

## ORIGINAL ARTICLE

## A Comparison of Alexithymia in Individuals with Suicidal Ideation, Attempted Suicide, and Non-Suicidal Self-Injury

## İntihar Düşüncesi Olan, İntihar Girişiminde Bulunan ve İntihar Amaçlı Olmayan Kendine Zarar Verme Davranışı Bulunan Bireylerde Aleksitiminin Karşılaştırılması

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## ABSTRACT

**Background/Aims:** Alexithymia is a concept characterized by the impairment of an individual's awareness of his feelings and ability to clearly identify and describe them. This study investigated whether alexithymia levels would differ in three different groups consisting of participants exhibiting suicidal ideation, attempted suicide, and non-suicidal self-injury (NSSI).**Methods:** Seventy-five patients admitted to the psychiatry clinic and emergency department due to suicidal ideation, attempted suicide, or non-suicidal self-injury and 25 healthy controls were included in the study. The Toronto Alexithymia Scale (TAS-20) and Hamilton Depression Rating Scale (HDRS) were applied to all participants. The individuals taking part were assigned into three different groups for comparisons: suicidal ideation, attempted suicide, and NSSI.**Results:** TAS-20 scores and HDRS scores were higher in the patient groups than in the healthy controls ( $p<0.001$ ). Significantly higher TAS-20 scores were determined in the group with NSSI than in the attempted suicide group. Mean scores for the TAS subscales TAS-A (difficulty identifying feelings) and TAS-B (difficulty describing feelings) were significantly higher in the NSSI group than in the attempted suicide group. Positive correlation was found between severity of depression and alexithymia levels, TAS-20 scores, TAS-A scores, TAS-B scores, and TAS-C (externally oriented thinking) scores.**Conclusion:** The data from this study indicate that alexithymia levels in NSSI are higher than in individuals with attempted suicide and suicidal ideation. This finding reveals the importance of examining individuals with NSSI in terms of alexithymia as well.**Keywords:** Alexithymia, attempted suicide, non-suicidal self-injury, suicidal ideation.

## ÖZ

**Amaç:** Aleksitimi, bireyin duygularının farkına varmasında, bunları tanıma ve açıkça tanımlama becerisinde bozulma ile karakterize bir kavramdır. Bu çalışma, intihar düşüncesi olan, intihar girişiminde bulunan ve intihar amaçlı olmayan kendine zarar verme (NSSI) davranışı sergileyen katılımcılardan oluşan üç farklı grupta aleksitimi düzeylerinin farklı olup olmayacağını araştırdı.**Gereç ve Yöntemler:** Çalışmaya intihar düşüncesi olan, intihar girişiminde bulunan veya intihar amaçlı olmayan kendine zarar verme nedeniyle psikiyatri kliniğine ve acil servise başvuran 75 olgu ve 25 sağlıklı kontrol dahil edildi. Tüm katılımcılara Toronto Aleksitimi Ölçeği (TAÖ-20) ve Hamilton Depresyon Derecelendirme Ölçeği (HAM-D) uygulandı. Olgular intihar düşüncesi olan, intihar girişiminde bulunan ve NSSI olmak üzere üç farklı gruba ayrılarak kendi aralarında ve sağlıklı kontroller ile karşılaştırıldı.**Bulgular:** Olgu gruplarında TAÖ-20 skorları ve HAM-D skorları sağlıklı kontrollere göre daha yüksekti ( $p<0,001$ ). NSSI grubunda intihar girişimi grubuna göre TAÖ-20 puanlarının anlamlı derecede yüksek olduğu belirlendi. TAÖ-20 alt ölçekleri TAÖ-A (duyguların tanımlama zorluk) ve TAÖ-B (duyguların tanımlamada zorluk) ortalama puanları, NSSI grubunda intihar girişiminde bulunan gruba göre anlamlı derecede yüksekti. Depresyonun şiddeti ile aleksitimi düzeyleri, TAÖ-20 puanları, TAÖ-A puanları, TAÖ-B puanları ve TAÖ-C (dışa dönük düşünme) puanları arasında pozitif korelasyon tespit edilmiştir.**Sonuç:** Bu çalışmadan elde edilen veriler NSSI'de aleksitimi düzeylerinin intihar girişiminde bulunan ve intihar düşüncesi olan bireylere göre daha yüksek olduğunu göstermektedir. Bu bulgu NSSI'li bireylerin aleksitimi açısından da incelenmesinin önemini ortaya koymaktadır.**Anahtar Kelimeler:** Aleksitimi, intihar girişimi, intihar amaçlı olmayan kendine zarar verme, intihar düşüncesi.

