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Relationship between MIDAS, depression, anxiety and alexithymia in migraine patients

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Abstract
The co-existence of psychiatric comorbidities with migraine is well known; however, the relationship between alexithymia and migraine has not been persuasively shown yet. The aim of the study was to assess the relationships between migraine-related disability, depression, anxiety and alexithymia. One hundred and forty-five migraine patients (33.18 ± 8.6; 111 females, 34 males), and 50 control subjects (29.06 ± 7.6; 34 females, 16 males) were prospectively enrolled for the study. The participants completed a demographic data form and Migraine Disability Assessment Scale, Beck Depression Inventory, Beck Anxiety Inventory and Toronto Alexithymia Score-20 (TAS-20). All migraine patients were more depressive ($p = 0.01$) and anxious ($p = 0.001$) than the healthy subjects. TAS-20 scores of the migraine sufferers and the control group did not indicate alexithymia. The migraine-related disability of all migraine patients was severe (27.84 ± 29.22). Depression and anxiety scores in the migraine patients were highly correlated with each other and TAS-20 ($r = 0.485$, $p = 0.001$) and all its subscales in turn: difficulty in identifying ($r = 0.435$, $p < 0.001$) and describing feelings ($r = 0.451$, $p = 0.001$) and externally oriented thinking ($r = 0.302$, $p = 0.001$). Moreover, logistic regression analysis revealed that depression and anxiety predicted alexithymia. Our findings showed a complex relationship between migraine, depression, anxiety and alexithymia. On the other hand, alexithymia apparently was not directly connected to migraine, but its presence could be predicted in migraine patients because of co-morbid depression and anxiety.

Keywords Alexithymia · Migraine · Depression · Anxiety · MIDAS

Introduction

Alexithymia (having no words for feelings) is a multidimensional psychological construct that is described with the following: (1) difficulty in discriminating between one emotion and another, with difficulty in distinguishing somatic states from emotions; (2) difficulty in communicating one's own emotions to others; (3) limited imaginative processes; with a deficient or absent activity of the imaginative faculty and restricted fantasy life; (4) externally oriented way of thinking; (5) inadequacy in intuition and empathy; and (6) reduced symbolic thought [1].

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Alexithymia is thought to be a personality trait consisting in a disorder of negative affect and the existence of alexithymia constitutes a risk factor for a variety of psychiatric disorders, such as depression, psychosomatic disorders, substance dependence and eating disorders and for developing psychiatric comorbidities in adults and also having a negative influence on the course of psychiatric disorders [2–4].

Psychiatric comorbidities co-occur in migraine sufferers at rates significantly higher than those in general population, especially the depression and anxiety disorders that are mainly common. This comorbidity can increase the risk of migraine-related disability, migraine chronification, poor treatment outcomes, medical costs, suicidal behaviors and can reduce the quality of life and can also affect adherence to treatment regime [5–8]. A few studies have yet addressed the relationship between migraine and alexithymia and convincing evidence of a link between alexithymia and migraine has not been revealed up to now [9–19]. The aim of the study was to assess the relationships between migraine-related

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disability, depression, anxiety and alexithymia in patients with migraine.

Methods

Participants

A total of 145 migraine patients were recruited in this study. The clinical sample enrolled at the Neurology Headache Clinic of Maslak Hospital, Acıbadem University, between January and October 2016. Migraine was diagnosed by means of a thorough clinical interview and neurological examination of the patients by three neurologists with expertise in headache according to the International Classification of Headache Disorders criteria, third edition (ICHD3 beta) [20].

First the participants were divided into two groups: (a) Migraine group (MG) ($n = 145$) and (b) control group (CG) ($n = 50$). Then MG was divided into three groups: (a) Infrequent episodic migraine (EM) ($n = 55$) (b) Frequent episodic migraine (EM) ($n = 40$) (c) Chronic migraine (CM) ($n = 50$). Infrequent EM is defined as one headache or fewer per week. If individuals have 2 or more headaches per week, it is coded as frequent EM. Chronic migraine is diagnosed on the basis of the ICHD-3 beta [20].

