

# Sleep Quality in Comorbid Generalized Anxiety Disorder and Major Depressive Disorder: Comparison with Healthy Controls

# Abdullah Burak Uygur<sup>1</sup>, Ece Özdemir Öktem<sup>2</sup>

<sup>1</sup> Department of Psychiatry, Faculty of Medicine, Alanya Alaaddin Keykubat University, Alanya, Turkey
<sup>2</sup> Department of Neurology, Faculty of Medicine, Alanya Alaaddin Keykubat University, Alanya, Turkey

ORCID; 0000-0001-7056-7553, 0000-0002-1264-5696

Abstract: It is well known that poor sleep quality is related with depression and anxiety. As we know, sleep quality in Generalized Anxiety Disorder (GAD)-Major Depressive Disorder (MDD) comorbidity has not been investigated in any study conducted in clinical settings in our country. In addition to determining the relationship between anxiety and depression levels with sleep quality, we conducted research determining similarities and differences between the comorbid MDD-GAD patient group and healthy control group in terms of sleep quality. In a cross-sectional study, patients who were diagnosed with MDD and GAD according to DSM-V diagnostic criteria and who did not have any other primary axis psychiatric disorder were included in the study. Individuals, who did not have a psychiatric disease according to DSM-V diagnostic criteria formed the healthy control group. The Sociodemographic Data Form, Pittsburgh Sleep Quality Index (PSQI), Beck Anxiety Inventory (BAI) and Beck Depression Inventory (BDI) were administered to 31 MDD-GAD patients and 30 healthy controls. Patients with poor sleep quality scored an average of 4,096 points higher on the BDI compared to patients with a good sleep quality (p=0,042). Depression scores showed a positive correlation of at a level of 42,5% with the PUKI Sleep Disturbances subtest (p=0,017) and 47,4% (p=0,007) Daytime Dysfunction subtest. Our study indicates that depression may be more related to sleep quality than anxiety. Problems related to sleep are shown as the first symptom that prompts many depressive patients to seek help. Detecting sleep related abnormalities can play a stimulating role for clinicians in many areas, including the risk of developing depression and implementing preventive therapy. The PSQI appears to be a very useful tool in identifying sleep related problems and can be very helpful to clinicians. Our findings reveal the importance of controlling individuals with sleep problems, especially in terms of depressive symptoms.

# INTRODUCTION

Sleep is an active process in which the brain works effectively and involves complex neurophysiological and biochemical processes<sup>1</sup>. The oldest study looking at the relationship between sleep and health was conducted by Hammond et al.<sup>2</sup>. During the two year follow up, Hammond observed that those who slept seven hours had the lowest mortality. He found higher mortality rates among those who reported shorter or longer sleep duration<sup>2</sup>. The conceptualization of sleep as duration and quality began only after Ford and Kamerow discovered that insomnia greatly increased the risk of psychiatric disorders<sup>3</sup>, and research on sleep quality began to attract more attention<sup>4</sup>. It is well known that poor sleep quality is related with anxiety and depression<sup>5</sup>. According to DSM V, one of the diagnostic criteria of Generalized Anxiety Disorder (GAD) is a sleep disorder defined as having difficulty falling asleep or maintaining sleep or a non-satisfying sleep that does not rest. The decreased or increased sleep duration is also one of the diagnostic criteria of Major Depressive Disorder (MDD)<sup>6</sup>. MDD patients often wake up during the night or very early in the morning. They may also have difficulty falling asleep at night<sup>7</sup>. Difficulties falling asleep or maintaining sleep are considered to be part of anxiety disorders and depression; clinical signs of sleep are not limited to these. They may also appear as symptoms related to sleep quality, such as lower sleep duration, worse sleep efficiency, and daytime dysfunctions<sup>7</sup>.

Major Depressive Disorder is a disease that has serious consequences and is becoming more common with increasing disease burden and mortality rates. Despite numerous treatment options, complete remission cannot be achieved in many patients with major depression<sup>8</sup>. Sleep-related disorders in particular may be at least partially responsible for these problems. Approximately three-quarters of the patients with Generalized Anxiety Disorder with a lifelong prevalence of 5-6% complain of insomnia<sup>9</sup>. The possibility of sleep disturbance in GAD patients was found to be much higher than healthy controls<sup>10</sup>. This may be a warning feature for individuals at risk of developing GAD<sup>11</sup>.

 Received
 : 01.04.2021

 Received in revised form
 : 09.05.2021

 Accepted
 : 15.07.2021

 Available online
 : 15.09.2021

#### Keywords:

Sleep Quality Major Depressive Disorder Generalized Anxiety Disorder Comorbidity

Corresponding Author: Abdullah Burak Uygur E-mail; burak.uygur@alanya.edu.tr http://dx.doi.org/10.29228/jamp.49971

Int J Acad Med Pharm, 2021; 3 (3); 201-207



MDD is the most severe among the depressive disorder subgroups. It has a great ratio of comorbidity with other psychiatric diseases<sup>12</sup>. In a comorbidity study, prevalence of MDD with anxiety disorders was found to be 56,8%<sup>13</sup>. Epidemiological data show that 59,0% of individuals with GAD also carry criteria of MDD<sup>14</sup>. Comorbid MDD-GAD is the most prevalent form of comorbidity which includes depression and anxiety<sup>15</sup>. MDD and GAD comorbidity is an important clinical problem among individuals receiving psychiatric treatment. When compared with patients with only MDD, patients with MDD and GAD comorbidity; They were found to show worse prognosis<sup>16</sup>, more severe clinical symptoms<sup>15,16</sup>, earlier age of onset<sup>15</sup>, higher relapse<sup>17</sup>, higher risk of suicide<sup>18</sup> and lower quality of life<sup>19</sup>.