## Introduction

Despite having been described a long time previously, alexithymia is still a foreign concept for many clinicians. In terms of etymology, alexithymia means 'lacking words to express feelings' and is a condition characterized by the impairment of an individual's awareness of his feelings and inability to clearly identify and describe them (1). Problems encountered in an individual's awareness and expression of his feelings and selecting correct behaviors in the light of his emotions can lead to deterioration of mental well-

being and a disposition to mental disorders (2). Various studies have estimated alexithymia prevalence in the community at 10–19% (3). Since more than one variable is involved in the etiology, alexithymia is defined using a multifactorial model. These include exposure to stressful events, the quality of attachment relationships in childhood, and congenital factors (4). Alexithymia is not recognized as a disorder in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (5). Therefore, it is routinely evaluated using self-report

scales rather than diagnostic criteria. Five principal characteristics of alexithymia are described: difficulty identifying one's own feelings, difficulty expressing one's own feelings, inability to experience emotions, an externally focused thinking style concentrating on the concrete details of events, and weak fantasizing or symbolic thinking (6). The ability to correctly interpret emotional facial expressions is of primary importance for healthy interpersonal interaction. Studies have observed deficiencies in perceiving emotions from the facial expressions of others in cases of alexithymia (7). Impaired perception of facial emotional signals can result in dysfunctional interpersonal relationships, frequently observed in alexithymic individuals (8).

Since alexithymic individuals are unable to verbally convey the problems they encounter and their feelings, they turn to physical reactions for external expression and employ a primitive method of expression in which emotions are externalized through the body (6). Patients presenting with physical symptoms of undeterminable cause represent difficult cases for primary physicians. Many such patients have lengthy histories regarding somatic symptoms similar or different to their current symptoms and usually respond weakly or are resistant to standard medical treatment. Physicians generally respond with helplessness and feelings of frustration and anger, thus making treatment even more problematic. These patients are frequently included under categories such as somatoform disorders, depressive disorders, anxiety disorders, and sometimes malingering (9).

Despite being formerly associated with psychosomatic disorders, several studies have revealed an association with depression, alcohol and substance disorder, eating disorders, autism spectrum disorders, particularly Asperger's syndrome, post-traumatic stress disorder, and personality disorders (6). Longitudinal studies have reported that alexithymia can exhibit a stable course and also represent a transient phenomenon, and that the causal relationship between it and depression is still unclear. In other words, in addition to being a chronic condition accompanying personality disorder, alexithymia can also encapsulate a transient phenomenon such as post-traumatic stress disorder. It should, therefore, be regarded as both a trait and a state phenomenon (10).

Alexithymic individuals have been observed to produce superficial and concrete solutions to problems they encounter, rather than examining the root of the difficulty. These physical forms of expression can sometimes also emerge in the form of suicide, because individuals with difficulty in recognizing their feelings are reported to be capable of regarding suicide as a solution and to externalize unspoken conflicts by means of attempted suicide (11). Although a powerful relationship has been revealed between alexithymia and psychiatric disorders, the association with suicide only began being addressed more recently (12). In addition to suicide, non-suicidal self-injury is another form of behavior widely seen in society (13). Although non-suicidal self-injury (NSSI) has a protective function

against suicide in the short term, it is also a risk factor for attempted suicide since the individual develops the capacity to self-injury during this process (14). There has been reference to it serving the individual's emotional regulation or avoidance function in theoretical models of NSSI (15). The most frequently reported function of NSSI is emotion regulation, followed by self-punishment and interpersonal relationship difficulties (16). Findings supporting the idea that alexithymia is a risk factor for NSSI in the general and psychiatric populations have been published in recent years (17).

