# Association of Insomnia with Anxiety and Depression in Type 2 Diabetic Patients: A Cross-Sectional Study

Karlyghash Shinalieva, PhD candidate; Asemgul Kasenova, PhD; Zauresh Akhmetzhanova, MSc; Dinara Alzhanova, PhD candidate; Laura Eszhanova, PhD candidate; Ainur Bekenova, PhD candidate

Department of Neurology, National Joint Stock Company, Medical University Astana, Astana, Kazakhstan

#### Correspondence:

Karlyghash Shinalieva, PhD candidate; Medical Center Senim, Department of Neurology, National Joint Stock Company, Medical UniversityAstana, No. 28, MangilikYel Ave., Postal code: 010000, Astana, Kazakhstan **Email:** shinalievak@mail.ru Received: 06 July 2022 Revised: 04 October 2022 Accepted: 11 November 2022

#### What's Known

• Insomnia is a common problem in patients with type 2 diabetes mellitus (T2DM).

• In these patients, there is a direct causal relationship between insomnia and poor carbohydrate control, quality of life, anxiety, and depression.

#### What's New

• The severity of insomnia is associated with an increased risk of anxiety and depression symptoms.

• Patients with T2DM exhibiting signs of anxiety and depression should be assessed for sleep disorders and vice versa.

#### Abstract

**Background:** Type 2 diabetes mellitus (T2DM) is associated with sleep disorders, which in turn may lead to anxiety and depression. Sleep deprivation impairs glucose metabolism causing a decrease in insulin sensitivity and glucose tolerance. The present study aimed to determine the association of insomnia with anxiety and depression in patients with T2DM.

Methods: A cross-sectional study was conducted in 2020 at the Endocrinological Department of City Clinical Hospital №1, affiliated with Astana Medical University (Astana, Kazakhstan). A total of 376 patients with decompensated T2DM were included in the study. Insomnia was assessed using the Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI). Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS). Multivariable logistic regression was used to assess the association of insomnia with anxiety and depression.

**Results:** All patients showed signs of sleep disturbances. Based on the HADS cutoff score >8, anxiety and depression were observed in 48 (12.80%) and 46 (12.20%) patients, respectively. PSQI, ISI, and HADS indicators were associated with an increased risk of anxiety and depression symptoms. In terms of anxiety, the adjusted odds ratio for PSQI and ISI scores were 1.09 (P=0.08) and 1.07 (P=0.01), respectively. These for depression were 1.10 (P=0.06) and 1.07 (P=0.01), respectively.

**Conclusion:** Sleep quality is an important indicator of psychological health in patients with T2DM, especially those who exhibit signs of anxiety and depression.

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**Keywords** • Anxiety • Depression • Sleep disorders • Type 2 diabetes mellitus

#### Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disease characterized by insulin resistance.<sup>1</sup> According to the International Diabetes Federation, half a billion people worldwide have diabetes, and the number is projected to increase by 25% and 51% by 2030 and 2045, respectively.<sup>2</sup>

Poor glycemic control can lead to major complications. To control blood glucose levels and avoid complications, patients with T2DM must adhere to a certain diet throughout their lives,

Copyright: ©Iranian Journal of Medical Sciences. This is an open-access article distributed under the terms of the Creative Commons Attribution-NoDerivatives 4.0 International License. This license allows reusers to copy and distribute the material in any medium or format in unadapted form only, and only so long as attribution is given to the creator. The license allows for commercial use. maintain physical activity, take medications, and regularly monitor their blood glucose levels. These in turn may lead to chronic stress and emotional problems such as anxiety, fear, and poor sleep quality.<sup>3</sup> Sleep disturbance is very common in people with T2DM, 30-50% of whom have poor sleep quality.<sup>4</sup> Sleep disturbance can lead to blood glucose dysregulation and reduced diabetes-related quality of life (QoL) irrespective of the age of onset, disease duration, number of comorbidities, number of complications, insulin use, and signs of depression.<sup>5, 6</sup>

Insomnia is characterized by difficulty in initiating and/or maintaining sleep, waking up too early followed by inability to fall back asleep, and disruption of daytime activities due to drowsiness; provided that sleep disturbances are not associated with the lack of opportunities or conditions for normal sleep.7 This condition becomes chronic if the symptoms are present at least three times a week for at least three months.8 Insomnia is associated with an increased risk of psychiatric disorders.9 Studies suggest common biological pathways in the development of T2DM and depression/ anxiety. Anxiety activates the autonomic and hypothalamic-pituitary-adrenal (HPA) axis and induces immuno-inflammatory dysregulation.10 It is also known that the hypothalamus regulates the sleep-wake cycle.

