



❧ Türk Psikiyatri Dergisi ❧

Turkish Journal of Psychiatry

CİLT | Volume 35

BAHAR | Spring 2024

SAYI | Issue 1

ISSN: 1300 – 2163

E-ISSN: 2651-3463

TÜRKİYE
SİNİR VE
RUH SAĞLIĞI
DERNEĞİ

Türk Psikiyatri Dergisi

Turkish Journal of Psychiatry

ISSN: 1300 – 2163 • E-ISSN: 2651-3463

VOLUME 35 • SPRING 2024 • ISSUE 1

Turkish Journal of Psychiatry

Turkish Journal of Psychiatry (*Türk Psikiyatri Derg*) is the scientific journal of Turkish Association of Nervous and Mental Health.
www.turkpsikiyatri.com

Four issues annually: *March, June, September, December*

Publication Category

Widespread, Periodical, Scientific Publication

Published by Turkish Association of Nervous and Mental Health

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Turkish Journal of Psychiatry is indexed in
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TÜRKİYE CITATION INDEX.

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E-mail: info@bayt.com.tr

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Network Design and Online Publishing Services

Seres Yazılım Ltd. Co.

Graphic Design

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Online Access : March 31, 2024

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P-ISSN: 1300-2163, E-ISSN: 2651-3463

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Contents

Research Papers

- 1 **Serum HMGB1 and Beclin 1 Levels in Patients with a Diagnosis of Schizophrenia**
Sevler YILDIZ, Aslı KAZĞAN KILIÇASLAN,
Burcu SİRLİER EMİR, Kerim UĞUR, Faruk KILIÇ
- 8 **Online Group Psychotherapy to Increase Self-acceptance and Reduce Shame Among Transgender Migrants: An Observational Report**
Mihriban Heval ÖZGEN, Cato MH de VOS,
Özgün YAĞMUR, Jae SEVELIUS
- 14 **Comparison of Clinical Characteristics, Gender Perceptions, and Rape-Related Beliefs of People Assessed for Criminal Liability for Rape Against Children and Adults**
Ender CESUR, Görkem YILMAZ, İlker TAŞDEMİR,
Barış SANCAK, Fatma Nuray CANSUNAR
- 24 **Fear, Perceived Threat, and Anxiety During COVID-19 Pandemic: The Mediating Role of Cognitive Control/Flexibility and Intolerance of Uncertainty**
Özge AKGÜL, Betül ÖNDER UZGAN, Melike TETİK,
Cansu AYKAÇ
- 34 **Symptom Exacerbations of Patients Attending a Community Mental Health Center During the COVID-19 Pandemic**
Remzi Erşah DİNDAR, Eren YILDIZHAN,
Nesrin Buket TOMRUK
- 46 **Validity and Reliability Study of the Prolonged Grief Disorder-Caregiver Turkish Form**
Gizem ÖNAL, Emrah KESER, Zeynep TÜZÜN GÜN

- 56 **Evaluation of Sexual Function According to Gender and Sexual Orientation during the COVID-19 Pandemic in Turkey: A National Online Survey Study**
Ardıl Bayram ŞAHİN, Emiralp BÜYÜKTOPCU,
Raşit TÜKEL

Review Article

- 63 **The Impact of Childhood Sexual Abuse on Adult Female Sexual Function and Sexual Distress: A Systematic Review and Meta-Analysis**
Özlem AŞCI, Meltem DEMİRGÖZ BAL,
Ferdane KOÇOĞLU

Case Report

- 75 **Neuroleptic Malignant Syndrome Concurrent with COVID-19 Infection: A Case Report**
Onur GÖKÇEN, Merve AKKUŞ
- 78 **Transient Fever Response After ECT in a Patient with Catatonic Schizophrenia: A Case Report**
Anıl ALP, Melike KARAÇAM DOĞAN, Elçin ÖZÇELİK
EROĞLU, Mevhibe İrem YILDIZ, Şeref Can GÜREL,
Suzan ÖZER

Letter to Editor

- 84 **Artificial Intelligence Innovations in Psychiatry: A Global Perspective from Young Psychiatrists**
Ahmet GÜRCAN, Victor PEREIRA-SANCHEZ,
Mariana PINTO da COSTA, Ramdas RANSING,
Rodrigo RAMALHO

Serum HMGB1 and Beclin 1 Levels in Patients with a Diagnosis of Schizophrenia



Sevler YILDIZ¹, Aslı KAZĞAN KILIÇASLAN², Burcu SIRLIER EMİR³, Kerim UĞUR⁴,
Faruk KILIÇ⁵

Objective: It is known that inflammation plays a role in the etiopathogenesis of schizophrenia. In this study, we examined high mobility group box 1 protein (HMGB1) and Beclin 1 levels and their relationship with clinical variables in patients with schizophrenia.

Method: Forty-three patients with schizophrenia and 43 healthy controls were included in this study. The patients were administered sociodemographic data form, the Positive Negative Symptoms Assessment Scale (PANSS) and the Clinical Global Impressions (CGI) scale. After the scales were filled, venous blood samples were taken from both the patient and control groups to measure serum HMGB1 and Beclin 1 levels. Serum samples obtained at the end of centrifugation were measured by Enzyme-Linked ImmunoSorbent Assay (ELISA) method.

Results: The mean serum HMGB1 levels were significantly increased and the mean serum Beclin 1 levels were significantly decreased in the schizophrenia group compared to the control group. In addition, a negative correlation was found between HMGB1 and Beclin 1 levels.

Conclusion: In conclusion, current research shows that HMGB1 is increased and Beclin 1 is decreased in patients with schizophrenia, and these findings may contribute to the role of autophagy in the pathogenesis of schizophrenia.

Keywords: Schizophrenia, High Mobility Group Box 1, Beclin 1, Autophagy

INTRODUCTION

Schizophrenia is a psychiatric disorder characterized by symptoms such as hallucinations, delusions, disorganized speech and behaviors, and withdrawal from society and results in significant disability due to the deterioration of cognitive, emotional, and social functions (APA 2013). The lifetime prevalence of schizophrenia is reported to be 1% (Charlson et al. 2018, McGrath et al. 2008). In recent years, it has been investigated whether neuroinflammatory processes may play a role in the development of psychiatric diseases, and it has also been suggested that these processes contribute to the development of schizophrenia (Arıcıoğlu et al. 2016). It is known that neuroinflammation causes white matter and myelin damage with axonal degeneration in schizophrenia (Najjar and Pearlman 2015). In addition, studies evaluating peripheral blood cytokine levels in patients

with schizophrenia have found that some interleukin levels may be associated with clinical symptoms measured using the Positive and Negative Symptom Scale (PANSS) (Dahan et al. 2018). Furthermore, some proteins have been shown to be associated with these inflammatory processes, although this has not yet been fully clarified.

High mobility group box 1 (HMGB1) is a non-histone protein that has the ability to regulate DNA repair, enhance transcription in the nucleus, and regulate cell differentiation, apoptosis, and autophagy in the cytoplasm after cell damage (Livesey et al. 2012, Dumitriu et al. 2005). In addition to acting as a proinflammatory cytokine (Wang et al. 1999), HMGB1 also affects the release of pro-inflammatory cytokines/chemokines, such as tumor necrosis factor, interleukin-1 β , and CXCL8 (Bertheloot and Latz 2017). HMGB1 triggers inflammation and disrupts the vascular

Received: 02.12.2021, Accepted: 06.05.2022, Available Online Date: 12.10.2023

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barrier in tissues (Nawaz and Mohammad 2015), and therefore it is a biological marker of neuroinflammation and neurodegeneration that can cause blood-brain barrier dysfunction (Festoff et al. 2016). This protein is considered to be a risk factor for the progression of inflammation in the nervous system in Alzheimer's disease, Parkinson's dementia, and multiple sclerosis (Angelopoulou et al. 2018, Paudel et al. 2020, Andersson et al. 2008). Makris et al. (2021) showed that HMGB1 serum concentrations changed in children with autism spectrum disorder, and HMGB1-mediated inflammatory processes affected certain cognitive features. In another study, the HMGB1 level was found to be high in patients with schizophrenia, and the authors suggested that the neurotoxic effects of this protein could explain neurocognitive disorders and various symptom clusters in schizophrenia (Al-Dujaili et al. 2021).

Autophagy, the cleaning system for cellular waste, is particularly important in neurons since it balances the production and destruction of cellular components. Blocking autophagy in neurons results in the accumulation of misfolded protein aggregates and damaged organelles, leading to apoptosis and consequently neurodegeneration (Mortensen et al. 2010, Hara et al. 2006). To date, more than 30 mammalian autophagy genes have been identified to play an important role in the occurrence and regulation of the autophagy process. In addition, many other proteins, including HMGB1, have been investigated in terms of their role in the autophagy process. HMGB1 is involved in the regulation of autophagy in the cell cytoplasm together with Beclin-1. HMGB1 induces autophagy by binding to Beclin-1, which plays a role in the regulation of autophagosome formation and maturation in autophagy (Kang and Tang 2016). Beclin-1 is a protein in the regulation of autophagy and plays a role in the formation of autophagosomes (Qu et al. 2003); therefore, a decrease in the level of Beclin-1 can trigger apoptotic processes (Wang 2008).

In the central nervous system, basal autophagy can degrade misfolded and damaged protein aggregates that cause neurodegenerative diseases, reduce protein toxicity, and oxidative stress, and prolong neural cell lifespan. In addition, disruptions in autophagy pathways, dysfunctional autophagosome accumulation, and overstimulation of autophagy can also lead to cell death (Puyal et al. 2012). Beclin-1 is a protein-structured molecule synthesized from neurons and glia (Liang et al. 1998), known to play a role in the pathogenesis of certain heart diseases and Parkinson's and Alzheimer's diseases (Esteyes et al. 2019, Zhu and He 2015, Spencer et al. 2009). It has been suggested that this protein may also have a role in autism due to the defect in the autophagy system (Dana et al. 2020). In schizophrenia, disruptions during autophagy in neurons can lead to cellular dysfunction and global changes in different brain regions, thereby contributing to the development of disease symptoms

(Schneider et al. 2016). A decrease in Beclin-1 levels was detected in the hippocampus of these patients, and this protein was shown to play a very important role in the initiation of the autophagy process associated with the initiation of apoptosis (Wagner et al. 2015). HMGB1 is a new Beclin-1-binding protein that is important in maintaining autophagy (Kang et al. 2010). It has been shown that HMGB1 causes autophagy dysfunction by affecting Beclin-1 levels and results in neurotoxicity (Huang et al. 2017). However, to our knowledge, it has not yet been clarified whether this relationship is related to the development of any disease.

It has been reported that the cytoplasmic HMGB1-Beclin-1 complex is increased in resistant oral squamous cell cancer (Min et al. 2019). Similarly, Beclin-1 inhibition has been found to have decreased in epithelial ovarian tumors, and that HMGB1 has been shown to play a role in the pathogenesis of this disease (Ju et al. 2016). Therefore, in the current study, our hypothesis is that the serum levels of HMGB1 and Beclin-1 proteins, which play a role in inflammation, are affected in patients with schizophrenia and can be considered among factors involved in disease etiopathogenesis. In our review of the literature, we did not find any study examining the relationship between schizophrenia, a disease associated with inflammatory responses, and HMGB1 and Beclin-1, proteins that play a role in inflammation. Therefore, this study aimed to compare the serum concentrations of HMGB1 and Beclin-1 between patients with schizophrenia and healthy controls and to examine the possible relationship between HMGB1 and Beclin-1 and schizophrenia symptoms.

METHOD

Approval for this study was obtained from the Non-Invasive Ethics Committee of the Faculty of Medicine of Firat University (Elazığ, Turkey) (approval number: E-97132852-050.01.04-87772). All stages of the study were carried out in accordance with the ethical standards of the Declaration of Helsinki as revised in 1983. Patients that were diagnosed with schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5) at the High-Security Forensic Psychiatry Ward of Elazığ Fethi Sekin Hospital were included in the study. Since the women's section of this ward was not active, all the patients and controls were men. The healthy control group consisted of individuals educated in our hospital and agreed to participate in the study. All the participants were provided detailed information concerning the study, and written consent was obtained from their legal guardians, if any. After obtaining the psychiatric history of the patients with schizophrenia, those that were diagnosed with malignancy or active infection and those that used corticosteroids or any other drug that

could affect the immune system within the last six months were excluded from the study. The control group consisted of volunteer hospital workers who did not have a history of mental disorder, history of alcohol and substance use disorder, diagnosis of malignancy or active infection, and had not used corticosteroids or any other drug that could affect the immune system within the past six months.

Procedure

After obtaining written consent from all the participants, a sociodemographic data form, PANSS, and the Clinical Global Impression (CGI) scale were administered to both the patients and control groups by a mental health specialist in the patient interview room over 45-minute interview periods. The height and weight measurements of both groups were made using the Seca machine, and body mass index (BMI) was calculated. Venous blood samples were taken from both groups immediately after the measurements were finished.

Data Collection Tools

PANSS

PANSS is a semi-structured 30-item scale that measures psychopathology based on positive, negative, and general schizophrenia symptoms. As a result of measurements, four scores are obtained: positive, negative and general psychopathology scores and the total PANSS score (Kay et al. 1987). The validity and reliability analyses of the Turkish version of PANSS were undertaken by Kostakoğlu et al. (1999).

CGI scale

This scale was developed to make a general assessment of the severity of depression and the patient's response to treatment during clinical studies and is divided into two main categories as the severity of the disease and general improvement achieved with drug therapy (Guy 1976).

Determination of serum HMGB1 and Beclin-1 Levels

Venous blood samples taken from the left forearm were placed into heparinized tubes between 08.00-09.00 o'clock after overnight fasting. To remove the plasma, the blood samples were centrifuged at 3,000 rpm for 10 minutes at 4 °C. The serum samples were stored at -80 °C until analysis. Commercial enzyme-linked immunosorbent assay kits [Human HMGB-1 (High Mobility Group Protein B1); Catalog No: E-EL-H1554; Elabscience Biotechnology Inc., Human BECN1 (Beclin-1); Catalog No: E-EL-H0564; Elabscience Biotechnology Inc.] were used to measure the serum concentrations of HMGB1 and Beclin-1 according to the manufacturer's instructions. The serum HMGB1 levels were recorded as pg/mL, and Beclin-1 levels as ng/mL.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) v. 20 (IBM Corp., Armonk, NY, USA) was used for statistical analyses. The Kolmogorov-Smirnov test was conducted to determine the normality of the distribution of variables. Data were presented as mean and standard deviation and evaluated using descriptive analyses. Relationships between categorical data were evaluated with the chi-square test. The psychiatric outcomes and biochemical parameters of the patient and control groups were compared using Student's t-test or the Mann-Whitney U test. The Spearman rank correlation coefficient was used to analyze correlations between clinical features and serum HMGB1 and Beclin-1 levels. P values of <0.05 were considered significant.

RESULTS

Sociodemographic Characteristics

The study included 43 male patients with schizophrenia and 43 healthy controls with similar sociodemographic characteristics. Descriptive statistics regarding the sociodemographic data of the patients are given in Table 1. There was no significant difference between the two groups in terms of age and BMI ($p>0.05$). Of the patients with schizophrenia, 26 (56%) were married, and 17(%) were single or widowed, and in the healthy control group, 11(36%) were married, and 32(64%) were single or widowed ($t=12.592$, $p=0.002$).

Thirty-eight of the patients were still using medication. While 26(60.5%) of these patients were using a single antipsychotic, 12(27.9%) were using multiple antipsychotics. The number of patients that did not use medication was 5(11.6%).

Thirty (65%) individuals diagnosed with schizophrenia and 19(41%) of the healthy control group were smokers ($\chi^2=5.740$, $p=0.017$). In addition, a history of alcohol use was present in six (13%) patients in the schizophrenia group but none of the controls had such a history ($\chi^2=6.450$, $p=0.011$).

Group Comparisons

The patients' mean PANSS positive score was 18 ± 4.7 , the mean PANSS negative score was 16.2 ± 5.1 , the mean PANSS general psychopathology score was 33.7 ± 5.9 , and the mean PANSS total score was 67.7 ± 10.2 . Lastly, the mean CGI score of the patients was 7.9 ± 1.8 (Table 1).

Serum HMGB1 and Beclin-1 Levels

As a result of the analyses, the mean serum HMGB1 level was measured as 2115.80 ± 444.48 pg/ml in the patients with schizophrenia and 1632.58 ± 396.21 pg/ml in the control group. The serum HMGB1 level was found to be significantly

Table 1. Demographic and Clinical Characteristics of the Patients with Schizophrenia and Controls

	Schizophrenia Group (n = 43)	Control Group (n = 43)	t/x ²	p
Age (years)	39.3 ± 13.4	39.9 ± 14.7	-0.176	0.861
Marital status				
Single/married/widowed	26/12/5	11/28/4	12.592	0.002
Education level				
Primary school/high school/university	23/11/9	29/10/4	2.663	0.264
Employment status				
Employed/unemployed	18/25	24/19	1.675	0.196
Smoking status				
Smoker/non-smoker	30/13	19/24	5.740	0.017
Alcohol use				
Present/absent	6/37	0/43	6.450	0.011
Body mass index	27.2 ± 4.4	27.6 ± 4.0	-0.418	0.677
History of suicide attempt				
Present/absent	5/38	0/43	5.309	0.021
Disease duration (years)	9.97 ± 8.01			
PANSS positive score	18 ± 4.7			
PANSS negative score	16.2 ± 5.1			
PANSS general psychopathology score	33.7 ± 5.9			
PANSS total score	67.7 ± 10.2			
CGI scale score	7.9 ± 1.8			

PANSS: Positive and Negative Syndrome Scale

CGI: Clinical Global Impression

Student t-test; Chi-square test

Table 2. HMGB1 and Beclin-1 Levels of the Patients with Schizophrenia and Controls

	Schizophrenia Group (n = 43)	Control Group (n = 43)	t	p
HMGB1 (pg/ml)	2.115.80 ± 444.48	1.632.58 ± 396.21	0.167*	<0.001*
Beclin-1 (ng/ml)	1.02 ± 0.40	1.34 ± 0.35	-3.852*	<0.001*

*p<0.001; *Student t-test

Table 3. Correlation Between the Biochemical and Clinical Parameters in the Patients with Schizophrenia

	BMI	PANSS positive	PANSS negative	PANSS general	PANSS total	CGI	HMGB1	Beclin-1
Age	-0.056	0.176	0.310*	0.328*	0.427*	0.237	0.272	-0.143
BMI	-	0.176	-0.066	0.096	0.105	0.065	0.075	0.1490
PANSS positive		-	-0.356*	0.101	0.327*	0.449**	-0.120	-0.041
PANSS negative			-	0.446**	0.620**	0.258	-0.159	0.173
PANSS general				-	0.865**	0.374*	-0.090	0.051
PANSS total					-	0.542**	-0.152	0.089
CGI						-	-0.212	0.128
HMGB1							-	-0.386*

Pearson correlation test; *p<0.05 **p<0.01

BMI: body mass index

PANSS: Positive and Negative Syndrome Scale

CGI: Clinical Global Impression

higher in the schizophrenia group compared to the control group ($t=0.167$, $p<0.001$) (Table 2).

The mean serum Beclin-1 level was found to be 1.02 ± 0.40 ng/ml in the schizophrenia group and 1.34 ± 0.35 ng/ml in the control group, indicating a significantly lower value in the patient group ($t=0.3.852$, $p<0.001$) (Table 2).

Correlation Analyses

No correlation was found between the HMGB1 and Beclin-1 levels and clinical parameters ($p>0.05$) (Table 3).

DISCUSSION

In this study, the serum HMGB1 and Beclin-1 levels of the patients with schizophrenia and healthy controls were examined. The main finding of our study is that the serum HMGB1 levels were significantly higher, and the serum Beclin-1 levels were significantly lower in the schizophrenia group compared to the healthy control group. To our knowledge, there is no other study comparing the serum HMGB1 and Beclin-1 levels of patients with schizophrenia and healthy controls. Therefore, this is the first study to describe this relationship.

Consistent with the literature, in our study, we determined the HMGB1 level to be higher in patients with schizophrenia than in the healthy control group. In a study conducted with 68 patients with chronic schizophrenia, it was shown that the HMGB1 levels were significantly higher in the patient group than in healthy controls, and this was attributed to the association of this disease with neuroinflammation (Kozłowska et al. 2021). Although that study was also conducted with schizophrenic patients, the authors did not exclude those using antipsychotics, which are known to affect serum cytokine levels (Tourjman et al. 2013). In a 2021 study, the serum HMGB1 levels were found to be significantly higher in 30 patients with schizophrenia in the exacerbation period of the disease and in 29 patients with schizophrenia in the remission period of the disease compared to the healthy control group. A positive correlation was observed between the HMGB1 levels and symptom severity scores in patients in remission, and it was suggested that HMGB1 could be a biomarker in the remission period of schizophrenia (Yılmaz et al. 2021). Similarly, Zhu et al. (2015) reported that the serum HMGB1 levels were higher in schizophrenic patients compared to controls. The authors suggested that HMGB1 could play a proinflammatory role in schizophrenia, and a decrease in the HMGB1 level after risperidone treatment might be an indicator of remission of mental symptoms. Although some studies state that antipsychotic use and disease duration do not affect the serum levels of HMGB1 (Lee et al. 2017, Xiu et al. 2015), it has also been reported

that antipsychotic drugs can reduce serum cytokine levels (Borovcanin et al. 2013). It is known that HMGB1 increases by secretion, especially in microglia cells in the hippocampal region, especially immediately after exposure to stress. Therefore, the known effects of HMGB1 on stress-induced neuroinflammatory response (Yao et al. 2019, Weber et al. 2015) may explain the high serum HMGB1 levels in patients with schizophrenia, as also observed in our study.

In the literature, we did not find any study investigating serum Beclin-1 levels in individuals diagnosed with schizophrenia; therefore, our study is the first one in this regard. It is known that autophagy plays a role in the pathogenesis of psychiatric diseases, such as major depressive disorder, schizophrenia, and bipolar disorder, and Beclin-1 plays a regulatory role in autophagy (Kang et al. 2011, Bar-Yosef et al. 2019). It has been shown that serum Beclin-1 levels in patients with a diagnosis of major depressive disorder who do not respond to antidepressant treatment are significantly higher compared to those that respond to antidepressant treatment, suggesting that the serum Beclin-1 level may be a predictive biomarker of response to antidepressant treatment (He et al. 2019). In a study conducted in rats, Zheng et al. (2017) determined that the prefrontal cortex was sensitive to stress, and increased exposure to stress resulted in changes in Beclin-1 levels due to autophagy. In human and mouse models of schizophrenia, low Beclin-1 mRNA and protein levels were found in the postmortem hippocampus, and antipsychotic treatment was shown to increase the Beclin-1 level (Merelender et al. 2014). In addition, it has been stated that adequate Beclin-1 expression and apoptosis are needed to effectively treat schizophrenia (Merelender et al. 2014). Furthermore, it has been determined that a protein regulated by Beclin-1 may lead to the development of schizophrenia and autism by leading to autophagosome formation (La Barbera et al. 2019). We also found that the serum Beclin-1 levels of the patients with a diagnosis of schizophrenia were lower than those of the healthy controls. This suggests that this decrease may be related to the disruptions in autophagosome formation in the pathogenesis of the disease.

HMGB1 competes with Bcl2 to interact with Beclin-1 and directs the latter toward autophagosomes (Kang et al. 2010). Preventing HMGB1 from binding to Beclin-1 in mice inhibits autophagy, thus leading to improvement in neurological functions (Pan et al. 2020). A study conducted in vitro showed that while the HMGB1 level increased in lung injury, Beclin-1 decreased (Le et al. 2020). In our literature review, we did not find any study examining the relationship between serum HMGB1 and Beclin-1 at the disease level. According to our results, there was no correlation between these two proteins measured by kits and other clinical parameters, but we found a negative correlation between HMGB1 and Beclin-1 ($r=-0.417$ $p<0.001$). We can state that our study is the first one in this respect.

Limitations

The strength of our study is that the participants were only male schizophrenic patients. However, the cross-sectional design and the lack of evidence showing that the measured parameters reflected the concentrations of serum levels in the brain are among our limitations. In addition, the patient group diagnosed with schizophrenia included people that used antipsychotic drugs, which are known to affect inflammatory markers (Momtazmanesh et al. 2019). Furthermore, the sample included individuals admitted to the forensic psychiatry ward after committing crimes, and the results may have been different due to the more impulsive behaviors of this patient population. There is a need for longitudinal studies to evaluate unmedicated or more homogeneous antipsychotic treatment groups.

CONCLUSION

Our results showed that the HMGB1 levels were higher, and the Beclin-1 levels were lower in the patients with schizophrenia compared to the healthy controls. We consider that these two parameters may play a role in the pathogenesis of schizophrenia. To our knowledge, serum HMGB1 and Beclin-1 levels have not been previously investigated in patients with a diagnosis of schizophrenia; therefore, this is the first study on this subject. The clarification of the role of HMGB1 and Beclin-1 in the etiopathogenesis of schizophrenia can contribute to the development of new treatment methods.

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Acknowledgment: *The authors thank all the patients that participated in this study.*

Online Group Psychotherapy to Increase Self-acceptance and Reduce Shame Among Transgender Migrants: An Observational Report



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ABSTRACT

Objective: Transgender and gender diverse (TGD) people experience higher levels of stigma, discrimination, and interpersonal violence due to their gender identity and/or expression, particularly TGD people with a migration background. This study aimed to conduct and evaluate group psychotherapy for TGD migrants to provide opportunities for exploring and developing interpersonal skills and relationships.

Method: The group therapy included five individuals who identified as TGD and originated from the Middle East. The TGD group therapy consisted of 12 weekly sessions of 90 minutes each and was facilitated by a psychiatrist. All sessions were conducted online and in Turkish. The sessions were guided by the group process and discussions.

Results: After completing 12 group therapy sessions, members of the group reported benefiting from observing and emulating others who shared their problem constellation. Through the interpersonal skills that they built up throughout the sessions, they became more open to share their feelings experiencing fewer social barriers, and reduced anxiety.

Conclusion: This observational study indicates the significance of offering group-based psychotherapy to enhance affirmation and social connection within gender minority groups and emphasizes the need to empirically evaluate the effectiveness of group psychotherapy with TGD individuals, with special attention to the unique needs of TGD migrants.

Keywords: Migrant, Transgender, Gender-diverse, Online Therapy, Group Therapy

INTRODUCTION

Transgender and gender diverse (TGD) people have a different gender identity and/or expression from the sex they were assigned at birth. They experience an incongruence between their gender identity and the sex assigned at birth which manifests as gender dysphoria for some TGD people (American Psychiatric Association 2013). TGD people face higher levels of stigma, discrimination, and interpersonal violence because of their gender identity and/or expression than cisgender people (Hendricks and Testa 2012, White Hughto et al. 2015), while frequently lacking the necessary social support from family, friends, and peers (Davey et al. 2014).

Experiences of stigma are amplified for TGD people of color, resulting in higher rates of depression and anxiety relative to white TGD people (Lefevor et al. 2019). In

addition, TGD refugees experience increased discrimination and violence because they often come from countries that hold traditional values of gender and sexuality (Alessi et al. 2018). TGD refugees frequently face discrimination from other refugees, particularly cisgender heterosexuals, while leaving their country of origin and residing in migration camps. Consequently, they experience elevated levels of persecution, violence, abuse (including sexual abuse), death threats, suicides, and even homicides (Grungras et al. 2009). Consequently, it comes as no surprise that by the time TGD refugees arrive in their destination country, their mental health has significantly deteriorated (Fox et al. 2020).

Mental healthcare providers serving TGD migrants encounter the challenge of addressing the resulting trauma that can lead to subsequent mental health issues. Common psychopathologies observed in this population consist of post-traumatic stress

Received: 10.05.2022, Accepted: 19.06.2023, Available Online Date: 02.11.2023

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disorder (PTSD), anxiety, depression, and suicidal ideation (Alessi et al. 2016). Individual psychotherapy can be used to treat these concerns. Furthermore, feelings around gender identity and expression can also be addressed in therapy, as TGD migrants may be halted in their social and physical transition for several reasons (e.g., lack of affirmative treatment or stigmatizing and unsafe social environments). Studies conducted among Western TGD people highlights the significance of an affirmative approach to medical treatment and social transition, as it considerably enhances the mental health and overall well-being of TGD adults (Hughto et al. 2020, Lelutiu-Weinberger et al. 2020, Murad et al. 2010) and adolescents (Fontanari et al. 2020, van der Miesen et al. 2020).

Access to mental health therapies and gender-affirming care is critical for TGD individuals. Prior to the COVID-19 pandemic, the rate of mental health problems, particularly depression, anxiety, and suicide risk among TGD individuals was significantly higher than in heterosexual and cisgender populations (Hidalgo et al. 2019, Yüksel et al. 2017). The COVID-19 pandemic was often associated with an increased level of distress, depressive and anxiety symptoms in the general population due to unpredicted circumstances, lacking social support and socioeconomic outcomes (Manchia et al. 2022) along with the neuropsychiatric effects of COVID-19 infection (Dinakaran et al. 2020). Individuals and populations at high risk of psychological distress or resilience for the stressful environment have been affected more than the general population by the detrimental effects of the COVID-19 pandemic. Like other vulnerable groups such as elderly, healthcare workers and children, healthcare access to gender-affirming services and mental well-being of TGD individuals have deteriorated during the COVID-19 pandemic (Koehler et al. 2021, Szücs et al. 2021). According to Meyer's minority stress theory, culturally defined norms and social stigma have inimical effects on the mental health of minority groups (Meyer et al. 2015). Therefore, the COVID-19 pandemic enhanced stress for TGD individuals. External stressors such as discrimination, victimization, rejection, and non-affirmation towards TGD individuals may also disrupt self-view, which may be turned into increasing self-blaming, social avoidance, experiencing non-affirmation and internalized stigmatization among their own or toward other gender minority groups.

Group psychotherapy for TGD people is considered a promising treatment modality that capitalizes on the inherent resilience of TGD communities (Heck 2017, Heck et al. 2015, Mills et al. 2019). Many psychologists report being unfamiliar with the challenges faced by this population. Training programs provide minimal exposure to transgender issues by way of coursework and practicum experiences, and many barriers prevent transgender persons from accessing quality mental health care. The provision of group psychotherapy services in psychology training clinics may help reduce barriers to treatment, but

there is little literature to guide professionals interested in facilitating such a group. The limited studies investigating group psychotherapy for TGD population show promising results. A study conducted in the United States demonstrated that group therapy with trans women with co-morbid PTSD and substance use disorders is promising (Empson et al. 2017). Further, several randomized controlled trials and meta-analyses demonstrate the efficacy of group psychotherapy for a range of mental health issues that disproportionately affect TGD people (Lo Coco et al. 2019, Okumura and Ichikura 2014, Wersebe et al. 2013, Yüksel et al. 2000). Group psychotherapy also allows TGD persons to explore and develop interpersonal skills and relationships, which is vital considering the high levels of isolation typically experienced by TGD people, particularly TGD migrants (Fox et al. 2020). In addition, group psychotherapies often include several non-specific therapeutic factors that promote authenticity, personal growth, and identity exploration (Yalom and Leszcz 2020). However, research on the effectiveness of group psychotherapy for TGD persons is limited, particularly for TGD with a migration background. Therefore, this observational study aims to evaluate the effectiveness of a therapy group focused on TGD migrants. This article provides psychologists with a description of an experiential/process psychotherapy group for transgender clients that was offered at a university training clinic. Logistical aspects of forming the group are reviewed. Prominent themes that emerged over the course of three 12-session groups are discussed. Considerations for other professionals and training clinics interested in offering similar groups are also provided.