The question of the relationship between alexithymia and suicidal ideation and behavior has received little attention to date. Understanding whether or not alexithymia is a potential indicator of the risk of suicide will be an important step in selecting an appropriate method of treatment. Research in the literature has generally evaluated the relationships between alexithymia and suicidal ideation, attempted suicide, and NSSI separately. The purpose of this study was to investigate whether alexithymia levels would differ in three different groups consisting of participants exhibiting suicidal ideation, attempted suicide, and NSSI, and thus to clarify the relationship between these states.

### Material and Methods

This study was performed at the Erzurum City Hospital Psychiatry Clinic and Emergency Medicine Clinic, Türkiye, with the approval of the University of Health Sciences Erzurum Medical Faculty ethical committee (Erzurum Medical Faculty no. 2023/01-02 dated 31/05/2023). The research was conducted in conformity with the principles of the Declaration of Helsinki, and informed consent was obtained from all patients and controlled prior to enrolment.

### Participants

One hundred four cases admitted to the Erzurum City Hospital emergency medicine and mental health and diseases clinics due to suicidal ideation, attempted suicide, or NSSI were included in the study. Individuals with psychotic disorder, depression with psychotic features, bipolar disorder, alcohol and substance users, dissociative disorder, mental disability, epilepsy, or other neurological diseases were excluded. Eight cases were excluded due to psychotic symptoms, five due to histories of bipolar disorder, four due to neurological disease, and 12 for refusing to take part. The study was thus conducted with 100 cases (47 female and 53 male).

The controls consisted of 25 individuals presenting to the Health Sciences University Erzurum Medical Faculty Psychiatry Clinic for good health status reports and evaluated as healthy. The healthy controls enrolled in the study were matched with the patient group in terms of age and sex.

### Tools

Structured Clinical Interview for DSM-5 Disorders, Clinician Version (SCID-5/CV): This was used to

investigate Axis I psychiatric disorders on the basis of DSM-5. This semi-structured interview guideline was developed by First et al. for identifying principal DSM-5 diagnoses (18). The validity and reliability of the Turkish version were investigated by Elbir et al. (19).

Sociodemographic data form: The sociodemographic data form was prepared by the authors in accordance with the literature to examine the sociodemographic and clinical data of the participants.

Toronto Alexithymia Scale (TAS-20): This five-point Likert-type, self-evaluation scale, developed to investigate alexithymia, consists of 20 items and three subscales. The TAS-20 was developed by Bagby et al. (20). These subscales; difficulty identifying feelings (TAS-A), difficulty describing feelings (TAS-B), and externally oriented thinking (TAS-C). The scores that can be obtained from the scale varies between 20-100. Higher scores indicate higher levels of alexithymia. The Turkish validity and reliability study of the scale was conducted by Sayar et al. in 2001 (21). According to the Turkish version, the score to be obtained from the scale is less than or equal to 51. It has been suggested that it can be categorized as “non-alexithymic”, between 52 and 58 as “borderline condition”, and being equal to or greater than 59 as “alexithymic”. In the internal reliability evaluation of the Turkish version, the Cronbach alpha coefficient was found as 0.78 (22).

Hamilton Depression Rating Scale (HDRS): HDRS was developed by Williams in 1978 and is the most widely used assessment scale for depression, consisting of 17 items (23). The total scale score is calculated by adding the scores for each item. Scores lower than 7 are regarded as indicating no depression, scores of 7-17 as mild depression, scores of 18-24 as moderate depression, and scores above 25 as severe depression. The Turkish validity and reliability study was conducted by Akdemir et al. (24).

**Statistical Analysis**

The data were analyzed on SPSS version 25.0 software. Normality of distribution of variables was examined using histogram graphs and the Kolmogorov-Smirnov test. Descriptive analyses were expressed using mean, standard deviation, and minimum-maximum values. Non-normally distributed (non-parametric) variables were compared between the groups using the Mann Whitney U test. Spearman's correlation test was applied in the analysis of measurement data. P values less than 0.05 were regarded as statistically significant.

**Results**

Seventy-five cases (36 female and 39 male) and 25 healthy controls (11 female and 14 male) participated in this study (Table 1). The patient and control group sociodemographic and clinical characteristics are shown in Table 1.

The alexithymia level in the healthy controls in this study was 16.00% (Table 1). The cases included in the study were divided into three subgroups; individuals

with suicidal ideation, attempted suicide, and NSSI. The healthy controls' mean TAS-20, TAS-A, and TAS-B scores were lower than those in the other groups (Table 2).