Pittsburgh Sleep Quality Index (PSQI) which indicates presence of problems with sleeping is widely used in studies conducted all over the world<sup>20</sup>. Most of the current comorbidity studies on sleep quality have focused on the comorbidity of physical diseases such as cerebrovascular diseases, cancer with anxiety and depression rather than comorbidity with psychiatric disorders<sup>21</sup>. As we know, sleep quality in MDD-GAD comorbidity has not been investigated in any study conducted in clinical settings in our country. In addition to determining the relationship between anxiety and depression levels with sleep quality, with this study we conducted to determine similarities and differences between the comorbid MDD and GAD patient group and healthy control group in terms of sleep quality. Better understanding of sleep-related clinical symptoms, which is one of the basic criteria to be considered in GAD and MDD; by contributing to the improvement of patients' compliance with treatment, daytime performance and general functionality will also contribute to the improvement of prognosis and treatment outcomes.

# **MATERIALS and METHODS**

### Ethics committee approval

Ethics committee approval of the study was obtained from Alanya Alaaddin Keykubat University Faculty of Medicine Clinical Research Ethics Committee with the decision number 02-05, dated 27.01.2021.

# Sample and Study Design

The cross-sectional study was conducted between 01.02.2021 and 01.03.2021at the Alanya Alaaddin Keykubat University (ALKU) Training and Research Hospital (TRH). Patients who were applied to the psychiatry outpatient clinic of ALKU TRH and who were diagnosed with MDD and GAD according to DSM-V diagnostic criteria and who did not have any other primary axis psychiatric disorder, additionally who could answer the research questions and continue the interview with no mental impairment or organic brain disease and who gave written consent to participate in the study were included in the study.

Individuals who applied to ALKU TRH health board within the same dates, between the ages of 18-65, who were not found to have any physical disease in the health board examination, who did not have a psychiatric disease according to DSM-V diagnostic criteria, and who did not have organic brain disease or mental retardation formed the healthy control group. The sample of the study consisted of 31 GAD-MDD patients and 30 healthy controls, a total of 61 volunteers.

After the approval of the ethics committee, volunteer participants who applied to Alanya Alaaddin Keykubat University Training and Research Hospital psychiatry outpatient clinic and health board and met the conditions for participation in the study constituted the sample of the study. Participants were informed about the study, their informed consents were obtained in writing, and the Sociodemographic Data Form, Pittsburgh Sleep Quality Index, Beck

MDD is the most severe among the depressive disorder subgroups. Anxiety Inventory and Beck Depression Inventory were administered.

#### **Data Collection Tools**

found to be  $56,8\%^{13}$ . Epidemiological data show that 59,0% of Sociodemographic Data Form, Pittsburgh Sleep Quality Index individuals with GAD also carry criteria of MDD<sup>14</sup>. Comorbid (PSQI), Beck Anxiety Inventory (BAI), and Beck Depression MDD-GAD is the most prevalent form of comorbidity which includes Inventory (BDI) were used to collect data in the study.

1. Sociodemographic Data Form: It is a form that is prepared by researchers for obtaining information: Age, gender, marital status, ... etc.

2. Pittsburgh Sleep Quality Index (PSQI): In this study, the Pittsburgh Sleep Quality Index (PSQI), which is a self-report scale, was used to evaluate sleep quality. The scale developed by Buysse<sup>20</sup> and adapted in Turkish by Ağargün<sup>22</sup>; it consists of seven components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping pills, and daytime dysfunction. The index consists of open-ended questions (When did you go to bed frequently in the evening during the last month?) And multiple choice questions (How was your sleep quality often during the last month? Very good, quite good, quite bad, very bad). Each of the multiple choice questions is scored between 0 and 3 by the individuals. Although the PSQI consists of 24 items, it is calculated over 19 items. The total PSOI score is obtained with the sum of the seven component scores. The total score ranges from 0 to 21, and those who score above 5 are considered to have "poor sleep quality", and those who score 5 and below are considered to have "good sleep quality".

3. Beck Depression Inventory (BDI): It is a self-report scale consisting of 21 categories and scored between 0 and 3 to evaluate the severity of depression. It was developed by Beck<sup>23</sup> and adapted to Turkish by Hisli<sup>24</sup>. The score that can be obtained from the scale varies between 0 and 63. The higher of the total score shows the greater the susceptibility to depression. When grouping the BDI scores; 0-9 points: normal, 10-16 points: mild, 17-29 points: moderate, and those who score 30 and above are considered as severe.

4. Beck Anxiety Inventory (BAI): It is a self-report scale questioning physical symptoms in situations where people are anxious and consists of 21 categories and scored between 0 and 3 to evaluate the severity of anxiety. It was developed by  $Beck^{25}$  and adapted to Turkish by Ulusoy<sup>26</sup>. The score that can be obtained from the scale varies between 0 and 63. When grouping BAI scores; 0-7 points: normal, 8-15 points: mild, 16-25 points: moderate, and those who score 26 and above are considered as severe.