METHODS

Transgender Therapy Group: Description

TGD group therapy consisted of 12 weekly sessions, of 90 minutes each, which were facilitated by a psychiatrist. All 12 sessions were held online, during the COVID-19 lockdown. After the COVID-19 lockdown the group met twice in person as a follow-up, 1 and 6 months after the last online session. The sessions were guided by the experiential framework of Yalom and Leszcz (2020), which includes existential, interpersonal, and emotion-focused interventions. The group process and discussions guided the intervention selection. There were no themes selected in advance for discussion. The initial sessions focused on developing trust, personal goals, and group cohesion. The following sessions primarily attended to in-the-moment interpersonal processes with the aim of facilitating individual members' goals. The concluding sessions focused on a reflection of the process and goals achieved, with an orientation towards integration and future plans.

Group Member Recruitment and Characteristics

Members of the therapy group were recruited from the LGBTQ (lesbian, gay, bisexual, trans, queer) transcultural outpatient

clinic at Parnassia Group Psychiatric Institute in Amsterdam. They were referred to the therapist after announcement of the group therapy. Recruitment was restricted to Turkish speaking adult (≥ 18 years of age) TGD individuals, who remained constant across sessions. Individuals that were unable to attend online and with acute suicidality were excluded. Five people were enrolled in group therapy; three of them were previous patients of the therapist, and two were new. Group members suffered from anxiety disorders, including panic disorder, or depressive disorder, PTSD, or comorbidity of these psychopathologies as diagnosed according to DSM-5 criteria (American Psychiatric Association 2013). All members identified as migrants originating from the Middle East (Armenian, Kurdish, Turkish and Syrian). One group member migrated 20 years ago, four members migrated around four years ago. The sex assigned at birth was female for one member, who identifies as trans man, with the remaining four group members were assigned male at birth and identify as trans women. The group members were aged between 35 and 52 years. In terms of education, two people had completed high school and three had completed college. All five members were unemployed. Four members were single and one was in a relationship.

Group Therapist Characteristics

The group meetings were facilitated by a Turkish-speaking cis-gender female psychiatrist experienced in migrant TGD mental health. The therapist regularly prompted the members to reflect on and discuss how her identity as a cis-gender woman impacted their therapeutic relationship. This allowed the members and the therapist to become more aware of how their beliefs around gender affected the group process. It also created the necessary space for members and the therapist to reflect on how the therapist's identity impacted the therapeutic processes of self-revelation and group cohesion. For example, when a group member showed a non-accepting response to the therapists' identity as a cis-gender woman, the therapist needed to process this to remain in full acceptance towards the group member and group cohesion.

Initial Consultation and Consent

Group members provided written and verbal informed consent to be part of the evaluation study. Members were informed that the group work could be used for research purposes, including the possibility of publication of the group therapy content. The study did not require the permission of an ethical committee due to its observational and low interference nature. The therapist met with each member individually for an initial consultation meeting to outline the forthcoming process and to address expectations and concerns. The therapist assessed each member regarding potential challenges they might encounter, within or outside the group process, which could interfere with their participation. In the case of potential challenges, additional

information was collected and the potential implications of these challenges for the member and the group was discussed. Finally, the therapist prompted each member to reflect on their previous experiences with groups, specifically to note their interpersonal strengths and weaknesses as well as to identify how past experiences might influence their position and engagement within the forthcoming group therapy. An agreement on no socialization outside the group was made to prevent attrition. This was continued till the termination of the therapy.

RESULTS

Process

Prior to the therapy sessions, the therapist informed the group members about the structure of the sessions, norms of trust, privacy and the importance of being on time. They were explained that there would be weekly meetings at a set time and day and with a fixed duration of 90 minutes for twelve weeks, without exceptions. Group members were able to maintain this attitude throughout, so no further coaxing was needed. Self-disclosure was explicitly explained to each member individually before the group-sessions began. Moreover, group members were informed that the therapist would apply a passive role, to hold space rather than intervene, and allow the members to console each other. At the beginning of the sessions there were always a period of silence. The group's creation of a safe environment allowed for both support and confrontation. The confrontation started in the last five to six sessions. For instance, when some members did not consider one of the members to be a "she" despite the fact that this member identified as a trans woman. The confrontation was friendly and positive. Due to the limited number of group members, time, and cultural dynamics, this confrontation was not addressed further by the therapist.

The initial sessions of the group therapy focused on building interpersonal relationships. Psychoeducation was also provided to clarify and attune the group process. The 'here-and-now' approach was explained and emphasized as an essential means of promoting progress. The safe and secure atmosphere provided in the group encouraged members to be self-disclosing. Hereafter, the goals of individual group members were identified. The group members were challenged by their differences within the group in defining gender and identifying as a man or woman. None of them identified as non-binary or other gender. Acknowledging and accepting these differences were essential for improvement and restoration of group member's well-being. To facilitate this process, the therapist helped members by differentiating and integrating their differences, which promoted recognition and reduced feelings of loneliness and guilt. During all sessions, the atmosphere was full of appreciation, respect and

support. At the end of the 12th session group members were interviewed on the effects of the therapy by the therapist.

Therapeutic Factors

The evaluation of processes that contributed to the improvement of the group members' symptom reduction and perceived mental health was based on clinical observations by the therapist are discussed below.

Installation of Hope

Research has shown that client's expectations correlate with subsequent therapeutic outcomes (Bloch et al. 1976). Bloch and colleagues (1976) suggest inducing and reinforcing positive expectations in three ways: by discussing the healing properties of the group and framing these in the context the member's difficulties, by repeatedly calling attention to the improvement of previous or present group members, and by nurturing and sharing a sense of confidence in one's own therapeutic effectiveness. During the preparation of this group, benefits of group therapy were discussed with each member personally and then within the group too. After four sessions, group members started commenting on each other's change and experiences which created more open space to share and talk confidently for them.

Universality

Particularly individuals who experience social isolation tend to assume that they alone struggle with certain potentially shameful or frightening problems, thoughts, and behaviors. Hearing other group members disclose similar situations and concerns creates relief, allowing for greater authenticity in communication and the experience that one is 'welcome to the human race'. The revealing of the member's own difficulties in such context creates the opportunity to experience acceptance from the other group members. Challenging discussions around race, sexual orientation and gender identity has been facilitated by the atmosphere that built of courage and trust within the group.

Imparting Information

Rather than psychoeducation and advising group members, in this study installation of hope was the main focus of dynamics/process to cope with social isolation, especially the isolation during the COVID-19 pandemic.

Altruism

Individuals may often feel worthless, as though they have nothing of value to give. Throughout the therapeutic process of group therapy, group members will inevitably give and receive from one another in the form of support, suggestions, reassurance, and share their own experiences. The process of giving empowers individual members by allowing them to demonstrate and develop their strengths, a mechanism

emphasized in positive psychology. In our study, altruism was shown by all group members towards one member that was very emotional during the first couple of sessions. After they observed how the therapist asked how this group member felt, in a non-judgmental and caring manner, the group members started spontaneously checking-in with her over the next sessions. Altruism was a strong dynamic of the group for acceptance and influencing self-worth and shame.

The Corrective Recapitulation of the Primary Family Group

The authors liken the therapy group to a family, including parental figures and siblings who engage in strong emotions, revelations, and intimacy. Such a structure creates the opportunity for re-exposure to early familial conflicts which can then be addressed and repaired. The therapist took mother and father roles during the sessions and created an environment for questioning gender pronouns and becoming more aware of male and female aspects within a self. After a few sessions, group members started to call the group a family.

Development of Socialization Techniques

The group provided opportunities for the development of social skills through encouraging constructive feedback. One example was when a group member shared to have difficulty to speak in public. Other group members encouraged this member by giving positive, constructive comments. This example of group members giving advice to each other made all group members more aware of their capabilities in terms of social interactions, and that they can mean something to someone. This contributed to trust building within themselves and the group. This also allowed members to learn about their interpersonal skills and how this might be contributing to their experience of isolation and loneliness. Overall, through the interpersonal skills that they built up throughout the sessions, they became more open to share their feelings with less social barriers and anxiety.

Imitative Behavior

The authors suggest that groups members benefit from observing and imitating other group members who share their problem constellation. This is called vicarious or spectator therapy. Imitating others' behaviors allows individuals to become aware of which behaviors suit them and which do not. Group members had observed each other's expressions and behaviors, and then applied it later, as shown by the example of altruistic behavior.

Group Dynamics

Group dynamics can be influenced by many factors, such as ethnic background, interpersonal feelings, ego structure, education level and status of gender-affirming surgical procedures. Considering the migration background and

ethnic diversity of the group, difficulties arising from members' ethnic identities could be expected during the group therapy sessions. However, no difficulties or setback regarding the common cultural and ethnical background arose, instead there were feelings of acceptance, warmth and friendship among group members that increased over the course of sessions. The group members shared similar interpersonal feelings such as lack of trust, shame, isolation, loneliness, and rejection. They have been suffering from emotional pain due to a similar background of trauma. This similarity of suffering and sharing similar emotional distress enhanced cohesion and symptom relief as well as trust in each other. Differences in group dynamics appeared in terms of ego structure, education level and status of gender-affirming surgical procedures. Half of the group considered themselves introvert and the other half as extrovert. Interestingly, after a few sessions the group cohesion allowed space for everyone, diminishing the differences in ego structures. This occurred through mimicking behavior: the extraverts gave space to the introverts by inviting them to share their feelings and experiences. Members gained new perspectives to positively change their lives as their education levels differed. Differences in gender-affirming surgical procedures that group members have been through were openly discussed and resolved. This included a discussion about the right to name yourself a woman between two trans women, of whom one still had her male genitalia and one who had been through surgical procedures concerning her genitals. The discussion brought more cohesion as well as it broadened their perspectives. Especially, differences in gender identity helped to balance group dynamics and their perspectives.

Advantages of having online group therapy outweighed disadvantages in terms of the group dynamics. Group members reported that being in their home environment during therapy made them feel safe and helped more, especially considering the extra isolation period of the COVID-19 pandemic. No need for transportation was another advantage, as it reduced costs, anxiety about social interactions and exposure to COVID-19. A major disadvantage of online group therapy was the lack of body language for interpreting interactions during the group process; however, empathy between group members remained intact. Another disadvantage of the online sessions was technical challenges, which caused one group member to be late for a few sessions.

DISCUSSION

This observational report represents the first online study on group therapy involving Turkish-speaking TGD individuals, to the best of our knowledge. Following 12 sessions of group therapy, members benefited from observing and imitating others who shared their problem constellation. By the interpersonal skills that they built up throughout the sessions,

they became more open sharing their feelings experiencing fewer social barriers and reduced anxiety. Online group psychotherapy facilitated improved affirmation and social connection within gender minority groups.

Some limitations should be considered when interpreting the findings of this study. Due to the observational character of the study empirical measures and a control group were not included, and member's responses were solely accessed through the therapist's interpretation. Further research could build upon this initial study by incorporating a control group, larger sample sizes with more diverse cultural dynamics, measure psychological constructs of the participants with validated quantitative measures and include follow-up measures. Despite these limitations, this study is unique in evaluating group psychotherapy in TGD individuals, particularly TGD migrants, during times of extreme isolation caused by the COVID-19 pandemic which had increased feelings of loneliness and increased the connectedness within the group. This observational report emphasizes the need to empirically evaluate the effectiveness of (online) group psychotherapy with TGD individuals, with special attention to the unique needs of TGD migrants.

According to the minority stress theory, depending on the diversity of ethnic and cultural backgrounds, belief systems within therapy groups may influence group dynamics in directions of attachment or discrimination due to social isolation and internalized stigmatization. Therefore, bringing together individuals who share a similar cultural background and emotional distress may foster attachment and group cohesion. Establishing a sense of safety and engendering tolerance and cultivating cultural awareness are essential for fostering group cohesion and community, and can contribute to therapy adherence (Reading and Rubin, 2011), while also helping to prevent conflicts within the group. This emphasizes the importance of therapists being aware of ethnic and cultural differences and creating a safe space for group therapy, with the therapist playing a crucial role in this process.

Similarly, therapists conducting group psychotherapy for TGD individuals should remain aware of their own biases and countertransference responses to ensure effectiveness, as demonstrated by our study. This is especially important when working with migrants, as it requires an understanding of and respect for their cultural perspectives on mental health and psychotherapy (Reading and Rubin 2011). Group therapists should cultivate self-awareness regarding their own gender identities, beliefs about gender, cultural perspectives and life experiences as these factors can influence the dynamics of the group. Ongoing feedback should be elicited from the group members about how the gender identities and expressions of the therapists may be influencing the group dynamics.

As the COVID-19 pandemic has been linked to an increase in cases of depression and anxiety, particularly among populations with low resilience (Manchia et al. 2022). In addition to these mental health effects, there has been a decline in access to in-person healthcare services due to pandemic-related restrictions. Consequently, offering online therapy is now more relevant offering benefits such as lower costs and increased convenience for both clients and therapists. Numerous studies also suggest that online therapy is an effective method for self-expression, intimacy, and connection, with no significant disadvantages compared to in-person psychotherapy (Simpson et al. 2020, Wind et al. 2020, Craig et al. 2021). TGD populations have been more susceptible to mental health issues than heterosexual populations even before the COVID-19 pandemic. Therefore, it is crucial to implement comprehensive and integrative digital mental health care to enhance resilience amongst TGD individuals against psychological stressors during the COVID-19 pandemic and in future pandemics.

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Comparison of Clinical Characteristics, Gender Perceptions, and Rape-Related Beliefs of People Assessed for Criminal Liability for Rape Against Children and Adults



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ABSTRACT

Objective: This study aimed to compare the criminal, sociodemographic and clinical characteristics, paraphilic behaviors, sexual attitudes, gender perceptions, and rape-related beliefs of people assessed for criminal liability for rape against adults and children.

Method: The study compared 40 people investigated for criminal liability for rape against an adult (RAA) with 40 individuals investigated for criminal liability for crime of rape against a child (RAC), and 43 age, sex and education matched individuals without any sexual crime history using the Structured Clinical Interview form for DSM-5 disorders, Hendrick Brief Sexual Attitude Scale, Gender Perception Scale, Illinois Rape Myth Acceptance Scale, and Barratt Impulsiveness Scale-11.

Results: All participants were male. There was no difference between the groups in terms of lifelong or existing psychiatric diseases. All participants had full criminal responsibility during the crime. No participant in any group was diagnosed with a paraphilic disorder. It was determined that people in both RAC and RAA groups tended to use sexuality as a tool, paid less attention to birth control methods, had a far less egalitarian perception of gender, and their myths about rape were significantly higher compared to the control group. The control group was much more impulsive than the sex offenders.

Conclusion: Our results show that the act of sexual assault should not be explained only by impulsivity or psychiatric disorders, and that gender perception and sexual myths may also be influential. The fact that all individuals had full criminal responsibility emphasizes the need for more research on the social and cultural origins of sexual violence.

Keywords: Rape, Sexual Assault, Criminal Responsibility, Gender, Rape Myths

INTRODUCTION

Sexual assault is the violation of a person's body immunity by sexual acts without the consent of the person (Golge et al., 2006). Types of sexual assault include acts ranging from verbal abuse to child sexual abuse and rape. In the United States, it is estimated that 19.3% of women and 1.7% of men have been raped during their lifetime (Breiding et al., 2015). A meta-analysis evaluating 65 studies in 22 countries revealed that 7.9% of men and 19.7% of women were exposed to sexual abuse before the age of 18 (Pereda et al., 2009).

There are some differences and similarities between people who sexually assault adults and people who sexually assault

children (Gudjonsson and Sigurdsson, 2000). It has been reported that people who sexually assault adults experience more anger problems, use more alcohol and substances during the crime, and are more likely to be diagnosed with a personality disorder than those who sexually assault children. On the other hand, people who sexually assault a child experience anxiety disorders and depression more, and their crime is more premeditated and planned (Salter, 1998). Sexual assaults can be perpetrated by strangers or by someone from the immediate environment, including family members of the victim (Golge et al., 2006). Especially in child sexual abuse, offenders are mostly family members, relatives, or acquaintances (Kara et al., 2004). It has been revealed that

Received: 26.09.2021, Accepted: 14.03.2022, Available Online Date: 19.10.2023

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many sexual aggressors have negative views about women, have internalized myths about sexuality and rape, are impulsive, and overly identify themselves with the masculine role (Robertiello and Terry, 1997).

The society and the media often claim that sexual assaults, especially those against children, occur concomitantly with psychiatric diseases, that child abusers are actually pedophiles and need treatment (Murray, 2000), that paraphilias may be common in these people, and that sexual aggressors have more sexual problems (Whitaker et al., 2008). In addition to personality disorders and mental illnesses that can be seen in perpetrators, sexual assaults can be the subject of forensic psychiatry due to the belief that sexual aggressors are 'sick' and may need to be evaluated in terms of criminal liability (Harsh et al., 2006).

This study aimed to contribute to the literature by comparing the criminal characteristics, sociodemographic and clinical characteristics, paraphilic behaviors, sexual attitudes, gender perceptions, and rape-related beliefs of sexual offenders assessed for criminal responsibility for sexual assault against adults and children.

METHOD

A total of 123 literate people over the age of 18 examined in the 4th Forensic Medicine Specialization Board of the Council of Forensic Medicine (CFM) were included in the study; 40 of them were evaluated for criminal liability for sexual assault against adults, 40 of them for criminal liability were evaluated for sexual assault against children, and 43 individuals who were matched with these people in terms of age and education were assessed for criminal liability for a non-sexual, non-violent crime. The research was conducted between March-April 2020 and April-May 2021. Due to the need for a face-to-face meeting with patients and worsening COVID-19 pandemic conditions in the country, the research was suspended between May 2020 and March 2021. While choosing the individuals alleged to have committed a sexual crime, attention was paid to including people in detention or pending trial who were judged to have committed the crime and questioned whether they had an accompanying psychiatric illness (criminal responsibility). The control group was comprised of people in detention or pending trial who were found guilty by the court for a crime that did not include physical or sexual violence (theft, slander, fraud crimes) and who were questioned whether they committed the crime with the influence of any psychiatric illness (criminal responsibility). The research group was divided into two groups, those alleged for rape against children (RAC) and those alleged for rape against adults (RAA). According to the United Nations Convention on the Rights of the Child, anyone under the age of 18 is considered a child (UN

Commission on Human Rights, Convention on the Rights of the Child, 1990). Those who committed rape crimes against persons under the age of 18 were included in the RAC group, and those who committed rape crimes against persons aged 18 and over were included in the RAA group. Sexual crimes can be considered violent crimes. To determine whether the tendency to sexual violence is affected by the clinical characteristics and sexual attitudes of the individuals, people who were evaluated by the institution for a non-violent crime and who did not have a history of sexual crime were selected as the control group.

All participants were male. At the time of the study, only two women who were sexual aggressors were interviewed. Women were not included in the study, considering that there may be differences between sexual assault crimes committed by women and sexual assault crimes committed by men, and that the small amount of data obtained from female participants could not be generalized to all sexual assaults committed by women.

The interviews were held face-to-face by the psychiatrist conducting the research. Individuals were interviewed alone in an environment where privacy conditions were observed, and verbal and written consent was obtained by explaining that the research data would not be used for non-scientific purposes and that participating in this study would not affect the evaluations in terms of criminal liability. After the interview, the case files and past medical documents of the participants were examined, and those with inconsistent forensic and medical history were excluded from the study. Those with simulative behavior, mental retardation, impaired cooperation and cognitive functions due to a neurological disease or alcohol or substance abuse during the examination, and those with manic or psychotic symptoms were also excluded from the study. Scientific and ethical approval was obtained from the CFM Scientific Research Commission on 25/02/2020 with the number 2020/171 and on 30/03/2021 with the number 2021/301 for both dates the study was conducted.

Data Collection Tools

Evaluation Form

In our study, an evaluation form was developed by the researchers to evaluate the sociodemographic and clinical characteristics, criminal data, and paraphilic behaviors of the participants. With the form, the assailant's sociodemographic characteristics, medical and psychiatric history, type of aggression, other types of violence accompanying sexual assault, the way the assault was committed, the victim's age and gender, and any injuries were questioned. A validity and reliability study in Turkish was conducted, and since there is no diagnostic tool for paraphilia, paraphilic disorders

were assessed by the specialist psychiatrist interviewing the participants based on the diagnostic criteria specified in The Diagnostic and Statistical Manual of Mental Disorders 5th ed. (DSM-5) (Diagnostic and Statistical Manual of Mental Disorders Fifth ed., 2016). In DSM-5, paraphilic disorders are classified as voyeuristic disorder, exhibitionistic disorder, frotteuristic disorder, sexual masochism disorder, sexual sadism disorder, pedophilic disorder, fetishistic disorder, transvestic disorder, other specified paraphilic disorder, and unspecified paraphilic disorder.

Structured Clinical Interview for DSM-5 Disorders (SCID-5-CV)

It is a shortened and reformatted version of SCID-5-RV for use by clinicians (First et al., 2016). The Turkish validity and reliability study was conducted by Elbir et al. (Elbir et al., 2019).

The Brief Sexual Attitude Scale (BSAS)

It is a 5-point Likert-type scale developed by Hendrick et al. (2006) (Hendrick et al., 2006), and adapted to Turkish by Karacam et al. (2012). It has four sub-dimensions, which are permissiveness (items 1-10), birth control (items 11-13), communion (items 14-18), and instrumentality (items 19-23). Each item is scored between 1-5 points. Birth control and communion sub-dimensions of the scale are reversely scored. The resulting score of the total scale is not used in the evaluation. The Cronbach's alpha coefficient was reported as 0.86 for permissiveness, 0.84 for birth control, 0.66 for communion, and 0.69 for instrumentality. The scale does not have a cut-off point. Low scores in the permissiveness sub-dimension indicate that the respondent has a promiscuous sexual life and and proclivity to such living. A high score in the birth control dimension indicates that the individual tends to prefer responsible and tolerant sexuality. High scores obtained from the communion dimension indicate that the individual exhibits a sexual attitude that also considers the wishes of the partner. In the last dimension, instrumentality, a low score indicates that the individual is inclined towards a self-centered sexual life and a utilitarian sexual attitude.

Perception of Gender Scale (PGS)

It is a 25-item 5-point Likert-type scale developed in Turkish to evaluate the gender perceptions of individuals (Altinova and Duyan, 2013). High scores on the scale indicate a more egalitarian perception of gender.

The Illinois Rape Myth Acceptance Scale (IRMA)

It is a 7-point Likert-type scale developed by Payne et al. (1999) and validated in Turkish by Coklar and Mese (2015). The scale consists of seventeen items to determine opinions on rape myths. Higher scores on the scale yield also higher levels of acceptance of rape myths.

The Barratt Impulsiveness Scale-11 (BIS-11)

It is a self-report scale developed by Patton et al. (1995) and it used to assess impulsivity. It consists of 30 items and three subscales: attentional impulsivity, motor impulsivity, and non-planning impulsivity. The Turkish validity and reliability study of BIS-11 was performed by Gulec et al. (Gulec et al., 2008).

Statistics

SPSS 21.0 software package was used in all data analyses (SPSS Inc., Chicago, IL, USA). In the study, categorical independent variables were shown with frequency and percentage values; continuous independent variables were presented with mean, standard deviation, median, and range values; and continuous dependent variables were demonstrated with mean and standard deviation values. Skewness and kurtosis indices, histogram plot, QQ plot graph, and Kolmogorov-Smirnov normality test were used to assess the conformity of the variables to normal distribution. To statistically evaluate the relationship between categorical independent variables, groups were compared using the Chi-square test when appropriate and Fisher's exact Chi-square test when the expected value in any cell of the contingency table was less than 5. Analysis of covariance (ANCOVA) was used for the intergroup comparison of continuous dependent variables that met the normal distribution assumptions of the study. Age and education level variables were included in the analysis as covariates. Bonferroni-corrected alpha value of 0.016 (0.05/3) was applied in post hoc pairwise comparisons. The effect size was computed using the Cramer's V for Chi-square statistics and Cohen's effect size (d) values for ANCOVA post hoc pairwise comparisons. First, multinomial logistic regression analysis was performed to determine how categorical and/or continuous variables, which showed statistically significant differences between the groups in the previous steps, predicted belonging to the ASA or CSA group. In the first regression analysis, the control group variable was taken as the reference value. In the other regression analysis, binomial logistic regression analysis was performed by taking the CSA group variable as reference to determine how much the categorical variables, in which a statistically significant difference was detected between the ASA and CSA groups in the previous steps, predicted belonging to the CSA group. Odds ratios and 95% confidence intervals of the predictor variables were shown. $P < 0.05$ was considered statistically significant in all results, except the post hoc Bonferroni-corrected analyses ($p < 0.016$).

RESULTS

The Chi-square test was applied to compare the sociodemographic data, which constituted the independent categorical variables of our study, between the groups. The data are presented in Table 1.

Table 1. Comparison of the Groups in Terms of Sociodemographic Characteristics

	RAC (n:40)	RAA (n:40)	Control (n:43)	χ^2/z	Effect Size (Cramer's V)
Sociodemographic Characteristics					
*Age, Mean $\pm$ SD, Median(Interval)	31.6 $\pm$ 10.6 / 29(18-70)	33.7 $\pm$ 8.6/ 33(19-56)	31.2 $\pm$ 6.5/ 30(22-55)	3.13	
Marital Status, Single/Married/ Divorced-Widowed n(%)	27(68.0)/ 9(23.0) / 4(10.0)	27(68.0)/10(25.0)/3(8.0)	19(44.0)/19(44.0)/5(12.0)	6.75	
Educational Status, Primary School and below/Middle School/High School and above n(%)	20(50.0)/12(30.0)/8(20.0)	23(57.0)/10(25.0)/7(18.0)	23(53.0)/10(23.0)/10(23.0)	0.94	
Presence of Working Status, n(%)	14(35.0)	12(30.0)	11(26.0)	0.87	
Being Imprisoned, Yes n(%)	21(53.0)	14(35.0)	13(30.0)	4.72	
Assault type- anal/vaginal/anal+vaginal (%)	18(45.0)/	14(35.0)/20(50.0)/6(15.0)	19(47.5)/3(7.5)	1.52	
History of Being Sexually Assaulted, n(%)	^a 12(30.0)	7(17.5)	3(7.0)	7.49*	0.25
History of Applying Violence to a Partner in the Past, n(%)	^a 21(52.5)	^b 29(72.5)	7(16.3)	27.25***	0.47
Psychiatric Outpatient Treatment History, n(%)	14(35.0)	17(42.5)	^c 35(81.4)	20.91***	0.41
Psychiatric Inpatient Treatment History, n(%)	4(10.0)	5(12.5)	^c 15(34.9)	10.03**	0.29
Alcohol-Substance Addiction, n(%)	4(10.0)	4(10.0)	^c 12(27.9)	6.59*	0.23

RAC: Those incurred for Child Rape RAA: Those incurred for Adult Rape, SD: Standart Deviation, *p< 0.05, **p< 0.01, ***p<0.001

a: RAC>C b:RAA>C c:C>RAA ve C>RAC

Table 2. Comparison of Sexual Assault Convict Groups in Terms of the Crimes Committed and Their Victims

	RAC (n:40)	RAA (n:40)	χ^2	Effect Size (Cramer's V)
Characteristics of Convicted Offense				
Assault Venue, House/ Outdoor n(%)	^a 25(62.0)/15(38.0)	15(38.0)/ ^b 25(62.0)	5.00*	0.25
Assault's Type of Violence, ^y Verbal/ ^y Physical/ Mixed, n(%)	^a 29(72.0)/4(10.0)/7(18.0)	11(28.0)/9(22.0)/ ^b 20(50.0)	16.28***	0.45
Assault's Type of Act, Planned/Sudden, n(%)	^a 37(92.0)/3(8.0)	10(25.0)/ ^b 30(75.0)	37.64***	0.69
Presence of Proximity with the Victim, n(%)	^a 31(78.0)	17(43.0)	10.21**	0.36
Demographic Characteristics of the Victim				
Victim Age, Median (Interval)	14(4-17)	25(18-60)		
Gender of Victim: Female, n(%)	25(62.0)	30(75.0)	1.45	
Victim's Status After the Assault				
+Death-Severe Injury	0(0.0)	^b 7(17.5)	18.95***	0.49
Minor Injury	14(35.0)	^b 24(60.0)		
No Physical Findings	^a 24(60.0)	7(17.5)		
Pregnancy	2(5.0)	2(5.0)		

RAC: Those incurred for Child Sexual Assault RAA: Those incurred for Adult Sexual Assault, ^yVerbal: Only Verbal Violence, ^yPhysical: Only Physical Violence, *p<0.05, **p<0.01, ***p<0.001

a: RAC>RAA b:RAA>RAC

Table 3. Comparison of the Groups in Terms of the Presence of a Detected Mental Disorder

	RAC (n:40)	RAA (n:40)	Control (n:43)	χ^2
Schizophrenia – lifelong, n(%)	3(7.5)	1(2.5)	6(14.0)	3.67
Schizophrenia – at present, n(%)	1(2.5)	1(2.5)	4(9.3)	2.79
Bipolar Disorder – lifelong, n(%)	1(2.5)	3(7.5)	6(14.0)	3.67
Bipolar Disorder - at present, n(%)	0(0.0)	1(2.5)	4(9.3)	4.97
Unipolar Depression – lifelong, n(%)	4(10.0)	4(10.0)	5(11.6)	0.08
Unipolar Depression – at present, n(%)	2(5.0)	1(2.5)	2(4.7)	0.38
Personality Disorder, n(%)	3(7.5)	6(15.0)	10(23.3)	3.95
Substance Use Disorder - last 12 months, n(%)	4(10.0)	4(10.0)	11(25.6)	5.20
Other Mental Disorders – lifelong, n(%) ^a	4(10.0)	4(10.0)	6(14.0)	0.43
Other Mental Disorders – at present, n(%) ^b	1(2.5)	2(5.0)	5(11.6)	3.06
Paraphilic Behavior, n(%) ^c	5(12.5)	7(17.5)	5(11.6)	5(12.5)

*p<0.05, **p<0.01, ***p<0.001, RAC: Those incurred for Child Sexual Assault RAA: Those incurred for Adult Sexual Assault,

a: Panic Disorder in 4, Social Anxiety Disorder in 1, Generalized Anxiety Disorder in 6, Obsessive-Compulsive Disorder in 2, Adjustment Disorder in 1 of the participants were found to be lifelong

b: 3 of the participants had Panic Disorder, 3 had Generalized Anxiety Disorder, 1 had Obsessive Compulsive Disorder, 1 had Adjustment Disorder

c: In the RAA group, voyeurism was detected in 1 person, frotteurism in 1 person, obscene telephone conversations in 1 person, sexual masochism in 1 person, sexual sadism in 2 people, fetishism in 1 person; In the RAC group, frotteurism in 2 individuals, sexual sadism in 1 person, fetishism in 1 person, sexual relations with children in 1 person; In the control group, voyeurism in 2 people, obscene telephone conversations in 1 person, and fetishism in 2 people

The characteristics of the crime committed by the RAA and RAC groups of sexual aggressors and the demographic characteristics of crime victims were also compared using the Chi-square test. The findings indicate that those in the RAC group committed sexual assault at a higher rate than those in the RAC group (62% vs. 38%), while those in the RAA group committed sexual assault more frequently in open spaces ($X^2=5.00$, $p<0.05$). Analysis of the other forms of violence accompanying sexual assault during the attack revealed that 72% of the assaults against children were accompanied only by verbal violence, 10% only by physical violence, and 18% by both verbal and physical violence (combined). In assaults against adults, these rates were 28%, 22%, and 50%, respectively, indicating a significant difference between the groups ($X^2=16.28$, $p<0.05$). It was determined that premeditation and prior planning of the assault was largely characteristic of the participants in the RAC group (25% vs. 92%), while those in the RAA group committed the crime of sexual assault all of a sudden, without prior planning ($X^2=37.64$, $p<0.001$). Those in the RAC group were more likely to be relatives of the victims compared to those in the ASA group ($X^2=10.21$, $p<0.01$). There was a statistically significant difference between the groups in terms of the medical condition of the victim after the sexual assault ($X^2=18.95$, $p<0.001$), with a higher rate of death-severe injury or minor injury to the victim in the RAA group (18% vs. 0%, 60% vs. 35%, respectively). The proportion of participants with a past criminal history did not differ

significantly between the groups (RAA 33% vs. RAC 23% vs. C 23%, $p>0.05$). The data are presented in Table 2.