In order to be eligible for the study, the patients had to be between 18 and 65 years of age, with a history of migraine for at least 6 months. They were excluded if they presented any of the following criteria: illiteracy, secondary headache, any major medical and psychiatric condition that was unstable, pregnancy and breastfeeding. The control group was recruited among the relatives of patients who applied to Neurology Clinic for entrapment neuropathy or radiculopathy. The relatives of patients were questioned by researchers, and then they were invited to participate in the study. If they had any medical history of headache or active medical/psychiatric condition, they would not recruit the study. The exclusion criteria for the control group were similar to those for the patients' group.

The study received approval by the Ethics Committee of the Acıbadem University, School of Medicine. All of the participants gave their informed consent to participate to the study.

Main outcome measures

Demographics form: This semi-structured form included questions about patients' demographics, current cigarette smoking and alcohol consumption and first-order-migraine-related relatives.

Migraine features: The questionnaire was used to detect the duration (in years) and type (with aura/without aura) of each migraine, and medication intake (preventative treatment for migraine, depression or anxiety and medication overuse for migraine).

Migraine disability assessment scale (MIDAS): MIDAS is a tool assessing the headache-related disability in daily activities. Headache sufferers are asked to answer five questions related to their days of partial or total loss within the past 3 months with respect to three main activities: (1) paid work or school; (2) household chores; (3) family, social and leisure activities [21, 22]. The final score corresponds to the sum of missed days for three activities. Depending on the severity of attacks, the MIDAS questionnaire diagnoses: little or no disability (0–5); mild disability (6–10); moderate disability (11–20); severe disability (21 or higher). MIDAS-A evaluates headache frequency and MIDAS-B assesses pain intensity (0 = no pain; 10 = very severe pain) over the past 3 months.

Beck depression inventory (BDI): BDI is a 21-item self-reporting scale developed to measure the severity of depression [23, 24]. Each item can score from 0 to 3. The total score can vary from 0 to 63. BDI scores between 0 and 9 are considered to denote no depression, 10–18, mild depression, 19–29, moderate depression and 30–63 severe depression.

Beck anxiety inventory (BAI): BAI is a self-reporting scale that consists of 21 items. Each item can score from 0 to 3 in terms of the severity of the symptom over the past month. The total score is calculated by finding the sum of the 21 items. A high total score indicates more severe levels of anxiety [25, 26]. BAI scores between 0 and 21 are considered to denote low anxiety, 22–35, moderate anxiety, 36 and above, potentially concerning levels of anxiety.

Toronto Alexithymia Scale (TAS-20): The TAS is a 20-item self-reporting scale. Responses to each item are made on a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). Factor analysis has yielded the following three factors: F1, difficulty identifying feelings; F2, difficulty describing feelings, and F3, externally oriented thinking.

The total scores for the TAS-20 were categorized as follows: a score of < 51 indicates the absence of alexithymia; 59 is the top score indicating the presence of alexithymia [27, 28].

Statistical analyses

Data are expressed as mean ± standard deviation (SD). Data of categorical variables are shown as counts and percentages. Pearson's Chi square was used to compare the categorical variables between the study groups. Numeric variables were compared with the Kruskal–Wallis test and the Mann–Whitney *U*-test. Bonferroni correction was used to adjustment. Spearman rank correlation was used to evaluate the correlation between the variables. Multiple forward

logistic analysis regression was used to determine independent predictors for BDI, BAI and TAS-20 scores in all migraine patients. All the statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 24.0 (SPSS Inc., Chicago, IL, USA, 2005). The level of significance was set at $p < 0.05$.

Results

Demographic findings

Table 1 shows the demographic features of all subjects with the MG and the CG. In the patients with migraine was older than the CG ($p = 0.005$). The subgroup analysis of all groups (the infrequent EM vs the CG ($p = 0.42$)); (the frequent EM vs the CG ($p = 0.72$)); (the CM vs the CG ($p = 0.001$)) showed that the CM patients was older than the healthy volunteers.

Current cigarette smoking in the MG was statistically higher than the CG ($p = 0.018$). The migraine patients had more migraine in first-order relatives than the CG ($p = 0.022$).

Headache characteristics and MIDAS

Table 2 shows migraine-related features and MIDAS scores in all patients and their subgroups. The duration of migraine was statistically different between the migraine subgroups ($p = 0.007$). The subgroup analysis of the groups: the infrequent EM vs the frequent EM ($p = 0.009$); the infrequent EM vs the CM ($p = 0.006$), the frequent EM vs the CM ($p = 0.625$) showed that the duration of migraine in the frequent EM and the CM patients were longer than the infrequent EM patients.