Anxiety is one of the most common comorbidities in people with T2DM.<sup>11</sup> Diabetic patients with comorbid anxiety were shown to be prone to increased complications, blood glucose dysregulation, and poor adherence to treatment.<sup>12</sup> Depression is common in people with T2DM, and its prevalence is approximately two times higher than in the normal population.<sup>13</sup> According to the Diagnostic and Statistical Manual of Mental Disorders (fifth edition), the main symptoms of a major depressive episode are sadness and/or anhedonia with additional symptoms such as pessimistic thinking, suicidal tendencies, and changes in energy, appetite, and sleep patterns.<sup>14</sup> These symptoms may occur individually or in combination and are associated with an unfavorable clinical profile such as poorer glycemic control, dietary habits, and adherence to physical activity.15

Current evidence suggests that emotional disorders and sleep disturbances often occur concurrently. For example, individuals with insomnia are at a higher risk of mental disorders, especially depression.<sup>16</sup> It was reported that persistent sleep disturbance may increase the risk of recurrent depression. Moreover, insomnia is known to be a significant risk factor for suicide.<sup>17</sup> Furthermore, poor sleep quality

combined with anxiety may negatively affect the QoL of people with T2DM. It is estimated that 29% of the decline in QoL in these people is related to the interaction between poor sleep quality and anxiety symptoms.

Despite the high prevalence of anxiety, depression, and sleep disturbances in people with T2DM, studies examining the association between these conditions are scarce. Such information will allow timely diagnosis and treatment of emotional disorders and sleep disturbances in these patients, which in turn improves their QoL.<sup>18, 19</sup> Hence, the present study aimed to examine a potential mediating effect of insomnia on the relationship between pathological personality traits and the severity of depression in patients with T2DM.

# Patients and Methods

А cross-sectional study was conducted between September and October 2020 at the Endocrinological Department of City Clinical Hospital №1, affiliated with Astana Medical University (Astana, Republic of Kazakhstan). The target population was patients living in Astana with confirmed clinical and laboratory diagnoses of T2DM. Based on statistical power analysis, a sample size of 384 participants was calculated (error margin of 5% with a 95% confidence interval). The inclusion criteria were disease duration for at least one year as confirmed by an endocrinologist and hemoglobin glycation index (HbA1C) ≥6.5%. The exclusion criteria were the presence of severe or unstable concomitant somatic pathology, a history of stroke or transient ischemic attack, craniocerebral trauma, central nervous system tumors or disease (inflammatory, degenerative, epilepsy, cerebral palsy), severe psychiatric disorders, dementia, alcoholism, or drug addiction. We did not exclude participants based on sex, nationality, or ethnicity. Accordingly, 384 patients were enrolled in the study, of which eight were subsequently excluded due to untreated sleep apnea, score >4 on the STOP-Bang questionnaire (snoring, tiredness, observed apnea, blood pressure, body mass index (BMI), age, neck size, sex), or inability to participate due to cognitive impairment. All included patients were in a state of decompensation based on the level of carbohydrate control.

The study was approved by the Ethics Committee of Astana Medical University (code number 3, dated 16 January 2020). Written informed consent was obtained from all participants.

## Instruments

Based on the American Academy of Sleep Medicine (AASM) clinical practice guidelines,<sup>19</sup> three questionnaires were used to determine insomnia, namely the Pittsburgh sleep quality index (PSQI), Insomnia severity index (ISI), and Hospital anxiety and depression scale (HADS). These questionnaires were filled out during the interviews with the help of the first author.