Variables obtained from the SCID-5-CV form administered to the participants by the clinician were considered categorical diagnoses, and the groups were compared with the Chi-square test. There was no statistically significant difference between current and past psychiatric diagnoses between the groups ($p>0.05$). None of the participants had a paraphilic disorder. The groups were not significantly different in the proportion of participants describing paraphilic behavior ($p>0.05$).

The mean values of the data obtained from the Likert-type scales filled by the participants and constituting the continuous dependent variables of our study were compared between all three groups by analysis of covariance (ANCOVA). Age and education level independent variables were included in the analysis as covariates for control purposes. In post hoc pairwise comparisons, the null hypothesis was rejected based on the Bonferroni-adjusted significance value ($0.05/3=0.0167$). The comparison of mean BSAS scores of all three groups revealed that the groups had statistically different mean scores in all subscales, except the Communion subscale (Instrumentality: $F=40.21$, $p<0.001$; Birth Control: $F=7.38$, $p<0.001$; Permissiveness: $F=4.35$, $p<0.001$; Communion: $p>0.05$). Participants in the control group had statistically significantly higher scores on the instrumentality, birth control, and permissiveness subscales than those in both the RAA and RAC groups ($p<0.001$, $p<0.001$, $p<0.01$, respectively). The mean PGS scores of the participants in the control group

Table 4. Comparison of the Groups in Terms of the Dependent Variables of the Study

	RAC (n:40) Mean ± SD	RAA (n:40) Mean ± SD	Control (n:43) Mean ± SD	F	Post-Hoc Comparison	Effect Size (Cohen's d)
BSAS-I	9.7±2.2	9.0±2.8	16.8±3.2	40.21***	Control> RAA*** Control> RAC***	2.78 2.57
BSAS-BC	8.3±2.2	8.6±3.6	11.8±2.9	7.38***	Control> RAA*** Control> RAC***	1.19 1.10
BSAS-C	16.5±3.8	16.4±4.3	15.7±3.4	.55	-	-
BSAS-P	25.8±5.9	25.6±8.3	31.2±7.7	4.35***	Control> RAA** Control> RAC**	0.79 0.76
BIS-11 Attentional	18.1±3.0	19.6±3.4	20.7±3.2	4.20**	Control> RAC***	0.86
BIS-11 Motor	25.8±3.5	26.9±4.1	27.7±3.6	1.79	-	-
BIS-11 Non-planning	28.6±3.9	29.8±3.8	30.9±3.7	3.89*	Control> RAC*	0.61
BIS-11 Total	72.5±9.1	76.2±9.6	79.4±9.4	5.93**	Control> RAC**	0.76
PGS	60.0±9.1	62.4±13.0	85.3±8.9	29.43***	Control> RAC*** Control> RAA***	2.40 2.19
IRMA	63.4±6.4	62.9±9.1	35.9±9.5	60.52***	RAC>Control*** RAA>Control***	3.30 3.28

Analysis of Covariance (ANCOVA), age, and education level were taken as covariates.

*p<0.05, **p<0.01, ***p<0.001, RAC: Those incurred for Child Rape RAA: Those incurred for Adult Rape, SD: Standart Deviation, BSAS: The Brief Sexual Attitude Scale, I: Instrumentality, BC: Birth Control, C: Communion, P: Permissiveness, BIS-11: Barratt Impulsiveness Scale-11, PGS: Perception of Scale, IRMA: Illinois Rape Myth Acceptance Scale Brief Form

were significantly higher than those in the RAA and RAC groups ($F=29.43$, $p<0.001$). In terms of IRMA, the scores obtained in the RAA and RAC groups were statistically significantly higher than those in the control group ($F=60.52$, $p<0.001$). The comparison of the scores obtained from the overall BIS-11 and the BIS-11 subscales BIS-attentional impulsivity and BIS-non-planning impulsivity identified a significant difference only between the C and RAC groups. The participants in the control group had higher impulsivity scores than those in the RAC group ($p<0.05$) (Table 4).

Multinomial logistic regression analysis was performed to calculate the extent to which the dependent variables of the study predicted sexual assault crime. All categorical (alcohol-substance addiction history, psychiatric outpatient treatment history, inpatient psychiatric treatment history,

sexual assault history, history of violence to a partner in the past) or continuous (BSAS subscales, except for BSAS-P, and PGS, IRMA, BIS-11 subscales) dependent variables, which were determined to have significant differences between the groups in the previous statistical analysis steps, were included in the analysis. The nominal variable of being in the control group was determined as the reference category of the regression analysis. The regression model was significant with a Nagelkerke R^2 value of 0.57 (Pseudo R^2) ($X^2(8)=129.40$, $p<0.001$). The variables of history of violence against a partner, BSAS-permissiveness, PGS, and BIS-non-planning impulsivity were identified as the predictors of being in the RAA or RAC group compared to the control group ($p<0.05$). When other scale scores are kept constant, a history of violence against a partner in the past increases the probability of being in the RAA group by 21.1 times and being in the

Table 5. Multinomial Logistic Regression Analysis of Variables

Dependent Variables	RAA		RAC		Control
	OR	95% CI	OR	95% CI	OR
History of applying violence to a partner in the past ^a	21.10**	2.80-150.77	8.64*	1.09-68.41	1.00
BSAS-P	0.77**	0.65-0.91	0.77**	0.65-0.91	1.00
PGS	0.79***	0.71-0.88	0.76***	0.68-0.85	1.00
BIS-11 Non-planning impulsivity	0.63**	0.45-0.87	0.55***	0.39-0.78	1.00

*p<0.05, **p<0.01, ***p<0.001 $R^2=0.57$ (Nagelkerke), $X^2(8)=129.40$ OR= odds ratio, CI= confidence interval, RAC: Those incurred for Child Rape RAA: Those incurred for Adult Rape, BSAS: The Brief Sexual Attitude Scale, P: Permissiveness, BIS-11: Barratt Impulsiveness Scale-11, PGS: Perception of Gender Scale

RAC group 8.6 times compared to the control group. A one-unit decrease in BSAS-Permissiveness scores increases the probability of being in the RAA group by 1.3 times and being in the RAC group again by 1.3 times, compared to being in the control group. Likewise, a one-unit decrease in PGS scores increases the probability of being in the RAA group by 1.3 times, and the probability of being in the RAC group again 1.3 times, compared to being in the control group. A one-unit decrease in BIS-non-planning impulsivity scores increases the probability of being in the RAA group by 1.6 times and being in the RAC group 1.8 times, compared to being in the control group.

Binominal logistic regression analysis was performed to calculate the extent to which the dependent variables of the study predicted the crime of sexual assault against an adult or a child. Categorical dependent variables (the presence of affinity with the victim, the way that the attack was committed, the location of the attack, the type of violence, and the condition of the victim after the attack), which showed significant differences between the groups in the previous statistical analysis steps, were further analyzed. The nominal variable of being in the RAC group was determined as the reference category of the regression analysis. The regression model was significant with a Nagelkerke 47 adjusted R^2 ($F(8,71)=9.89$, $p<0.001$). It was found that only the variable of the way the assault was committed was a predictor of being in the RAA group compared to the RAC group ($b=-0.57$ (95% CI -0.81, -0.34), $t=-4.87$, $p<0.001$). The predictability of other variables was not statistically significant ($p<0.05$).

DISCUSSION

The results of this study show that gender perception is not egalitarian in both the RAA and RAC groups, and the myths about rape are significantly higher in these groups compared to the control group. There was no difference between the groups in terms of lifelong or existing diagnosis of psychiatric diseases and paraphilia, and it was determined that all participants had full criminal responsibility. This research is one of the few studies conducted by interviewing perpetrators of sexual assault in Turkey, aiming to provide information on the origins of sexual assaults and the approach to the aggressors.

It was determined that 17 of the RAA group, 14 of the RAC group, and 35 of the control group had a psychiatric diagnosis in the past. However, all participants had full criminal liability. In other words, there was no reduction in the perception of the legal meaning and consequences of the act or the ability to direct their behavior regarding this act. During sample selection, those with mental retardation, cognitive damage, and active psychotic or manic symptoms were excluded from the study. This may have prevented the inclusion of

individuals who do not have full criminal liability in the study. The widespread use of the terms 'pedophile', 'sex offender' and 'patient' in society leads to the false assumption that 'sex offender' is a diagnostic term and that sex offenders are thus mentally ill (Fagan et al., 2002). As none of the groups met the criteria for functionality and/or duration, the participants were not diagnosed with a paraphilic disorder. Unlike earlier versions of the DSM, paraphilias are not considered a pathology in the DSM-5 unless they cause clinically significant distress, or interpersonal or functional problems (Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, 2013). Despite not meeting the criteria for defining a disorder, paraphilic behaviors were detected in 7 of the RAA group, 5 of the RAC group, and 5 of the control group, and no significant difference was found between them. Only one person in the RAC group described a pedophilic interest. Others stated that their sexual assault was not caused by sexual interest in children. The individuals included in the study were sent to the institution for evaluation of criminal liability; hence, they might have hidden their paraphilic behavior due to stigmatization toward paraphilias (Lehman et al., 2021). Due to beliefs stemming from incomplete knowledge about paraphilias and psychiatric diseases, especially pedophilia, there is a common perception that every sexual aggressor can be paraphilic. These beliefs and discourses also lead to debates on treatment methods, which can reach up to chemical and surgical castration of sexual aggressors (Kim et al., 2016) and which have no effect on preventing sexual assaults at the social level. Because of the prejudice toward disorders, it is difficult for psychiatric patients to access treatment (Lehman et al., 2021). To both correct these false beliefs about sexual assaults and prevent attacks, it is crucial to avoid the use of stigmatizing language against sexual aggressors, especially among healthcare professionals, implying that these people are 'sick,' and to focus more on social values that pave the way for sexual violence.

It was determined, that, compared to the control group, people in both RAC and RAA groups tended to use sexuality as a tool, to have indiscriminate sexuality and to pay less attention to birth control methods. Sexual violence has also been reported to be used as a tool and even as a weapon (Kirby, 2013). It is stated that people who use sexuality only as a means of 'relaxation' also experience more random sex (Dubé et al., 2017) and that birth control methods are used less frequently in random sexual relations (Lescano et al., 2006). Analysis of the Brief Sexual Attitude Scale (BSAS)-The communion dimension revealed no difference between the groups. In the communion dimension, responses were sought for statements such as 'Sex is the closest form of communication between two people,' 'Sex is a very important part of life,' and 'Sex is usually an intense and shocking experience.' The responses to these statements may

have been given considering the positive aspects of gender, such as being a part of life and an important interaction tool, or the negative aspects of being superior to other forms of communication. The permissiveness sub-dimension included statements such as 'the best sex is sex without rules' or 'sex can just be a good physical relief.' A low score in this sub-dimension indicates that the person tends to engage in sexual relationships that require less attachment or do not involve emotional investment (Hendrick et al., 2006). The regression analysis also showed that the decrease in permissiveness scores predicts sexual assaults against both adults and children. It has been suggested that sexual aggressors have less capacity for empathy (Marshall and Moulden, 2001), they experience attachment problems, particularly insecure attachment (Ward et al., 1995), and they misinterpret sexual cues (Abbey and McAuslan, 2004). Although it is partially possible to associate the differences in sexual attitudes between the control group and the sexual aggressors in our study with the personality traits that effect interpersonal relationships, these data are insufficient to explain why most of the perpetrators are men. Besides, associating sexual assault with the individual distress experienced by individuals carries the risk of overlooking the cultural context that influences sexual attitudes. Therefore, it should be noted that the fact that the sexual aggressors in our study were using sexuality as a tool, in other words, they were seeking a more random and unbiased sexual relationship, is influenced not only by individual characteristics but also by social factors.

Sexual violence is a type of violence originating from gender hierarchy (Scarduzio et al., 2017). Myths are common in society that 'immoral' women are responsible for the sexual assault, or at least they provoke the aggressor, that the assault occurs because of the victim's reluctance to say 'no,' and that the assaults are performed by men who cannot control their impulses (Grubb and Turner, 2012). In our study, the perception of gender was far from being egalitarian, and myths about rape were significantly higher in both the RAA and RAC groups than in the control group. Regression analysis showed that a decrease in the Perception of Gender Scale (PGS) scores predicted being in the sexual aggressor group. Again, the Barratt Impulsivity Scale-11 (BIS-11) scores showed that the control group was much more impulsive than those who were alleged to have committed sexual crimes. These findings suggest that the act of sexual assault cannot be explained solely by impulsiveness, and that gender perception and sexual myths may also contribute to the emergence of this act.

Golge et al. (2006) found that most of the assaults against children were committed at home, the use of violence was lower, the assault was planned and the majority of the perpetrators were relatives of the victim, the victims showed less physical resistance, and most of them had no physical findings, whereas assaults against adults were committed more

in public places, injuries were more common, and victims showed more resistance (Golge et al., 2006). Our findings are in agreement with these data. The regression analysis shows that the way that the assault is committed differs in assaults against adults or children and is predictive. It is stated that child molesters exhibit less violence because children are open to manipulation and tend to choose victims from their close circles (Robertiello and Terry, 1997). This may make it difficult for sexually abused children to seek help or be heard.

The history of sexual assault was significantly higher in the RAC group than in the other groups. According to one theory, the person who was sexually abused in childhood re-enacts this trauma through their victims in their adulthood (Simons et al., 2002). It has been suggested that traumatic experiences caused by childhood abuse reduce the ability to empathize with others in adulthood (Bandura et al., 1975), and that these individuals commit more sexual assaults against children in adulthood (Simons et al., 2002). Although the identification of sexually assaulted individuals with the aggressor due to their past traumas seems to explain the dynamics of some assaults, most people exposed to sexual abuse in childhood do not resort to sexual violence in their adulthood (Greathouse et al., 2015). Besides, given that girls are at least as likely to be sexually abused as boys, these theories fail to explain why sexual aggressor women are less common. The psychopathological model reduces the problem to individuals only and may deny gender differences in cultural learning in male-dominated societies (Scully, 1990). This again suggests that more attention should be paid to the social causes of sexual assaults.

Participants in both the RAA and RAC groups had significantly higher rates of violent and sexual crime than those in the control group. While 29 in the RAA group and 21 in the RAC group applied physical violence to their partners in the past, this rate was 7 in the control group. The regression analysis showed that having a history of partner violence increased the risk of being in the RAA group by 21.1 times, and the risk of being in the RAC group by 8.6. The perpetrator's history of physical or sexual violence may be an important factor in predicting sexual assaults (Dhawan and Marshall, 1996). For this reason, it is thought that the appropriate determination of and imposing of sanctions against people who have committed physical or sexual assault in the past and raising public awareness on this issue may be effective in preventing repetitive sexual assaults.

Limitations

It was difficult to generalize the data to all perpetrators of sexual assault since only those sent for legal reasons were examined in the institution where the research was conducted, and the participants were confined to individuals sent for criminal liability assessment. Patients with mental retardation, cognitive

impairment, and active psychotic or manic symptoms were excluded from the study. This may have prevented people without full criminal responsibility from participating in the study. While choosing the people who were alleged to have committed a sexual crime, people who were judged to have committed the crime by the court and who were questioned whether they committed the crime under the influence of any psychiatric illness were included in the study. However, the trials of some participants were still ongoing, and therefore their decisions were not finalized. Although the individuals found to be simulative were not included in the study, the possibility of a biased response should not be excluded. Again, the number of those sent to the institution for sexual assault and child abuse is lower than those sent for other crimes. Therefore, the smaller number of people in the study and control groups is another limitation. It is crucial to conduct studies with more participants and groups other than those who are questioned for criminal liability. Only men were included in the study. Therefore, data obtained may not be valid for female offenders. Moreover, the nature of the crime, the sexual attitudes of the aggressors, and their perceptions of gender may vary according to the gender of the victims. Another limitation of the study is that the victims were not separated by gender. The research started in March 2020, but due to the pandemic, and the difficulty of meeting face-to-face, the interviews were interrupted for about a year and continued in April 2021. Considering that the frequency of domestic violence and sexual assaults increased during the pandemic and quarantine period (Kofman and Garfin, 2020), temporal differences in data collection may have also affected the results and the factors that can be associated with the results.

CONCLUSION

The causes of sexual assault, especially rape, which can be considered the most violent form of sexual assault, are quite complex. Although various psychiatric diseases, especially paraphilias, have been suggested to cause sexual assaults, the psychopathological model alone is insufficient to explain the motivation of the assaults. The full criminal responsibility of all participants reveals the necessity of thinking more about the social and cultural roots of sexual violence. We think that longitudinal studies with larger groups on the origins of sexual assault will improve our understanding of this issue.

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Fear, Perceived Threat, and Anxiety During COVID-19 Pandemic: The Mediating Role of Cognitive Control/Flexibility and Intolerance of Uncertainty



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ABSTRACT

Objective: In this study, we aimed to evaluate the relationship between fear of COVID-19, perceived threat of COVID-19, anxiety, cognitive control/flexibility, and intolerance to uncertainty. In addition, the mediating role of cognitive control/flexibility and intolerance to uncertainty were investigated.

Method: 224 volunteers aged between 18-55 years were included in the study. Cognitive Control and Flexibility Scale, Intolerance of Uncertainty Scale, Fear of COVID-19 Scale, Perceived COVID-19 Threat Form and Beck Anxiety Scales were administered to all participants via an online environment. In this context, Pearson correlation, linear regression, and mediation analyzes were performed.

Results: There were significant relationships among Cognitive Control and Flexibility, Intolerance of Uncertainty, Beck Anxiety, fear of COVID-19, perceived COVID-19 threat ($p<0,01$). Linear regression analysis showed that the Beck Anxiety Scale, Intolerance of Uncertainty and Cognitive Control/ Flexibility Scale scores significantly predicted fear of COVID-19 and the perceived threat of COVID-19 ($p<0,001$). In addition, mediation analysis revealed that intolerance to uncertainty and cognitive control/flexibility are mediating factors between anxiety and the perceived threat of COVID-19 ($p<0,01$).

Conclusion: There is a relationship between fear of COVID-19 and perception of threat, anxiety, intolerance of uncertainty, and cognitive control mechanisms. In accordance with these findings, psychosocial support and therapy programs can be created based on cognitive control/flexibility and intolerance of uncertainty in order to increase the mental health well-being of individuals.

Keywords: Cognitive Control, Flexibility, Intolerance To Uncertainty, Anxiety, Perceived Threat, COVID-19

INTRODUCTION

The COVID-19, which was caused by the SARS-CoV-2 virus and first appeared in Wuhan, China, in December 2019, quickly spread to the rest of the world, resulting in a significant public health concern. COVID-19 has caused 258,830,438 confirmed cases and 5,174,646 deaths as of November 25, 2021 (WHO Coronavirus (COVID-19) Dashboard, November 25, 2021). As a result of the unpredictability of the outbreak and the course of the disease, COVID-19 causes alarm in numerous regions. Fear of becoming infected, transmitting the virus to others, losing loved ones, losing

employment, not receiving sufficient medical care, isolation due to quarantine, and fear of dying from the virus are examples of these anxieties (Deniz 2021, Montemurro 2020, Satici et al. 2020a). Fear, as a fundamental emotion, can be viewed as an adaptive reaction to the threat posed by traumatic stimuli (Gratz et al. 2015), and it encourages people to take preventive and protective actions to avoid unpleasant events. Fear caused by the outbreak may heighten an individual's perception of risk and correspondingly alter their behavior. Fear of contracting a disease or infecting loved ones is a frequent response that can lead to anxiety-related

Received: 16.11.2021, **Accepted:** 15.11.2022, **Available Online Date:** 12.10.2023

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psychological issues (Kubb and Foran 2020). Dealing with an unidentified virus can induce considerable anxiety, which can lead to functional difficulties.

Due to its considerable association with anxiety and mental problems associated with the feeling of danger and worry, the significance of intolerance of uncertainty has been highlighted. (Birrell et al. 2011). Intolerance of uncertainty can be defined as the tendency of an individual to perceive ambiguous situations and events as threatening in emotional, behavioral, and cognitive aspects (Heimberg et al. 2004). Given the prevalence of unforeseen circumstances in life, intolerance of uncertainty will likely be inevitable and difficult for many individuals. According to Buhr and Dugas (2002), intolerance of uncertainty has four dimensions: uncertainty is stressful and disturbing, uncertainty impedes action, uncertain circumstances are undesirable and should be avoided, and uncertainty is unfair. (Buhr and Dugas 2002). COVID-19 has had harmful effects on both physical and emotional health (Wang et al. 2020). The findings of studies indicate that COVID-19 can cause a variety of neuropsychiatric illnesses, including depression, anxiety, and panic disorders (Qiu et al. 2020). Prior to the pandemic, the global prevalence of anxiety disorders was estimated to be 7.3% (Stein et al. 2017), however, a recent meta-analysis of 43 important research conducted during the COVID-19 outbreak indicates that this incidence is 25% (Santa Barbara et al. 2021). Anxiety is a future-focused response to big life events, and symptoms include a rapid heartbeat, perspiration, and apprehension that something negative may occur. Given that COVID-19 is known to have a severe course, particularly in those over 60 years old and those with concomitant chronic disorders, it is reasonable to assume that those who live with someone over 60 will suffer higher levels of anxiety as a result. (Zhou et al. 2020). Additionally, research indicates that those with high anxiety levels are more prone to seek psychiatric assistance in this regard. (Russell et al. 2022). According to Morris et al. (2016), intolerance of uncertainty is one of the fundamental components of anxiety disorders, and it has been suggested that intolerance of uncertainty promotes anxiety (Rettie and Daniels 2020). In a study conducted by Satici et al., intolerance of uncertainty was found to be a significant component of COVID-19 fear (Satici et al. 2020b). According to another study, fear of COVID-19 is associated with intolerance of uncertainty, stress, despair, and anxiety (Bakioglu et al. 2020). Additionally, psychological flexibility and intolerance of uncertainty have been shown to predict state anxiety levels (Mallett et al. 2021).

Cognitive control is another concept that connects with intolerance of uncertainty. Numerous studies have demonstrated that cognitive control processes are at the core of uncertainty (Mushtaq et al. 2011). As cognitive control is the ability to focus on relevant information toward a specific

goal while suppressing irrelevant information (Morton et al. 2011); cognitive flexibility emphasizes the significance of being able to adapt one's reactions to a constantly changing environment (Moore and Malinowski 2009, Stemme et al. 2007). Cognitive control is one of the primary components that enable humans to adapt to difficult circumstances. For instance, research indicates that cognitive processes might be related to the working environment (Bosma et al. 2003, Potter et al. 2008), and today's dynamic working contexts make cognitive flexibility increasingly vital (Cascio 2003). As an executive function, cognitive control/flexibility is crucial for coping with the unpleasant features of the epidemic. Cognitive control and cognitive flexibility are widely used interchangeably in the literature since they overlap criteria and are evaluated using similar tasks (Daz-Blancat et al. 2018, Glascher et al. 2012). Cognitive flexibility has been identified as a component of cognitive control processes from a cognitive neuroscience perspective (Dajani and Uddin, 2015; Marko and Riečanský, 2018). Cognitive control is reported to be associated with goal-directed behaviors such as problem-solving and decision-making, as well as various executive functions such as working memory and inhibition (Deniz 2021, Gläscher et al. 2012, Mackie et al. 2013). In addition to executive functions, cognitive control is also associated with emotional control and emotional regulation (Gotlib and Joormann 2010, Hofmann et al. 2012).

Based on studies and evidence now available, it is possible to conclude that the psychological effects of COVID-19 are unavoidable. According to Smith et al., adaptability can play an essential role in minimizing the pandemic's detrimental health effects (Smith et al. 2020). In this context, identifying the risk factors as well as how individuals are affected by the pandemic process has become a key concern. The purpose of this study was to assess the association between fear and threat perception with psychological and cognitive factors that came with the COVID-19 pandemic process. The hypotheses of the study are as follows: 1) There is a positive relationship between COVID-19 fear and threat perception and intolerance of uncertainty; 2) There is a negative relationship between COVID-19 fear and threat perception and cognitive control and flexibility; and 3) Cognitive control/flexibility and intolerance of uncertainty mediate the relationship between COVID-19 fear and threat perception and anxiety. In addition, sociodemographic information will be evaluated based on cognitive control/flexibility and Beck anxiety levels.

METHOD

Sample

The study was granted permission by the Ethics Committee of Izmir Democracy University on April 7, 2021, with the decision number 2021/07-04, and the rules of the Helsinki

Declaration have been followed during the data collection process. The study was concluded between April and September 2021, and data was collected between July 8 and August 14, 2021. Due to the possible dangers of face-to-face interviews during the COVID-19 epidemic, the data was collected via an online survey. All subjects provided informed consent prior to the commencement of the study. Inclusion criteria included having at least a primary school education and being between the ages of 18 and 55. Exclusion criteria included having a medical condition that affects cognitive functions, being outside the specified age range, being unable to use a computer effectively, and refusing to participate in the study.

Out of 224 individuals in total, 134 (59.8%) of the participants were female, 85 (37.9%) were male, and 5 (2.2%) were queer. The participants had a mean age of 37.07 (SD=11.8) years. There were 4 (1.8%) elementary school graduates, 16 (7%) high school grads, 127 (56.7%) undergraduates, 55 (24.6%) graduates, and 22 (9.8%) PhD graduates among the participants.

Data Collection Instruments

The Socio-Demographic Form

This form was created by the researchers to collect information about the socio-demographic characteristics of the participants, such as age, gender, marital status, and education level, as well as their health status during the pandemic, the precautions they took, and their views on vaccination.

The Cognitive Control and Flexibility Questionnaire (CCFQ)

The scale, which was established by Gabrys et al. in 2018, evaluates the ability to manage undesirable thoughts and emotions, as well as the coping skills acquired in stressful situations. Demirtaş conducted the Turkish validity and reliability assessment of the scale in 2019, and the Cronbach alpha values were between 0.85 and 0.91. The CCFQ is composed of two factors, titled "Cognitive Control over Emotions" and "Appraisal and Coping Flexibility." The 18-item CCFQ is a self-report scale with a 7-point Likert scale, and participants are asked to rate between 1: I Do not agree at all and 7: I fully agree (Demirtaş, 2019).

Intolerance of Uncertainty Scale

This scale was initially developed in French and then translated into English and Turkish by Sarı and Dağ in 2009. It has a four-factor structure and comprises of a total of 26 items. These factors are: 1) uncertainty is stressful and upsetting, 2) negative self-assessment about uncertainty 3) disturbing thoughts about the uncertainty of the future; and 4) uncertainty keeps someone from acting. The internal

consistency coefficient for the IUS was found to be 0.93, and it is noted that the scale is a viable and reliable instrument for assessing the level of uncertainty tolerance in individuals (Sarı and Dağ, 2009).

The Fear of COVID-19 Scale

This scale was created by Ahorsu et al. in 2020 to measure individuals' fear of COVID-19 and has been modified for usage in the Turkish context. It is a seven-item, one-dimensional self-report questionnaire with a 5-point Likert scale (1: Definitely disagree and 5: Definitely agree). The lowest possible score on the scale is 7, and the maximum possible score is 35, with higher numbers indicating a greater level of fear towards COVID-19. The internal consistency and test-retest reliability of the scale are 0.82 and 0.72, respectively. Ladikli et al. conducted the Turkish validity and reliability research and reported a Cronbach's alpha coefficient of 0.86. (Ladikli et al. 2020).

Perceived COVID-19 Threat Form

This seven-item self-report scale was developed by Kavaklı et al. in 2020. It employs a 5-point Likert scale (1: Definitely disagree and 5: Definitely agree) to assess respondents' perceptions of the COVID-19 threat. The scale consists of a single element, with higher values indicating a greater perception of threat. The Cronbach's alpha coefficient for the scale is 0.75 (Kavaklı et al. 2020).

The Beck Anxiety Scale

It is a self-report scale consisting of 21 items. It was developed by Beck et al. and the Turkish validity and reliability study was conducted by Ulusoy et al. in 1998. It is a 4-point Likert scale that measures the anxiety symptoms experienced by individuals in the preceding week, ranging from 0 (not at all) to 3 (very severely). The range of possible scale scores is between 0 and 63.

Statistical Analyses

For statistical analysis of the data, SPSS 24.0 version was utilized. For all measurable data, the mean and standard deviation were provided, while percentages were provided for categorical data. A t-test was used to investigate the comparison of groups based on socio-demographic information, cognitive control/flexibility, and Beck anxiety levels. Using variance analysis, the mean COVID-19 fear scale scores of more than two groups were compared. COVID-19 fear, and perceived COVID-19 threat were evaluated using linear regression and Pearson correlation, respectively, to determine the association between variables. Then, SPSS was used to conduct mediation analyses with the bootstrap option of 1,000 resampling, as suggested by Preacher and Hayes (2004). If the 95% confidence intervals do not overlap zero, the indirect effects are considered substantial (Preacher and Hayes, 2004).

RESULTS

The average age of the participants was ($\bar{x}$ =37.1, SD =11.8) and the average number of years of education was ($\bar{x}$ =16.6, SD =4.3). Mean scores were as follows: fear of COVID-19 ($\bar{x}$ =15.3, SD =6.1), cognitive control and flexibility ($\bar{x}$ =86.5, SD =17.9), perceived threat of COVID-19 ($\bar{x}$ =16.46, SD =5.7), intolerance of uncertainty ($\bar{x}$ =72.9, SD =23.7), and Beck anxiety ($\bar{x}$ =8.7, SD =9.5). Additional socio-demographic factors are shown in Table 1. There was a statistically significant trend based on independent samples t-test results, $t(90.314)=-1.94$, $p=0.056$, indicating that people living with someone with a chronic illness or over 65 years old had higher anxiety levels than those who did not live with someone with a chronic illness during the COVID-19 pandemic. Moreover, during the pandemic, working individuals exhibited significantly greater cognitive control and flexibility ($\bar{x}$ =80.3, SD =18.2) than non-working individuals ($\bar{x}$ =89.4, SD =17.0), $t(222)=-3.61$, $p<0.01$. Those who received psychological help during the COVID-19 pandemic also had greater Beck anxiety levels ($\bar{x}$ =16.2, DS =9.8) than those who did not ($\bar{x}$ =8.2, SD =9.3), $t(222)=-3.21$, $p<0.01$. (Supplement 1).