## Statistical Analysis

Numerical variables with mean, standard deviation values; categorical variables are shown with numbers and percentages. Whether there was a difference between the groups in terms of categorical variables was investigated with the Chi-square test. In terms of numerical variables; To compare the variables that make up more than two independent groups; If parametric test conditions were met, one-way analysis of variance (ANOVA) was applied. In case of a statistically significant difference, post hoc tukey and tukey's b tests were performed for paired comparisons. If parametric test conditions could not be provided, Kruskal Wallis test was applied; If a statistically significant difference was found, paired comparisons were made using the Mann Whitney U test. Variables forming two independent groups; For comparison in terms of numerical variables, if parametric test conditions were met, t-test was used for independent groups, if not, the non-parametric equivalent of the test Mann Whitney U test was used. The data were evaluated with the SPSS 22,0 statistical program and the level of  $p \le 0.05$  was accepted for statistical significance<sup>27</sup>.

## RESULTS

Sociodemographic characteristics and clinical scale scores of 31 age of the Healthy Control group was  $35,17 \pm 16,63$  consisting of 15 and three-fifths were single.

Table 1. Sociodemographic characteristics and clinical scale scores of the Comorbid Major Depressive Disorder-Generalized Anxiety Disorder patient group and the Healthy Control group

		MDD-GAD Pati- ent Group N: 31		Healthy Control Group N: 30	
		N / Mean	%/SD	N / Mean	%/SD
Age		28,32	12,59	35,17	16,63
	18-24	20	64,5	14	46,7
	25-34	4	12,9	4	13,3
	35-44	3	9,7	2	6,7
	45-54	1	3,2	5	16,7
	$\geq$ 55	3	9,7	5	16,7
Gender	Female	20	64,5	15	50,0
	Male	11	35,5	15	50,0
	Married	7	22,6	11	36,7
Marital Status	Single	23	74,2	18	60,0
Status	Divorced	1	3,2	1	3,3
According to the PUKI	Good Sleep Quality	16	51,61	16	53,33
Cut-off Score Sleep Quality	Poor Sleep Quality	15	48,39	14	46,67
	Beck Depres- sion Inventory Score	18,42	5,66	2,77	2,70
Scales	Beck Anxiety Inventory Score	18,16	8,06	1,97	2,30
	Pittsburgh Sleep Quality Index (PUKI) Total Score	5,81	2,73	6,20	4,12
	PUKI 1. Item Subjective Sleep Quality Score	1,55	0,85	0,90	0,88
	PUKI 2. Item Sleep Latency Score	1,39	0,92	1,13	1,10
	PUKI 3. Item Sleep Duration Score	0,29	0,74	1,13	1,25
	PUKI 4. Item Habitual Sleep Efficiency Score	0,13	0,56	0,77	1,28
	PUKI 5. Item Sleep Distur- bances Score	1,48	0,51	1,40	0,56
	PUKI 6. Item Use of sleeping pills Score	0,13	0,56	0,00	0,00
	PUKI 7. Item Daytime Dysfunction Score	0,84	0,97	0,87	0,73

MDD: Major Depressive Disorder, GAD: Generalized Anxiety Disorder, N: Number of Samples, SD: Standard Deviation, PUKI: Pittsburgh Sleep Quality Index

The mean of the Beck Depression Inventory points of the comorbid MDD-GAD patient group was  $18,42 \pm 5,66$  and the mean of Beck Anxiety Inventory points was  $18,16 \pm 8,06$ . The mean of the Comorbid MDD-GAD patients and 30 Healthy Controls are shown in Beck Depression Inventory points of the healthy control group was Table 1. The mean age of MDD-GAD patient group was  $28,32 \pm 2,77 \pm 2,70$  and the mean of the Beck Anxiety Inventory points was 12,59 consisting of 20 women and 11 men, while two-thirds were  $1.97 \pm 2.30$ . The mean of PSQI total score was  $5.81 \pm 2.73$  in the between the ages of 18-24 and three-quarters were single. The mean MDD-GAD group, while it was  $6,20 \pm 4,12$  in the Healthy Control group. While poor sleep quality was determined in 48,39% of the women and 15 men, half of the group was between the ages of 18-24 MDD-GAD group, this rate was 46.67% in the healthy control group (Table 1).

> The comparison of comorbid MDD-GAD patient group and healthy control group in terms of age, gender, marital status and good or poor sleep quality is shown in Table 2. No statistically significant difference was found between the two groups in terms of age (p = 0.076), gender (p = 0.252), marital status (p = 0.476), and good or poor sleep quality (p = 0.893).

> The comparison of comorbid MDD-GAD patient group and healthy control group in terms of PSQI is shown in Table 3. Higher scores indicate a greater susceptibility to the presence of a sleeping problem in the area concerned. In terms of PUKI total score, no statistically significant difference was found between the comorbid MDD-GAD patient group and healthy control group (p = 0.663). While Healthy Control group compared to comorbid MDD-GAD group, Pittsburgh Sleep Quality Index Subjective sleep quality subtest was found on average 0,648 points lower (p = 0,005); and the Sleep duration subtest was 0,843 points higher (p = 0,003) and the Habitual sleep efficiency subtest was 0,638 points higher (p = 0,016). No statistically significant difference was found between the two groups in the subtests of Sleep latency (p = 0,333), Sleep disturbances (p = 0.543), Use of sleeping pills (p = 0.211), and Daytime dysfunction (p = 0.899).