# Pittsburgh Sleep Quality Index

The 19-item self-rated PSQI evaluates overall sleep quantity by assessing seven components, namely subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. The scores range from 0 to 21, where a score higher than five indicates poor quality sleep.<sup>20</sup>

The Russian version of the PSQI was developed by Semenov and colleagues, however, they did not evaluate its psychometric properties in the Russian population.<sup>21</sup> The content validity of the questionnaire was examined in our sleep laboratory using both quantitative and qualitative approaches. In the quantitative phase, the content validity ratio (CVR) and content validity index (CVI) were examined by a panel of nine experts at an interdisciplinary sleep medicine center. The expert panel included six somnologists and three neurologists. The essentiality of the PSQI items was scored based on a threepoint Likert scale (1=essential, 2=useful but not essential, and 3=not essential). Based on the Lawshe table (9 experts agreeing on which items are essential),22 items with CVR=0.90 were considered essential. Using the model purposed by Waltz and Bausell, the CVI of the questionnaire was assessed based on three criteria, namely relevancy, simplicity, and clarity.23 The relevancy of each item of the questionnaire was assessed using a four-point Likert scale (from 1=irrelevant, not simple, and not clear to 4=totally relevant, very simple, and very clear). Items with CVI>0.91 were accepted.

# Insomnia Severity Index (ISI)

The seven-item ISI assesses current sleep problems for the preceding two weeks. Each item of the questionnaire is scored based on a five-point Likert scale. A total score of 0-7 indicates normal, 8-14 indicates mild insomnia, 15-21 indicates moderate insomnia, and 22-28 indicates severe insomnia.<sup>24</sup> Psychometric properties of the Russian version of ISI were evaluated, and its reliability with a Cronbach's alpha coefficient of 0.77 was confirmed. The ISI was reported to have good sensitivity (90.2%) and specificity (95.2%).<sup>25</sup>

# Hospital Anxiety and Depression Scale (HADS)

HADS was developed by Zigmond and Snaith to assess anxiety and depression.26 The 14-item HADS includes seven items on anxiety (odd questions) and seven items on depression (even guestions). Each item is rated on a 4-point Likert scale, ranging from zero (no symptoms) to four (maximum severity). A total score of 0-7 indicates normal, 8-10 indicates borderline, and ≥11 indicates a significant case of anxiety/depression. A cutoff score of  $\geq 8$  were suggested as an optimal balance between sensitivity and specificity for anxiety and depression. This cutoff was used to group and compare the patients, i.e., patients with and without anxiety and depression. The validity and reliability of the questionnaire had been confirmed through approximately 200 studies with a total of 35,000 participants in various populations.<sup>27</sup> Pushkarev and colleagues have confirmed the validity and reliability of the Russian version of HADS.28

# Statistical Analysis

Data were analyzed using SPSS software, version 26.0 (IBM Corp., Armonk, NY, USA). Nominal data were expressed as absolute and relative (%) values. Continuous data were presented as mean±SD. Mann-Whitney U test was used to determine the difference between groups. Spearman's correlation was used to evaluate the relationship between variables. The association between insomnia and anxiety/ depression was assessed using binary logistic regression adjusted for age and sex.

# Results

A total of 376 patients with decompensated T2DM were included in the study, of which 232 were female and 144 were male patients. The mean age of the participants was 51.73±6.63 years (range: 45-59) (table 1). Evaluation of affective disorders showed that 87% of the patients did not have any symptoms of anxiety or depression. However, all patients showed signs of sleep disturbances.

# Between-group Comparison

There was a significant difference in insomnia indicators between patients with and without anxiety/depression (table 2). Sleep quality and insomnia severity were significantly worse in patients with anxiety and depression that those without.

Variables		Results
Age (years)		51.73±6.63
Sex	Female	232 (61.70)
	Male	144 (38.30)
BMI (Kg/m²)		29.78±6.30
HbA1C		11.20±3.05
Comorbidities	Arterial hypertension (AH)	204 (54,3)
	Ischemic heart disease (IHD)	12 (3,2)
	AH+IHD	24 (6,4)
Anxiety	Without anxiety (HADS≤7)	328 (87.20)
	Abnormal anxiety score (HADS>8)	48 (12.80)
Depression	Without depression (HADS≤7)	330 (87.80)
	Abnormal depression score (HADS>8)	46 (12.20)
Insomnia	Sleep quality, PSQI	7.90±3.99
	Severity of insomnia, ISI	8.90±7.14