The findings of the variance analysis revealed a statistically significant correlation between COVID-19 fear scores and the frequency of interaction with non-family members during the pandemic (none, once a week, once a month, every day), $F(3.220)=2.62$, $p=0.05$. Multiple comparisons revealed that, according to the results of the Tukey HSD test, the average scores of participants who did not speak to anyone during the pandemic and those who spoke to people outside their family every day were substantially different ($p=0.03$, 95% $CI=[0.31, 7.95]$). In addition, the variance analysis revealed a statistically significant difference in COVID-19 fear between subjects who had or will get the COVID-19 vaccine, $F(2.221)=6.45$, $p<0.01$. According to the results of the Tukey HSD test, the averages of individuals who have or will get the COVID-19 vaccine differed ($p=0.009$, 95% $CI=[-7.99, -0.94]$). Other socio-demographic variables associated with COVID-19 did not demonstrate statistically significant differences ($p>0.05$).

The findings of the correlation study revealed that COVID-19 fear was adversely associated with the total score of the cognitive control and flexibility scale ($r=-0.220$, $p<0.01$). In addition, there was a positive correlation between COVID-19 fear ratings and Beck anxiety scores ($r=0.42$, $p<0.01$) (Table 2). The perceived threat scores of COVID-19 were found to have a positive correlation with Beck Anxiety scores ($r=0.43$, $p<0.01$) and a negative correlation with cognitive control and flexibility ($r=-0.35$, $p<0.01$) (Table 2). Participants' fear of COVID-19 and their perceived threat scores were positively associated with the intolerance of uncertainty scale (respectively $r=0.34$, $p<0.01$; $r=0.45$, $p<0.01$) (Table 2). All Pearson correlation results are presented in Table 2.

Table 1. Sociodemographic Data

Variables	Frequency (%)
Sex	
Male	85 (37.9)
Female	134 (59.8)
Queer	5 (2.3)
Marital Status	
Single	105 (46.9)
Married	119 (53.1)
Did you receive psychological support during the Covid-19 pandemic?	
Yes	15 (6.7)
No	209 (93.3)
Who do you live with during the Covid-19 pandemic?	
Alone	28 (12.5)
Roommate	12 (5.4)
Family	184 (82.1)
Do you have any kids?	
Yes	97 (43.3)
No	127 (56.7)
Do you work?	
Yes	153 (68.3)
No	71 (31.7)
What is your mode of work during the Covid-19 pandemic?	
I don't work	67 (29.9)
From home	67 (29.9)
From office	90 (40.2)
Have you been diagnosed with Covid-19?	
Yes	21 (9.4)
No	203 (90.6)
Have you had a Covid-19 test?	
Yes	108 (48.2)
No	116 (51.8)
Have you been in quarantine during the Covid-19 pandemic?	
Yes	61 (27.2)
No	163 (72.8)
Has a relative of yours been diagnosed with coronavirus?	
No	74 (33)
Yes, but we don't live together	127 (56.7)
Yes, we live together	23 (10.3)
Is there anyone working in the Covid 19 clinic among the people you live with?	
Yes	21 (9.4)
No	203 (90.6)
Have you had the COVID-19 vaccine when it was your turn?	
Yes	188 (83.9)
I will make an appointment	17 (7.6)
I don't want to get vaccinated	19 (8.5)
How often do you meet with people outside the family?	
Everyday	35 (15.6)
Once a month	67 (29.9)
Several times a week	91 (40.6)
I don't see anyone outside the family	31 (13.8)
Have you lost a loved one due to coronavirus?	
Yes	38 (17)
No	186 (83)
Is there anyone over the age of 65 or with a chronic illness who lives with you?	
Yes	61 (27.2)
No	163 (72.8)

Supplement 1. Independent Samples T-test Results

Independent Variable	Dependent Variable	Yes	No	t	df	p
		Mean.±SD	Mean.±SD			
Living with a chronically ill person	Anxiety	10.93±11.0	7.90±8.8	-1.936	90.314	0.056
Working status	Cognitive Control/Flexibility	89.35±16.9	80.34±18.2	-3.612	222	0.000
Getting psychological support	Anxiety	16.20±9.8	8.19±9.3	-3.210	222	0.002

p<0.05 SD: Standard deviation

Table 2. Pearson Correlation Analyses Results

Variables	Fear of COVID-19	Perceived COVID-19 Threat	Intolerance of Uncertainty	Beck Anxiety
Cognitive Control and Flexibility Subtype 1	$r=-0.30$ $p=0.00$	$r=-0.40$ $p=0.00$	$r=-0.57$ $p=0.00$	$r=-0.45$ $p=0.00$
Cognitive Control and Flexibility Subtype 2	$r=-0.05$ $p=0.43$	$r=-0.18$ $p=0.01$	$r=-0.24$ $p=0.00$	$r=-0.26$ $p=0.00$
Cognitive Control and Flexibility Total	$r=-0.22$ $p=0.00$	$r=-0.35$ $p=0.000$	$r=-0.50$ $p=0.00$	$r=-0.43$ $p=0.00$
Beck Anxiety	$r=0.42$ $p=0.00$	$r=0.43$ $p=0.00$	$r=0.35$ $p=0.00$	-----
Intolerance of Uncertainty	$r=0.34$ $p=0.00$	$r=0.45$ $p=0.00$	-----	$r=-0.35$ $p=0.00$
Fear of COVID-19	-----	$r=0.72$ $p=0.00$	$r=0.34$ $p=0.00$	$r=0.42$ $p=0.00$

Note. Subtype 1: Cognitive Control Over Emotions; Subtype 2: Appraisal and Coping Flexibility
p<0.01

Table 3. Regression Analysis Results in Predicting Fear of COVID-19

Variables	B	t	P	95 % CI	R ²
Beck Anxiety	0.25	5.812	0.000	[0.17, 0.34]	0.16
Cognitive Control/Flexibility	-0.02	-0.761	0.448	[-0.06, 0.03]	
Age	0.01	0.150	0.881	[-0.06, 0.07]	

p<0.001, CI = Confidence Interval

As shown in Tables 3 and 4, the regression model constructed using the total Beck anxiety and cognitive control and flexibility scale scores is significant in predicting COVID-19 fear and perceived threat scores ($R^2=0.18$, $F(2,221)=23.45$, $p<0.001$; $R^2=0.22$, $F(2,221)=31.48$, $p<0.001$). The regression model created for fear of COVID-19 and perceived threat of COVID-19 with Beck anxiety and intolerance of uncertainty was found to be statistically significant (respectively, $R^2=0.22$, $F(2,221)=30.61$, $p<0.001$; $R^2=0.29$, $F(2,221)=44.86$, $p<0.001$). Beck anxiety and intolerance of uncertainty significantly predicted fear of COVID-19 (respectively;

$\beta:0.21$ $t(221)=5.30$ $p<0.001$; $\beta:0.06$ $t(221)=3.52$ $p<0.001$). Beck anxiety and intolerance of uncertainty also significantly predicted perceived threat of COVID-19 (respectively; $\beta:0.19$ $t(221)=5.08$ $p<0.001$; $\beta:0.08$ $t(221)=5.54$ $p<0.001$) (Table 5 and Table 6). A mediation analysis was conducted utilizing SPSS version 24 and the bootstrap technique described by Preacher and Hayes (2004). The bootstrap approach is applicable even when sample sizes are moderate or small and is supported by comparable methodologist guidelines (Koopman et al. 2015, Preacher and Hayes, 2004).

Table 4. Regression Analysis Results in Predicting Perceived COVID-19 Threat

Variables	B	t	P	95% CI	R ²
Beck Anxiety	0.21	5.20	0.00	[0.13, 0.28]	0.22
Cognitive Control/Flexibility	-0.07	-3.01	0.00	[-0.11, -0.22]	
Age	-0.01	-0.21	0.83	[-0.07, 0.05]	

p<0.001, CI = Confidence Interval

Table 5. Beck Anxiety, Intolerance of Uncertainty, and Age as Predictors of COVID-19 Fear

Variables	B	t	P	95% CI	R ²
Beck Anxiety	0.21	5.30	0.00	[0.13, 0.29]	0.22
Intolerance of Uncertainty	0.06	3.52	0.00	[0.03, 0.09]	
Age	0.01	0.37	0.71	[-0.05, 0.07]	

p<0.001, CI = Confidence Interval

Table 6. Beck Anxiety, Intolerance of Uncertainty and Age as Predictors of Perceived COVID-19 Threat

Variables	B	t	P	95% CI	R ²
Beck Anxiety	0.19	5.08	0.00	[0.12, 0.26]	0.29
Intolerance of Uncertainty	0.08	5.54	0.00	[0.05, -0.11]	
Age	-0.01	-0.33	0.74	[-0.06, 0.05]	

p<0.001, CI: Confidence Interval

Table 7. Path Coefficients and Indirect Effects in Mediation Analysis

IV ₁	MV	DV ₂	Path a			Path b			Indirect Effect		
			Coefficient	SE	p	Coefficient	SE	p	Coefficient	SE	95% CI
Anxiety	MV 1	Perceived threat	0.88	0.16	0.00	0.08	0.01	0.00	0.07	0.02	[0.04, 0.11]
Anxiety	MV 1	Fear	0.88	0.16	0.00	0.06	0.02	0.00	0.05	0.02	[0.02, 0.08]
Anxiety	MV 2	Perceived threat	-0.81	0.11	0.00	-0.07	0.02	0.00	0.05	0.02	[0.02, 0.10]

Not. IV₁: Independent Variable, DV₂: Dependent Variable, MV1: Mediating Variable 1, Intolerance of Uncertainty, MV 2: Mediating Variable 2, Cognitive Control/Flexibility, SE: Standard Error, p<0.01

Beck anxiety was found to have an indirect effect on COVID-19 fear via intolerance of uncertainty, $b=0.05$, 95% BCa CI [0.02, 0.08]. The direct effect of Beck anxiety on perceived threat of COVID-19 was found to be significant, and the role of intolerance of uncertainty in this relationship was also determined, $b=0.07$ 95% BCa CI [0.04, 0.11]. Additionally, Beck anxiety had a significant indirect effect on perceived threat of COVID-19 through the mediating role of cognitive control and flexibility, $b=0.05$, 95% BCa CI [0.02, 0.10]. The confidence intervals in the table do not intersect with zero, therefore, the indirect effects are reported as statistically significant. (Table 7 and Figure 1).

DISCUSSION

Since its onset, the physiological and psychological impacts of COVID-19 have been examined, and the negative effects have been elucidated in several studies. In order to shed light on the psychological component of COVID-19, the effects of intolerance of uncertainty, cognitive control/flexibility, and anxiety on the fear and perception of threat of COVID-19 were explored in this study. The following are the study's findings: 1) Fear and threat perception of COVID-19 were found to have a positive association with intolerance of uncertainty and anxiety levels, but a negative relationship with

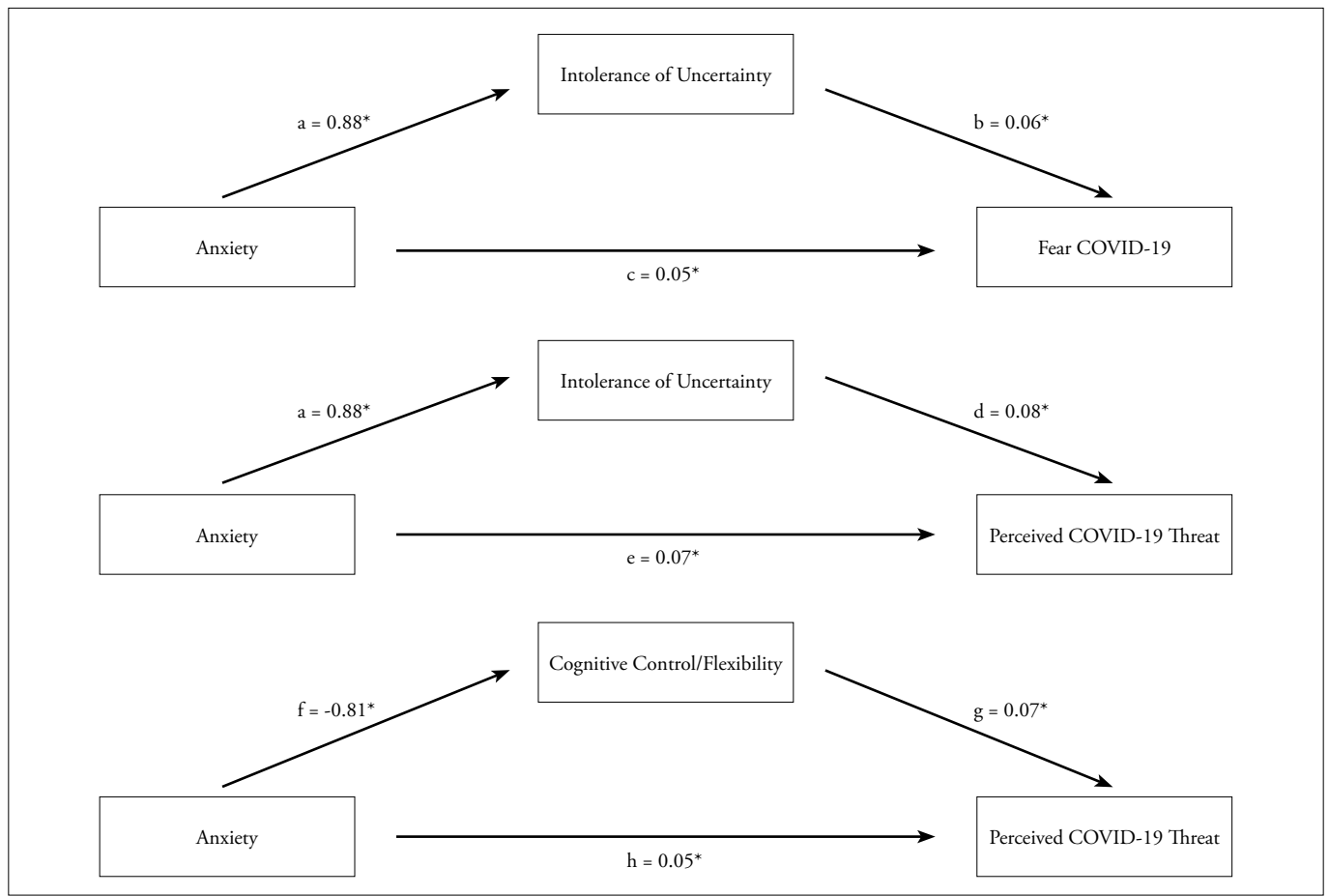


Figure 1. The Mediating Role of Fear, Perceived Threat, and Anxiety in Cognitive Control/Flexibility and Intolerance of Uncertainty during the COVID-19 Pandemic

a: the direct effects of anxiety (predictor variable) on intolerance of uncertainty (mediating variable); **b:** the direct effect of intolerance of uncertainty on fear of COVID-19 (outcome variable); **c:** the direct effect of anxiety on fear of COVID-19; **d:** the direct effect of intolerance of uncertainty on perceived threat of COVID-19 (outcome variable); **e:** the direct effect of anxiety on perceived threat of COVID-19; **f:** the direct effect of anxiety (predictor variable) on cognitive control and flexibility (mediating variable); **g:** the direct effect of cognitive control and flexibility on perceived threat of COVID-19 (outcome variable); **h:** the direct effect of anxiety on perceived threat of COVID-19

Note 1. The text notes that the reported beta coefficients are not standardized.

Note 2. * $p < 0.001$

total cognitive control and flexibility scores. 2) intolerance of uncertainty, Beck anxiety, and cognitive control/flexibility were found to be significant predictors of COVID-19 fear and threat perception. 3) Intolerance of uncertainty and cognitive control/flexibility were identified as mediators between anxiety and the perception of COVID-19 threat.

During the pandemic, an increase in an individual's level of fear is likely to be noted, and individuals will be compelled to respond accordingly. Anxiety is often coupled with the fear of losing loved ones or one's own life. (Kubb and Foran, 2020) Similarly, the threat perception and fear of COVID-19 showed a positive correlation with Beck anxiety levels in our study. A meta-analysis of 17 studies completed in 2020 revealed a prevalence of 31.9% for anxiety during the pandemic (Salari et al. 2020). Likewise, a second Lancet study published in 2021 found that the incidence of anxiety disorders increased

during the COVID-19 pandemic (Santomauro et al. 2021). In accordance with these research, the anxiety levels of the participants in our study during the pandemic were consistent with the expectations. This can be accepted as evidence that COVID-19 has a very harmful effect on the psychological state of humans. In this study, it was also noted that those with a chronic condition had higher anxiety levels, and those who were vaccinated scored higher on the COVID-19 fear scale than those who were considering vaccination.

According to a recent study (Knipe et al. 2020), individuals at risk for COVID-19 will likely take more preventative measures as their fear of the disease increases (Knipe et al. 2020), as predicted by Rogers' protection motivation theory (Rogers 1975). Similarly, Head et al. have shown a positive association between fear of COVID-19 and vaccination intent (Head et al. 2020).

Intolerance of uncertainty is the perception that uncertain situations are frightening and unacceptable (Carleton et al. 2007). Individuals with a high intolerance for uncertainty may feel anxiety symptoms due to their fear of unknown events (Greco and Roger, 2003; Swee et al. 2019) and may regard such situations as more threatening. During the H1N1 pandemic in 2009, a study found that people with high levels of intolerance of uncertainty had higher anxiety levels (Taha et al. 2014). Uncertainty regarding the duration of this process might cause psychological distress in individuals. It has been reported that intolerance of uncertainty is also associated with threat evaluation related to anxiety (Bredemeier and Berenbaum 2008, Dugas et al. 2005, Chen and Hong 2010). Due to the fact that everyone is at risk of losing themselves and/or their loved ones to the COVID-19 outbreak, feeling threatened is inevitable. Previous research has also demonstrated a positive relationship between COVID-19 fear and intolerance of uncertainty (Satıcı et al. 2020b). Additionally, some researchers suggest that people who are more prone to intolerance of uncertainty would perceive circumstances as more threatening and unpleasant (Freeston et al. 2020). The association between intolerance of uncertainty and emotional reactions has been proven to be consistent (Mertens et al. 2020, Rettie and Daniels 2020, Taha et al. 2014). Therefore, it is crucial to examine intolerance of uncertainty and fear of COVID-19 as connected ideas. In our study, like in other research (Bakioglu et al. 2020, Satıcı et al. 2020b, Gica et al. 2020, Bavolar et al. 2021, Akbari et al. 2021, Zhao et al. 2021), fear and perceived threat of COVID-19 were strongly associated with intolerance of uncertainty and anxiety levels.

Another key finding is that cognitive control/flexibility is negatively associated with both fear of COVID-19 and perception of threat. It is known that cognitive control and flexibility can be exposed through intensive focus, evaluations/re-evaluations, and persuasive coping techniques. Cognitive control involves avoiding extraneous information and concentrating on relevant stimuli. Therefore, people in a tense situation will focus on information linked to the threat. Additionally, when possibly confronted with a stressful situation, stimuli are evaluated for their possible hazard (Halk 2013). Cognitive control is believed to play a role in re-evaluation by altering the cognitive sets in which cognitive flexibility occurs (Ochsner et al. 2012, Zaehring et al. 2018). Given the negative emotional responses that develop in response to stressful events, cognitive control and flexibility are linked to the regulation of emotions. In a crisis situation like as the COVID-19 pandemic, cognitive control and emotional regulation are crucial for effective coping responses (Feder et al. 2019). Several research have examined the association between cognitive control and mental health during the

pandemic thus far. The data indicate that cognitive control deficiencies are predictive of elevated anxiety levels during the COVID-19 process (Brehl et al. 2021, Panayiotou et al. 2021, Weissman et al. 2021). According to a study, psychological flexibility mitigated the effects of COVID-19 (Pakenham et al. 2020). Similarly, our results have shown that as anxiety increases, cognitive control and flexibility decrease, or vice versa. Additionally, a moderate association was found between cognitive control and intolerance of uncertainty. Consequently, cognitive control becomes increasingly crucial in the pandemic's second-level danger context of rising uncertainty (Monninger et al. 2021). In addition, considering cognitive control and flexibility, which assess the ability to cope with difficult situations by controlling unwanted thoughts and feelings, our study reveals that working individuals during the pandemic have significantly greater cognitive control and flexibility than non-working individuals. Given that the majority of people were required to work throughout the pandemic and that they needed to maintain a psychologically stable life in order to overcome the stress they encountered during that time, it can be concluded that our findings are compatible with these notions. Additionally, regression analysis reveals that intolerance of uncertainty, cognitive control/flexibility, and anxiety levels can predict COVID-19 fear and virus threat. The results of a mediation analysis indicate that intolerance of uncertainty and cognitive control/flexibility serve as mediators between anxiety and the perception of COVID-19 threat. The investigation of these cognitive elements that influence people's mental health may have a protective effect on the regulation of present anxiety. Therefore, it may be advantageous to design cognitive-based interventions based on these variables in order to assist people with severe pandemic anxiety. It is crucial to provide individuals with effective cognitive control and flexibility tools and support procedures for managing intolerance of uncertainty in order to combat pandemic threat and anxiety.

Some limitations must be taken into account when evaluating the outcomes of this study. It's conceivable that not all populations were included in the study because it was conducted online to lessen the risk of infection during the COVID-19 pandemic. For instance, those without internet access or with limited internet connection may not have been able to participate in the study, which may have impacted the generalizability of the findings. Self-report measures may have also contributed to response bias. Additionally, the sample size may potentially be a limitation of the study; thus, sample size can be expanded in future studies to analyze these associations, additional variables can be included, and neuropsychological and neuroimaging approaches may also be effective. A detailed neuropsychological assessment of the role of cognitive processes in the pandemic by experts

will contribute to the field. Despite its limitations, this study has offered information on the association between cognitive variables and fear of COVID-19. It is anticipated that people will feel anxious about COVID-19 due to the fact that the pandemic has altered life standards across the globe, requiring people to adapt to a new order involving the use of masks and other restrictions; consequently, it is likely that people will be concerned about the virus. The aforementioned changes may have prompted the urge for individuals to exert control over the course of events. Cognitive flexibility may be viewed as a significant aspect in anxiety management and control. Increasing cognitive flexibility may assist individuals in regulating their beliefs of control, and research in this area may have a beneficial effect on fear and anxiety. Existing improvement initiatives may benefit from interventions concentrating on cognitive control/flexibility and intolerance of uncertainty in this regard. Individuals may benefit from psychological support in terms of reducing fear of COVID-19 and perceived threat of COVID-19 and enhancing mental health.

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Symptom Exacerbations of Patients Attending a Community Mental Health Center During the COVID-19 Pandemic



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ABSTRACT

Objective: The aim of this study was to examine the effect of the COVID-19 pandemic on the clinical conditions of the patients with bipolar disorder (BD) and schizophrenia spectrum disorders (SSD) in a community mental health center (CMHC).

Method: Symptom exacerbations, emergency service admissions, drug dose increases, additional medication prescriptions, and psychiatric hospitalizations of patients with BD and SSD in the CMHC were evaluated retrospectively. The data from the 1-year prior, 6-months prior, 6-months after the onset and 1-year after the onset of the pandemic were compared. Hospital and CMHC medical records were used for outcomes. Personal and Social Performance (PSP) Scale was used to assess the level of functioning.

Results: 107 patients with the diagnosis of BD and 121 patients with the diagnosis of SSD were recruited. In the BD group, there was increase in the frequency of symptom exacerbations ($p=0.001$) and additional medication prescriptions or increased dose ($p=0.007$), with decrease in emergency service admissions ($p=0.039$) during the pandemic. In the patients with SSD, the number of patients with exacerbation of symptoms ($p=0.001$) and with increased dose or additional medication prescriptions ($p=0.004$) were higher during the pandemic. There was no increase in the rate of hospitalized patients in the period of first 6 months and first one year. Symptom exacerbations were more frequent in the SSD group with Covid (+) in family ($p=0.016$).

Conclusion: The fact that the hospitalization rates remained the same despite an increase in the acute exacerbations provides info on the role of CMHCs and how mental health system functioned during the pandemic.

Keywords: COVID-19, Bipolar Disorder, Schizophrenia, Psychotic Disorders, Community Mental Health Center, Hospitalization

INTRODUCTION

Throughout the history pandemics such as the Spanish flu (1918-1920), the Asian flu (1956-1957), SARS (2002-2003), the swine flu (2009), Ebola (2013-2014) and others had impinged on people worldwide (Talevi et al. 2020). Data from the previous pandemics reveal that, there were remarkable public exposure of anxiety and panic with significant psychological consequences (Wang et al. 2020). First COVID-19 case was reported in 10th of March 2020 in our country (Turkish Ministry of Health 2020). High transmission speed and death rate, absence of a vaccine and vagueness of treatment protocols and side effects in the first months with the addition of uncertainty in recurrence risk,

survival and long-term sequela contributed to COVID-19 related anxiety and panic. In addition, increasing public concern, social restrictions and economic decline led to psychosocial problems (Holt-Lunstad et al. 2010). Social and economic disadvantages have made adaptation to the adversities of the pandemic even more difficult for patients with serious mental disorders like schizophrenia and bipolar disorder (BD) (Balaban et al. 2021).

The importance of social relationships gain prominence in times like the COVID-19 pandemic in which uncertainty and distress is high and these relationships can have a buffering effect on the stressors. Social restrictions may have important consequences on psychical and mental health

Received: 20.05.2022, Accepted: 11.10.2022, Available Online Date: 29.10.2023

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(Holt-Lunstad 2018). In addition to mortality risks, the COVID-19 pandemic can be seen as a global stressor with significant changes in social lives of the people because of the unprecedented social isolation precautions in the 21st century. Various levels of social restrictions including long curfews were implemented in many countries in order to limit the spread of virus. Many patients who were already socially isolated before the pandemic, the isolation problem only got worse in this period (Fahy et al. 2021).

Quickly imposed deviations in normal daily life and practices of social isolation results in anxiety, depression and increase in suicidal thoughts (Killgore et al. 2020). In a survey study, the participants reported that the COVID-19 pandemic had negative effect on psychological functions and mental health; they were sleeping less, using alcohol, tobacco and other substances with increasing amounts, displaying abnormal eating patterns with increasing frequency and having concentration difficulties together with learning problems because of the preoccupation with COVID-19 (American Psychiatric Association 2020). Furthermore, an increase in arguments with partners, some of which resulting in domestic violence, was observed (Stremikis 2020). The vulnerable groups towards the COVID-19 pandemic and its psychological effects were determined as: older people, homeless people, immigrant workers, patients with mental disorders, pregnant women and international students who travelled overseas for education (Rajkumar 2020). It was also reported that patients with mental disorders were using adaptive coping strategies less frequently than healthy controls and experienced more severe anxiety and depression during the pandemic (Sole et al. 2021).

Risk of getting infected with COVID-19 is higher for patients with BD as per reports from large scale studies (Wang et al. 2021). Because of the conflicting results in the literature, we do not exactly know the effect of the pandemic on BD (Fornaro et al. 2021). While studies reporting an increase in symptom severity and hospitalizations are present there are also studies reporting the diminishing symptom severity by comparison to the previous year (Tundo et al. 2021).

A study that focuses on the difficulties of coping with the pandemic for psychiatric patients in China, it is stated that although there were more than 300 patients with the diagnosis of COVID-19 in the mentioned facility, the number of trained mental health staff was insufficient due to the pandemic replacements and relocations which caused problems in treating mental health emergencies (Xiang et al. 2020). Implementation of infection control precautions was suboptimal due to shared dining and living places in psychiatric inpatient facilities, group activities that increase contact, judgement difficulties, self-care problems, effect of the psychotic symptoms and problems in reality testing are the factors that increase the vulnerability for viral pandemic

(Xiang et al. 2020). It was postulated that COVID-19 related adverse outcomes are higher in patients with schizophrenia especially because of the common comorbidity of cardiovascular and metabolic diseases (Mohan et al. 2021). A study with a large sample size consisting of 52078 participants reported that risk of being COVID-19 positive was lower for patients with schizophrenia, but when infected, risk of requirement for inpatient treatment was 2 times higher (Bitan et al. 2021). There are also reports of higher mortality in patients with schizophrenia who needed hospitalization for COVID-19 than other patients who were also hospitalized for COVID-19 (Fond et al. 2021). These results point to the increased risks related to inpatient psychiatric hospitalizations during the pandemic. After all, hospitalizations for reasons other than COVID-19 were diminished as a result of the changes in service utilizations in the times of crisis (Birkmeyer et al. 2020).

Further changes in the provision of health services were made in line with shifting demands during the pandemic. After emergency assignments to COVID-19 treatment units, the number of mental health professionals were diminished in some of the hospitals, resulting in the transient closure of community mental health centers (CMHC) linked to these hospitals and halting of inpatient treatment in some psychiatric units. In our study, we aimed a retrospective comparison of emergency admissions, medication dose increases and hospitalizations related to acute exacerbations for the period of 6 months before and after the COVID-19 pandemic in a CMHC that was continuously open during this period.

It can be anticipated that these periods could be more troublesome for patients who had COVID-19 infection or who had a family member with COVID-19 infection, for this reason, our secondary aim was to determine whether having infection personally or in the family had an effect on acute exacerbations in this particular 6-month period when vaccine was not available yet and the uncertainty with fear was extreme.

In addition, to overcome the effect of seasonality on hospitalizations and acute exacerbations, we also compared the relapses before and after the onset of the pandemic for the period of one year.

Hypothesis 1: Acute exacerbations, hospitalizations and emergency admissions in patients with BD have increased during the COVID-19 pandemic.

Hypothesis 2: Acute exacerbations, hospitalizations and emergency admissions in patients with schizophrenia spectrum disorders (SSD) have increased during the COVID-19 pandemic.

Hypothesis 3: Acute exacerbations, hospitalizations and emergency admissions between BD and SSD remained the same during the first 6 months and the first 12 months of the pandemic.

METHOD

Sampling

Data of the patients attending a CMHC were analyzed. During the pandemic, some of the CMHCs were closed across the country, however the CMHC which we conducted our study had continued clinical service without closure.

Patients with the diagnosis of BD and SSD (including schizophrenia and other psychotic disorders in the schizophrenia spectrum) were attending the CMHC. But, delusional disorder, substance induced psychotic disorder, schizotypal disorder and brief psychotic disorder were in our exclusion criteria although these disorders were also in the schizophrenia spectrum, because they were not be able to attend the CMHC according to the regulations of social insurance agency. Schizoaffective disorder which is classified as schizophrenia spectrum disorders in DSM-5 was also in exclusion criteria, because this diagnosis in the intersection area of BD and schizophrenia with regard to phenomenology and follow-up features. Medical records of all the patients between the age range of 18-65 were investigated. Other exclusion criteria were intellectual disability, mental disorders due to a medical condition, chronic neurological disorders and pregnancy or peripartum period. Ethical Approval was obtained from Bakırköy Dr. Sadi Konuk Research and Training Hospital Institutional Review Board for Clinical Researches in 19.10.2020 (Research Protocol Number: 2020/49, decision number: 2020-21-15). Additional approval was obtained from the Turkish Ministry of Mental Health Covid-19 Scientific Research Platform (Approval announcement date: 09.10.2020). After the review board approval procedure, the patients and relatives in the CMHC were informed and their informed consent were obtained for the retrospective use of their medical records. As a result of the above-mentioned recruitment criteria, 121 patients with SSD and 107 patients with BD were included to the study.