> The comparison of patients with good and poor sleep quality in the comorbid MDD-GAD group, in terms of Beck Depression Inventory and Beck Anxiety Inventory scores is shown in Table 4. According to the PSOI cut-off score; those who score 5 and below are considered to have good sleep quality, and those who score above 5 are considered to have poor sleep quality. Patients with poor sleep quality scored an average of 4,096 points higher on the Beck Depression Inventory scores compared to patients with a good sleep quality (p = 0.042). No statistically significant difference was found between the two groups in terms of Beck Anxiety Inventory scores (p = 0.945).

> The correlation of PSQI scores with BAI and BDI scores in the comorbid MDD-GAD patient group is shown in Table 5. Depression scores showed a positive correlation of at a level of 42,5% with the PUKI Sleep Disturbances subtest (r = ,425, p = 0,017) and a positive correlation with Daytime Dysfunction subtest at a level of 47,4% (r = .474, p = 0.007). There was no correlation found between BDI scores and PSQI total score (p = 0,156), and Subjective sleep quality (p = 0,298), Sleep latency (p = 0,606), Sleep duration (p = 0,773), Habitual sleep efficiency (p = 0,837), and Use of sleeping pills (p = 0.809) subtests.

> There was no correlation found between Beck Anxiety Inventory scores and PSQI total score (p = 0,605) and Subjective sleep quality (p = 0.861), Sleep latency (p = 0.925), Sleep duration (p = 0.778), Habitual sleep efficiency (p = 0.980), Sleep disturbances (p = 0.114), Use of sleeping pills (p = 0.228), and Daytime dysfunction (p = 0.668) subtests (Table 5).

## DISCUSSION

As we know, sleep quality in MDD-GAD comorbidity has not been investigated in any study conducted in clinical settings in our country. In addition to determining the relationship between anxiety and depression levels with sleep quality, with this study we conducted

to determine similarities and differences between the comorbid MDD scores of patients with poor sleep quality were found to be higher than and GAD patient group and healthy control group in terms of sleep patients with good sleep quality. However there was no difference quality. Two groups were compared with the PSQI which indicates the found between these two groups in terms of anxiety scores. This presence of sleep related problems by evaluating subjective sleep finding may indicate that depression may be more related to sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep quality than anxiety. When the correlation between sleep quality disturbances, use of sleeping pills and daytime dysfunction. Although patients with comorbid MDD-GAD had higher sleep duration and Depression scores were found to be related with Sleep Disturbances sleep efficiency compared to healthy controls, they perceived their subjective sleep quality worse than healthy controls. Cognitive distortions seen in major depression may be one of the factors affecting this condition. When the patients were divided into two groups in terms of sleep quality by the PSQI cut-off score: Depression depression may be more related to sleep quality rather than anxiety.

components and anxiety and depression levels was evaluated: and Daytime Dysfunction, which are components of sleep quality. As depression scores increase, related sleep problems also increase. On the other hand, no relationship was found between anxiety scores and sleep quality components. This result also supports our view that

Table 2. Comparison of Comorbid Major Depressive Disorder-Generalized Anxiety Disorder patient group and Healthy Control group in terms of Age, Gender, Marital Status and Sleep Quality

		MDD- GAD N: 31 Mean	HC N: 30 SD	Total / Difference of Means	Pearson Chi - Square Value / t Value	р
	Female	20	15	35		
Gender	Male	11	15	26	1,314	0,252ª
Gender	Total	31	30	61		
	Married	7	11	18		
Marital	Single	23	18	41	1,483	0,476 <sup>a</sup>
Status	Divorced	1	1	2	1,465	
Status	Total	31	30	61		
	Good Sleep Quality	16	16	32		
Sleep Quality	Poor Sleep Quality	15	14	29	0,018	0,893ª
	Total	31	30	61		
Age	18-24	20	14	34	1.0.00	0.1.(1)
	25 or above	11	16	8	1,969	0,161 <sup>a</sup>
2 Groups	Total	31	30	61		
Age		28,32	12,59	6,844	1,807	0,076 <sup>b</sup>
		35,17	16,63	0,044	1,007	0,076

MDD: Major Depressive Disorder, HC: Healthy Controls, GAD: Generalized Anxiety Disorder, N: Number of Samples, SD: Standard Deviation, PUKI: Pittsburgh Sleep Quality Index, Pa: Statistical significance for Pearson Chi-Square test,  $p \le 0.05$ , pb: Statistical significance for independent groups t-test,  $p \le 0.05$ 

Table 3. Comparison of Comorbid Major Depressive Disorder-Generalized Anxiety Disorder patient group and Healthy Control group in terms of Pittsburgh Sleep Quality Index