Data are expressed as mean±SD or number (%), BMI: Body mass index; HbA1C: Hemoglobin glycation; HADS: Hospital anxiety and depression scale; PSQI: Pittsburgh sleep quality index; ISI: Insomnia severity index

Table 2: The results of sleep disturbance indicators based on the cutoff score of the hospital anxiety and depression scale								
Indicators	Anxiety			Depression				
	HADS≤7 (n=328)	HADS>8 (n=48)	P value*	HADS≤7 (n=330)	HADS>8 (n=46)	P value**		
Sleep quality PSQI	7.53 (4, 10)	10.26 (7, 13)	0.34 (<0.001)	7.53 (4, 10)	10.26 (7, 13)	0.37 (<0.001)		
Severity of insomnia ISI	8.23 (2, 13)	13.42 (9.5, 9)	0.48 (<0.001)	8.26 (2, 11)	13.43 (9, 9)	0.33 (<0.001)		

\*Mann-Whitney U test; \*\*Spearman's correlation; HADS: Hospital anxiety and depression scale; PSQI: Pittsburgh sleep quality index; ISI: Insomnia severity index. Higher PSQI and ISI scores indicate poorer sleep quality and more severe insomnia, respectively. Data are presented as median (interquartile range: 25th-75th percentile).

Table 3: Association of anxiety and depression with demographic parameters and sleep indicators							
Variables		Adju	Adjusted*		Crude		
		OR (95% CI)	P value	OR (95% CI)	P value		
Anxiety	Sex	0.98	0.01	n/a			
	Age	0.00	0.89	n/a	n/a		
	PSQI	1.09 (0.99-1.20)	0.08	1.13 (1.02-1.25)	0.01		
	ISI	1.07 (1.02-1.13)	0.01	1.07 (1.02-1.13)	0.01		
Depression	Sex	1.16	0	n/a	n/a		
	Age	0.00	0.76	n/a	n/a		
	PSQI	1.10 (1.00-1.21)	0.06	1.14 (1.04-1.26)	0.01		
	ISI	1.07 (1.01-1.13)	0.01	1.07 (1.02-1.13)	0.01		

\*The multivariate model was adjusted for both age and sex rather than each variable; n/a: Not available; PSQI: Pittsburgh sleep quality index; ISI: Insomnia severity index

#### Logistic Regression Analysis

The association between insomnia and anxiety and depression was examined using the logistic regression analysis. The results showed that the anxiety score was moderately correlated with PSQI (r=0.34, P<0.0001) and ISI (r=0.48, P< 0.0001). Moreover, the depression score was correlated with PSQI (r=0.37, P<0.0001) and ISI (r=0.33, P<0.0001). The results of adjusted logistic regression showed a significant association of PSQI and ISI with both anxiety and depression (table 3).

#### Discussion

For the first time, an association between

insomnia and the risk of anxiety and depression symptoms in patients with T2DM were studied. The results showed that although less than 15% of these patients had signs of subclinical or clinical depression and anxiety, they had significantly lower QoL and severe insomnia. Anxiety and depression scores were moderately correlated with sleep quality and insomnia severity. However, the results of the logistic regression analysis showed a significant association between insomnia severity and the degree of anxiety and depression. We also found that anxiety and depression scores were negatively associated with the severity of daytime sleepiness.

We found a relationship between the severity

of insomnia and the intensity of affective disorders in our patients. To date, no studies have reported this specific relationship. However, some studies evaluated the association of insomnia with anxiety and depression in type 2 diabetic patients. Okun and colleagues evaluated the relationship between sleep quality and symptoms of depression and anxiety in 116 women during pregnancy and six months after childbirth using the Overall Anxiety Severity and Impairment Scale (OASIS), Patient Health Questionnaire. nine-item (PHQ9), and Edinburgh Postnatal Depression Scale (EPDS).<sup>29</sup> They reported that sleep indicators were significantly associated with more pronounced symptoms of depression and anxiety. Their results, after adjustment for covariates (prenatal depression and anxiety scores), showed higher total PSQI scores in women with significantly higher scores on the OASIS (anxiety) (β=0.530, P<0.001), PHQ9 (depression) ( $\beta$ =0.496, P<0.001), and EPDS (postpartum depression and anxiety) ( $\beta$ =0.585, P<0.001). They confirmed that sleep quality is a risk factor for postpartum anxiety and depression. Another study examined the association between affective disorders and insomnia in patients hospitalized for cardiovascular diseases.<sup>30</sup> They reported that depression and anxiety were strongly associated with poor sleep quality. A population-based study of rural populations in China found a positive association between poor sleep quality and anxiety symptoms in both men and women. After stratified analysis, they found stronger positive associations in people aged ≥60 years, smokers, low physical activity levels, obesity, and T2DM.31