Since the first reported COVID-19 case in our country was dated 10 March 2020, the comparisons were made for variables associated with the relapses of patients between the period of 6 months before (10 September 2019-10 March 2020) and after (10 March 2020-10 September 2020) this date. Accordingly, patients who had a history of COVID-19 infection in themselves or their family during these time periods and therefore experienced COVID-19 stress in the family in addition to the pandemic stress were defined as “Covid (+) in the family” and were divided into groups

according to whether the patients had this feature and they were further examined in terms of variables related to relapse.

In addition to the analysis of first 6 months when the vaccine was not available and uncertainty was extreme, we also analyzed one year before and after the date of 10 March 2020 in order to eliminate the confounding effect of seasonality on hospitalizations and relapses.

For all the patients with BD and SSD, acute exacerbations were coded as two different methods as being “symptom exacerbations” or “relapse” according to the clinical examination records. The relapse term defined not a nonspecific increase in symptom severity, but rather a full-blown syndrome as listed by the DSM-5 criteria which includes increase in symptom severity that results in significant decrease in functionality. According to this, in patients with BD, “relapse” represented of full-blown manic or depressive episodes resulting in hospitalization or significant decrease in general functioning in addition to increase in symptom severity. In patients with SSD, “relapse” represented increase in symptom severity when the DSM-5 criterion A symptoms for schizophrenia were met, including significant loss of functioning or need for hospitalization as recorded in clinical examination. In our study, the increase in antipsychotic medications were coded as “dose increase” only if the increase also results in an increase of daily antipsychotic equivalent dose for that patient. The “Dose increase/addition of new medication” coding was not used if a change in medication was made that does not result in an increase in daily antipsychotic equivalent dose, but merely an increase in dosing frequency because of daily division of total dose to smaller and more frequent dosing with different pharmaceutical forms.

Instruments

Sociodemographic Data Form: Sociodemographic features of the patients were recorded in this form. While structuring this form the authors used hospital records, CMHC follow-up notes, patient registry data in the Ministry of Health and Social Insurance Agency system.

Personal and Social Performance (PSP) Scale: PSP scale which was routinely implemented for all the patients in the CMHC was used in order to make comparisons related to the functionality level of patients. PSP scale is an instrument for measuring social functionality in patients with severe mental disorders (Nafess et al. 2012). Reliability and validity study of the Turkish version has been conducted by Aydemir et al. 2009. This scale gives a general impression about the functionality level of the patients and it has been used in our study for describing the study sample. We used the PSP scale not for measuring a pandemic related effect, but for giving descriptive information about general functionality of the sample and it was implemented once for every patient in the

6-month period before the pandemic by the second author during the routine clinical practice.

Statistical Analysis

SPSS (Statistical Package for the Social Sciences) Windows version 20.0 statistical software was used for the analysis in the study. Symptom exacerbations, relapse, suicide attempt, hospitalization, emergency admission, dose increase/ addition of new medication were defined as dependent variables in the periods of 6 months and 12 months. For the period of the first 6 months, comparisons were also made for the history of COVID-19 infection in the patient or in the family of the patient. Sociodemographic and clinical features of the study sample were analyzed with descriptive statistics, Sapiro-Wilk test was used for evaluation of normal distribution. Demographic features, clinical features, socioeconomic status (independent variables) of the sample were compared between both the diagnostic groups (SSD and BD) and for the relapses. In the comparisons between two groups, Mann-Whitney U test was used for numerical variables when the data was not normally distributed and Chi-square test was used for categorical variables. McNemar test was used for the before and after comparisons of categorical variables in dependent groups. Level of significance was adopted as $p < 0.05$ for all the tests comparing the groups and analyzing the statistical relationships.

RESULTS

Patients with Diagnosis of BD

The data of 107 patients with BD, consisting of 61 (57%) women and 46 (43%) men were analyzed. Mean age of the patients were 39 ± 10.53 (range: 18-64). Mean age of Family-Covid (+) group were 38.5 ± 9.91 , mean age of the group with no COVID-19 history were 40.7 ± 12.7 . The difference was not statistically significant ($p = 0.31$). PSP scale scores of the patients ($n:107$) were 72.82 ± 12.4 (range: 40-91). Sociodemographic features and treatment related characteristics of the patients are given in table 1.

During the first 6 months of the pandemic, the number of patients who had symptom exacerbations or dose increase with/without addition of medications were significantly higher than the period of 6 months before the pandemic ($p < 0.001$ and $p = 0.007$ respectively). There was no patient who attempted to suicide in the period of 6 months before the pandemic. During the first 6 months of the pandemic, there were 2 patients who attempted to suicide. Emergency admissions were significantly lower during the first 6 months of the pandemic compared to before ($p = 0.039$).

The comparison of before and after pandemic period for the clinical features of the 22 Family-Covid (+) patients revealed

that before the pandemic there were 4 patients with symptom exacerbations and in pandemic period there were 9 patients with symptom exacerbations, but the difference was not significant. Relapse related variables of the patients with BD are shown in table 2.

Patients with Diagnosis of SSD

The data of 121 patients with BD, consisting of 47 (39%) women and 75 (61%) men were analyzed. Mean age of the patients was 37.12 ± 11.29 (range: 18-63). PSP scale scores of the patients ($n:121$) were 59.99 ± 15.3 (range: 22-90). Sociodemographic features and treatment related characteristics of the patients are given in table 3.

While 31 patients (26%) had symptom exacerbations during the period of 6 months before the pandemic, the number of patients with symptom exacerbations increased to 55 (46%) during the first 6 months of pandemic. There was significant increase in the number of patients with symptom exacerbations in the pandemic period ($p < 0.001$). In the period of 6 months before the pandemic, no suicide attempts were recorded. One patient attempted to suicide during the first 6 months of the pandemic. There were more patients with a dose increase with/without addition of new medication during the pandemic and the difference was significant ($p = 0.004$). There was no difference in hospitalizations or emergency admissions.

In the group of 23 (19%) Family-Covid (+) patients, there were significantly more patients with symptom exacerbations during the pandemic ($p = 0.016$). Hospitalizations and emergency admissions were yet similar. Relapse related variables of the patients with SSD are shown in table 4. Further detailed analysis could not be executed since the number of patients in the sample is limited.

Comparison of the One Year Period Before the Pandemic and the First One Year Period During the Pandemic in terms of Acute Exacerbations and Hospital Admissions

The comparisons were made for the records of acute exacerbations and hospital admissions of the patients with BD and SSD in the first 1 year during the pandemic and 1 year period before the pandemic. In the group of patients with BD, 24% of the patients had symptom exacerbations in the period of 6 months before the pandemic, but 50% of the patients had symptom exacerbations during the first one year of the pandemic, the difference was significant ($p = 0.001$). In addition, in BD group, there were more patients with a dose increase with/without addition of new medication during the first year of the pandemic ($p = 0.001$) (Table 5). During the period of 6 months before the pandemic 32% of the SSD patients in the group had symptom exacerbations, meanwhile during the first one

Table 1. Demographic and Clinical Features of Patients with BD

Demographic and Clinical Features of Patients with BD	All Patients with Diagnosis of BD (D:107)	Family-Covid(+) Patients (n:22)	Not Family-Covid(+) Patients (n:85)	Significance (p)
Age	39±10.53	38.5±9.91	40.7±12.7	0.31*
PSPS	72.8±12.40	76.6±12.35	71.8±12.28	0.10*
Sex	61 F (57%) 46 M (43%)	12 F (55%) 10 M (45%)	49 F (%58) 36 M (%42)	0.79**
Smoking	44 (41%)	5 (23%)	39 (46%)	0.04**
Alcohol Use Disorder	8 (7%)	0	8 (9%)	-
Substance Use Disorder	5 (5%)	1 (5%)	4 (5%)	1.00***
Suicide Attempt	19 (18%)	2 (9%)	17 (20%)	0.35***
History of ECT	11 (10%)	2 (9%)	9 (11%)	1.00***
Medications	All Patients with Diagnosis of BD (n:107)	Family-Covid(+) Patients (n:22)	Not Family-Covid(+) Patients (n:85)	
Mood Stabilizer	95 (89%)	21 (96%)	74 (87%)	
Lithium	42 (39%)	10 (46%)	32 (38%)	
Valproate	40 (37%)	8 (36%)	32 (38%)	
Carbamazepine	3 (3%)	1 (5%)	2 (2%)	
Lamotrigine	5 (5%)	0	5 (6%)	
Antidepressant	9 (8%)	0	9 (11%)	
Antipsychotic	75 (70%)	11 (50%)	64 (75%)	
Long Acting Injectable Antipsychotic	10 (9%)	1 (5%)	9 (11%)	

BD: Bipolar Disorder, PSPS: Personal and Social Performance Scale, ECT: Electroconvulsive Therapy, F: Female, M: Male

*Mann-Whitney U test, **Chi-square test, ***Fisher exact test, p<0.05 significance.

Table 2. Comparison of Acute Exacerbations of Patients with BD Before and After the Pandemic

Patients with BD (n=107)	6 Months Period Before Pandemic	6 Months Period During Pandemic	Significance* (p)
Symptom exacerbations	22	43	0.001
Relapse	12	15	0.63
Suicide Attempt	0	2	0.50
Hospitalization	11	5	0.109
Emergency Admission	13	6	0.039
Dose increase/ addition of new medication	18	32	0.007
Family-Covid(+) Patients with BD (n:22)	6 Months Period Before Pandemic	6 Months Period During Pandemic	Significance* (p)
Symptom exacerbations	4	9	0.125
Relapse	2	4	0.625
Suicide Attempt	0	1	1.00
Hospitalization	2	2	1.00
Emergency Admission	2	1	1.00
Dose increase/ addition of new medication	3	6	0.375

BD: Bipolar Disorder

*McNemar test, p<0.05 significance.

Table 3. Demographic and Clinical Features of Patients with SSD

Demographic and Clinical Features of Patients with SSD	All Patients with Diagnosis of SSD (n:121)	Family-Covid (+) Patients (n:23)	Not Family-Covid (+) Patients (n:98)	p
Age	37.12±11.29	37.5±12.16	37.04±11.14	0.87*
PSPS	59.9±15.53	57.0±13.70	60.62±15.91	0.29*
Sex	47 F (39%) 74 M (61%)	7 F (30%) 16 M (70%)	40 F (41%) 58 M (59%)	0.36**
Smoking	69 (57%)	15 (65%)	54 (55%)	0.38**
Alcohol Use Disorder	5 (4%)	1 (4%)	4 (4%)	1.00***
Substance Use Disorder	20 (17%)	3 (13%)	17 (17%)	0.76***
Suicide Attempt	31 (26%)	5 (22%)	26 (27%)	0.64**
History of ECT	30 (25%)	7 (30%)	23 (23%)	0.48**
Medications	All Patients with Diagnosis of SSD (n:121)	Family-Covid(+) Patients (n:23)	Not Family-Covid(+) Patients (n:98)	
Mood Stabilizer	11 (9%)	0	11 (11%)	
Antidepressant	26 (21%)	7 (30%)	19 (19%)	
Single Antipsychotic	78 (64%)	15 (65%)	63 (64%)	
Multiple Antipsychotic	43 (35%)	8 (34%)	35 (35%)	
Clozapine	22 (19%)	3 (13%)	19 (19%)	
Long Acting Injectable Antipsychotic	63 (52%)	11 (47%)	52 (53%)	

SSD: Schizophrenia Spectrum Disorders, PSPS: Personal and Social Performance Scale, ECT: Electroconvulsive Therapy, F: Female, E: Male

*Mann-Whitney U test, **Chi-square test, ***Fisher exact test, p<0.05 significance.

Table 4. Comparison of Acute Exacerbations of Patients with SSD for 6 Months Before and After the Pandemic

Patients with SSD (n=121)	6 Months Period Before Pandemic	6 Months Period During Pandemic	Significance* (p)
Symptom exacerbations	31	55	0.001
Relapse	14	19	0.405
Suicide Attempt	0	1	1.00
Hospitalization	12	12	1.00
Emergency Admission	16	14	0.832
Dose increase/ addition of new medication	21	38	0.004
Family-Covid (+) Patients with SSD (n=23)	6 Months Period Before Pandemic	6 Months Period During Pandemic	Significance* (p)
Symptom exacerbations	4	11	0.016
Relapse	12	16	1.00
Suicide Attempt	0	0	1.00
Hospitalization	2	2	1.00
Emergency Admission	3	2	1.00
Dose increase/ addition of new medication	3	7	0.125

SSD: Schizophrenia Spectrum Disorders

*McNemar test, p<0.05 significance.

Table 5. Comparison of Acute Exacerbations of Patients with BD and SSD for 12 Months Before and After the Pandemic

Patients with BD (n=103)	12 Months Period Before Pandemic	12 Months Period During Pandemic	Significance* (p)
Symptom exacerbations	25 (24%)	52 (50%)	0.001
Relapse	13 (13%)	19 (18%)	0.63
Suicide Attempt	0 (0%)	3 (3%)	1.00
Hospitalization	13 (13%)	11 (11%)	0.774
Emergency Admission	13 (13%)	10 (10%)	0.508
Dose increase/ addition of new medication	21 (20%)	41 (39%)	0.001

Patients with SSD (n=117)	12 Months Period Before Pandemic	12 Months Period During Pandemic	Significance* (p)
Symptom exacerbations	38 (32%)	61 (52%)	0.001
Relapse	22 (19%)	26 (22%)	0.541
Suicide Attempt	1 (1%)	0 (0%)	1.000
Hospitalization	18 (15%)	18 (15%)	1.000
Emergency Admission	24 (21%)	21 (18%)	0.690
Dose increase/ addition of new medication	33 (28%)	50 (48%)	0.003

BD: Bipolar Disorder, SSD: Schizophrenia Spectrum Disorders

*McNemar test, $p < 0.05$ significance.**Table 6.** Comparison of CMHC admissions of patients with BD and SSD for one year before the pandemic and one year follow up during the pandemic

CMHC admissions of Patients with BD	12 Months Period Before Pandemic	12 Months Period During Pandemic	Significance* (p)
Mean Admissions	16.23	9.44	0.001
Standard Deviation	14.36	6.84	
Range	2-98	2-32	

CMHC admissions of Patients with SSD	12 Months Period Before Pandemic	12 Months Period During Pandemic	Significance* (p)
Mean Admissions	21.59	10.13	0.001
Standard Deviation	23.00	6.60	
Range	2-111	3-27	

CMHC: Community Mental Health Center, BD: Bipolar Disorder, SSD: Schizophrenia Spectrum Disorders

*Wilcoxon test, $p < 0.05$ significance.

year of the pandemic the rate increased to 52% once again the difference is significant ($p=0.001$). In SSD group, more patients with a dose increase with/without addition of new medication during the first year of the pandemic ($p=0.003$) (Table 5). In both of the groups, there was no difference between clinical deteriorations that were in the severity of a full-blown relapse. There was no significant difference in the before and after one-year comparisons of hospitalizations and emergency admissions for both the patients with BD and SSD (Table 5). The treatments of patients having symptom exacerbations were followed-up at the CMHC and clinical deteriorations had not resulted in an increase in the number of emergency admissions to hospital.

In the one-year before and after comparisons of CMHC admissions, there was a significant decrease both in the BD group and SSD group ($p=0.001$ for both comparisons). The mean number of CHMC admissions of patients with BD was 16.23 ± 14.36 in the one year before the pandemic, but 9.44 ± 6.84 in the first one year during the pandemic and the mean number of CHMC admissions of patients with SSD was 21.59 ± 23 in the one year before the pandemic, but 10.13 ± 6.6 in the first one year during the pandemic (Table 6).

In the period of one year before the pandemic, there was no significant difference between the patients with BD and SSD for acute exacerbations, hospital admissions, dose increase /

Table 7. Comparisons Between Patients with BD and SSD Group for Acute Exacerbations, Emergency Admissions and Hospitalizations

Period of One Year Before Pandemic	Patients with BD (n=103)	Patients with SSD (n=85)	Significance* (p)
Symptom exacerbations	25 (24%)	38 (32%)	0.143**
Relapse	13 (13%)	22 (19%)	0.222**
Suicide Attempt	0 (0%)	1(1%)	1.00***
Hospitalization	13 (13%)	18 (15%)	0.576**
Emergency Admission	13 (13%)	24 (21%)	0.081**
Dose increase/ addition of new medication	21 (20%)	33 (28%)	0.138**
Period of One Year During Pandemic	Patients with BD (n=103)	Patients with SSD (n=117)	Significance* (p)
Symptom exacerbations	52 (50%)	61 (52%)	0.752**
Relapse	19 (18%)	26 (22%)	0.511**
Suicide Attempt	3 (3%)	0(0%)	0.099***
Hospitalization	11 (11%)	18 (15%)	0.316**
Emergency Admission	10 (10%)	21 (18%)	0.085**
Dose increase/ addition of new medication	41 (39%)	50 (48%)	0.704**

BD: Bipolar Disorder, SSD: Schizophrenia Spectrum Disorders

*p<0.05 significance, **chi-square test, ***Fisher exact test.

addition of medications. In the same manner, there was also no significant difference between the BD and SSD groups for these relapse related parameters (Table 7).

DISCUSSION

Demographic Data and Clinical Features

No difference was encountered in sociodemographic and clinical features such as age, gender, smoking, alcohol use, substance use, suicide attempts or history of electroconvulsive therapy that would complicate the group comparison between patients who were Family-Covid (+) and who were not in the BD group. For the patients with the diagnosis of SSD in our study, history of suicide attempt was rather high (26%), but there was no difference in the comparisons of demographic and clinical features for being Family-Covid (+) or not.

In accordance with the previous reports in the literature, 9.3% of the patients with BD were using long-acting injectable (LAI) antipsychotics (Greene et al. 2017). 52% of the patients in the schizophrenia spectrum were using LAI antipsychotics. Use of more than one antipsychotic (35%) was not rare and 19% of the patients with SSD were using clozapine.

In order to accommodate with the restrictions implemented for dealing with the intensity of the pandemic, it was stated (by the regulatory agencies) that patients could take their

regular medications from the pharmacies without needing new prescription. Since face-to-face contact with a medical professional is needed for during LAI antipsychotics use or during clozapine use which requires monthly monitoring of leukocyte levels, it is of paramount importance that mental health services should stay open in the pandemic. It has also been suggested that the requirement of face-to-face contact with medical services may be a protective factor for depressive and anxiety symptoms (Fahy et al. 2021).

It is possible to further suggest that, although the frequency of the CMHC admissions have diminished; continuity of the service in the CMHC may have a protective role in preventing hospitalizations or suicide (MacLaurin et al. 2021). Rehabilitation services, courses and social skill related interventions were halted during the pandemic, yet clinical psychiatric services continued. Decrease in the CMHC admissions is in line with our impressions that during the pandemic, the continuously open CMHC has transformed into a purely medical unit for medical examinations and treatment rather than a daily activity or rehabilitation center.

We did not use an instrument measuring drug compliance to treatment in our study, but psychoeducation and guiding services in the CMHC were activities increasing the drug compliance. If a patient does not show up in the appointment, the staff calls the patient on phone and reminds the CMHC admission for examination and prescription. Increasing

treatment adherence is also targeted in family interviews. 89% of the patients with BD were using a mood stabilizing agent and serum levels of the mood stabilizers were regularly measured in the CMHC for optimum dose arrangement and checking for treatment adherence. In addition, 52% of the patients with SSD were using LAI antipsychotics and this was also a treatment form increasing treatment adherence. As a result, it should be considered in the evaluation of our results that there were factors reinforcing treatment adherence in our study sample.

Symptom Exacerbations and Increase in the Dose and Number of Medications

In the BD group, there were significantly more patients who had symptom exacerbations and had increase in the dose and number of medications in the pandemic period. There were more patients with symptom exacerbations or medication dose increase in the subgroup of Family-COVID-19 (+) with BD, but the difference between before and after pandemic was not significant.

In the SSD group, there were significant increase in the number of patients with symptom exacerbations and increase in medication dose. In the subgroup of patients with SSD who are Family-COVID-19 (+), the increase was significant only for the variable of symptom exacerbations. There was no significant increase for the variables of hospitalizations of suicide attempt during the pandemic.

Although there was no significant difference in relapse related variables in Family-Covid (+) patients with BD, there was significant difference for symptom exacerbations in Family-Covid (+) patients with SSD. There are reports in the literature pointing to lower frequency of relapse and symptom increase in patients with BD in the pandemic (Orhan et al. 2021, Tundo et al. 2021). Sample size in our study is not enough to conclude that mental health of SSD patients with close contact to COVID-19 has been more profoundly affected than patients with BD. There is also numerical increase in patients with symptom exacerbations in the BD group during the pandemic.

In the pandemic, although there was significant increase in symptom severity in patients with BD and SSD as recorded by clinical examination, there was no difference in full-blown relapses which is described as increase in symptom severity to such an extent that significantly disrupts functionality or results in hospitalization. These results underline the fact that if we solely count on relapse parameters with high severity such as hospitalizations and new episodes, subtle changes such as clinical deteriorations with low severity but also with clinical importance can be overlooked when evaluating the effect of the pandemic.

Emergency Admission and Difficulties in Accessing Mental Health Services

In our study, there is a significant decrease in the emergency admissions of patients with BD during the pandemic. Although there was an increase in the symptoms, most of the patients with BD had not admitted to emergency services as frequent as they did before the pandemic. These results remind the importance of CMHCs being continuously open during the pandemic and the role of CMHCs in diminishing the burden of psychiatric emergencies in general hospitals.

Though the frequency of emergency admissions has diminished in BD yet it is not the case for SSD. The main reason for the decrease in emergency admissions of patients diagnosed with BD compared to patients diagnosed with SSD may be that patients diagnosed with BD were more likely than patients diagnosed with SSD to comply with precautions such as not going to the hospital unless it is absolutely necessary and staying at home. There are reports indicating that patients with BD are more compliant with pandemic restrictions than patients with SSD (Pinkham et al. 2021).

Hoyer and colleagues (2021) reports decrease in emergency psychiatric admissions, but no detail related to diagnoses in a psychiatric hospital in Germany during the pandemic. A study in our country points to the decrease in the frequency of emergency admissions in patients attending a CMHC in the pandemic (Usta Sağlam et al. 2022). In our study, although there were increase in symptom exacerbations in the pandemic period for the patients with SSD too, we did not detect neither any change or an increase in emergency admissions in SSD group as the observation of the increase in admissions in the BD group. This may be related to the failure in compliance with pandemic restrictions in patients with SSD because of diminished interest to the environment or lack of knowledge (Barlati et al. 2021).

A study about the influence of the pandemic on first episode psychosis cases reports decrease in hospitalizations and emergency admissions with an increase in psychiatric symptoms (Szmulewicz et al. 2021). Various factors have been listed as risks for worsening of psychosis in patients with SSD. Some of these factors are pandemic fear and stress, viral transmission, distress and isolation during viral infection and steroids or other agents used for treatment (Kozloff et al. 2020). In our study, increase in symptom severity were also significant in Family-COVID-19 (+) subgroup of the patients with SSD but not in the Family-COVID-19 (+) subgroup of patients with BD. Patients with schizophrenia generally have smaller social networks and for this reason, restrictions of their already poor social support may be related with negative consequences. Social isolation is related to poor quality of life and paranoia. It is suggested that misinformation in social media has potential

to worsen psychotic symptoms (Hamada and Fan 2020). These studies provide explanations about the increased vulnerability in patients with SSD in the pandemic. A study from Portugal reports 52% decline in emergency room examinations in the pandemic which is more prominent for patients with a mood disorder diagnosis, besides, decline is in the admissions of patients with SSD were limited, being only 9% (Goçaves-Pinho et al. 2020). These results support our findings.

Hospitalizations

In our study, no significant difference was encountered neither regarding the hospitalizations nor suicide attempts in the comparisons of before or during the pandemic. All the patients in our analysis were patients attending the CMHC. Our results, indicating no increase in hospitalizations despite the increase in symptoms, may be a favorable consequence of continuously open CMHC providing outpatient mental health service during the pandemic. Our study underlines the importance of providing uninterrupted mental health service from the open CMHCs even in the pandemic. On the other hand, sample size of our study is inadequate for making detections about suicide, for this reason, studies with large sample sizes are needed for comparing the difference in suicide rates of patients attending CMHCs and outpatient clinics of general hospitals.

In England, a general decrease in psychiatric hospitalizations, but increase in hospitalizations of patients with BD and SSD were reported in the first 4 weeks of the pandemic in a study with relatively small sample size (63 patients, one center) (Abbas et al. 2021). A study conducted in Italy reports decrease in general psychiatric hospitalizations in the pandemic with comparison to the previous year (Clerici et al. 2020). Sidana and colleagues (2021) reported a general decrease in hospitalizations in a psychiatry clinic in India in the first 6 months of the pandemic, but a specific increase in the hospitalizations due to treatment discontinuation and hospitalizations of patients with the diagnosis of schizophrenia or BD. Decrease in both emergency admissions and hospitalizations were reported in the study of Usta Sağlam and colleagues (2022) that investigated the hospitalization and admission rates of patients in attending CMHC linked to a mental hospital in our country. These results are in line with our findings. In addition to this, our study also includes a point that is not addressed in the studies that only analyze admission rates and hospitalizations: Although there is an increase in the number of patients with clinical deterioration, it does not reflect to the emergency admissions and hospitalizations in terms of numbers.

In the pandemic, we observed that since there is a high risk of COVID-19 contagion in crowded psychiatric services, patients were generally treated in outpatient setting even during acute exacerbations if possible and hospitalizations were only made

in the most obligatory cases. According to this, even though symptom severity increased for all the groups in our study, it does not reflect in hospitalizations in terms of numbers and the reason for this may be the overly selective decision making of the doctors because of the pandemic. Besides, although the symptoms have increased, not all newly emerging symptoms are identical to a full-blown relapse, so this may be another reason for the discrepancy between symptom exacerbations and hospitalizations.

Acute Exacerbations and Hospital Admissions in the Period of One Year Before and After the Onset of the Pandemic

There was significant increase in the frequency of patients with symptom exacerbations and the patients with dose increase/addition of new medications during the first one year of the pandemic with comparison to the previous year. These differences in the one-year comparisons which shows increase in acute exacerbations underlines the detrimental effect of the pandemic for the patients attending the CMHC.

The differences in 6-month comparisons of the emergency admissions of patients with BD is not apparent in the one-year comparisons. The reason for this discrepancy may be the effect of seasonality in 6-month comparisons, and absence of this effect of seasonality in one-year comparisons, but the reason may also be the avoidance of patients with BD from the emergency services due to the fear of COVID-19 contagion. To be more precise about these conclusions; more detailed measurement of the fear related to COVID-19 is needed.

The reports from another CMHC in our country informs that after the closure of that CMHC during the pandemic because of the shortages and relocations of medical professionals to other institutions, there were interruptions in the long-acting injectable treatments of patients in the first months and there were relapses especially apparent in this group of patients (Mutlu et al. 2021). These results show the importance of uninterrupted medical services for the patients using long-acting injectable antipsychotics.

Considering both of the diagnostic groups emergency admissions and hospitalizations were similar in the first year of the pandemic with comparison to the previous year. These results, which can be interpreted as repetition of the results of 6-month comparisons, shows that clinical deteriorations which are salient as the worsening of symptoms, were treated with dose increase or addition of new medications, but these deteriorations were visible from the frequency of emergency admissions and hospitalizations. According to this, it can be seen that considering only the parameters of hospitalizations and emergency admissions will lead to overlooking the various aspects of clinical worsening of patients, when evaluating the effect of the pandemic.

Strengths and Limitations

One of the strong aspects is that comparisons within the framework of the study were made for the first 6-month of the pandemic which corresponds to a time span that is before the availability of vaccination. According to a study, even the first dose of a COVID-19 vaccine is effective in decreasing the distress for most of the people (Perez-Arce et al. 2021). The implementation of vaccination affects stress related risk perception and changes the extent of restrictions in daily life, limiting the attribution of results to the pandemic. In our country, public vaccination started in January 2021 (Turkish Ministry of Health 2021). This date is after the 6-month comparison period in our study so the confounding effect of vaccination could be excluded while evaluating the effect of the pandemic on mental health in our study.

Retrospective design of the study is a limitation. A mirror-image comparison of the same patient group for the period before and after the onset of pandemic was made, but symptom severity before the pandemic might have a predictive role about the relapses during the pandemic, for this reason; analysis of variables including previous number of episodes and hospitalizations could be productive for firmer conclusions.

It is also a limitation that clinical examination records have been used instead of structured scales for the measurement of symptom severity. Recording of the symptom severity with application of structured clinical scales in routine practice will increase the quality of the results in future studies in our country, but high patient/practitioner ratio is currently one of the biggest problems.

Besides, it is a strength of our study that the CMHC constituting our sample were continuously open for medical service during the pandemic and all the patients who are under follow-up at this CMHC were included in our evaluations.

CONCLUSION

During the pandemic, both in the BD and SSD groups, there was increase in the number of patients with increase in symptom severity and the number of patients with medication dose increase or addition of new medication. On the other hand, there was no increase in hospitalizations for both of the groups. The pattern of increase in symptom severity without concomitant increase in hospitalizations underlines the importance of outpatient mental health services in the CMHC and this may also be related to the difficulties in hospitalization decisions in order to prevent overcrowding in psychiatric wards which have been reduced in terms of the number of beds after clinical closures during the pandemic.

Considering only variables with low sensitivity such as full-blown relapses or hospitalizations will lead to overlooking of

other clinically significant deteriorations such as symptom exacerbations in various severity when conducting studies about the effect of the pandemic on mental health.

Psychopathological differences between schizophrenia and BD may be the reason for the observation of a decrease in the emergency admissions in patients with BD, but not in patients with SSD in the first 6 month of the pandemic. Although we observed no increase in psychiatric hospitalizations, our results point to the fact that both patients with BD and SSD were in the need of intensive psychiatric treatment for the worsening of symptoms in the pandemic.

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Acknowledgement: *This article was written with the collaboration of the psychiatry resident Remzi Erşah Dindar, her medical specialty dissertation supervisor Eren Yıldızhan and training coordinator Nesrin Buket Tomruk.*

Validity and Reliability Study of the Prolonged Grief Disorder-Caregiver Turkish Form



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ABSTRACT

Objective: The aim of this study was to adapt the Prolonged Grief Disorder – Caregiver Form (PG-12), which is used to measure grief symptoms of caregivers providing care to their relatives with a chronic diseases that cause functional disability to Turkish and to investigate its psychometric properties. We also aimed to investigate the prevalence of prolonged grief disorder in the caregiver sample.

Method: The sample consisted of 120 adult participants (70.8% female) who acted as caregivers. The participants were administered Prolonged Grief Disorder-Caregiver Form, Zarit Caregiver Burden Scale, Beck Depression Inventory and Life Satisfaction Scale.

Results: The results of confirmatory factor analysis showed that the single-factor structure of PG-12, consistent with the original form, was supported. PG-12 scores showed a positive correlation with depression and caregiver burden scores and a negative correlation with life satisfaction scores. The internal consistency coefficient of the scale was 0.85. The prevalence of prolonged grief disorder calculated using PG-12 was found to be 31.66%.

Conclusion: The results showed that PG-12 is a valid and reliable tool for assessing the grief symptoms of people who provides care for a relative. In addition, the prevalence of prolonged grief disorder in our study population was high. Additional studies are needed in Turkey to confirm this rate and develop new strategies for caregivers.