The migraine sufferers who were taking medicines for depression or anxiety or migraine were numbered as follows: 2 of 50 patients with the infrequent EM patients (1 fluoxetine, 1 amitriptyline), 4 of 40 patients with the frequent EM (2 fluoxetine, 1 amitriptyline, 1 metoprolol) and 9 of 50 patients with the CM patients (4 topiramate, 2 Botulinum toxin-A, 1 metoprolol, 2 bupropion). Nine of the 50 CM patients (18%) had comorbid medication overuse for headache.

Psychopathological symptoms (BDI, BAI) and TAS-20

Table 3 shows the BDI, BAI and TAS-20 scores of all patients and the CG.

BDI and BAI scores were statistically different between the MG and the CG. BDI scores showed statistically difference between the groups ($p = 0.01$) in turn: the infrequent EM vs the frequent EM ($p = 0.023$); the infrequent EM vs the CM ($p = 0.001$); the frequent EM vs the CM ($p = 0.065$).

Anxiety symptoms showed difference between the MG and the CG ($p = 0.001$) although the BAI scores of the migraine subgroups were not different.

Alexithymia symptoms in the MG were not different compared to the CG. On the other hand, the F2 dimension of TAS-20 showed difference between the migraine subgroups: the infrequent EM vs the frequent EM ($p = 0.029$);

Table 1 The demographic findings of all subjects with migraine and control

	Migraine ($n = 145$) Mean ± SD	Control ($n = 50$) Mean ± SD	p
Age	33.18 ± 8.6	29.06 ± 7.6	**0.005**
	n (%)	*n* (%)	
Gender			
Female	111 (76.6%)	34 (68%)	0.232
Male	34 (23.4%)	16 (32%)	
Employment status			
Unemployed	29 (20%)	15 (30%)	0.145
Employed	116 (80%)	35 (70%)	
Education			
Up to high school	5 (3.4%)	5 (10%)	0.139
College graduate	121 (83.5%)	41 (82%)	
Graduate degree	19 (13.1%)	4 (8%)	
Current cigarette smoking	59 (40.7%)	11 (22%)	**0.018**
Occasional alcohol intake	48 (33.1%)	18 (36%)	0.709
Migraine in first-order relatives	58 (40%)	11 (22%)	**0.022**

N number of subject, *SD* standard deviation

Bold indicates statistically difference, $p < 0.05$

Table 2 Migraine types and MIDAS scores in all migraine patients and the subgroups

Variables	All migraine patients *n* (%)	Infrequent EM patients *n* (%)	Frequent EM patients *n* (%)	CM patients *n* (%)	*p*
Type					
With aura	25 (17.2%)	10 (18.2%)	7 (17.5%)	8 (16%)	0.956
Without aura	120 (82.8%)	45 (81.8%)	33 (82.5%)	42 (84%)	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Duration of migraine (years)	9.3 ± 8.0	6.5 ± 6.1	10.2 ± 7.8	11.7 ± 9.2	**0.007**
MIDAS	27.8 ± 29.2	10.8 ± 14.1	28.3 ± 26.6	46.2 ± 32.5	**0.001**
MIDAS-A	33.4 ± 24.3	10.4 ± 5.6	30.8 ± 5.9	60.9 ± 17.4	**0.001**
MIDAS-B	7.1 ± 1.3	7.1 ± 1.4	6.9 ± 1.2	7.4 ± 1.1	0.184

N number of subjects, *MIDAS* migraine disability assessment scale, *MIDAS-A* headache frequency over the past 3 months, *MIDAS-B* pain intensity of migraine attacks (0 = no pain; 10 = very severe pain) over the past 3 months, *SD* standard deviation

Bold indicates statistically difference, $p < 0.05$

Table 3 Psychopathological symptoms and TAS-20 scores of all migraine patients and the control group