Mean HDRS, TAS-20, TAS-A, TAS-B, and TAS-C scores were compared between the suicidal ideation, attempted suicide, and NSSI groups. Accordingly, the group with the highest HDRS score was the group with suicidal ideation, followed by the NSSI group, and it was lowest in the group with suicide attempts. TAS-20 score was highest in the NSSI group, followed by the group with suicidal ideation, and was lowest in the group with suicide attempts. (Table 3).

Correlations between scales were examined in patient groups. This revealed positive correlation between HDRS scores and TAS-20, TAS-A, and TAS-B scores. Analysis in the attempted suicide group revealed positive correlations between HDRS scores and TAS-20, TAS-A, and TAS-B scores. In NSSI group, positive correlations were determined between HDRS scores and TAS-20, TAS-A, TAS-B, and TAS-C scores (Table 4).

The relationship between severity of depression, and the presence of alexithymia, and TAS-20, TAS-A, TAS-B, and TAS-C scores was examined in all the case groups. Positive correlations were observed between severity of depression and the presence of alexithymia, and TAS-20, TAS-A, and TAS-B scores in all the case groups (Table 5).

**Table 1:** Comparison of sociodemographic and clinical characteristics of the groups

		n	%
		mean±SD	
Total number of patients		75	
Sex	Male	39	52.00 %
	Female	36	48.00 %
Age, years		29.79±8.562	
<b>Subgroups</b>			
Suicidal ideation		25	33.33 %
Attempted suicide		25	33.33 %
NSSI		25	33.33 %
<b>Scale scores</b>			
HDRS		18	
TAS-20		29.00±4.640	
		39	
		23.77±8.845	
Depression severity	None	3	4.00 %
	Mild	15	20.00 %
	Moderate	39	52.00 %
	Severe	18	24.00 %
<b>Alexithymia (according to TAS)</b>			
None		20	26.66 %
Probable		22	29.33 %
Present		33	44.00 %
<b>Control group</b>			
Sex	Male	14	56.00 %
	Female	11	44.00 %
Age, years		25	
Alexithymia		30.40±9.428	
None		21	84.00 %
Probable		0	
Present		4	16.00 %

**Table 2:** A comparison of the case groups' TAS-20, TAS-A, TAS-B, and TAS-C scores with those of the healthy controls

	Suicidal ideation (1)		Attempted suicide (2)		NSSI (3)		Healthy controls (4)		p (1-4)	p (2-4)	p (3-4)
	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)			
TAS-20 score	56.92±13.4	60 (26-76)	50.12±13.45	53 (26-73)	60.6±10.97	61 (28-81)	38.44±11.72	39 (20-59)	<0.001	0.001	<0.001
TAS- A score	18.46±7.95	17.5 (6-36)	13.16±5.89	13 (4-26)	16.64±4.95	16 (4-27)	8.56±4.53	8 (2-19)	<0.001	0.004	<0.001
TAS- B score	16.04±8.12	15 (2-32)	18.52±6.8	20 (7-39)	23.96±6.6	23 (8-36)	9.32±3.88	9 (4-19)	0.001	<0.001	<0.001
TAS- C score	21.44±5.66	19 (14-29)	18.88±4.87	20 (10-28)	19.76±4.21	20 (10-27)	20.52±5.25	20 (11-30)	0.712	0.325	0.527

Mann Whitney-U Test, TAS: Toronto alexithymia scale, TAS-A: Difficulty identifying feelings, TAS-B: Difficulty describing feelings, TAS-C: Externally oriented thinking, NSSI: Non-suicidal self-injury

**Table 3:** A comparison of the case groups' HDRS, TAS-20, TAS-A, TAS-B, and TAS-C scores

	Suicidal ideation (1)		Attempted suicide (2)		NSSI (3)		p (1-2)	p (1-3)	p (2-3)
	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)	Mean±SD	Median (min-max)			
HDRS score	24.24±8.2	21 (12-41)	18.56±9.28	16 (4-42)	22.88±9.27	23 (4-39)	0.015	0.600	0.072
TAS-20 score	56.92±13.4	60 (26-76)	50.12±13.45	53 (26-73)	60.6±10.97	61 (28-81)	0.082	0.437	0.008
TAS- A score	18.46±7.95	17.5 (6-36)	13.16±5.89	13 (4-26)	16.64±4.95	16 (4-27)	0.016	0.477	0.022
TAS- B score	16.04±8.12	15 (2-32)	18.52±6.8	20 (7-39)	23.96±6.6	23 (8-36)	0.296	0.002	0.004
TAS- C score	21.44±5.66	19 (14-29)	18.88±4.87	20 (10-28)	19.76±4.21	20 (10-27)	0.213	0.572	0.585