Keywords: Prolonged Grief Disorder, Caregiver, Anticipatory Grief, Validity, Reliability

INTRODUCTION

Along with developments in medicine, the pharmaceutical industry, and technology, people's average life expectancy has increased over time. The period between becoming ill and dying was shorter a few centuries ago, but nowadays people can survive for many years, even when they suffer from various chronic diseases (World Health Association 2011). This increase in survival times for people with chronic diseases has created a need for long-term treatment and care. The diagnosis of a loved one's life-threatening chronic illness and that person's need for care can be experienced as traumatic life events (Lai et al. 2017), and many studies have found that prolonged grief, depression, anxiety, and post-traumatic stress are more common in caregivers than in the normal population (Aoun et al. 2020, Schulz et al. 2006, Wadhwa et al. 2013).

The mourning caregivers experience has been emphasized and hotly debated in recent years (Chiambretto et al. 2010, Lichtenthal et al. 2011). Caregivers lose their previous relationships with care recipients, who cease to be the people they used to know and become dependents who cannot meet their own needs and require care (Boss and Yeats 2014). Moreover, providing uninterrupted care can cause caregivers to forfeit social relations, restrict their autonomy, and feel a loss of control over their lives (Boss and Yeats 2014, Coelho and Barbosa 2016). Hence, as a result of these cumulative losses, caregivers of people with severe chronic illnesses may experience grief despite their relatives still being alive. The phenomenon of grief in caregivers may manifest as anticipatory grief (Large and Slinger 2015, Rando 1988), pre-death grief, or pre-loss grief (Nielsen et al. 2016, Trembl et al. 2021).

Received: 05.12.2021, Accepted: 29.04.2022, Available Online Date: 30.10.2023

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Grief after a loss is normal and expected. After a loss, certain symptoms are likely to occur, but they decrease over time as people adapt to their work and social lives after the loss (Prigerson et al. 2009). Although most people go through this process as expected, some people fail to adapt to daily life even long after the loss; there is no decrease in the severity of their symptoms, and it is as if time has stopped for them. This condition is called prolonged grief disorder (Prigerson et al. 2009). Prolonged grief disorder usually results from the loss of a loved one, but it is also observed in caregivers struggling to care for people with serious illnesses (Jacobsen et al. 2010, Prigerson et al. 2009, Tomarken et al. 2008).

Ignoring caregivers' grief symptoms may decrease their ability to provide care, as well as cause them to be unsatisfied with life, feel exhausted, and be at risk of psychiatric disorders (Chiambretto et al. 2010, Lichtenthal et al. 2011). Therefore, it is crucial to be able to measure caregivers' grief symptoms and to provide professional help to people with high symptom severity. In the literature, we found no assessment tool that could measure the prolonged grief symptoms of relatives caring for chronic patients and could be used as an auxiliary tool to detect prolonged grief disorder cases in Turkey. To eliminate this absence, we reviewed international studies and found that the Prolonged Grief Disorder-Caregiver Form (PG-12), developed by Prigerson and Maciejewski (2008), is an internationally accepted measurement and diagnostic tool used for different samples in different countries.

The first 11 items of the PG-12 assess the severity of grief symptoms, such as longing, denial, sadness, sorrow, resentment, avoidance, and diminished sense of self. The last item examines whether these symptoms are causing impaired socio-occupational functioning. Prolonged grief disorder can be diagnosed by evaluating all items of the scale together, and the severity of anticipatory grief symptoms can be evaluated by merely using the first 11 items (Prigerson and Maciejewski 2008). It is well known that one should not make a clinical diagnosis based solely on a self-report measurement tool. Hence, the PG-12 should not be considered a standalone diagnostic measurement tool, but only an auxiliary measurement tool to support physicians' diagnoses. A diagnosis of prolonged grief disorder made with PG-12 means that the severity of prolonged grief symptoms is higher than the threshold value and may impair the ability to function in important areas of a person's life (Prigerson et al. 2009).

PG-12 is widely used to measure anticipatory grief symptoms and to diagnose pre-death prolonged grief disorder in many different countries. In a study conducted in Denmark, the prevalence of pre-death prolonged grief disorder ($n=2865$) was 15.2% in a sample of caregivers of cancer patients (Nielsen et al. 2017a). Another study conducted with caregivers of individuals treated by palliative services in

Australia found that the prevalence of pre-death prolonged grief disorder ($n=301$) was 14.9% (Hudson et al. 2011). Similarly, the prevalence was 33% in a study of caregivers of cancer patients ($n=94$) in Portugal (Coelho et al. 2017), and 38.5% in a study of caregivers of vegetative patients ($n=52$) in Italy (Bastianelli et al. 2016). It is clear that PG-12 can be used for diagnostic purposes and to measure caregivers' prolonged grief symptoms in various countries.

According to the World Health Organization (2018) Noncommunicable Diseases Country Profiles report, approximately 89% of deaths in Turkey in 2016 were due to chronic diseases. When the Turkish Statistical Institute (2020) examined the cause-of-death statistics, it found quite similar results. Cancer, circulatory system diseases, nervous system diseases, respiratory system diseases, and metabolic diseases affect hundreds of thousands of people, meaning that the high prevalence of chronic diseases leads to a large number of people assuming the role of caregiver. Caregivers' grief and impaired psychological well-being can have a significant negative impact on their socio-occupational functioning (Cooper et al. 2007, Goldberg and Rickler 2011, Lim and Zebrack 2004). Therefore, the grief process of hundreds of thousands, or maybe millions, of caregivers has become a serious public mental health concern. Although using PG-12 as a measurement tool in Turkey would not, in itself, provide a holistic solution for caregivers' grief, it may be an important tool for supporting projects, research, and psychosocial interventions. Therefore, in this study, we aimed to investigate the psychometric properties of PG-12 for a sample of Turkish participants. We also aimed to investigate the prevalence of pre-death prolonged grief disorder among caregivers in Turkey.

METHOD

Participants

Within the scope of the research, we reached out to 120 adults aged between 18–65 who cared for adults with chronic diseases and who were relatives of the people they cared for. Participants were reached by convenience sampling method. Children, even if not ill, are naturally in a care-receiving position, and parents are naturally expected to care for their children. Therefore, it is thought that there may be great differences in psychological burdens of caring for an adult or a child (Raina et al. 2004). For this reason, it was thought that the people who care for an ill child could be the sample of a different study and we excluded people cared for patients under the age of 18 from this study. In addition, Prigerson and Maciejewski (2008) used a sample of adult caregivers in their original study, which developed the PG-12 instrument we adapted in the current study. Information about the participants is presented in Table 1.

Instruments

Within the scope of this study, we administered the Sociodemographic Information and Caregiver Form, Prolonged Grief Disorder Scale-Caregiver Form, Zarit Caregiver Burden Scale, Beck Depression Inventory and Life Satisfaction Scale to the participants.

Sociodemographic Information and Caregiver Form: It is an information form prepared by the researchers in which the participant is asked about themselves, the person they care for, and other demographic characteristics in Table 1.

Prolonged Grief Disorder Scale-Caregiver Form (PG-12): PG-12, developed by Prigerson and Maciejewski (2008), evaluates the symptoms of pre-death prolonged grief disorder in caregivers, including separation anxiety, emotions, cognitions, and behaviors. The first 11 items of the 12-item instrument are measured using a five-point Likert-type response scale. The first four items are rated as follows: 1="Not at all," 2="At least once," 3="At least once a week," 4="At least once a day," and 5="Several times a day." The next 7 items are rated as follows: 1="Not at all," 2="Slightly," 3="Somewhat," 4="Quite a bit," and 5="Overwhelmingly." The twelfth item of the scale concerns impaired functioning and is answered with "Yes/No". The total score for the scale is determined by the first 11 items and varies between 11 and 55. An increase in score means an increase in the severity of grief symptoms. The twelfth item evaluates impaired functioning and is required for diagnosis. Although the first 11 items can be used to measure the severity of grief symptoms, the instrument can also be used as an auxiliary tool for diagnosing prolonged grief disorder by including item 12. A diagnosis of pre-death prolonged grief disorder is made if the following criteria are met:

- A. **Event Criterion:** The person to whom it is applied must be caring for a relative with a serious illness.
- B. **Separation Anxiety:** The person must experience at least one of the symptoms listed in PG-12 items 1 and 2 (1=longing and yearning, 2=emotional pain, intense sadness, or sorrow) at least once a day.
- C. **Cognitive, Emotional, and Behavioral Symptoms:** The person must have answered at least five of items 3–11 (3=avoidance, 4=feeling stunned, shocked, or dazed, 5=diminished sense of self, 6=trouble accepting the illness, 7=difficulty in trusting others, 8=feeling bitter, 9=difficulty in moving on, 10=numbness, 11=feeling that life is unfulfilling, empty, or meaningless) with "at least once a day," "several times a day," "quite a bit," or "overwhelmingly."
- D. **Impairment Criterion:** The person must have a significant impairment in social, occupational, or other important areas of life (for example, household responsibilities).

In other words, if impairment exists, item 12 will be answered with "Yes."

In the original study, the internal consistency coefficient for PG-12 was found to be 0.78 (Prigerson and Maciejewski 2008). In the present study, the Cronbach's alpha value was found to be 0.85.

Zarit Caregiver Burden Scale (ZCBS): This is a five-point Likert-type measurement tool developed by Zarit et al. (1980), consisting of 19 items and is used to measure subjective caregiver burden. The score that can be obtained from the scale is 19–95. An increase in score means an increase in caregivers' subjective burden. The Cronbach's alpha coefficient of the original scale was found between 0.87 and 0.94, and the test–retest reliability was 0.71. It was adapted into Turkish by Özlü et al. (2009). The Cronbach's alpha coefficient of the Turkish version of the scale was 0.83. In this study, the Cronbach's alpha value of the scale was determined as 0.92.

Beck Depression Inventory (BDI): The BDI, developed by Beck et al. (1961), is a measurement tool that consists of 21 Likert-type items, scored 0–3, which evaluates the cognitive, emotional, and behavioral symptoms of depression. Hisli (1989) adapted the scale for use in Turkey, and in the current study, the Cronbach's alpha value of the scale was found to be 0.91.

Satisfaction With Life Scale (SWLS): This is a five-point Likert-type measurement tool developed by Diener et al. (1985), consisting of five items that determine individuals' life satisfaction levels. An increase in the scores obtained from the scale indicates an increase in life satisfaction. The test–retest correlation coefficient of the original scale was 0.82, and the Cronbach's alpha coefficient was 0.87. The adaptation of the scale for use in Turkey was carried out by Köker (1991), and the test–retest reliability coefficient for the scale was 0.85. In a second adaptation study conducted by Dağlı and Baysal (2016), the Cronbach's alpha coefficient of the scale was calculated as 0.88. In the current study, the Cronbach's alpha value of the scale was found to be 0.83.

Procedure

First, a psychologist who had a good level of proficiency in English and Turkish translated the PG-12 instrument into Turkish after obtaining the necessary written permissions for the adaptation study from the PG-12 developers. The Turkish version was translated back to English by three experts (two clinical psychologists and one psychologist) who were fluent in both languages, and the Turkish version was finalized by comparing the translation with the original scale.

Ethical permission to conduct the research (approval date, 27.10.2020; document no., E-12908312-300-00001306011) was obtained from the Hacettepe University Ethical Board.

Table 1. Sociodemographic Characteristics of Caregivers and Patients and Information Regarding Diagnosis and Caregiving Process

Variables	f	%	M	SD	Range
Gender					
Female	85	70.8			
Male	34	28.3			
Age			42.48	12.08	46.00
Education					
Primary	13	10.8			
Middle	7	5.8			
High School	37	30.8			
Collage	49	40.8			
Master's Degree	11	9.2			
Doctoral Degree	3	2.5			
Marital status					
Single	30	25			
Married	79	65.8			
Divorced	5	4.2			
Widow	6	5			
Economic status					
Low	31	25.8			
Middle	83	69.2			
High	6	5			
Employment status					
Employed	45	37.5			
Unemployed	75	62.5			
Relationship to patient					
Sibling	4	3.3			
Spouse	37	30.8			
Daughter/Son	67	55.8			
Partner	1	0.8			
Daughter-in-law/Son-in-law	6	5			
Grandchild	5	4.2			
Patient's age			63.13	14.7	73
Diagnosis					
Amyotrophic Lateral Sclerosis	52	43.3			
Cancer	25	20.8			
Alzheimer's Disease/Dementia	12	10			
Cardiovascular diseases	6	5			
Parkinson's Disease	5	4.2			
Respiratory Diseases	3	2.5			
Kidney Failure	2	1.7			
Other	15	12.5			
Duration of diagnosis (month)			62.19	73.44	381.5
Duration of caregiving (month)			52.29	66.75	479.5
Weekly caregiving duration (hour)			72.83	62.81	167.0

The data collection process took approximately three months, from December 2020 to February 2021. We conducted the study online using Google Forms software. We reached out to participants in various regions of Turkey through welfare associations, support groups for patients' relatives, and social media. After obtaining written and verbal consent from the administrators of the associations and support groups, we shared the invitation to participate in the research which included the purpose of study and the criteria for being a participant in the communication groups. First, we distributed an informed consent form to the participants, which included the conditions for voluntary participation in the study, the purpose of the study, confidentiality and other similar issues. In the online data collection process, we determined the time it took the participants to complete the questionnaires and whether they had completed the scales multiple times from their computers. We identified no situations that could threaten the study.

Statistical Analysis

We conducted the analyses using IBM® Statistical Package for the Social Sciences® (SPSS) version 24 AMOS 21 program. We examined all items for all the measurement tools to identify missing values, and the missing value rate did not exceed 1% for any item. We then analyzed outliers by calculating the z-values for the total scores of the scales. The z-values for the total scores of all scales were between -3.2 and +3.2. No participant was excluded from the data as an outlier. We examined normality and multivariate normality assumptions in order for confirmatory factor analysis (CFA) to produce robust results. For the analysis carried out using the AMOS program, the critical values for kurtosis and skewness were between -3 and +3, and the multivariate kurtosis value was less than 10. These values showed that the data were appropriate for the analysis.

We conducted CFA to test the construct validity of the PG-12 for the Turkish sample. CFA evaluates Chi-Squared and degrees of freedom ratio Chi-Squared divided by degrees of freedom value ($X^2/df < 3$), Comparative Fit Index ($CFI > 0.90$), Goodness of Fit Index ($GFI > 0.90$), Adjusted Goodness of Fit Index ($AGFI > 0.90$) and Root Mean Square Residual ($RMSA < 0.08$) criteria (Byrne 2016, Hu and Bentler 1998). To examine convergent and divergent validity, we evaluated the relationships between the PG-12 and ZCBS, BDI, and SWLS instruments using Pearson's correlation analysis. We used the between-group separation method to evaluate criterion validity, and we conducted t-tests for independent samples to examine the differentiation of the PG-12 total scale score between the groups with low and high BDI and ZCBS scores. We examined the internal consistency coefficient and item-total score correlations to evaluate the reliability of PG-12.

RESULTS

Confirmatory Factor Analysis

To test whether the single-factor measurement model in the original PG-12 form was valid for the Turkish version, we examined the single-factor model using the maximum likelihood method. In the analyses we carried out, the fit indices were $X^2/df=1.60$, $p=0.008$, $CFI=0.95$, $IFI=0.95$, $GFI=0.91$, $AGFI=0.85$, and $RMSEA=0.07$. When we reviewed these indices, we found that the X^2/df , CFI, and IFI values for the collected data perfectly overlapped with the theoretical model (Byrne 2016, Hu and Bentler 1998). The RMSEA and AGFI values indicated an acceptable level of conformity (Byrne 2016, Hu and Bentler 1998). When we evaluated all of these indices together, the data collected using PG-12 were compatible with the single-factor 11-item model; that is, the factor structure was confirmed. In addition to the model fit indices, we examined whether the standardized regression coefficients for all 11 Likert-type items in PG-12 were significant. We observed that all items, except for the third item, had factor loadings above 0.40, and all of these loadings were statistically significant ($p < 0.001$). As shown in Figure 1, the standardized regression coefficient for the third item was 0.29, but this value was not statistically significant at the 0.001 level ($p=0.02$).

Convergent and Divergent Validity

To evaluate the convergent and divergent validity of the PG-12 instrument, we examined the Pearson's correlation coefficients between PG-12, ZCBS, BDI, and SWLS and found that the coefficients for the relationships between PG-12 and the other scales were statistically significant. The positive correlations of PG-12 with BDI and ZCBS and the negative correlation of PG-12 with SWLS supported convergent and discriminant validity, according to the literature (Holley and Mast 2009, Hudson et al. 2011, Nielsen et al. 2017b, Chan et al. 2017). Table 2 presents Pearson's correlation coefficients for these variables.

Criterion Validity

To test the criterion validity of the PG-12 instrument, we used the intergroup differentiation method. For this purpose, we ranked all participants according to their largest to smallest BDI total scores. The participants fell into two separate groups with the highest 25% and the lowest 25% depression scores, and these groups' scores were compared with each other in terms of PG-12 scores. The same procedure was repeated for the ZCBS scores. T-test findings showed that the participants in the highest 25% quantile of depression scores had statistically significantly higher scores on PG-12 than the group in the lowest quantile. Similarly, participants in the highest 25% quantile in terms of ZCBS scores obtained

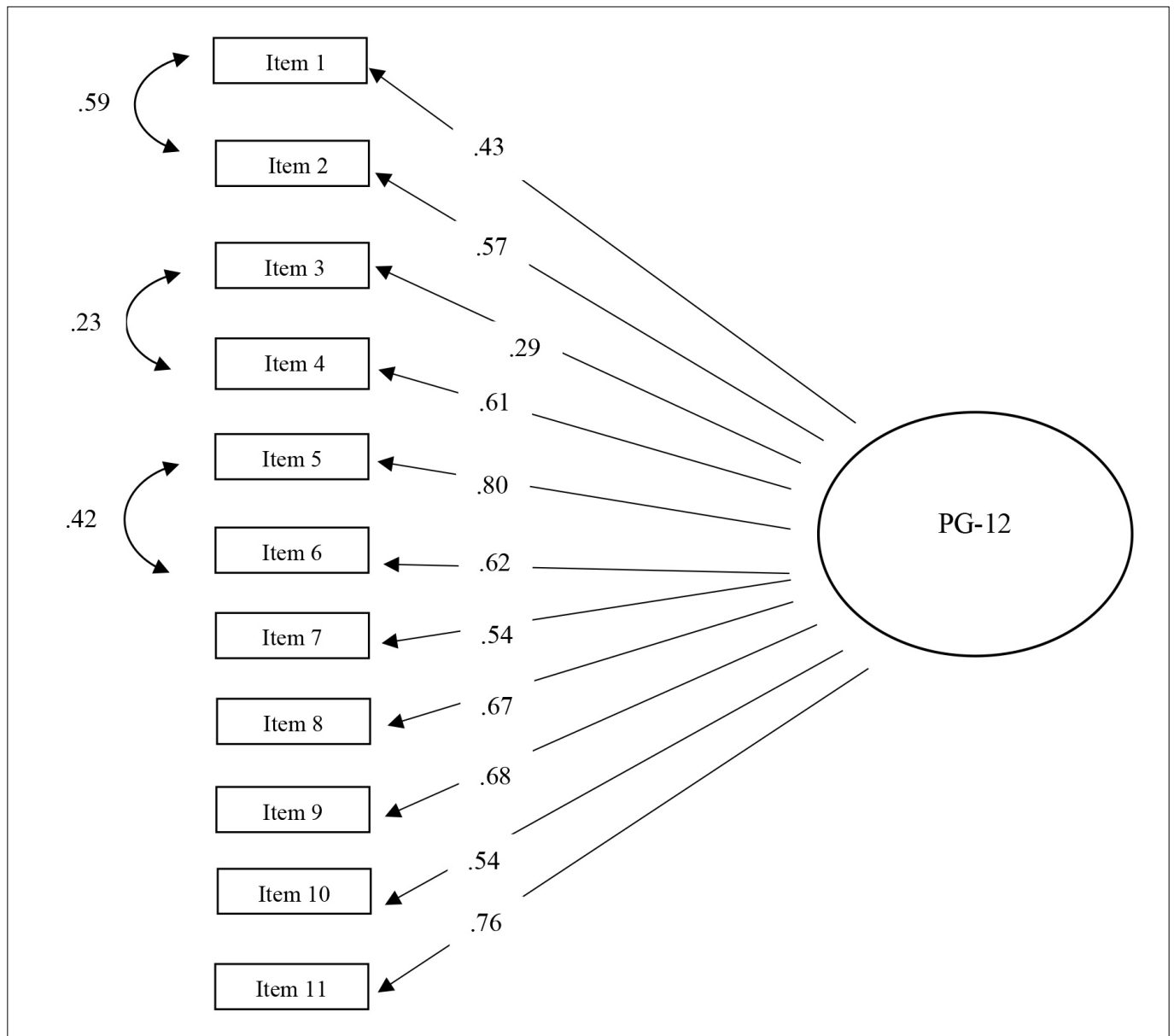


Figure 1. Results of the CFA of the PG-12 Turkish Version

CFA: Confirmatory Factor Analysis, PG-12: Prolonged Grief Disorder Scale-Caregiver Form

significantly higher PG-12 scores than those in the lowest 25% quantile. Table 3 presents the t-test findings.

Reliability

We calculated the Cronbach's alpha value as an indicator of the internal consistency coefficient to determine the reliability level of PG-12, and this value was $\alpha=0.85$. George and Mallery (2010) stated that Cronbach's alpha values above 0.80 indicate a high level of internal consistency. In addition to the internal consistency coefficient, we examined the item-total score correlations of PG-12, and the correlation values ranged between 0.44 and 0.74. Since the item-total test correlation coefficients for all items in PG-12 were over 0.40 and statistically significant ($p<0.01$), PG-12 is clearly a highly

distinctive and reliable measurement tool (Büyüköztürk 2015).

Prevalence of Prolonged Grief Disorder in Caregivers

We investigated the prevalence of prolonged grief disorder in a sample of 120 caregivers who were caring for their relatives with chronic illnesses, considering criteria A, B, C, and D in the PG-12 instructions (see the Methods section). It was evident that 31.66% of the caregivers met the diagnostic criteria for pre-death prolonged grief disorder. The mean age of the participants who met these diagnostic criteria was 41.82 years ($SD=12.24$), and the mean age of the relatives they cared for was 64.47 years ($SD=15.29$). Of the participants who met the diagnostic criteria, 68.4% were children of people with

Table 2. Pearson Correlation Coefficients Between PG-12 and BDI, ZCBS, and SWLS

	1	2	3	4
1.PG-12	1	0.60**	0.36**	-0.41**
2.BDI		1	0.31**	-0.51**
3.ZCBS			1	-0.19*
4.SWLS				1

* $p < 0.05$ ** $p < 0.01$

PG-12: Prolonged Grief Disorder Scale-Caregiver Form, BDI: Beck Depression Inventory, ZCBS: Zarit Caregiver Burden Scale, SWLS: Satisfaction with Life Scale.

Table 3. Comparison of Groups with Low and High Caregiver Burden and Depression in terms of PG-12 Scores

	N	M	SD	t	df	p
Group with Low Depression Score	30	31.83	7.25	-6.92	58	0.000
Group with High Depression Score	30	45.60	8.14			
Group with Low Caregiver Burden Scores	30	35.03	10.27	-3.13	51.14	0.003
Group with High Caregiver Burden Scores	30	42.13	6.99			

PG-12: Prolonged Grief Disorder Scale-Caregiver Form,

chronic diseases. Also, 78.9% of the diagnosed participants were women, 60.5% had a college or postgraduate education, 57.9% were unemployed, and almost all (97.4%) were of low to middle socioeconomic status. The diagnosed participants reported that they spent an average of 82 hours ($SD=65.02$) per week caring for their relatives, and 50% of the diagnosed participants cared for bedridden relatives.

DISCUSSION

In this study, the Prolonged Grief Disorder Scale-Caregiver Form was adapted for use in Turkey. The analyses showed that the validity and reliability values were close to those for the original form and were statistically significant. The CFA results supported the single-factor model according to the original scale and adaptation studies conducted in various cultures (Chiambretto et al. 2008, Coelho et al. 2017, Prigerson and Maciejewski 2008). The correlation values for convergent and discriminant validity and the t-test results for criterion validity supported construct validity, and the Cronbach's alpha value was a good indicator of the reliability of the scale for the Turkish sample.

When we examined the standardized regression coefficients using CFA to determine whether they were significant, the factor loadings were above 0.40 for all items except the third item, for which the standardized regression coefficient was .29 ($p=0.02$). In this case, we evaluated two possibilities. One possibility was that item 3, asking about avoidance, was not understood by the participants, either because they understood something other than what was meant by

the avoidance item or did not understand the psychology-related terminology. Another possibility was that because the participants were caregivers who constantly shared the same environments as the people they cared for, avoidance was not an option. In other words, the necessity of constantly being in the same environments as the care recipients and inevitably confronting the reality of the situation may have made it difficult for caregivers to avoid reminders of their relatives' illnesses. Based on the findings in the CFA that the third item did not work as well as the other items, we had to make a decision about whether to remove this item from the scale. Since the PG-12 instrument has frequently been used in studies published in prominent journals by outstanding researchers in many countries, and it has also been used in cross-cultural comparison studies, we decided to retain the original form and keep the third item in the scale. Another reason for keeping the third item in the scale was that the fit indices were extremely high, and the 11-item version of the scale was compatible with the data.

When we examined the prevalence of prolonged grief disorder in the sample, we found that approximately 32% of caregivers met the diagnostic criteria for prolonged grief disorder. In previous studies that examined the anticipatory grief symptoms of caregivers using PG-12, the prevalence of prolonged grief was 15.2% in Nielsen et al.'s (2017a) study of caregivers of cancer patients ($n=2865$), 14.9% in Hudson et al.'s (2011) study of caregivers of relatives treated by palliative services ($n=301$), 33% in Coelho et al.'s (2017) sample of caregivers of cancer patients ($n=94$), and 38.5% in Bastianelli et al.'s (2016) study of caregivers of patients

in a vegetative state (n=52). Although the prevalence of prolonged grief disorder in Italy, Portugal, and Turkey, which are Mediterranean countries, is similar, cultural differences in family ties may explain the lower prevalence of prolonged grief in studies conducted in Australia and Denmark which is Northern European countries. While family ties are less important and more individualistic cultures are predominant in Northern Europe, close family ties are the norm in the Mediterranean region, and the family is prioritized over the individual (Reher 1998). Hence, caregivers in Mediterranean countries may experience more severe effects from relational losses associated with their relatives' illnesses. Also, they may experience a higher pressure to assume the role of caregiver due to cultural codes, however reluctantly (Mahoney et al. 2005). Identity of caregivers also vary depending on the cultures in which studies are conducted. While 64% of caregivers in Nielsen et al.'s (2017a) study were the spouses of patients, 60% of caregivers in Coelho et al.'s (2017) study were the patients' children. In the present study, although the caregivers were mostly patients' children (55.8%), spouses took second place (30.8%). Although a limited number of studies have revealed that caregivers of spouses experience more anticipatory grief than caregivers of parents, the loss of competence of a parent for a caregiver, even if he/she has reached adulthood, and the consequent change in roles may affect the severity of the grieving experience (Ar 2017, Hudson et al. 2011, Nanni et al. 2014).

The caregivers providing care for their relatives with chronic diseases experience an extended period of grief due to the loss of social relations, restriction of their autonomy, loss of control over their lives, suppression of their own emotional and physical needs, and interruption of their future plans as well as their relatives' struggles with diseases, declining health status of the relatives they care for, the loss of relationships with those relatives, and their relatives' impending deaths (Boss and Yeats 2014, Coelho and Barbosa 2016). The fact that 31.66% of the participants met the diagnostic criteria for prolonged grief disorder revealed that these individuals experienced severe grief symptoms in terms of emotions, cognitions, behaviors, and separation anxiety in the face of loss, which impaired their functioning in important areas of their lives. Although most patients' caregivers experience similar losses, a minority of caregivers have symptoms that meet the criteria for prolonged grief. Also, individual differences between caregivers may play a role in their different experiences of prolonged grief disorder. In this study, consistent with the literature, the participants who met the diagnostic criteria for prolonged grief disorder had low income levels and dedicated most of their time (an average of 82 hours per week) to providing care as primary caregivers. Anticipatory grief is likely to occur in people with high relational dependency tendencies, low education levels, low income levels, people who are neurotic, have trouble with

intimacy, who have an inability to make sense of loss, and less attachment to spiritual values (Burke et al. 2015, Tomarken et al. 2008). However, assuming the role of primary caregiver and living with the patient are also risk factors (Areia et al. 2019, Hudson et al. 2011). In particular, low levels of social support for caregivers and the grieving process increase the likelihood of anticipatory grief (Burke et al. 2015).

Limitations of the Study

The main limitation of this research was that the measurements were based on self-reports. Self-reports can lead to the possibility of participants not being able to evaluate themselves objectively and/or giving answers they believe to be acceptable to society, potentially biasing the results. Another limitation of the study was the lack of a representative sample. Besides the inclusion in the sample only of individuals who cared for their adult relatives, the participants had particularly high levels of education. These factors could limit the generalizability of the findings. Also, reaching the participants through support groups for patients' relatives suggests that the sample received social support and therefore did not reflect the experiences of the wider population. Another limitation of the study is that it was cross-sectional. Also, the high ratio of women to men in the sample was compatible with the literature, which may have biased the research findings, since we do not yet know whether there are gender-related differences in the grieving process (Gopalan and Brannon 2006).

Implications for Clinical Practice

Bringing PG-12 into the national literature as a valid and reliable measurement tool for Turkey is of critical importance. The PG-12 instrument, which is internationally recognized and accepted, has been used in many studies of caregivers' anticipatory grief (Breen et al. 2020, Coelho et al. 2017, Hudson et al. 2011, Lai et al. 2017, Nielsen et al. 2016, Nielsen et al. 2017a, Nielsen et al. 2019, Thomas et al. 2014). Besides being a short and easily applicable measurement tool, the fact that it can be used to both evaluate the severity of anticipatory grief and diagnose pre-death prolonged grief disorder makes PG-12 convenient for clinicians in Turkey. Also, the fact that it is valid and reliable for any serious illness of a loved one expands its applicability compared to similar measurement tools that evaluate anticipatory grief in caregivers. Also, we believe that this scale will help shape psychological support services for caregivers according to their specific needs. Considering the caregiver population in Turkey and the prevalence of bereavement in this population, the necessity and benefits of this measurement tool are obvious.

In summary, the PG-12 is suitable for evaluating the grief symptoms of caregivers in Turkey in terms of its psychometric properties, and we foresee that it will be useful in both research and clinical practice.

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Acknowledgement: *This article is a part of the master's thesis of the first author Gizem Önal, conducted under the supervision of the last author Assoc. Prof. Zeynep Tüzün Gün.*

Evaluation of Sexual Function According to Gender and Sexual Orientation During the COVID-19 Pandemic in Turkey: A National Online Survey Study



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ABSTRACT

Objective: Coronavirus Diseases-19 (COVID-19) pandemic that has caused the death of thousands of people affected negatively not only people's physical wellbeing but also their mental health. The aim of this study was to evaluate the sexual function, depression, anxiety and stress, and fear of COVID-19 of individuals according to gender and sexual orientation during the COVID-19 pandemic.

Method: The questionnaire form included sociodemographic data form, the Arizona Sexual Experiences Scale (ASEX), the Depression, Anxiety and Stress Scale-Short Form (DASS-21), and the Fear of COVID-19 Scale (FCV-19S). The form was distributed on social media platforms.

