26.
16 Lipton RB, Hamelsky SW, Kolodner KB, Steiner TJ, Stewart WF. Migraine, quality of life, and depression: a population-based case-control study. *Neurology* 2000; **55**: 629–35.
17 Dodick DW, Eross EJ, Parish JM, Silber M. Clinical, anatomical, and physiologic relationship between sleep and headache. *Headache* 2003; **43**: 282–92.
18 Alberti A. Headache and sleep. *Sleep Med. Rev.* 2006; **10**: 431–7.
19 Rains JC, Poceta JS, Penzien DB. Sleep and headaches. *Curr. Neurol. Neurosci. Rep.* 2008; **8**: 167–75.
20 Brennan KC, Charles A. Sleep and headache. *Semin. Neurol.* 2009; **29**: 406–18.
21 Gilman DK, Palermo TM, Kabbouche MA, Hershey AD, Powers SW. Primary headache and sleep disturbances in adolescents. *Headache* 2007; **47**: 1189–94.
22 Ødegård SS, Engstrøm M, Sand T, Stovner LJ, Zwart JA, Hagen K. Associations between sleep disturbance and primary headaches: the third Nord-Trøndelag Health Study. *J. Headache Pain* 2010; **11**: 197–206.
23 Kelman L, Rains JC. Headache and sleep: examination of sleep patterns and complaints in a large clinical sample of migraineurs. *Headache* 2005; **45**: 904–10.
24 Miller VA, Palermo TM, Powers SW, Scher MS, Hershey AD. Migraine headaches and sleep disturbances in children. *Headache* 2003; **43**: 362–8.
25 Hargreaves RJ, Bigal ME. Why does sleep stop migraine? *Curr. Pain Headache Rep.* 2013; **17**: 369.
26 Barbanti P, Fabbrini G, Aurilia C, Vanacore N, Cruccu G. A case-control study on excessive daytime sleepiness in episodic migraine. *Cephalalgia* 2007; **27**: 1115–19.
27 Peres MF, Stiles MA, Siow HC, Silberstein SD. Excessive daytime sleepiness in migraine patients. *J. Neurol. Neurosurg. Psychiatry* 2005; **76**: 1467–8.
28 Gori S, Lucchesi C, Maluccio MR *et al*. Inter-critical and critical excessive daily sleepiness in episodic migraine patients. *Neurol. Sci.* 2012; **33**: 1133–6.
29 Suzuki S, Suzuki K, Miyamoto M *et al*. Evaluation of contributing factors to restless legs syndrome in migraine patients. *J. Neurol.* 2011; **258**: 2026–35.
30 Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia* 2013; **33**: 9629–808.
31 Backhaus J, Junghanns K, Broocks A, Riemann D, Hohagen F. Test-retest reliability and validity of the Pittsburgh Sleep Quality Index in primary insomnia. *J. Psychosom. Res.* 2002; **53**: 737–40.
32 Spira AP, Beaudreau SA, Stone KL *et al*.; Osteoporotic Fractures in Men Study. Reliability and validity of the Pittsburg Sleep Quality Index and the Epworth Sleepiness Scale in older men. *J. Gerontol. A. Biol Sci. Med Sci* 2012; **67**: 433–9.
33 Carpenter JS, Andrykowski MA. Psychometric evaluation of the Pittsburgh Sleep Quality Index. *J. Psychosom. Res.* 1998; **45**: 5–13.
34 Buysse DJ, Reynolds CF, Monk TH, Berman SR *et al*. The Pittsburgh Sleep Quality Index: a new instrument for

psychiatric practice and research. *Psychiatry Res.* 1989; **28**: 193–213.
35 Fictenberg NL, Putnam SH, Mann NR, Zafonte RD, Millard AE. Insomnia screening in postacute traumatic brain injury: utility and validity of the Pittsburg Sleep Quality Index. *Am. J. Phys. Med. Rehabil.* 2001; **80**: 339–45.