	MG Mean ± SD	CG Mean ± SD	*p*	Infrequent EM Mean ± SD	Frequent EM Mean ± SD	CM Mean ± SD	*p*
BDI	10.3 ± 6.9	6.8 ± 5.4	**0.001**	7.6 ± 6.0	10.4 ± 6.5	13.2 ± 6.9	**0.001**
BAI	14.0 ± 9.4	6.3 ± 6.5	**0.001**	13.7 ± 10.3	15.2 ± 10.2	13.3 ± 7.8	0.586
F1	13.3 ± 5.1	13.5 ± 5.1	0.768	12.1 ± 4.5	14.6 ± 5.6	13.7 ± 5.1	0.074
F2	10.9 ± 3.5	12.0 ± 6.1	0.347	10.0 ± 3.1	11.7 ± 3.9	11.3 ± 3.4	**0.041**
F3	20.7 ± 3.9	21.5 ± 3.7	0.171	20.3 ± 4.2	21.2 ± 3.1	20.8 ± 4.1	0.500
Total TAS-20	45.0 ± 9.9	47.1 ± 11.3	0.351	42.4 ± 9.8	47.4 ± 10.4	45.8 ± 9.1	0.052

BDI beck depression inventory, *BAI* beck anxiety inventory, *TAS-20* Toronto Alexithymia Scale, *F1* identifying feelings and distinguishing them by bodily sensations, *F2* difficulty expressing feelings, *F3* externally oriented thinking, *SD* standard deviation, *MG* migraine group, *CG* control group, *EM* episodic migraine, *CM* chronic migraine

Bold indicates statistical difference, $p < 0.05$

the infrequent EM vs the CM ($p = 0.043$); the frequent EM vs the CM ($p = 0.067$).

The relationship between age, the duration of migraine, MIDAS, depression, anxiety and alexithymia for all migraine patients

Table 4 shows the correlation between the variables in MG.

Regression analysis

A multivariable logistic regression analysis was used to predict for depression, anxiety and alexithymia (Table 5). In the first model, a forward multiple regression analysis revealed that depression independently associated with headache frequency (MIDAS-A) [adjusted odds ratio (AOR) 1.023, $p = 0.041$, (1.001–1.045) 95% CI] and BAI [AOR 1.122, $p = 0.001$, (1.059–1.189) 95% CI].

In the second model, a forward multiple regression analysis revealed that anxiety independently associated with TAS-20 [AOR = 1.051, $p = 0.047$, (1.001–1.105) 95% CI] and BDI [AOR 1.098, $p = 0.006$, (1.027–1.175) 95% CI].

In the third model, a forward multiple regression analysis revealed that alexithymia independently associated with BDI [AOR 1.077, $p = 0.019$, (1.002–1.145) 95% CI] and BAI [AOR 1.061, $p = 0.012$, (1.013–1.111) 95% CI].

Discussion

Alexithymia was first used by Sifneos and is a personality variable that describes incapacity to express emotions through words [29]. Our findings showed that depression and anxiety are closely associated with each other and in the meantime they are correlated with alexithymia and all its subscales in the migraine sufferers; in turn, difficulty in identifying and describing feelings and externally oriented thinking. Moreover, regression analysis revealed that depression and anxiety symptoms in the migraine patients predict alexithymia.