In the present study, in addition to the PSQI questionnaire to assess sleep quality, the ISI questionnaire was used to evaluate the severity of insomnia. Both insomnia symptoms and poor sleep quality can cause physiological changes (activation of the sympathetic nervous system, impaired glucose tolerance) and behavioral disorders (inattention, anxiety, depression). Therefore, it is important to determine the exact mechanisms underlying the relationship between sleep quality, the development of insomnia, and affective disorders.32 A recent meta-analysis reported a 39% (95% CI=34-44) prevalence of insomnia in people with T2DM and insomnia was associated with higher HbA1c levels (mean difference=0.23% [0.1-0.4]) and higher fasting glucose levels (mean difference=0.40 mmol/L [0.2-0.7]) with a low grade of evidence.<sup>33</sup> Our results showed a much higher prevalence of insomnia, which could be due to a higher number of patients with decompensated T2DM and higher HbA1c levels.

A previous study using the International Prevalence and Treatment of Diabetes and Depression (INTERPRET-DD) protocol reported an overall prevalence of 18% for anxiety disorders among 3,170 people with T2DM across various countries (56.2% women, mean duration of diabetes: 10.01 (7.0) years).<sup>34</sup> This is in line with our result of 15%, although their target population consisted mainly of ambulatory patients, and our study only included non-ambulatory patients. Chaturvedi and colleagues further specified the prevalence of anxiety disorders per country. The highest prevalence was observed in Ukraine, Saudi Arabia, and Argentina (72.7%, 52.2%, and 37.6%, respectively) and the lowest in Bangladesh and India (0.5% and 0.0%, respectively). Variation in the reported prevalence could be due to differences in research methodology (assessment tools) and demographic and clinical parameters (ethnicity, culture, or diabetes-related factors). In our study, variables significantly associated with anxiety disorder were sex (female), the presence of diabetic complications, and poorer glycemic control (HbA1c levels).

Our research findings have clinical significance for healthcare practice. We recommend a specific focus on timely diagnosis of sleep disorders to reduce psychological effects on diabetic patients who are already dealing with the emotional aspect of the disease. It is also important that practitioners screen and identify poor sleep quality in these patients.<sup>35</sup>

As the main limitation, all participants in our study had decompensated T2DM, due to which poor sleep quality was prevalent. This limits the generalizability of our findings to all people with T2DM, particularly those with good glycemic control. In addition, although the cross-sectional study design allowed us to determine a temporal relationship between insomnia and anxiety, and depression, a longitudinal study is strongly recommended.

# Conclusion

The severity of insomnia could be an important indicator of psychological health in patients with T2DM, especially those suffering from sleep disorders with signs of anxiety and depression. Timely evaluation of these patients is therefore recommended. Further studies are required to better understand the mechanisms underlying the association between anxiety and depression and sleep disorders in these patients. In addition, the feasibility and effectiveness of assessment techniques are recommended to improve affective and sleep disorders in clinical settings.

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## **Authors' Contribution**

K.Sh, A.K: Study concept and design; K.Sh, A.K, A.B, L.E: Data acquisition; K.Sh, A.K, A.B, L.E: Recruitment and screening of the participants, data collection; K.Sh, A.K, Z.A, D.A: Statistical analysis; K.Sh, A.K: Data analysis and interpretation; K.Sh, Z.A, D.A: Drafting the manuscript; K.Sh, A.K, A.B, L.E: Coordination and supervision of the study. All authors have revised and approved the final version of the manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

#### Conflict of Interest: None declared.

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