Scales	HC &	N Mean SD		SD p	Diff. of Means	95% CI		
Scales	a MDD-GAD	IN	Mean	5D	р	Wieans	Lower	Upper
BDI	HC	30	2,77	2,700	< 0,001	15 (52	17.021	12 274
Score	MDD-GAD	31	18,42	5,661	< 0,001	-15,653	-17,931	-13,374
BAI	HC	30	1,97	2,297	< 0,001	16 105	-19,257	-13,133
Score	MDD-GAD	31	18,16	8,067		-16,195		
PUKI 1. Item	HC	30	,90	,885	0.005	(10	-1,093	-,204
Score	MDD-GAD	31	1,55	,850	0,005	-,648		
PUKI 2. Item	HC	30	1,13	1,106	0,333	-,254	-,774	,267
Score	MDD-GAD	31	1,39	,919		-,234	-,//4	,207
PUKI 3. Item Score	HC	30	1,13	1,252	0,003	,843	,311	1,375
	MDD-GAD	31	,29	,739	0,005	,045		
PUKI 4. Item Score	HC	30	,77	1,278	0,016	,638	,124	1,152
	MDD-GAD	31	,13	,562	0,010	,050	,124	
PUKI 5. Item Score	HC	30	1,40	,563	0,543	-,084	-,358	,191
	MDD-GAD	31	1,48	,508	0,010	,001	,500	,-/1
PUKI 6. Item Score	HC	30	,00	,000	0,211	-,129	-,335	,077
	MDD-GAD	31	,13	,562	- )		)	,
PUKI 7. Item Score	HC	30	,87	,730	0,899	,028	-,413	,469
	MDD-GAD	31	,84	,969			, ·	,
PUKI Total Score	HC	30	6,20	4,122	0,663	,394	-1,412	2,199
	MDD-GAD	31	5,81	2,738			,	,

HC: Healthy Controls, MDD: Major Depressive Disorder, HC: Healthy Controls, GAD: Generalized Anxiety Disorder, N: Number of Samples, SD: Standard Deviation, Diff: Difference, CI: Confidence Interval, PUKI: Pittsburgh Sleep Quality Index, P<sup>a</sup>: Statistical significance for Pearson Chi-Square test, p ≤ 0,05, p<sup>b</sup>: Statistical significance for independent groups t-test,  $p \le 0.05$ 

 Table 4. Comparison of patients with Good Sleep Quality and patients with Poor Sleep Quality in the Comorbid Major Depressive

 Disorder-Generalized Anxiety Disorder group, in terms of Beck Depression Inventory and Beck Anxiety Inventory scores

								%95 CI	
	Sleep Quality Group	Ν	Mean	SD	t Value	р	Diff. of Means	Lower	Upper
Beck Depression Inventory Score	Good Sleep Quality	16	16,44	4,75	-2,128	0,042	-4,096	-8,032	-0,159
	Poor Sleep Quality	15	20,53	5,94					
Beck Anxiety Inventory Score	Good Sleep Quality	16	18,06	9,34	-0,069	0,945	-0,204	-6,235	5,826
	Poor Sleep Quality	15	18,34	6,77					

N: Number of Sample, SD: Standard Deviation, Diff: Difference, CI: Confidence Interval, p: Statistical significance for independent groups t-test, p ≤ 0.05

**Table 5.** Correlation of Pittsburgh Sleep Quality Index Scores of Patients in the Comorbid Major Depressive Disorder -Generalized Anxiety Disorder group with Beck Depression Inventory and Beck Anxiety Inventory Scores

	Beck Depression Inventory Score		Beck Anxiety Inventory Score	
	r	р	r	р
PUKI 1. Item				
Subjective Sleep Quality Score	,193	,298	-,033	,861
PUKI 2. Item				
Sleep Latency Score	-,096	,606	-,018	,925
PUKI 3. Item				
Sleep Duration Score	-,054	,773	-,053	,778
PUKI 4. Item				
Habitual Sleep Efficiency Score	-,039	,837	-,005	,980
PUKI 5. Item				
Sleep Disturbances Score	,425	,017	,289	,114
PUKI 6. Item				
Use of sleeping pills Score	,045	,809	,223	,228
PUKI 7. Item				
Daytime Dysfunction Score	,474	,007	,080	,668
Pittsburgh Sleep Quality				
Index (PUKI) Total Score	,261	,156	,097	,605

PUKI: Pittsburgh Sleep Quality Index, r: Pearson correlation coefficient, p: Statistical significance for Pearson correlation test,  $p \le 0.05$ 

In the study patients with comorbid MDD-GAD, higher sleep duration and sleep efficiency were determined compared to healthy controls. Although it has individual characteristics, it is stated that the most appropriate sleep duration should be between 7 and 9 hours for a young adult and between 7 and 8 hours for an older adult<sup>28</sup>. Studies in the literature found inconsistent results related to sleep duration and sleep quality. In some studies, lower sleep duration was found in MDD-GAD patients compared to healthy controls<sup>5,29,30</sup>. On the other hand, in a study comparing the usual sleep duration, similar sleep duration was found between the group complaining of insomnia and using sleeping pills with the group consisting of those without sleep problems<sup>31</sup>. In another study, it was found that individuals with low sleep quality also had sufficient sleep duration<sup>32</sup>. Our study shows that evaluating only sleep duration does not seem sufficient in determining the sleep related problems of the patients. Evaluating both sleep duration and sleep quality together will contribute more to determine the sleep related problems of MDD-GAD patients.

Major Depression patients show negative cognition and are extremely concerned and sensitive to their own body. Therefore, the negative perceptions of the patients about their sleep may cause the symptoms to become worse. Cognitive distortions refer to seeing and interpreting events in an unrealistic way different from what they actually are, stemming from the individual's basic beliefs. These erroneous thoughts have become so involved in daily life that these thoughts which can be very difficult to notice can cause mental disorders. In the study MDD-GAD patients perceived their subjective sleep quality worse than healthy controls. In the treatment of Major Depression, in addition to biological treatments, cognitive behavioral therapy can help patients perceive their subjective sleep quality better by changing their erroneous cognition.