Table 4 Correlation between variables in all migraine patients

Variables	Age	Duration of migraine	MIDAS	MIDAS-A	MIDAS-B	BDI	BAI	F1	F2	F3	TAS-20
Age											
Rho	1.000	0.479**	0.052	0.103	0.194*	0.168*	0.013	0.024	0.017	0.109	0.71
p	–	**0.001**	0.536	0.219	**0.020**	**0.044**	0.874	0.777	0.836	0.192	0.395
Duration of migraine											
Rho	0.479**	1.000	0.205*	0.221**	0.225**	0.184*	0.099	0.23	− 0.001	0.072	0.26
p	**0.001**		**0.014**	**0.007**	**0.006**	**0.026**	0.234	0.785	0.994	0.391	0.759
MIDAS											
Rho	0.052	0.225*	1.000	0.636*	0.232**	0.330**	0.126	0.094	0.210*	0.102	0.139
p	0.536	**0.014**		**0.001**	**0.005**	**0.001**	**0.132**	0.262	**0.011**	0.222	0.095
MIDAS-A											
Rho	0.103	0.221**	0.636**	1.000	0.109	0.335**	0.069	0.148	0.190*	0.048	0.170*
p	0.219	**0.007**	**0.001**		0.193	**<0.001**	0.407	0.076	**0.022**	0.566	**0.040**
MIDAS-B											
Rho	0.194*	0.225**	0.232**	0.109	1.000	0.022	0.002	− 0.012	− 0.038	0.081	0.012
p	**0.020**	**0.006**	**0.005**	0.193		0.795	0.978	0.978	0.652	0.335	0.889
BDI											
Rho	0.168*	0.184*	0.330**	0.335**	0.022	1.000	0.468**	0.435**	0.451**	0.302**	0.485**
p	**0.044**	**0.026**	**0.001**	**0.001**	0.795		**0.001**	**0.001**	**0.001**	**0.001**	**0.001**
BAI											
Rho	0.013	0.099	0.126	0.069	0.002	0.468**	1.000	0.473**	0.398**	0.220**	0.456**
p	0.874	0.234	0.132	0.407	0.978	**0.001**		**0.001**	**0.001**	**0.001**	**0.001**
F1											
Rho	0.024	0.023	0.094	0.148	− 0.012	0.473**	0.473**	1.000	0.651**	0.260**	0.837**
p	0.777	0.785	0.262	0.076	0.885	**0.001**	**0.001**		**0.001**	**0.002**	**0.001**
F2											
Rho	0.017	− 0.001	0.201*	0.190*	− 0.038	0.451**	0.398**	0.651**	1.000	0.437**	0.857**
p	0.836	0.994	**0.011**	**0.022**	0.652	**0.001**	**0.001**	**0.001**		**0.001**	**0.001**
F3											
Rho	0.109	0.072	0.102	0.048	0.081	0.302**	0.220**	0.260**	0.437**	1.000	0.661**
p	0.192	0.391	0.222	0.566	0.335	**0.001**	**0.008**	**0.002**	**0.001**		**0.001**
TAS-20											
Rho	0.071	0.026	0.139	0.170*	0.012	0.485**	0.456**	0.837**	0.857**	0.661**	1.000
p	0.395	0.759	0.095	**0.040**	0.889	**0.001**	**0.001**	**0.001**	**0.001**	**0.001**	

MIDAS migraine disability assessment scale, *MIDAS-A* headache frequency over the past 3 months, *MIDAS-B* pain intensity of migraine attacks (0 = no pain; 10 = very severe pain) over the past 3 months, *F1* identifying feelings and distinguishing them bodily sensations, *F2* difficulty expressing feelings, *F3* externally oriented thinking, *BDI* beck depression inventory, *BAI* beck anxiety inventory, *TAS-20* Toronto Alexithymia Scale, *SD* standard deviation, *rho* Spearman rho correlation

Bold indicates statistical difference, *$p < 0.05$, * $p \leq 0.001$

To date, psychiatric comorbidity with migraine has been widely studied and the bidirectional relationship between them is known. In our study, all migraine patients were more depressive and anxious than the healthy ones. The depression and anxiety scores of the infrequent EM sufferers did not indicate any psychiatric comorbidity, whereas the frequent and CM patients had mild depressive symptoms but with low anxiety levels. We did not find statistically difference for alexithymia between the MG and the CG. In addition to that, alexithymia in migraine subgroups did not show any difference; however, in the frequent EM and the CM patients, difficulty with describing feelings (F2) was slightly higher compare to the infrequent EM patients.

Researches have shown that alexithymia is linked to decreasing or increasing age, low educational level, poor perceived health and depression [30–32]. In this study, age did not show correlation with alexithymia, but depression and anxiety were highly correlated with not only each other but also with alexithymia and all its subscales in the migraine patients. Depression also showed strong correlation with