36 Johns MW. Reliability and factor analysis of the Epworth Sleepiness Scale. *Sleep* 1992; **15**: 376–81.
37 Beaudreau SA, Spira AP, Stewart A *et al*. Validation of the Pittsburgh Sleep Quality Index and the Epworth Sleepiness Scale in older black and white women. *J. Gerontol. A. Biol Sci. Med Sci* 2012; **67A**: 433–9.
38 Johns M. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. *Sleep* 1991; **14**: 540–5.
39 Beck AT, Ward C, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch. Gen. Psychiatry* 1961; **4**: 561–71.
40 Salkind MR. Beck depression inventory in general practice. *J. R. Coll. Gen. Pract.* 1969; **18**: 267–71.
41 Wang YP, Gorenstein C. Psychometric properties of the Beck Depression Inventory-II: a comprehensive review. *Rev. Bras. Psiquiatr.* 2013; **35**: 416–31.
42 Piotrowski C. The status of the Beck Anxiety Inventory in contemporary research. *Psychol. Rep.* 1999; **85**: 261–2.
43 Stewart WF, Lipton RB, Dowson AJ, Sawyer J. Development and testing of the Migraine Disability Assessment (MIDAS) Questionnaire to assess headache-related disability. *Neurology* 2001; **56**: S20–8.
44 Ertaş M, Siva A, Dalkara T *et al*.; Turkish MIDAS group. Validity and reliability of the Turkish Migraine Disability Assessment (MIDAS) questionnaire. *Headache* 2004; **4**: 786–93.
45 Lipton RB, Stewart WF, Sawyer J, Edmeads JG. Clinical utility of an instrument assessing migraine disability: the Migraine Disability Assessment (MIDAS) questionnaire. *Headache* 2001; **41**: 854–61.
46 Langley GB, Sheppeard H. The visual analog scale: its use in pain measurement. *Rheumatol. Int.* 1985; **5**: 145–8.
47 Carlsson AM. Assessment of chronic pain. I. Aspects of the reliability and validity of the visual analogue scale. *Pain* 1983; **16**: 87–101.
48 Karthik N, Kulkarni GB, Taly AB, Rao S, Sinha S. Sleep disturbances in 'migraine without aura'–a questionnaire based study. *J. Neurol. Sci.* 2012; **321** (1–2): 73–6.
49 Seidel S, Hartl T, Weber M *et al*.; PAMINA Study Group. Quality of sleep, fatique and daytime sleepiness in migraine – a controlled study. *Cephalalgia* 2009; **29**: 662–9.
50 Walters AB, Hamer JD, Smitherman TA. Sleep disturbance and affective comorbidity among episodic migraineurs. *Headache* 2014; **54**: 116–24.
51 Barbanti P, Aurilia C, Egeo G, Fofi L, Vanacore N. A case-control study on excessive daytime sleepiness in chronic migraine. *Sleep Med.* 2013; **14**: 278–81.
52 Engstrøm M, Hagen K, Bjørk MH *et al*. Sleep quality,arousal and pain thresholds in migraineurs: a blinded controlled polysomnographic study. *J. Headache Pain* 2013; **14**: 12.
53 Yavuz BG, Aydinlar EI, Dikmen PY, Incesu C. Association between somatic amplification anxiety, depression, stress and migraine. *J. Headache Pain* 2013; **14**: 53.
54 Jelinski SE, Magnusson JE, Becker WJ, CHORD Study Group. Factors associated with depression in patients referred to headache specialists. *Neurology* 2007; **14**: 489–95.
55 Bruni O, Russo PM, Ferri R, Novelli L, Galli F, Guidetti V. Relationships between headache and sleep in a non-clinical population of children and adolescents. *Sleep Med.* 2008; **9**: 542–8.
56 Hamel E. Serotonin and migraine: biology and clinical implications. *Cephalalgia* 2007; **27**: 1293–300.
57 Peres MF, Sanchez del Rio M, Seabra ML *et al*. Hypothalamic involvement in chronic migraine. *J. Neurol. Neurosurg. Psychiatry* 2001; **71**: 747–75.
58 Barden N. Implication of the hypothalamic–pituitary–adrenal axis in the physiopathology of depression. *J. Psychiatry Neurosci.* 2004; **29**: 185.