Results: 1593 sexually active participants were included in the study. 47.5% of the participants were females and 52.5% were males. 86.9% of them were heterosexuals and 13.1% were lesbian, gay, and bisexual (LGB) individuals. ASEX, DASS-21 Depression, Anxiety, and Stress, and FCV-19S scores were significantly higher in females than males ($p<0.001$). When anxiety, depression, stress, and fear of COVID-19 were controlled, level of sexual dysfunction continued to be higher in women. We found that while the ASEX and FCV-19S scores were similar between the heterosexuals and LGBs (respectively $p=0.66$ and $p=0.31$), the DASS-21 Depression, Anxiety, and Stress scores were higher in LGBs ($p<0.001$).

Conclusion: Our results reveal the effect of the pandemic period on female sexual functions and the importance of addressing this topic in clinical practice and research.

Keywords: Sexual Dysfunction, Mental Health, Gender, Sexual Orientation, COVID-19

INTRODUCTION

The first Novel Coronavirus Disease (COVID-19) case in Turkey was reported on 11 March 2020 when the World Health Organization announced the outbreak as a pandemic. On 16 March 2020, some measures restricting social mobility were introduced across the country to prevent the rapid increase in the number of new cases, and these measures reduced interaction between people. Various changes were experienced at personal and social levels due to this unexpected life event. The outbreak that caused the death of thousands of people affected not only people's physical wellbeing but also their mental health negatively (Liu et al. 2020, Shigemura et al. 2020, Wang et al. 2020, Zhu et al. 2020). Major changes in people's daily routines, feeling useless in the workplace, and

uncertainty about pandemic caused depression and anxiety symptoms and a sense of panic, fear, anger, guilt, despair, and loss (Ibarra et al. 2020).

The fact that people had to stay at home affected both interpersonal and partner relationships (Li et al. 2020a). Some changes were observed in people's sexual life and behaviors as a result of modifications in the daily routines such as always being at home with children and/or partners due to closed schools or home-office working conditions and fear of getting infected with COVID-19 (Fuchs et al. 2020, Ibarra et al. 2020). A consistent and good sexual function is associated with physical and mental wellbeing (Anderson 2013, Bach et al. 2013, Jackson et al. 2020). On the other hand, low levels of sexual desire and satisfaction are shown in

Received: 28.09.2021, Accepted: 22.08.2022, Available Online Date: 05.30.2023

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people with a high level of depression and anxiety (Carcedo et al. 2020, Ko et al. 2020, Nimbi et al. 2020). Studies conducted during the pandemic (Cito et al. 2020, Ko et al. 2020, Li et al. 2020b) have shown significant changes in the sexual behavior of individuals, in the form of a decrease in sexual activities with partners and an increase in sexual activities without any. Although the researchers investigated the changes in sexual behavior during the pandemic, a few studies assessed sexual function according to gender and sexual orientation which are important factors in evaluating sexual practices (Fuchs et al. 2020, Sanchez et al. 2020, Schiavi et al. 2020).

Aim of this study is to investigate the relationship between sexual function and depression, anxiety, stress, and fear of COVID-19. In this study, we also compared sexual function, depression, anxiety and stress, and fear of COVID-19 according to gender and sexual orientation. Lastly, we investigated the effects of age, depression, anxiety and stress, and fear of COVID-19 on differences in sexual function between men and women, and heterosexuals and LGBs during the pandemic.

METHODS

We conducted a cross-sectional survey using an online questionnaire. Between 15 June and 15 July 2020, the questionnaire form, created on Google Forms by the researchers and which included sociodemographic data form, the Arizona Sexual Experiences Scale (ASEX) (McGahuey et al. 2000), the Depression, Anxiety and Stress Scale-Short Form (DASS-21) (Henry ve Crawford, 2005), and the Fear of COVID-19 Scale (FCV-19S) (Ahorsu et al. 2020), was distributed on social media platforms (Facebook, Twitter, Instagram). A study announcement image was created, and this announcement image was distributed through the researchers' social media accounts.

Sample

Before answering the questionnaire, all participants were informed about the content of the questionnaire and were able to proceed with the questionnaire after giving informed consent. Participation in this study was voluntary and participants had the option to withdraw consent until they completed the questionnaire. Incomplete questionnaires were not submitted to the system.

The participants were included in the study if they fulfilled all the following inclusion criteria: (a) Providing informed consent for the study (b) being between 18-64 years old, (c) living in Turkey (d) being sexually active, which we define as people who engage in sexual acts with or without partners during the pandemic period. Whether the participants were

sexually active or not was determined according to the answers given to the following question "Did you have an active sex life before the COVID-19 pandemic? (Including all sexual activities with or without a partner) a) Yes b) No". The applied questionnaire form does not allow the recording of the answers unless all the questions are answered. The answers of the recorded questionnaires were checked by the researchers, and 53 questionnaire responses that gave inappropriate answers to non-multiple-choice questions, duplicated records, and did not meet the criteria for participation in the study were not evaluated. The sexual orientation of the participants was determined according to the answers given to the following question, "Your sexual orientation? a) Heterosexual b) Homosexual c) Bisexual".

1593 participants who met these inclusion criteria were included in the study. Data collection conducted in accordance with the Helsinki Declaration. This research was approved by Clinical Research Ethics Committee of Istanbul University Istanbul Faculty of Medicine (File Number: 2020/782).

Measures

Arizona Sexual Experiences Scale (ASEX)

The ASEX is a self-report scale developed by McGahuey et al. (2000) to examine sexual functions. It has two separate forms, male and female, and each consists of 5 questions that examine sexual drive, psychological arousal, physiological arousal, ability to orgasm, and satisfaction as a result of orgasm. Rated on a 6-point Likert scale, scores for each domain and/or the total scale are taken into account. Total scores range from 5 to 30, with the higher scores indicating more sexual dysfunction. "Clinical sexual dysfunction is defined as a score of >19 for the whole scale, >5 for any domain, or ≥4 for any three domains. The Turkish validity and reliability study of the ASEX was conducted by Soykan, Cronbach's alpha values were found as 0.89 and 0.90 (0 and 6 months, respectively) (Soykan 2004).

Depression, Anxiety and Stress Scale-Short Form (DASS-21)

The DASS-21 is a scale consisting of 21 questions selected from the DASS-42 scale by Lovibond and Lovibond (1995)). This scale has three 7-item sub-scales measuring Depression, Anxiety and Stress. Answers to each item is graded with Likert-type scoring ranging from 0 to 3. Higher score shows the severity of the distress. The validity and reliability study of the 21-item short form of the scale in Turkish was conducted by Sariçam (2018) and, the Cronbach's alpha internal consistency coefficient of the scale was 0.85 for the depression subscale, 0.80 for the anxiety subscale, and 0.77 for the stress subscale.

Fear of COVID-19 Scale (FCV-19S)

The FCV-19S is a reliable and valid unidimensional scale for assessing COVID-19-related fear that was recently developed by Ahorsu et al. (22). This is a 7-item self-report tool, measuring fear based on a 5-point scale (1 = strongly disagree, 5 = strongly agree). Total scores range between 7 and 35. Higher scores indicate the greater fear of COVID-19. The Turkish validity and reliability study of the scale was performed by Satıcı et al. (2021), and the Cronbach alpha internal consistency coefficient was found to be 0.85.

Statistics

SPSS 20.0 for Windows was used for statistical analyses. Descriptive variables were expressed as mean $\pm$ standard deviation (SD). Age and distribution of scores from scales were evaluated with Kolmogorov-Smirnov test; The Mann-Whitney U test was used to compare the age and scale scores that did not fit the normal distribution between the two groups. Chi-square test was used for categorical variables in comparisons between the two groups. Spearman correlation coefficient was calculated to examine the correlations between continuous variables. One-way analysis of covariance (ANCOVA) was performed, in which ASEX scores were taken as the dependent variable, gender as the independent variable, and DASS-21 and FCV-19S scores as covariates. In addition, in this study, two-way ANCOVA, in which ASEX scores as dependent variables, gender and sexual orientation as independent variables, and DASS-21 and FCV-19S scores as covariates, was applied to investigate the interaction effect between gender and sexual orientation.

RESULTS

Responses of 1593 people between the ages of 18-60 were evaluated. The mean age of the participants was 29.9 (SD=8.9). 47.5% of the participants were females. 94.1% of the participants resided in an urban place, 5.9% in the countryside. 86.9% of them were heterosexuals while 13.1% were lesbian (0.6%), gay (5.9%), and bisexual (6.6%) (LGB). 36.7% of the participants were married. 84.9% of the participants were university graduates, 12.7% were high school graduates and the other 2.4% were primary school graduates. 30.8% of the participants were unemployed, 35% were working from home and 34.2% were working outside the home.

The mean ASEX score was 29.86 (SD=8.92); the mean DASS-21 Depression score was 7.96 (SD=5.73); the mean DASS-21 Anxiety score was 5.39 (SD=4.57), the mean DASS-21 Stress score was 8.46 (SD=5.09) and the mean FCV-19S score was 16.57 (SD=6.99). The Spearman correlation analysis results

Table 1. Spearman Correlation Analysis Results Between Arizona Sexual Experiences Scale Scores and Age and Other Scale Scores

All participants		
		ASEX
Age	r	- 0.05
	p	0.05
DASS-21 Depression	r	0.25
	p	< 0.001
DASS-21 Anxiety	r	0.17
	p	< 0.001
DASS-21 Stress	r	0.22
	p	< 0.001
FCV-19S	r	0.07
	p	0.004

ASEX: Arizona Sexual Experiences Scale; DASS-21: Depression, Anxiety and Stress Scale-Short Form; FCV-19S: COVID-19 Fear Scale

between ASEX scores and age, DASS-21 Depression, DASS-21 Anxiety, DASS-21 Stress and FCV-19S scores are given in Table 1.

Age, ASEX, DASS-21 Depression, DASS-21 Anxiety, DASS-21 Stress mean scores were compared between male and female groups, and are given in Table 2. In one-way ANCOVA, ASEX total scores were found to be higher in women than in men, even when ASEX total scores were taken as the dependent variable and age, DASS-21 Depression, DASS-21 Anxiety, DASS-21 Stress, and PCV-19S scores as covariates [$F(1, 1586) = 70.690, p < 0.001, \text{partial } \eta^2 = 0.043$].

Age, ASEX, DASS-21 Depression, DASS-21 Anxiety, DASS-21 Stress mean scores were compared between heterosexual and LGB groups, and the results are given in Table 3. In two-way ANCOVA, after controlling for covariants age, DASS-21 Depression, DASS-21 Anxiety, DASS-21 Stress and PCV-19S scores, sexual orientation (heterosexual/LGB) and gender (female/male) were determined in terms of ASEX scores. There was no interaction between them [$F(1, 1584) = 2.452, p = 0.12, \text{partial } \eta^2 = 0.002$].

DISCUSSION

In our study, the levels of sexual dysfunction, depression, anxiety, stress and fear of COVID-19 were found to be significantly higher in women than in men; and when anxiety, depression, stress and fear of COVID-19 levels were examined, the level of sexual dysfunction was found to be higher in women. Our results also revealed that while the levels of sexual dysfunction and fear of COVID-19 did not differ between heterosexual and LGB individuals, the levels of depression, anxiety and stress were significantly higher in LGB individuals.

Table 2. Comparisons of Sexual Dysfunction, Depression, Anxiety and Stress, and the Fear of COVID-19 Levels of Participants According To Gender

	Female (n=756)	Male (n=837)			
	Mean (SD)	Mean (SD)	Mann-Whitney U	z	p
Age	28.80 (8.11)	30.81 (9.50)	280631.0	-3.90	<0.001
ASEX- Total	13.49 (4.86)	11.52 (3.61)	237045.5	-8.68	<0.001
ASEX- desire	2.38(1.22)	1.91(1.02)	246060.0	-0.80	<0.001
ASEX- arousal	2.62(1.16)	2.23(1.02)	257147.0	-0.67	<0.001
ASEX- lubrication/erection	2.56(1.15)	2.15(1.01)	253014.0	-7.16	<0.001
ASEX- orgasm	3.28(1.30)	2.92(1.05)	262950.5	-6.04	<0.001
ASEX- orgasm satisfaction	2.65(1.42)	2.31(1.08)	281645.5	-3.92	<0.001
DASS-21 Depression	8.69 (5.79)	7.30 (5.60)	271491.0	-4.91	<0.001
DASS-21 Anxiety	6.17 (4.91)	4.69 (4.12)	261850.0	-5.97	<0.001
DASS-21 Stress	9.50 (5.20)	7.53 (4.80)	247069.5	-7.57	<0.001
FCV-19S	18.05 (6.88)	15.24 (6.82)	236185.5	-8.76	<0.001

ASEX: Arizona Sexual Experiences Scale; DASS-21: Depression, Anxiety and Stress Scale-Short Form; FCV-19S: COVID-19 Fear Scale; SD= Standard Deviation

Table 3. Comparisons of Sexual Dysfunction, Depression, Anxiety and Stress, and the Fear of COVID-19 Levels of Participants According To Sexual Orientation

	Heterosexual (n=1385)	LGB (n=208)			
	Mean (SD)	Mean (SD)	Mann-Whitney U	z	p
Age	30.33 (9.11)	26.76 (6.79)	112822.5	-5.05	<0.001
ASEX- Total	12.48 (4.34)	12.33 (4.50)	138785.0	-0.85	0.39
ASEX- desire	2.13(1.14)	2.18(1.18)	140718.0	-0.56	0.57
ASEX- arousal	2.43(1.10)	2.34(1.15)	136074.5	-1.34	0.18
ASEX- lubrication/erection	2.36(1.10)	2.25(1.11)	135585.5	-1.42	0.16
ASEX- orgasm	3.11(1.19)	3.00(1.17)	135444.0	-1.44	0.15
ASEX- orgasm satisfaction	2.46(1.26)	2.57(1.29)	136518.0	-1.26	0.21
DASS-21 Depression	7.78 (5.70)	9.12 (5.82)	124465.0	-3.17	0.002
DASS-21 Anxiety	5.24 (4.50)	6.39 (4.93)	124251.5	-3.21	0.001
DASS-21 Stress	8.29 (5.01)	9.59 (5.44)	124501.5	-3.16	0.002
FCV-19S	16.50 (7.00)	17.03 (6.93)	137055.0	-1.13	0.26

LGB: Lesbian, Gay and Bisexual; ASEX: Arizona Sexual Experiences Scale; DASS-21: Depression, Anxiety and Stress Scale-Short Form; FCV-19S: COVID-19 Fear Scale; SD= Standard Deviation

In our study, we found a positive correlation between levels of depression, anxiety, stress, and fear of COVID-19, in addition to a negative correlation between sexual dysfunction levels and age. Several stress factors caused by the pandemic negatively affected the mental health of individuals and caused them to feel more depressed, anxious, stressed, and lonely (Rajkumar 2020, Xiong et al. 2020). Previous studies (Angst 1998, Deumic et al. 2016, Forbes et al. 2017, Basson ve Gilks 2018) also indicated that high levels of depression and anxiety are related to higher levels of sexual dysfunction. Furthermore, the fear of contagion itself reduced intimacy within partners, from

simple kissing to intense sexual relations (Ibarra et al. 2020). A study (Baran and Aykac 2021) found that the fear of transmission of the virus to partners may manifest itself as a decrease in the frequency and quality of sexual intercourse during the COVID-19 pandemic. Most of the studies on sexuality in the COVID-19 period focused on the changes in all sexual activities. In these studies, which assess the changes in sexual behavior during the global pandemic, decrease in the frequency of sexual intercourse and pleasure from intercourse (Li et al. 2020b) and increase in sexual desire and individual sexual activities (such as masturbation, watching pornographic broadcasts) (Cocci. et al. 2020)

have been reported. An internet-based study (Karşıyakalı 2021) conducted in Turkey found a significant decrease in sexual activity during COVID-19. In two different studies conducted in our country, it has been reported that individuals experience an increase in depression (Gül 2021) and anxiety (Eroğlu 2022) levels due to COVID-19, and this situation negatively affects sexual functions.

In this study, we found that sexual dysfunction levels were significantly higher in females than males. Consistent with our results, a study reported that women had more sexual dysfunction than men before (Laumann et al. 1999) and during the COVID-19 pandemic (Gondwal et al. 2020). Also, a few studies (Fuchs et al. 2020, Ramón-Arbués et al. 2020, Yuksel and Ozgor 2020) reported that women's sexual functions worsened further during this pandemic. In a review study conducted by McCool-Myers et al. (2018), it was reported that there are many biological, psychological, and social predictors of sexual dysfunction in women, and these predictors vary according to the location of the study, gender norms and gender inequalities in that country/region.

We found that depression, anxiety, and stress were significantly higher in women compared to men, like sexual dysfunction. Previous studies (Liu et al. 2020, Karagoz et al. 2020, Ramón-Arbués et al. 2020, Wang et al. 2020) showed that women had higher depression, anxiety, and stress during the pandemic, and they were more affected by the COVID-19 outbreak related to mental distress. In line with our results, a study conducted in Egypt (Omar et al. 2020) showed that females suffered more anxiety and depression and thereby greater risk of sexual function difficulties. We found that women had significantly more fear of COVID-19 in addition to experiencing higher levels of depression, anxiety, and stress. Similarly, it was reported that women have three times more fear of COVID-19 than men, and being a woman is a predictor of the fear of COVID-19 (Ahorsu et al. 2020). In the present study, weak but significant positive correlations were found between the levels of sexual dysfunction and depression, anxiety, stress, and fear of COVID-19. In addition, after controlling for age, depression, anxiety, stress, and fear of COVID-19, it was observed that women had significantly higher sexual dysfunction levels than men.

Our findings show that the higher level of sexual dysfunction in women compared to men has reasons other than age and psychological variables such as depression, anxiety, stress, and fear of COVID-19. The reasons for the higher sexual dysfunction levels in women may be related to the importance given to sexuality and the higher level of knowledge about sexuality in men than in women (Lau et al. 2005). In our country, it can be thought that male-dominated sexuality and gender inequality may play a negative role on women's sexuality.

In this study, we found that there was no difference between LGBs and heterosexuals in terms of sexual dysfunction during the COVID-19 pandemic. While previous studies (Ko et al. 2020, Lehmler et al. 2020) showed significant differences in sexual activity (more decrease in sexual activity with a partner, more increase in no-partner and new sexual activity) according to sexual orientation, most did not compare sexual functions during the pandemic. A study (Gondwal 2020) showed that sexual functions do not differ according to sexual orientation. When comparing heterosexuals and LGBs, we observed that although the fear of COVID-19 level was similar, levels of depression, anxiety, and stress were significantly higher in LGBs during the pandemic. In fact, many studies (Baams et al. 2015, Meyer, 2003, Meyer 2015) showed that LGB individuals have higher levels of depression, anxiety, and stress before the pandemic period as a result of the sexual minority groups' experience. In our study, there was also no correlation effect between sexual orientation and gender in terms of sexual dysfunction, after controlling for the age, depression, anxiety, and stress, and COVID-19 levels. These results suggest that higher levels of anxiety, depression, and stress compared to heterosexuals do not mean that they have more sexual dysfunction than heterosexuals.

This study has some potential limitations. The study is cross-sectional and therefore it is not possible to evaluate the change in sexual function during the pandemic. Although all assessments were made with validated and reliable self-report scales, not questioning the sexual behavior of the participants in the study should be taken as a limitation of the study.

All evaluations were performed with self-report scales. The questionnaire was conducted online instead of face-to-face. Individuals without internet or who are unable to use digital platforms could not be included in the study. On the other hand, it was inevitable to use an online questionnaire due to the risk of disease spread during the peak of the pandemic. Although the number of participants included is sufficient, the sample may not be representative of all segments of the society. The results of our study should be evaluated considering these limitations.

In our study, significant positive correlations were found between the levels of depression, anxiety, stress and fear of COVID-19 and the level of sexual dysfunction. It has been observed that women have higher levels of sexual dysfunction, depression, anxiety, stress and fear of COVID-19 than men. When anxiety, depression, stress, and fear of COVID-19 were controlled for, the level of sexual dysfunction continued to be higher in women. Although LGB individuals have higher levels of depression, anxiety and stress compared to heterosexual individuals, there was no significant difference between the two groups in terms of sexual function. Since

sexuality is a fundamental determinant of well-being, we should not ignore it, but rather take it into account, as is the case with other challenges during the pandemic. Our study may contribute to the understanding of whether sexual functions differ by gender and sexual orientation during the COVID-19 pandemic, taking into account the impact of clinical variables. Further studies on sexuality during COVID-19 pandemic are needed to clarify the results.

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The Impact of Childhood Sexual Abuse on Adult Female Sexual Function and Sexual Distress: A Systematic Review and Meta-Analysis



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ABSTRACT

Objective: In this study, it was aimed to examine the impacts of exposure to childhood sexual abuse (CSA) on women's sexual function and sexual distress.

Method: In this systematic review and meta-analysis study, eight international (EBSCO, Psyc-Info, Proquest, PubMed, Science Direct, Scopus, Ovid, Web of Science) and two national electronic databases (Dergipark and Thesis Database of the Turkish Council of Higher Education) were searched. Studies reporting outcomes of sexual function and sexual distress in women with and without a history of CSA were included. The data were synthesized by meta-analysis and narrative methods.

Results: Two dissertations and five research articles published between 2010 and 2021 were included in the study. In some studies that were not included in the meta-analysis, it was reported that there was no difference in the prevalence of sexual dysfunction, and sexual satisfaction in women with and without a history of CSA. Meta-analysis results demonstrated lower sexual function (sexual arousal, MD: -0.83, $p<0.001$; sexual desire, MD: -0.55, $p<0.001$; lubrication, MD: -0.78, $p<0.01$; pain, MD: -0.52, $p<0.001$) and more sexual distress (SMD: -0.79, $p<0.05$) in women with CSA history.

Conclusion: This study showed that CSA negatively affects female sexual function and increases sexual distress. Healthcare professionals should be aware that women with a CSA history may have worse sexual functions and more sexual distress. More research is needed on the role of CSA in the etiology of sexual function problems and its possible mechanisms of action.

Keywords: Childhood sexual abuse, sexual health, women, sexual dysfunctions

INTRODUCTION

Childhood sexual abuse (CSA) is generally defined as forcing or persuading a child or young person under the age of 18 to participate in contact (such as touching genital organs or penetrating) or non-contact (such as exhibitionism, watching pornography) sexual acts (Fisher et al. 2017). CSA, a global problem, affects the physical and mental health of victims throughout their lives (World Health Organization 2006). Studies have found that the prevalence of CSA worldwide varies between 8-31% in women and 3-17% in men (Barth et al. 2013). Systematic reviews and meta-analysis studies have indicated that CSA victims are at risk for various physical and psychological problems (Hailes et al. 2019). These risks are

schizophrenia, post-traumatic stress disorder, substance use, increase in chronic pain complaints, obesity, and recurrent sexual victimization (Hailes et al. 2019, Irish et al. 2010, Maniglio 2009). In addition, although the underlying mechanisms are not yet fully understood, it is reported that CSA has a high risk of adversely affecting sexual health (Kilimnik et al. 2018, Lacelle et al. 2012, Pulverman et al. 2018, Seehuus et al. 2015). CSA affects sexual health more than other childhood traumas in adulthood, since it usually occurs in relationships with which the child establishes close bonds, abuses the child's trust, and includes sexual acts (Bigras et al. 2021).

Sexual function is the individual's ability to respond to or enjoy sexuality (Seehuus et al. 2015). Sexual dysfunction

Received: 23.10.2021, Accepted: 22.08.2022, Available Online Date: 12.10.2023

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is considered in the presence of a problem (such as orgasm disorder) that causes personal and/or interpersonal distress in a sexual function-related dimension (such as sexual desire, sexual arousal, and sexual satisfaction) (Basson et al. 2010, Bigras et al. 2021).

As a mental disorder category, the International Classification of Diseases and Related Health Problems (ICD-11) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) are often used to diagnose female sexual dysfunctions (ICD-11 for Mortality and Morbidity Statistics 2022, IsHak and Tobia 2013). In both DSM-5 and ICD-11, sexual dysfunction must be associated with a clinically evident distress in order to establish the diagnosis of sexual dysfunction (ICD-11 for Mortality and Morbidity Statistics 2022, IsHak and Tobia 2013). In this context, sexual distress, which refers to feelings such as frustration and anxiety related to the sexual act, is considered an important component of sexual dysfunction (Santos-Iglesias et al. 2018).

Individuals with a history of CSA have more negative cognitive and affective problems related to sexuality, which may lead to negative sexual health outcomes (Pulverman et al. 2018). In the literature, it is stated that CSA may be associated with sexual dysfunction, decreased sexual desire and satisfaction, and risky sexual behaviors (Kilimnik et al. 2018, Lacelle et al. 2012, Pulverman et al. 2018, Rellini 2008). Some studies have reported that the risk of contracting a sexually transmitted disease increases due to reasons such as the early onset of voluntary sexual intercourse, increase in the number of sexual partners and unprotected sexual intercourse, and the use of drugs or alcohol during sexual intercourse after CSA (Abajobir et al. 2017). A recent study suggested that CSA is not related to all areas of sexuality, contrary to what was predicted (Bigras et al. 2021). Although CSA is strongly associated with increased sexual dysfunction, sexual functions have not been adequately investigated in individuals with a history of CSA. In addition, the study has stated that the wide variety and methodological differences in the definition of CSA lead to inconsistent and complex results (Bigras et al. 2021, Gewirtz-Meydan and Lahav 2020b, Kilimnik et al. 2018, Lacelle et al. 2012). For this reason, healthcare professionals may have difficulty in accessing credible information about sexual problems they frequently encounter (Bigras et al. 2021).

Sexual function is an important determinant of an individual's quality of life (Carreiro et al. 2016, Flynn et al. 2016). Evaluation of the effect of CSA on sexual function and sexual distress may be beneficial in determining the ways of increasing the quality of life of individuals who have been abused (Carreiro et al. 2016). In addition, it is recommended to confirm the negative health outcomes caused by CSA with

quality studies for planning post-abuse health services (Hailes et al. 2019).

In the literature, the effect of CSA on sexual health outcomes has been investigated relatively more in women than in men (Bigras et al. 2021, Gewirtz-Meydan and Opuda 2022). On the other hand, there are no recent studies that systematically reviewed and synthesized the results of studies evaluating the effect of CSA on female sexual function and sexual distress. Studies in the nature of traditional literature reviews reported the results of previous studies (Kilimnik et al. 2018, Pulverman et al. 2018), and in some parts of these studies, the methodological differences of existing studies were discussed. In a systematic review study dealing with some results related to sexual well-being in men and women, CSA and sexual functions were found to be associated in individuals with psychiatric problems and therefore high potential for sexual problems, and adolescents (Bigras et al. 2021). In addition, there are systematic reviews and meta-analysis studies that address the relationship between gynecological diseases, including sexual dysfunction and a history of sexual assault in women (Hassam et al. 2020). However, considering sexual assault in adulthood and childhood together in these studies makes it difficult to understand the effects of CSA on sexual function. The purpose of this systematic review and meta-analysis is to determine the effect of CSA on female sexual function and sexual distress, based on the above-mentioned information. The questions aimed to be answered in the study are as follows;

1. What is the effect of CSA exposure on sexual function of adult women?
2. What is the effect of CSA exposure on sexual distress in adult women?
3. What is the effect of CSA exposure on the prevalence of sexual dysfunction in adult women?

METHOD

This study was prepared in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA) Checklist (Moher et al. 2009). Before starting, the study protocol was recorded in the PROSPERO database (CRD42021237119). In order to reduce the risk of possible bias in this study, literature review, study selection, data extraction, and quality assessment of the included studies were performed independently by the first and third researchers, and all these processes were checked by the second researcher. In addition, in order to carry out this study in an appropriate manner and with good quality, pilot studies were carried out with online sessions attended by all researchers, for reviewing, study selection, data extraction and study quality assessment. When there was any difference of opinion

among the researchers, the issue was discussed, and consensus was reached in an online meeting attended by all researchers.

Inclusion and Exclusion Criteria

Original research articles and theses published in Turkish or English, which reported the main results on sexual function and sexual distress in women over 18 years of age with and without a history of CSA, were included in this study. Since previous studies on the subject did not include studies published in the last ten years (Kilimnik et al. 2018, Pulverman et al. 2018), this study was limited to studies conducted between 2010-2021.

The studies eligible for this systematic review and meta-analysis conformed to the following PECOS components;

Participant (P): Adult women over 18 years old

Exposure (E): History of CSA

Comparison (C): No history of CSA

Outcomes (O): Sexual arousal, physiological and subjective sexual response to sexual stimuli, sexual desire, lubrication, orgasm, pain, sexual dysfunction, sexual satisfaction, and sexual distress

Study Design (S): Cross-sectional, experimental, or quasi-experimental studies that provide an opportunity to compare results in women with and without CSA

Qualitative studies and letters to the editor, case reports, systematic reviews, and traditional literature reviews were excluded from this study. Since it is known that sexual difficulties increase in high-risk samples (adolescents, alcohol abusers, patient groups diagnosed with posttraumatic stress disorder) (Bigras et al. 2021), studies conducted with these sample groups were excluded. Studies that did not define CSA separately from other trauma types, did not report male and female participant outcomes by gender, and did not examine the sexual health outcomes considered in this study were excluded. It was planned to include studies that evaluated sexual function and sexual distress outcomes with a scale and/or clinical interview. In studies that met PECOS criteria and were included in this study, outcome variables were evaluated with a scale.

Literature Review

In this study, the literature review was carried out between March 2021 and March 2022. Research articles were sought through EBSCO, Psyc-Info, Proquest, PubMed, Science Direct, Scopus, Ovid, Web of Science and Dergipark. "EBSCO Open Dissertations" and "ProQuest Dissertation" were used to screen international theses, and "The Council of Higher Education National Theses Center" was used to screen national theses. The review was limited

to studies published in Turkish and English between 2010 and 2021. In the review, the keywords "child sexual abuse, child molestation, sexual violence, sexual health, sexual (dys) function, sexual satisfaction, sexual distress, and abused women" in accordance with the Medical Subject Headings (MeSH) to access studies in English were used. The keywords "çocuk, ergen, cinsel istismar, cinsel işlev, cinsel sıkıntı, cinsel memnuniyet, and cinsel işlev bozukluğu" were used when searching national databases. In order to reach additional studies, the reference lists of the literature reviews on CSA and women sexual function, which were obtained as a result of the database search, were examined.

Study Selection

All studies obtained from databases were uploaded to a free computer application called Rayyan (Ouzzani et al. 2016). Duplicate studies were removed from the reviews using this application. Then, two researchers, blinded to each other's selection decisions through the application, selected the studies to be examined according to the title and abstract text. After the selection process was completed by two researchers, the final decision about the study was made with an online meeting attended by all researchers. Then, full texts of the studies were examined according to the inclusion criteria and the studies to be analyzed were determined. Among the studies being conducted within the scope of the same project and having overlapping sample results, the study containing the most comprehensive result was selected. In addition, some studies were excluded due to inconsistent data detected during the data extraction phase. Data were requested by e-mail from the authors of the studies that were not included in the study due to reporting deficiencies. However, due to the lack of feedback, no additional study could be included in this way. Figure 1 shows the selection process of the studies according to the PRISMA flowchart.

Data Extraction

A data extraction tool developed by the researchers was used to obtain the data in this study (Table 1). With this data extraction tool, data on the place and year of publication, study design, participant selection, sample size, female average age, CSA definition, measurement technique, and outcome variables of the studies included in the systematic review and meta-analysis were obtained. In studies reporting results by gender or different trauma types, only the data of women with and without CSA were extracted.