Table 5 Logistic regression analysis for BDI, BAI and TAS-20 scores

	p	OR ratio	95% CI	
			Lower	Upper
Dependent: BDI				
Enter Metot				
Age	0.275	1.045	0.965	1.132
Gender (male)	0.845	0.848	0.163	4.415
Current cigarette smoking	0.951	0.958	0,241	3.800
Occasional alcohol intake	0.089	3.606	0.823	15.797
Migraine type (with aura)	0.201	0.287	0.043	1.940
Duration of migraine	0.896	1.005	0.929	1.088
MIDAS	0.331	0.986	0.958	1.015
MIDAS A	**0.043**	1.029	1.001	1.058
MIDAS B	0.106	1.549	0.912	2.632
TAS-20	0.512	1.022	0.957	1.093
BAI	**0.001**	1.146	1.062	1.238
Forward Metot				
MIDAS A	**0.041**	1.023	1.001	1.045
BAI	**0.001**	1.122	1.059	1.189
Dependent: BAI				
Enter Metot				
Age	0.703	0.986	0.920	1.058
Gender (male)	0.052	0.211	0.044	1.010
Current cigarette smoking	0.108	2.563	0.812	8.091
Occasional alcohol intake	**0.040**	0.230	0.057	0.934
Migrane type (with aura)	0.235	2.164	0.605	7.742
Duration of migraine	0.818	1.008	0.941	1.081
MIDAS	0.556	0.992	0.968	1.018
Midas A	0.105	0.976	0.948	1.005
Midas B	0.385	0.820	0.523	1.284
TAS-20	0.057	1.061	0.998	1.128
BDI	**0.006**	1.120	1.034	1.214
Forward Metot				
TAS-20	**0.047**	1.051	1.001	1.105
BDI	**0.006**	1.098	1.027	1.175
Dependent: TAS-20				
Enter Metot				
Age	0.274	1.032	0.975	1.093
Gender (male)	0.087	2.468	0.878	6.936
Current cigarette smoking	0.958	0.976	0.384	2.477
Occasional alcohol intake	0.355	0.613	0.217	1.730
Migraine type (with aura)	0.433	1.549	0.519	4.618
Duration of migarine	0.260	0.966	0.910	1.026
MIDAS	0.326	0.991	0.972	1.010
MIDAS A	**0.038**	1.022	1.001	1.043
MIDAS B	0.234	1.232	0.874	1.738
BDI	0.082	1.061	0.993	1.134
BAI	**0.003**	1.083	1.027	1.143
Forward Metot				
BDI	**0.019**	1.077	1.012	1.145
BAI	**0.012**	1.061	1.013	1.111

TAS-20 Toronto Alexithymia Scale-20 item version, *BDI* Beck depression inventory, *BAI* beck anxiety inventory, *MIDAS* migraine disability assessment scale, *MIDAS A* headache frequency over the past 3 months, *MIDAS B* pain intensity of migraine attacks (0 = no pain; 10 = very severe pain) in the past 3 months, *SD* standard deviation, *OR* odd ratio, *CI* confidence Interval

Bold indicates $p < 0.05$

migraine-related disability and higher migraine frequency. In the present study, age and the duration of migraine were also the important determinants for depression but not for anxiety or alexithymia. Duration of migraine was also highly correlated with migraine-related disability, higher migraine frequency and pain intensity for migraine attacks over the past 3 months.

Similar to our findings, Honkalampi et al. showed a link between depression and alexithymia in a large sample ($n = 7087$) of Finnish adolescents [33]. A meta-analysis reviewed 19 studies to examine any possible association between depression severity and alexithymia [34]. Authors concluded that alexithymia was closely related to depression. Kojima revealed that the ability to identify and express emotions plays an important role in the construction of health and disease [35]. Besides, depressive patients engage in emotional inhibition strategies to cope with their symptoms and thus demonstrate more difficulties in subjectively identifying and describing their feelings [36]. Thus depression indicates reduced emotional awareness and expression and has a bidirectional relationship with alexithymia.

Wise et al. compared to depression, anxiety and alexithymia in patients with migraine and tension-type headache (TTH). They did not find any difference for depression, anxiety or alexithymia between two groups [9]. Muftuoglu et al. made the comparison of 50 migraine patients with 50 healthy subjects to search for any association between migraine, alexithymia, depression and anxiety [10]. Authors found that the migraine sufferers were much more depressive, anxious and alexithymic than the CG and anxiety was significantly correlated with alexithymia in patients with migraine. In our study, the migraine sufferers showed more depressive and anxious symptoms compare to the healthy subjects and depression and anxiety highly correlated with alexithymia in the MG similar to their study, but we did not find any difference in alexithymia between the MG and the CG on the contrary. Yalug et al. searched for correlations between alexithymia, pain severity, depression and anxiety among patients with CM and EM [11]. According to the study, the total TAS-20 scores of the EM (57.91 ± 14.43) and the CM (59.29 ± 14.92) patients did not show any difference similar to our findings, although alexithymia scores of their patients were little higher than ours. They found that the CM patients had significantly higher depression scores but not alexithymia or anxiety similar to our patients and depression and anxiety were significantly correlated with alexithymia in both migraine groups. Gatta et al. investigated alexithymia in a sample of pediatric patients suffering from migraine or tension-type headache (TTH) and their mothers, to establish whether alexithymic traits related to the primary caregiver [12]. The children/preadolescents in the primary headache group showed higher levels of alexithymia compared to the CG and correlation between levels of