In studies evaluating sleep objectively with polysomnography, there is inconsistent evidence of decreased sleep efficiency in patients with GAD. In most studies, no significant difference was found between patients with Generalized Anxiety Disorder and healthy

controls in terms of sleep efficiency<sup>33,34</sup>. However in studies morning, going to the toilet by interrupting sleep, not being able to evaluating sleep subjectively with clinical scales, such as the Pittsburgh Sleep Quality Index: When compared with healthy controls, worse subjective sleep quality was found in adults with GAD, consistent with our findings<sup>35</sup>. In studies evaluating the sleep quality of the same patient group both objectively and subjectively, inconsistencies were found between objective and subjective sleep findings<sup>5</sup>. Combined with the results in the literature, our results show the importance of subjective assessment of patients' sleep quality as well as objective assessments.

In the study, depression scores of patients with poor sleep quality in the comorbid MDD-GAD group were found to be higher compared to patients with good sleep quality. On the other hand no significant difference was found between two groups in terms of anxiety scores. Almost half of the patients with MDD cannot be cured with current treatments<sup>8</sup>. This disappointing aspect of depression treatment may also be due to difficulties in recognizing depressive disorders early. The time interval between the onset of the first symptoms of depression and the initiation of treatment is quite long. It was found that the period between the onset of the first symptoms of depression and the beginning of benefiting from treatment was more than 3 years in approximately one quarter of the patients, in the study by Dietrich. In the same study it was detected that only one third of the patients received treatment within three months immediately after the onset of the first symptoms of depression<sup>36</sup>. In the study conducted by Sun, sleep related abnormalities were identified as the first symptom that prompted many depressive patients to seek help<sup>37</sup>. The detection of sleep related abnormalities can play a stimulating role for clinicians in many areas, including the risk of developing depression and implementing preventive therapy. In addition, symptoms of ongoing sleep disorders in a patient in remission may also predict recurrence of the disease<sup>5,38</sup>

In the MDD-GAD patient group the relationship was determined between Sleep disturbances and Daytime Dysfunction which are the sleep quality components of PSOI and depression scores. As depression scores increase, related sleep problems also increase. On the other hand no relationship was found between sleep quality components and anxiety scores. The relationship between depression and sleep which is an important regulator of circadian systems and a supporter of homeostasis and environmental adaptation has been well established in studies<sup>39,40</sup>. Sleep problems and the resulting inability to synchronize with the outside world (chrono disruption) can change the basic properties of the brain systems that regulate neuroendocrine, immune and autonomic functions. These changes also play a very important role in the development of stress-related disorders through impaired homeostatic balance<sup>41,42</sup>.

Consistent with our results, Daytime dysfunction which is one of the important components of sleep quality was also found to be related with major depression in the study conducted by Sun<sup>37</sup>. Daytime dysfunction is directly related to a lack of willingness to do something, which is one of the main symptoms of depression. In the study by Huang, it was detected that depressed mothers in the early postpartum period showed more daytime dysfunction than non-depressive mothers<sup>43</sup>. In the study conducted by Ji, Daytime dysfunction was found to be related with changes in depressive symptoms rather than changes in nighttime sleep in patients with comorbid major depression and primary sleep disorder<sup>44</sup>. In a study conducted in the geriatric age group, it was found that geriatric depression scale scores were perfectly associated with daytime dysfunction<sup>45</sup>. In our study, the component of Sleep Quality most associated with Depression scores was found to be Daytime dysfunction.

Sleep disturbances which is an important component of sleep quality include waking up in the middle of the night or early in the

breathe comfortably during sleep, feeling extremely cold or extremely hot, having bad dreams, feeling pain, coughing, and snoring loudly in the sleep<sup>20</sup>. Sleep disturbances was found to be another sleep quality component associated with depression scores in our study. Other studies have also found that sleep disturbances were associated with depression<sup>5,29,30</sup>. In our study no relationship was found between sleep latency and use of sleeping pills which are the other components of the PSOI and levels of depression and anxiety. There are studies in the literature showing that sleep latency<sup>5,29,30</sup> and use of sleeping pills<sup>46</sup> are associated with depression. The fact that our study was conducted with a small sample may be one of the factors in not determining the relationship in these areas.

This study has some limitations: This study was conducted with a small sample, in a single center. The findings were obtained with self-report scales, not objective sleep measurements such as Polysomnography. Information on comorbid physical diseases such as asthma, heart diseases that may affect the sleep quality results of the participants is not included. Since there are not many studies investigating the sleep quality in Comorbid MDD-GAD in the literature, the findings obtained in our study were compared with studies in which patient groups were studied separately rather than studies involving comorbid MDD-GAD patients. Finally as in all cross-sectional studies, a causal relationship could not be established.