Mann Whitney-U Test, TAS-20: Toronto alexithymia scale, TAS-A: Difficulty identifying feelings, TAS-B: Difficulty describing feelings, TAS-C: Externally oriented thinking, NSSI: Non-suicidal self-injury

**Table 4:** Correlations between scales were examined in patient groups

		HDRS score	TAS-20 score	TAS-A score	TAS-B score
<b>Suicidal ideation</b>	r	0.690			
	p	<0.001			
	r	0.650	0.858		
	p	<b>0.001</b>	<b>&lt;0.001</b>		
	r	0.531	0.912	0.786	
	p	<b>0.008</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>	
<b>Attempted suicide</b>	r	-0.115	-0.365	-0.478	-0.361
	p	0.585	0.073	<b>0.018</b>	0.083
	r	0.686			
	p	<b>&lt;0.001</b>			
	r	0.780	0.856		
	p	<b>&lt;0.001</b>	<b>&lt;0.001</b>		
<b>NSSI</b>	r	0.664	0.910	0.853	
	p	<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>	
	r	0.246	0.544	0.162	0.257
	p	0.236	<b>0.005</b>	0.440	0.215
	r	0.664			
	p	<b>&lt;0.001</b>			
<b>NSSI</b>	r	0.410	0.691		
	p	<b>0.042</b>	<0.001		
	r	0.520	0.821	0.628	
	p	<b>0.008</b>	<b>&lt;0.001</b>	<b>0.001</b>	
	r	0.518	0.354	-0.240	0.138
	p	<b>0.008</b>	0.083	0.248	0.509

Spearman Correlation Test, TAS-20: Toronto alexithymia scale, TAS-A: Difficulty identifying feelings, TAS-B: Difficulty describing feelings, TAS-C: Externally oriented thinking, HDRS: Hamilton depression rating scale, NSSI: Non-suicidal self-injury

**Table 5:** The relationship between severity of depression, and the presence of alexithymia, and TAS-20, TAS-A, TAS-B, and TAS-C scores in the case groups

	p	r
<b>Suicidal ideation</b>		
Alexithymia level	0.628	<b>0.001</b>
TAS-20 score	0.691	<b>&lt;0.001</b>
TAS-A score	0.596	<b>0.002</b>
TAS-B score	0.595	<b>0.002</b>
TAS-C score	-0.231	0.267
<b>Attempted suicide</b>		
Alexithymia level	0.755	<0.001
TAS-20 score	0.775	<b>&lt;0.001</b>
TAS-A score	0.794	<b>&lt;0.001</b>
TAS-B score	0.725	<b>&lt;0.001</b>
TAS-C score	0.358	0.079
<b>NSSI</b>		
Alexithymia level	0.608	0.001
TAS-20 score	0.750	<0.001
TAS-A score	0.416	0.039
TAS-B score	0.569	0.003
TAS-C score	0.484	0.014

Spearman Correlation Test, TAS-20: Toronto alexithymia scale, TAS-A: Difficulty identifying feelings, TAS-B: Difficulty describing feelings, TAS-C: Externally oriented thinking, NSSI: Non-suicidal self-injury

**Discussion**

In this study, we aimed to compare alexithymia levels in three different groups consisting of participants with suicidal ideation, suicide attempt, and non-suicidal self-injury (NSSI) behavior. Previous studies have reported prevalences of alexithymia of 5-10% in women and 9-17% in men (25). A previous study involving university students determined no gender



difference in terms of alexithymic symptoms, while similar prior research reported alexithymic symptoms in 9.5% of men and 7.2% of women (26). The alexithymia level in the healthy controls in this study was 16.00%, with the values of 12.00% in women and 4.00% in men. The difference between the data from the present study and the previous literature may be due to our relatively low number of healthy controls. The alexithymia rate in the patient group in the present study was 44.00%. Previous studies involving patient groups have reported symptoms in 32.7% of outpatient psychiatric patients and 47.3% of hospitalized patients (27). Our finding is, therefore, consistent with the previous literature.