alexithymia in children/adolescents and in their mothers did not find. A different study revealed that the pediatric patients with TTH were more alexithymic than the migraine sufferers [13]. A meta-analysis was performed to examined psychopathological symptoms in child and adolescent sufferers with migraine and TTH [14]. Their findings demonstrated that the patients with migraine and TTH showed more psychopathological symptoms than the healthy controls. Alexithymia and post-traumatic stress disorder were found more common in students with migraine than in other students [15]. Brazilian women with migraine without aura ($n = 40$) showed higher levels of depression, anxiety and alexithymia than in a group of matched controls [16]. Similar to our findings, the authors found that pain frequency in the previous 3 months had been significantly correlated to depression and also anxiety. In a different study, alexithymia was compared between patients with CM and EM and healthy subjects [17]. A statistical difference in the F1, F2 and total TAS-20 scores was revealed between groups (EM, CM, control). However, they did not find meaningful differences between the CM and EM patients of the TAS-20 scores in post hoc analysis. Bottiroli et al. found that in migraine patients with medication overuse had higher alexithymia scores than the EM patients had [18]. Their findings suggested that alexithymia could be a risk factor in the transformation from episodic migraine to the chronic subtype with medication overuse. A recent study aimed to clarify whether alexithymia may be a predictor of psychological distress in adolescent outpatients and mothers suffering from migraine [19] Authors compared them with healthy adolescents and their mothers. Linear regression analysis affirmed that TAS-20 scores were a significant predictor of psychopathology in both adolescents and mothers suffering from migraine, so the authors concluded that the co-occurrence of migraine and alexithymia enhanced the risk of psychopathology for such patients.

The present study has some limitations. First, we evaluated the presence of depressive symptoms and anxiety symptoms and alexithymia in subjects only from a self-reported questionnaire; we did not use structured interviews. It is hard to predict how alexithymic subjects will perform on the psychological test batteries, which essentially rely on the verbal expression of feelings. Second, we analyzed hospital-based migraine patients, not those from the general population and our selected sample does not allow our results to be generalized. Third, the gender distribution of our sample is remarkably biased towards females, though this can partly reflect the fact that there is distinct female bias in the distribution of migraine. Gender distribution is important for in evaluating alexithymia; the studies showed that alexithymia was associated with male respondents [37]. Fourth, the age difference between the patients and the control subjects could be a weak point in this study. Because age is one of the determinants for alexithymia, if our healthy subjects had been older, their depression and alexithymia scores might have been higher. The final limitation is that a small percentage of the migraine patients were using preventative treatment when they were recruited the study. This may affect the depression and anxiety levels of our migraine patients, which would be higher than reported. At the same time, the strength of the present study is that the patients with migraine were evaluated by neurologists who were experts in headache. In addition, we categorized migraine groups according to the frequency of their attacks and compared them both with each other and with healthy subjects. As far as we know, our study is the first one which investigated migraine patients and healthy subjects for a possible association between psychiatric comorbidities and alexithymia and MIDAS at the same time.

Our findings showed that depression and anxiety were both closely associated with not only each other but also alexithymia and they were significant predictors for alexithymia. Depression also showed a marked relationship with migraine-related disability and migraine frequency, which were connected to F2 subscale of TAS-20. Difficulty in describing feelings was the only shared negative affect with psychiatric symptoms (depression/anxiety) and migraine-related disability and migraine frequency. Finally, our findings showed a complex relationship between migraine, depression, anxiety and alexithymia. On the other hand, alexithymia apparently was not directly connected to migraine, but its presence could be predicted in migraine patients because of co-morbid depression and anxiety.

Compliance with ethical standards

Conflict of interest No disclosures for both authors.

Ethical approval The study received approval by the Ethics Committee of the Acıbadem University, School of Medicine.

Informed consent All of the participants gave their informed consent to participate to the study.

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