## Conclusion

In our study, although patients with comorbid MDD-GAD had higher sleep duration and sleep efficiency compared to healthy controls, they perceived their subjective sleep quality worse than healthy controls. This result shows that evaluating only sleep duration does not seem sufficient in determining the sleep related problems of the patients. Evaluating both sleep duration and sleep quality together will contribute more to determine the sleep related problems of MDD-GAD patients. Our study indicates that depression may be more related to sleep quality than anxiety. Problems related to sleep are shown as the first symptom that prompts many depressive patients to seek help. Detecting sleep related abnormalities can play a stimulating role for clinicians in many areas, including the risk of developing depression and implementing preventive therapy. The PSQI appears to be a very useful tool in identifying sleep related problems and can be very helpful to clinicians. Our findings reveal the importance of controlling individuals with sleep problems, especially in terms of depressive symptoms. Arranging treatment for sleep problems in addition to standard treatment will contribute to increase the effectiveness of psychiatric treatment.

## **Conflict of interest**

All authors declare that they have no financial interests or personal conflicts that could affect the work reported in this article.

# REFERENCES

- Öztürk O. Uyku Bozuklukları, Ruh Sağlığı ve Bozuklukları, 9. Baskı, Ankara: Nobel Tıp Kitabevleri, p. 479-488; 2002.
- Hammond EC. Some Preliminary Findings on Physical Complaints from a Prospective Study of 1,064,004 Men and Women. Am J Public Health Nations Health. 1964;54:11-23.
- Ford DE, Kamerow DB. Epidemiologic study of sleep disturbances and psychiatric disorders. An opportunity for prevention? JAMA. 1989;262 (11):1479-84.
- 4 Seow LSE, Tan XW, Chong SA, Vaingankar JA, Abdin E, Shafie S, et al. Independent and combined associations of sleep duration and sleep quality with common physical and mental disorders: Results from a multi -ethnic population-based study. PLoS ONE. 2020;15(7):e0235816. doi.org/10.1371/journal.pone.0235816.

- Salah AB, Nakajima M, N DeAngelis B, al'Absi M. Effects of tobacco 27. addiction on links between early life adversities, sleep disturbance, and depression: A moderated mediation approach, *Preventive Medicine* 28. *Reports*. 2020;20:101225. doi.org/10.1016/j.pmedr.2020.101225.
- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Washington DC: American Psychiatric Publishing; 2013.
- Potvin O, Lorraine D, Belleville G, Grenier S, and Préville M. Subjective sleep characteristics associated with anxiety and depression in older adults: a population-based study, *Int J Geriatr Psychiatry*. 2014;29:1262-1270.
- Guilbert JJ. The world health report 2002 reducing risks, promoting healthy life. *Educ Health*. 2003; 16(2):230.
- Bélanger L, Morin CM, Langlois F, Ladouceur R. Insomnia and generalized anxiety disorder. J. Anxiety Disord. 2004;18(4):561-571.
- Berger A, Dukes E, Wittchen HU, Morlock R, Edelsberg J, Oster G, et al. Patterns of healthcare utilization in patients with generalized anxiety disorder in general practice in Germany. *European Journal of Psychiatry* 2009;23:90-100.
- Neckelmann D, Mykletun A, Dahl AA. Chronic insomnia as a risk factor 33. for developing anxiety and depression. *Sleep*. 2007;30(7):873-880.
- Gao K, Wang Z, Chen J, Kemp DE, Chan PK, Conroy CM, et al. Should an assessment of Axis I comorbidity be included in the initial diagnostic 34. assessment of mood disorders? Role of QIDS-16-SR total score in predicting number of Axis I comorbidity. *J Affect Disord*. 2013;148:256-264.
- Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, et al. The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). Jama. 2003;289:3095-3105.
- 14. Carter RM, Wittchen HU, Pfister H, Kessler RC. One-year prevalence of subthreshold and threshold DSM-IV generalized anxiety disorder in a nationally representative sample. *Depress A nxiety*. 2001;13:78-88.
- Lamers F, van Oppen P, Comijs HC, Smit JH, Spinhoven P, van Balkom AJ, et al. Comorbidity patterns of anxiety and depressive disorders in a large cohort study: the Netherlands Study of Depression and Anxiety 38. (NESDA). J Clin Psychiatry. 2011;72:341-348.
- Hofmeijer-Sevink MK, Batelaan NM, van Megen HJ, Penninx BW, Cath DC, van den Hout MA, et al. Clinical relevance of comorbidity in anxiety disorders: a report from the Netherlands Study of Depression and Anxiety 39. (NESDA). *J Affect Disord*. 2012;137:106-112.
- 17. Cyranowski JM, Schott LL, Kravitz HM, Brown C, Thurston RC, Joffe H, et al. Psychosocial features associated with lifetime comorbidity of 40. major depression and anxiety disorders among a community sample of mid-life women: the SWAN mental health study. *Depress Anxiety*. 2012;29:1050-1057. 41.
- Nock MK, Hwang I, Sampson NA, Kessler RC. Mental disorders, comorbidity and suicidal behavior: results from the National Comorbidity 42. Survey Replication. *Mol Psychiatry*. 2010;15:868-876.
- D'Avanzato C, Martinez J, Attiullah N, Friedman M, Toba C, Boerescu DA, et al. Anxiety symptoms among remitted depressed outpatients: prevalence and association with quality of life and psychosocial functioning. *J Affect Disord*. 2013;151:401-404.
- Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The 44. Pittsburgh sleep quality index: a new instrument for psychiatric practice and research. *Psychiatry Res.* 1989;28(2):193-213.
- Hsu MF, Lee KY, Lin TC, Liu WT, Ho SC. Subjective sleep quality and association with depression syndrome, chronic diseases and health-related 45. physical fitness in the middle-aged and elderly. BMC Public Health. 2021 Jan 19;21(1):164. doi: 10.1186/s12889-021-10206-z.
- Ağargün MY, Kara H, Anlar Ö. Pittsburgh The Validity and Reliability 46. of the Pittsburgh Sleep Quality Index. *Türk Psikiyatri Dergisi* 1996;7:107 -15.
- Beck AT, Ward C, Mendelson M, Mock J, Erbaugh J. Beck depression inventory (BDI). Arch Gen Psychiatry. 1961;4(6):561-71.
- Hisli N. Beck Depresyon Envanterinin üniversite öğrencileri için geçerliliği, güvenilirliği. J Psychol. 1989;7:3-13.
- Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol. 1988;56(6):893.
- 26. Ulusoy M, Sahin NH, Erkmen H. The Beck anxiety inventory: psychometric properties. *J Cogn Psychother*. 1998;12(2):163-72.