Depression severity was evaluated in the alexithymic cases in this study with mild depression being detected in 33.3%, middle depression in 48.48%, and severe depression in 18.52%. These data are consistent with the previous literature. Earlier studies have revealed a significant association between alexithymia and depression (28). Research involving depressive patients has detected significantly greater difficulty in identifying feelings, describing feelings, and total alexithymia scores in such individuals compared to a healthy group, with alexithymic symptoms being observed in approximately one third of patients with depression (29). In the present study, alexithymia was determined in 6.66% of the patients with mild depression, 41.02% of those with moderate depression, and 88.88% of those with severe depression. Severity of depression also exhibited positive correlation with alexithymia levels and TAS-20 scores ( $p=0.001$  and  $p<0.001$ , respectively). Separate examination of all the groups revealed similar positive correlation between HAM-D scores and TAS-20 scores.

The causality of this association between alexithymia and depression remains unclear. In other words, the question of whether alexithymia predisposes individuals to depression (the vulnerability hypothesis) or whether depression produces alexithymic symptoms is still controversial (6). Several studies have reported that the severity of depression mediates the association between alexithymia and suicidal behavior (30). However, more recent research has revealed that the connection between alexithymia and suicide persists even after the effect of depression has been eliminated (31). One long-term observational study has suggested that alexithymia is a significant predictor of subsequent suicidal ideation (32). A large part of previous studies supports the idea that alexithymia is more powerfully associated with suicidal ideation than suicidal behavior (29). Nonetheless, a few studies have reported a stronger link between alexithymia and suicidal behavior than with suicidal ideation (33). TAS-20 scores in the present study were lowest in the attempted suicide group and highest in the NSSI group. The difference was also statistically significant ( $p= 0.008$ ). This picture may show that the individual embarks on behavior to concretize the difficulty in identifying and describing feelings and turns to self-injury as a form of expression, rather than suicide. This supports the hypothesis that individuals with difficulty in understanding their own emotional

states may be less capable of identifying and applying strategies for tolerating stress or solving underlying problems in the short term and may therefore employ self-injury behavior to reduce disturbing arousal (34). Other factors may also be capable of affecting the relationship between alexithymia and suicide and NSSI. For example, there is evidence showing that low self-esteem, low social support levels, and attachment styles are separately associated with both the disposition to suicide and alexithymia (12).

### Conclusion

The findings of this study show that the relationship between alexithymia and NSSI is stronger than those between alexithymia and suicidal ideation and attempted suicide. This reveals the need to evaluate alexithymia in individuals presenting due to self-injury behavior and ideation, and its critical importance in determining therapeutic strategies.

### Limitations and future directions

Future research should concentrate on longitudinal studies detailing the association between alexithymia and NSSI and including its interaction with other variables. The limitation of our study is that we have insufficient number of patients and controls. It is possible to reach more generalizable data with studies with larger populations. We think that the data yielded by such studies will be useful in eliciting a better understanding of the relationship between alexithymia and emotion perception and in the application of more specific therapeutic approaches for the improvement of social skills in alexithymic individuals.

### Declarations:

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#### Author Contributions:

Conception: S.Z., O.D., Data Collection and Processing: S.Z., O.D., Design: S.Z., O.D., H.U., Supervision: S.Z., O.D., Analysis and Interpretation: S.Z., Literature Review: S.Z., O.D., H.U. Writer: S.Z., Critical Review: O.D., H.U.

#### Availability of data and materials

The data sets analyzed are available from the corresponding author.

#### Declaration of conflicting interests

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## Ethical approval

This study was performed at the Erzurum City Hospital Psychiatry Clinic and Emergency Medicine Clinic, Türkiye, with the approval of the University of Health Sciences Erzurum Medical Faculty ethical committee (Erzurum Medical Faculty no. 2023/01-02 dated 31/05/2023). The research was conducted in conformity with the principles of the Declaration of Helsinki

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