- Corp I. IBM SPSS statistics for windows, version 22.0. Armonk, NY: IBM Corp. 2013.
- Hirshkowitz M, Whiton K, Albert SM, Alessi C, Bruni O, DonCarlos L, et al. National Sleep Foundation's sleep time duration recommendations: methodology and results summary. *Sleep Health.* 2015;1(1):40-3. doi.org/10.1016/j.sleh.2014.12.010.
- Liu Y, Peng T, Zhang S, Tang K. The relationship between depression, daytime napping, daytime dysfunction, and snoring in 0.5 million Chinese populations: exploring the effects of socio-economic status and age. *BMC Public Health*. 2018;18(1):759.
- Benca RM, Peterson MJ. Insomnia and depression. Sleep Med. 2008;9 (Suppl 1):3-9.
- Kripke DF, Simons RN, Garfinkel L, Hammond EC. Short and long sleep and sleeping pills. Is increased mortality associated? *Arch Gen Psychiatry*. 1979;36(1):103-16.
- Carskadon MA, Dement WC, Mitler MM, Guilleminault C, Zarcone VP, Spiegel R, et al. Self-reports versus sleep laboratory findings in 122 drug-free subjects with complaints of chronic insomnia. *Am J Psychiatry*. 1976;133(12):1382-8.
- Lund HG, Beach P, Eplov L, Jennum P, WildSchütz G. An epidemiological study of REM latency and psychiatric disorders J. Affect. Disord. 1991;23:107-112.
- Papadimitriou GN, Kerkhofs M, Kempenaers C, Mendlewicz J. EEG sleep studies in patients with generalized anxiety disorder. *Psychiatry Res.* 1988;26:183-190.
- Brenes GA, Miller ME, Stanley MA, Williamson JD, Knudson M, McCall WV, et al. Insomnia in older adults with generalized anxiety disorder. *The American Journal of Geriatric Psychiatry*. 2009;17:465-472.
- Dietrich S, Mergl R, Rummel-Kluge C. From the first symptoms of depression to treatment. When and where are people seeking help? Does stigma play a role? *Psychiatr. Prax.* 2016;44:461-468.
- Sun Q, Tan L. Comparing primary insomnia to the insomnia occurring in major depression and general anxiety disorder. *Psychiatry Res.* 2019;282:112514. doi: 10.1016/j.psychres.2019.112514.
- Rachel M, Edinger JD, Gress JL, San Pedro-Salcedo MG, Kuo TF, Tasha K, et al. Cognitive behavioral therapy for insomnia enhances depression outcome in patients with comorbid major depressive disorder and insomnia. *Sleep.* 2008;31(4):489.
- Fang H, Tu S, Sheng J, Shao A. Depression in sleep disturbance: A review on a bidirectional relationship, mechanisms and treatment. *J. Cell Mol. Med.* 2019;23(4):2324-2332.
- Deboer T. Sleep homeostasis and the circadian clock: Do the circadian pacemaker and the sleep homeostat influence each other's functioning? *Neurobiol. Sleep Circad. Rhythm.* 2018;5:68-77.
- Morris CJ, Aeschbach D, Scheer FA. Circadian system, sleep and endocrinology. *Mol. Cell. Endocrinol.* 2012;349(1):91-104.
- Wulff K, Gatti S, Wettstein JG, Foster RG. Sleep and circadian rhythm disruption in psychiatric and neurodegenerative disease. Nat. *Rev. Neurosci.* 2010;11(8):589-599.
- Huang C, Carter PA, Guo JL. A comparison of sleep and daytime sleepiness in depressed and non-depressed mothers during the early postpartum period. J. Nurs. Res. 2004;12(4):287-296.
  - Ji XW, Ng SM, Chan CLW, Chan JSM, Chan CHY, Chung KF, et al. Integrative body-mind-spirit intervention for concurrent sleep and mood disturbances: sleep-specific daytime functioning mediates sleep and mood improvements. J. Sleep Res. 2018;27(1):56-63.
- Yu J, Rawtaer I, Fam J, Jiang MJ, Feng L, Kua EH, et al. Sleep correlates of depression and anxiety in an elderly Asian population. *Psychogeriatrics* 2016;16(3):191-195.
- Greenfield EA, Lee C, Friedman EL, Springer KW. Childhood abuse as a risk factor for sleep problems in adulthood: evidence from a U.S. national study. *Ann. Behav. Med.* 2011;42(2):245-256.