Assessment of the Quality of Studies

By following the steps suggested for systematic review studies (Karaçam 2013), the quality of the studies included in this study was evaluated. In this way, it was ensured that studies

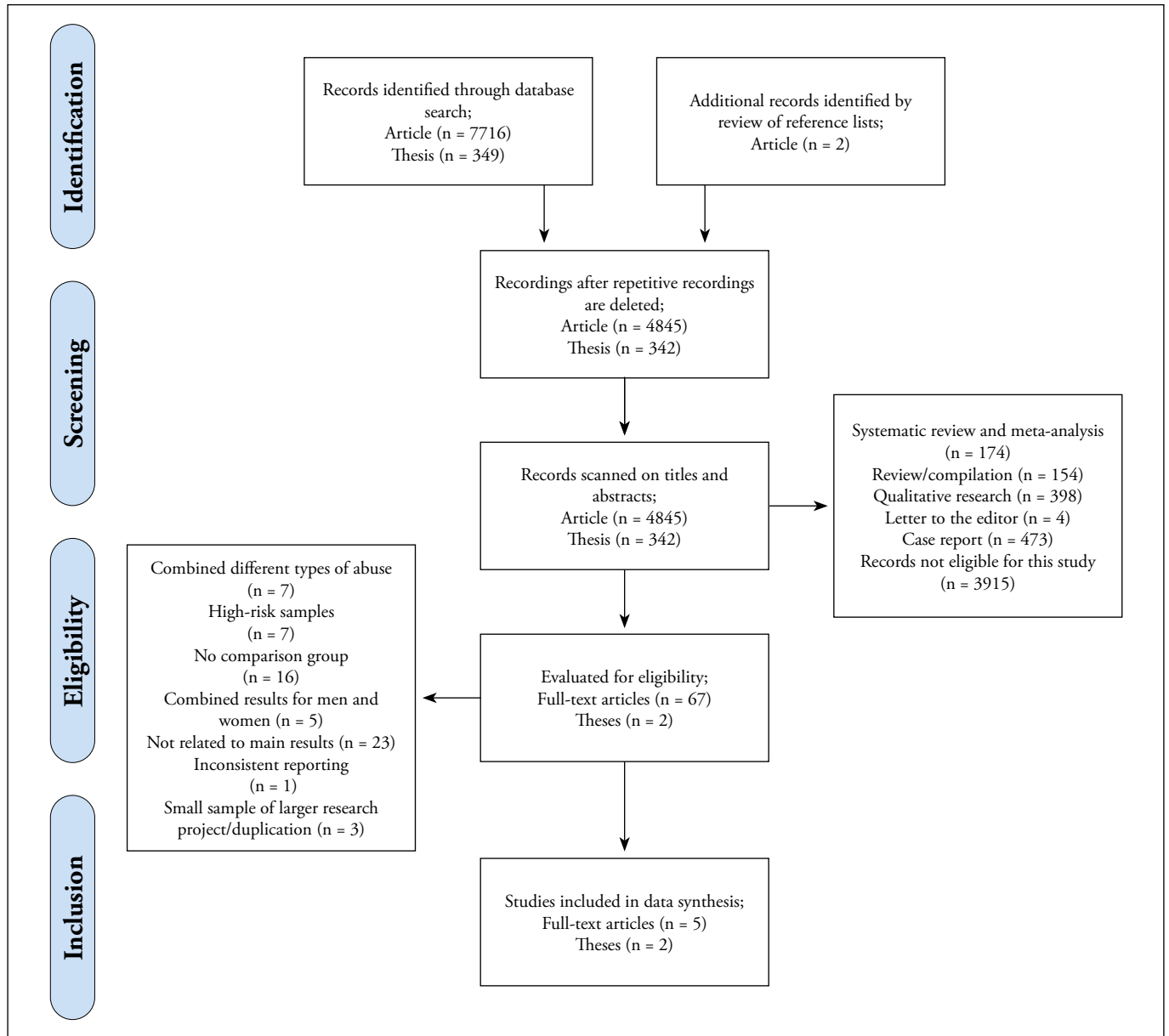


Figure 1. Selection of studies according to the flow chart of Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA)

of low quality were not included in the meta-analysis. Quality assessment tools of the Joanna Briggs Institute were used for quality assessment. Since all included studies were conducted in accordance with the cross-sectional study design, the eight-question quality assessment tool (JBI Critical Appraisal checklist for Analytical Cross-Sectional Studies) used for this design was chosen (Moola et al. 2017). Every item in this tool is rated with “Yes, No, Uncertain and Not Applicable” options. In this context, the evaluation results of each study were presented as “Quality score” in Table 1.

Data Synthesis

The studies included in this study had different measurement methods and outcome variables. Meta-analysis was performed if there were at least two study results related to the outcome

variables examined in this study and obtained with similar measurement methods (Ryan 2016). Data that were not included in the meta-analysis were tabulated and presented in the form of narrative synthesis.

Meta-analysis was performed using Review Manager 5.3 (The Nordic Cochrane Centre, Copenhagen, Denmark). The effect size was calculated using the mean difference (MD) in outcomes of sexual function and sexual distress obtained with similar measures, and the standardized mean difference (SMD) in outcomes obtained with different measures. In the included studies, sexual distress was assessed with different scales which has scoring differences. Therefore, low scores in some results and high scores in others indicated increased sexual distress. In order to combine the results of studies using different measurement methods for the same outcome

Table 1. Characteristics of Studies Included in Systematic Review and Meta-analysis

Authors, Year, Country	Study design	Participant selection	Sample size	Age (years)	CSA definition	Outcome Variables (Mean or Frequency)			Quality Score *
						CSA	NSA		
Bird et al. 2014**, America	Cross- sectional	Community, clinical interview with CTQ	CSA:30-39 NSA:21-24	CSA:30 NSA:28	Forced or persuasive sexual intercourse where touching or penetration of the genitals occurs with someone at least 5 years older before the age of 16	FSFI-Arousal Arousal based on laboratory evaluation: Physiological Subjective	4.42±1.01 35.50±33.47 74.81±28.94	5.06±1.03 40.59±34.95 71.73±27.09	Yes:7 Unclear:1
Camuso and Rellini 2010, America	Cross- sectional	Community, online survey with CSAM	CSA:60 NSA:120	CSA:33 NSA:28	Forced touching or oral/anal/vaginal intercourse by someone at least 5 years of age before the age of 14	FSFI- arousal disorder	17	31	Yes:6 Unclear:2
Gewirtz- Meydan et al. 2020a, Israel	Cross- sectional	Community, online survey with CTQ	CSA:308 NSA:312	-	-	Total ASEX Total FSDS-R***	18.69±5.45 20.49±15.47	20.11±4.67 14.50±13.81	Yes:5 Unclear:3
Khouri 2010, America	Cross- sectional	Community, telephone interview	CSA:70 NSA:30	CSA:32 NSA:33	Unwanted sexual activity before the age of 16 (including oral, anal or vaginal intercourse, penetration into the vagina or anus using objects or fingers, or genital touching or caressing)	Total SSS-W Total FSFI	84.3±22.8 22.1±6.3	105.7±28.3 26.9±4.6	Yes: 5 Unclear:3
Pulverman 2017, America	Cross- sectional	Community, clinical interview with THQ	CSA:59 NSA:46	CSA:28 NSA:26	Unwanted sexual experience before age 16 (including oral, anal or vaginal intercourse, penetration into the vagina or anus using objects or fingers, or genital touching or caressing)	Total FSFI Sexual dysfunction	24.12±5.89 31	26.12±5.07 19	Yes: 7 Unclear:1
Staples et al. 2012, America	Cross- sectional	Community, clinical interview with CTQ	CSA:34 NSA:22	CSA:30 NSA:27	Unwanted sexual experience before the age of 16, including touching or penetrating the genitals with someone 5 years or older	FSFI sub- dimension: Desire Arousal Lubrication Orgasm Satisfaction Pain Arousal based on laboratory evaluation: Physiological Subjective	4.2±1.2 4.5±1.0 5.0±0.9 4.5±1.2 4.0±1.4 5.2±1.1 1.7±2.0 80.5±27.3	4.6±0.9 5.0±1.0 5.5±0.8 4.8±1.1 4.4±1.6 5.6±0.9 2.4±2.0 72.0±27.8	Yes: 7 Unclear:1
Stephenson et al. 2012, America	Cross- sectional	Community, and university students, telephone interview, screening with THQ	CSA:105 NSA:71	CSA:33 NSA:32	Unwanted sexual activity before the age of 16 (including oral, anal or vaginal intercourse, penetration into the vagina or anus using objects or fingers, or genital touching or caressing)	FSFI sub-dimension Desire Arousal Lubrication Orgasm Pain SSS-W Sub dimension: Personal distress	3.83±1.54 3.63±1.48 4.23±1.43 3.03±1.74 4.27±0.56 14.48±5.82	4.45±1.06 4.68±0.84 5.25±0.74 4.36±1.56 4.80±0.65 22.37±7.57	Yes:7 Unclear:1

*Refers to the total number met out of the eight items on the Joanna Briggs Institute critical appraisal checklist for analytical cross-sectional studies.

** The sample size reported for this study differs according to the outcome variables. Therefore, the sample size is presented as range. Details about the sample sizes of the study are included in the meta-analysis findings (Figures 2 and 3).

*** For this result, the direction of the scale score was adjusted so that a low score indicates increased sexual distress, then included in the meta-analysis. For this arrangement, the reported score was subtracted from 58, which is the highest score that can be obtained from the FSDS-R scale, without changing the standard deviation.
CSA, Women with a history of childhood sexual abuse; NSA, Comparison group without a history of childhood sexual abuse; FSFI, Female Sexual Function Index; SSS-W, Self-Sexual Satisfaction Scale for Women; ASEX, Arizona Sexual Experiences Scale; FSDS-R, Female Sexual Distress Scale-Revised; CTQ, Childhood Trauma Scale; CSAM, Child Sexual Abuse Scale; THQ, Trauma History Questionnaire.

measurement, the differences in direction between the scales were corrected by subtracting the reported average value from the highest possible value for the scale without changing the standard deviation (Higgins and Green 2011).

Q test and Higgins I^2 value are frequently used to evaluate heterogeneity in meta-analysis. In case of few studies, the Q test has lower power and does not provide information about the extent of heterogeneity when compared to I^2 (Melsen et al. 2014). Since the number of studies included in the meta-analysis was small in this study, heterogeneity was evaluated using I^2 . A value greater than 50% for I^2 indicates significant heterogeneity. In cases where heterogeneity is high, the random effects model was used to estimate the difference between the means. Fixed effect model was used for I^2 values less than 50% (Higgins and Green 2011, Melsen et al. 2014). In this way, the effect of heterogeneity on the strength of the evidence obtained was controlled (Higgins and Green 2011). All tests were calculated in two ways and $p < 0.05$ value was considered as statistically significant.

RESULTS

Systematic Review Findings

Screening Findings

As a result of the screening, 7718 articles and 349 theses were reached from the databases. As a result of removing the repetitive records and examining according to the title and abstract, respectively, 69 studies that could be examined in full text were obtained. As a result of the analysis on the full text, a total of 7 studies, including 2 theses and 5 research articles, that met the inclusion criteria were identified (Figure 1). No published articles of thesis studies were found in the screenings.

Characteristics of the Studies

All included studies were cross-sectional studies conducted in community samples and published in English. The sample consisted of American women in six of the studies and Israeli women in one. In the studies, the age ranged from 28-32 in American women with and without a history of CSA and 26-33 in their Israeli female counterparts. The total sample size of the studies ranged between 30 and 308 individuals in women with a history of CSA, and between 21 and 312 individuals in women without a history of CSA. CSA was defined as an unwanted/forced/persuasive contact sexual encounter/activity/experience before the age of 16 in five studies and before the age of 14 in one study. In one study, the diagnosis way of CSA was not reported, but CSA was evaluated with the 'Childhood Trauma Scale', which is a valid and reliable scale (Gewirtz-Meydan and Lahav 2020a).

Therefore, although no clear definition of CSA was made, this study was not excluded.

In the studies, sexual function was evaluated using the Female Sexual Functioning Index (FSFI), Arizona Sexual Experiences Scale (ASEX) and The Sexual Satisfaction Scale for Women (SSS-W). In the studies, the "The Female Sexual Distress Scale-Revised (FSDS-R)" and "The Sexual Satisfaction Scale for Women (SSS-W)" personal distress subscale were used in the evaluation of sexual distress. The decrease in FSFI total and subscale scores and total ASEX scores indicates a lower level of sexual function and an increased risk of sexual dysfunction (McGahuey et al. 2000, Wiegel et al. 2005). The decrease in total SSS-W scores indicates that sexual satisfaction is lower (Meston and Trapnell 2005). The increase in total FSDS-R scores (Derogatis et al. 2008) and the decrease in SSS-W personal distress subscale scores represent less sexual distress (more well-being) (Meston and Trapnell 2005). Table 1 shows the general characteristics and main findings of the included studies.

Quality Evaluation of the Studies

Eight items of the quality assessment tool were answered as 'Yes' with 7 for four studies, 6 for one study, and 5 for two studies (Table 1). Study subject, setting, and confounding/ contributing factors were unclear in 71.4% ($n=5$) of the studies. In addition, methods used to cope with confounding factors in two studies (28.5%), inclusion criteria in one study (14.2%) and the assessment method of exposure in one study (14.2%) were not defined.

The Effect of Childhood Sexual Abuse on Sexual Function and Sexual Distress

The Study Findings That Could Not Be Included in the Meta-analysis

In studies with results that could not be included in the meta-analysis, there was no significant difference in sexual satisfaction (Staples et al. 2012), prevalence of sexual arousal disorder (Camuso and Rellini 2010), and prevalence of sexual dysfunction (Pulverman 2017) in women with and without a history of CSA (Table 1). One study reported that women with a history of CSA generally had lower sexual satisfaction (Khouri 2010).

Meta-analysis Findings

In a meta-analysis conducted based on the results of three studies included in this study (Bird et al. 2014, Staples et al. 2012, Stephenson et al. 2012), the level of sexual arousal was found to be lower in women with a history of CSA compared to their counterparts (MD: -0.83, $p < 0.001$). In a meta-analysis based on two studies (Staples et al. 2012, Stephenson

et al. 2012), it was determined that women with a history of CSA experienced less sexual desire (MD: -0.55, $p < 0.001$) and lubrication (MD: -0.78, $p < 0.01$) and more pain during sexual intercourse (MD: -0.52, $p < 0.001$). There was no significant difference in orgasmic function in women with and without a history of CSA (MD: -0.83, $p > 0.05$). A meta-analysis conducted based on three studies reporting results on the effect of CSA on overall sexual function (Gewirtz-Meydan and Lahav 2020a, Khouri 2010, Pulverman 2017) revealed that the level of sexual function was significantly lower in women with a history of CSA compared to their counterparts (Figure 2 SMD: -0.43, $p < 0.01$). In addition, two studies reported the results of physiological and subjective sexual arousal elicited by visual erotic stimuli in the laboratory environment in women with and without a history of CSA (Bird et al. 2014, Staples

et al. 2012). In the meta-analysis based on these studies, it was determined that the physiological (SMD: -0.24, $p = 0.21$) and subjective (SMD: -0.21, $p = 0.29$) sexual responses of women with and without a history of CSA to erotic videos in the laboratory environment were similar (Figure 3; $p > 0.05$).

Results regarding the effect of CSA on sexual distress were reported in two studies. In the meta-analysis based on the results of these studies, sexual distress was found to be higher in women with a history of CSA compared to those without a history of CSA (Figure 4; SMD: -0.79; $p < 0.05$).

In these meta-analyses, the I^2 value for sexual arousal, sexual desire, pain, subjective and physiological sexual arousal results was below 50%. For lubrication, orgasm and general sexual function results, the I^2 value varied between 60% and 94%.

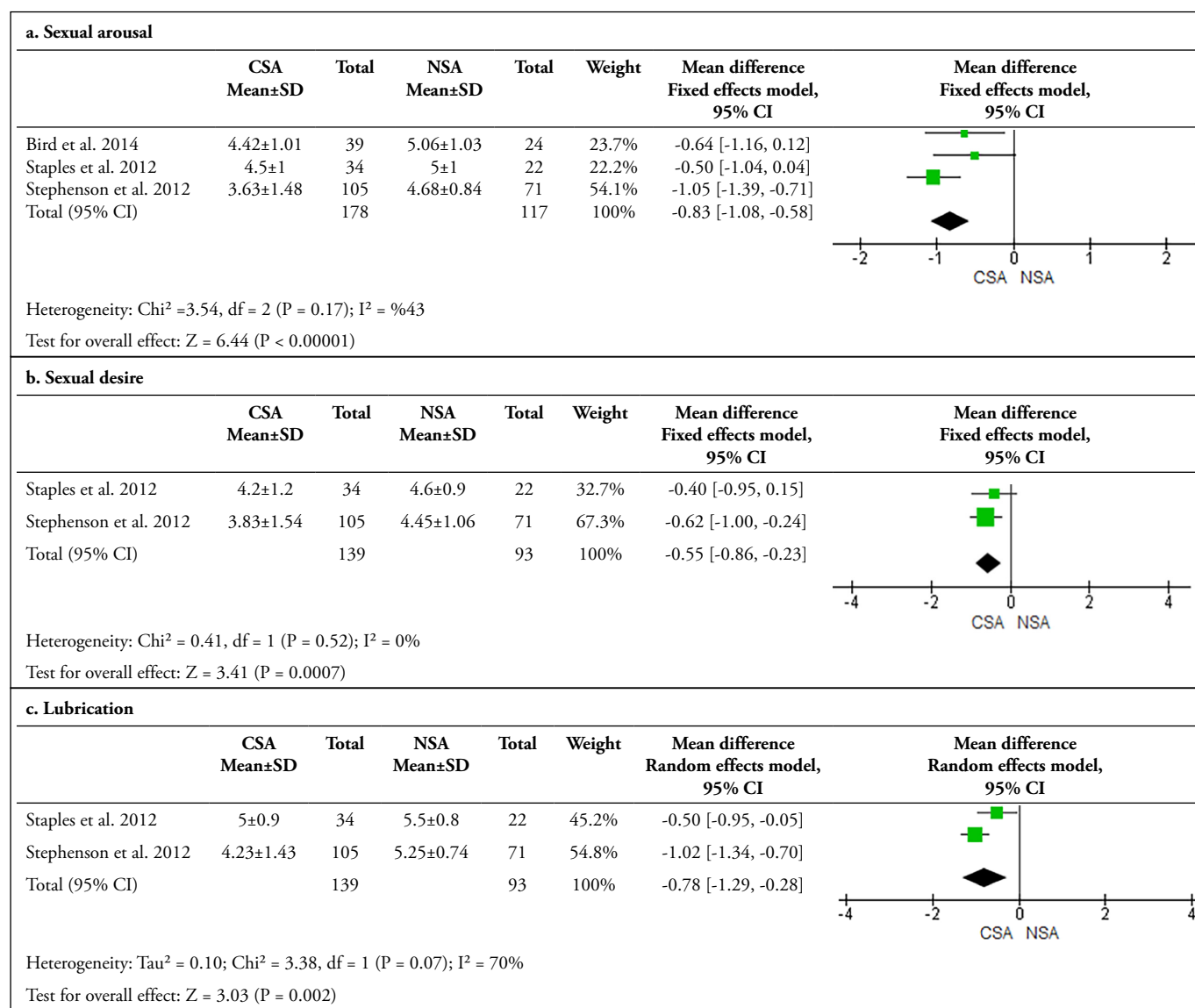


Figure 2. Meta-analysis results on sexual functions of women with and without a history of childhood sexual abuse

SD, Standard deviation; CI, Confidence Interval; CSA, Women with a history of childhood sexual abuse; NSA, Comparison group with no history of childhood sexual abuse

d. Orgasm							
	CSA Mean±SD	Total	NSA Mean±SD	Total	Weight	Mean difference Random effects model, 95% CI	Mean difference Random effects model, 95% CI
Staples et al. 2012	4.5±1.2	34	4.8±1.1	22	48.4%	-0.30 [-0.91, 0.31]	
Stephenson et al. 2012	3.03±1.74	105	4.36±1.56	71	51.6%	-1.33 [-1.82, -0.84]	
Total (95% CI)		139		93	100%	-0.83 [-1.84, 0.18]	
Heterogeneity: Tau² = 0.45; Chi² = 6.61, df = 1 (P = 0.01); I² = 85%							
Test for overall effect: Z = 1.62 (P = 0.11)							
e. Pain							
	CSA Mean±SD	Total	NSA Mean±SD	Total	Weight	Mean difference Fixed effects model, 95% CI	Mean difference Fixed effects model, 95% CI
Staples et al. 2012	5.2±1.1	34	5.6±0.9	22	11%	-0.40 [-0.93, 0.13]	
Stephenson et al. 2012	4.27±0.56	105	4.8±0.65	71	89%	-0.53 [-0.72, -0.34]	
Total (95% CI)		139		93	100%	-0.52 [-0.69, -0.34]	
Heterogeneity: Chi² = 0.21, df = 1 (P = 0.65); I² = 0%							
Test for overall effect: Z = 5.78 (P < 0.00001)							
f. General sexual function							
	CSA Mean±SD	Total	NSA Mean±SD	Total	Weight	Standardized mean difference Random effects model, 95% CI	Standardized mean difference Random effects model, 95% CI
Gewirtz-Meydan et al. 2020a	18.69±5.45	308	20.11±4.76	312	47.6%	-0.28 [-0.44, -0.12]	
Khouri 2010	22.1±6.3	70	26.9±4.6	30	24.4%	-0.81 [-1.26, -0.37]	
Pulverman 2017	24.12±5.89	59	26.12±5.07	46	28.0%	-0.36 [-0.75, 0.03]	
Total (95% CI)		437		388	100%	-0.43 [-0.72, -0.14]	
Heterogeneity: Tau² = 0.04; Chi² = 5.02, df = 2 (P = 0.08); I² = 60%							
Test for overall effect: Z = 2.88 (P = 0.004)							

Continuation of Figure 2. Meta-analysis results on sexual functions of women with and without a history of childhood sexual abuse

SD, Standard deviation; CI, Confidence Interval; CSA, Women with a history of childhood sexual abuse; NSA, Comparison group with no history of childhood sexual abuse

DISCUSSION

The findings of this systematic review and meta-analysis study, which aimed to examine how childhood sexual abuse affects female sexual function and sexual distress, supported that CSA negatively affected female sexual function and increases sexual distress in adulthood and CSA could be an important risk factor for sexual dysfunctions (Kilimnik et al. 2018, Pulverman et al. 2018). In the studies included in this study, the FSFI scores reported for women with history of CSA were below 26.55, which is considered as a clinical cut-off value for sexual dysfunction (Wiegel et al. 2005). Numerous researchers used this value to determine the risk of sexual dysfunction in samples including women with a history of CSA (Witting et al. 2008). In addition, meta-analysis findings in this study

showed that women with a history of CSA generally had worse sexual functions, had more problems related to sexual desire, arousal and pain, and increased sexual distress. These findings are compatible with the literature (Loeb et al. 2002, Pulverman et al. 2018). However, the results of some studies included in this study on the prevalence of sexual arousal disorder and sexual dysfunction in women with and without a history of CSA (Camuso and Rellini 2010, Pulverman 2017) were similar differently from the meta-analysis findings. It was thought that the reason for this difference between the related studies (Camuso and Rellini 2010; Pulverman 2017) and the literature and this meta-analysis might be associated with a real effect or sampling error due to the sample characteristics of the studies, or to overlooked confounding/contributing factors.

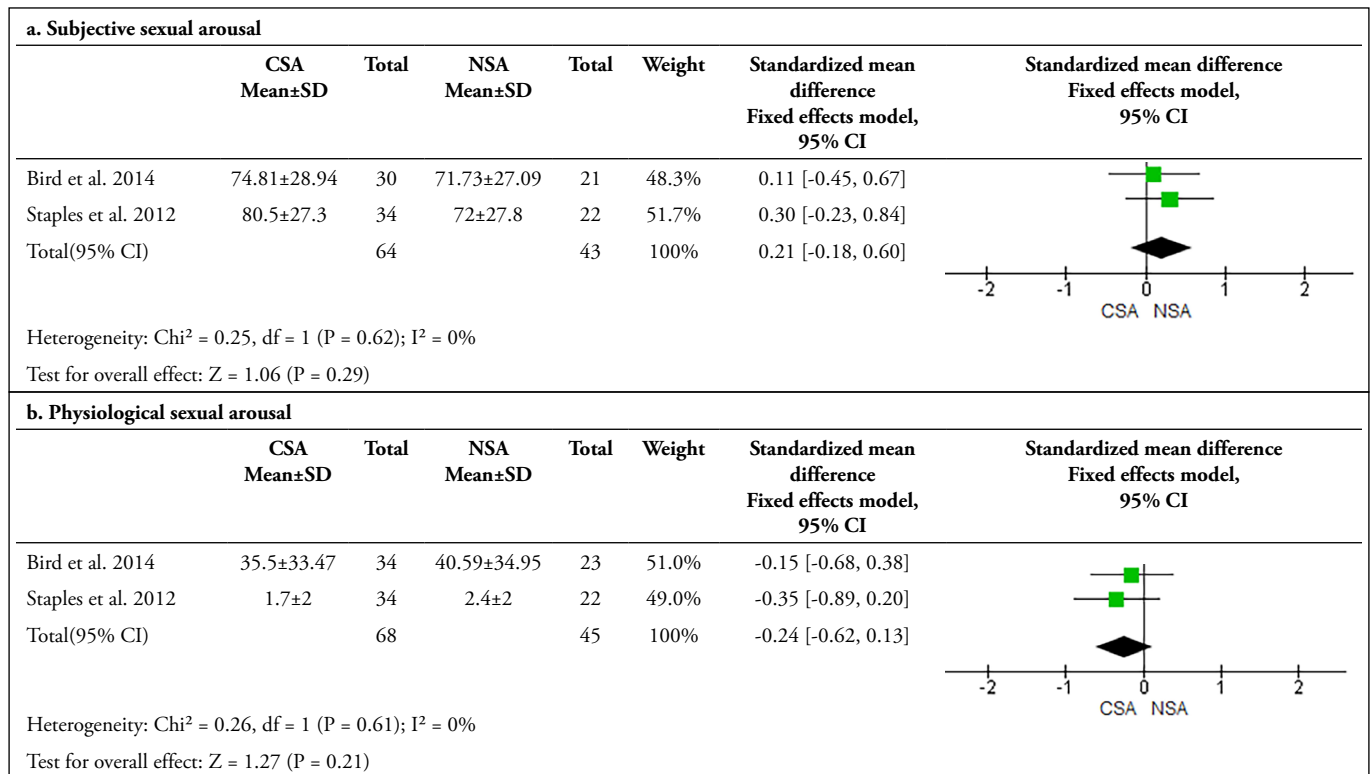


Figure 3. Meta-analysis results of subjective and physiological sexual responses to visual erotic stimuli in the laboratory setting of women with and without a history of childhood sexual abuse

SD, Standard deviation; CI, Confidence Interval; CSA, Women with a history of childhood sexual abuse; NSA, Comparison group with no history of childhood sexual abuse

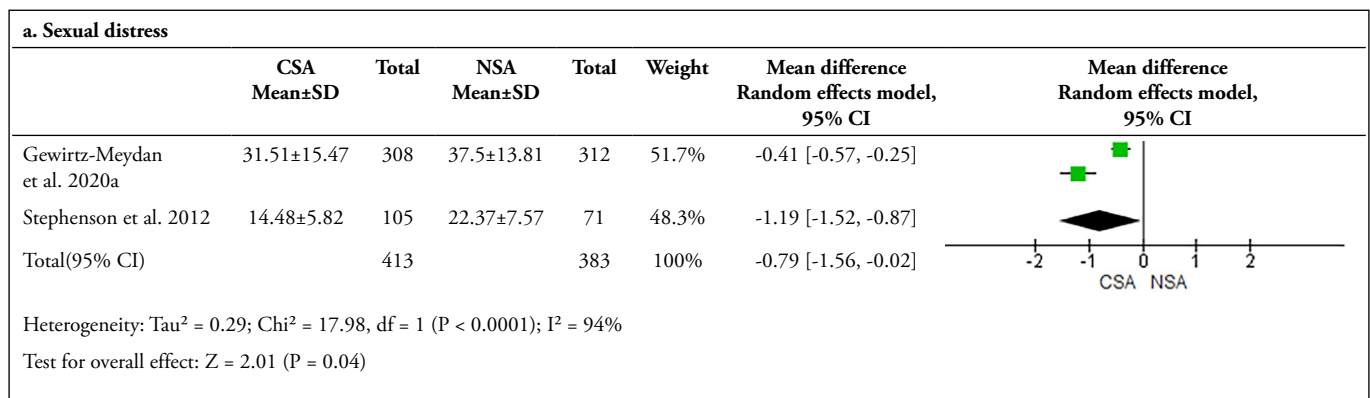


Figure 4. Meta-analysis results on sexual distress in women with and without a history of childhood sexual abuse

SD, Standard deviation; CI, Confidence Interval; CSA, Women with a history of childhood sexual abuse; NSA, Comparison group with no history of childhood sexual abuse

In a previous study, it was found that 23-62% of women with a history of CSA had arousal disorders and 18-45% had orgasmic disorders (Pulverman et al. 2018). It has been stated that women with a history of CSA may ignore the pleasurable aspect of sexual experience due to their tendency to avoid negative emotional experiences, and therefore may have difficulty in sexual arousal or reaching orgasm (Lacelle et al. 2012, Pulverman et al. 2018). Contrary to the literature (Klimnik et al. 2018, Loeb et al. 2002, Pulverman

et al. 2018), no significant difference was found in orgasm in women with and without a history of CSA in this study. This difference may be associated with the fact that findings of the present study were based on studies conducted in community samples and did not include the results of studies conducted on women with sexual problems.

Sexual arousal in women consists of two components, physiological and subjective. Physiological genital arousal includes genital vasocongestion and other physiological

changes that occur in response to sexual stimuli. Subjective arousal represents mental preoccupation in sexual acts (Meston and Stanton 2019). It has been reported that only two therapeutic approaches (mindfulness-based therapy and impressive writing therapy) have been empirically validated for treating sexual problems, including sexual arousal disorders, in women with a history of CSA (Gewirtz-Meydan 2020). There is a need for further studies on the subject. Figuring out the subjective and physiological arousal processes of women with a history of CSA can guide the development of effective treatments (Gewirtz-Meydan 2020, Meston and Stanton 2019). This study showed that the results of sexual arousal evaluated by FSFI and measured in the laboratory were not compatible with each other in women with history of CSA. Physiological and subjective arousal components can be evaluated together with FSFI. However, due to its structure, FSFI cannot separate the physiological component of arousal from its subjective component. For this reason, it may be more limited in evaluating sexual arousal when compared to laboratory measurements (Meston and Stanton 2019). The findings of this study revealed that although women with and without CSA history displayed similar physiological and subjective sexual arousal results against visual erotic stimuli, they were less aroused when they evaluated their own sexual functions. Due to a limited number of studies addressing the effects of CSA exposure on psychophysiological, emotional, and cognitive sexual response, it is difficult to interpret the present study's findings on sexual arousal. It is thought that the history of sexual abuse or negative sexual experience may cause low subjective sexual arousal in women by affecting beliefs and attitudes towards sexuality and sexual acts. The time of abuse may affect subjective sexual arousal and increase sexual shame and conservatism. It has been reported that abuses which occur after menarche or before the person's consensual sexual experience may affect women's ability to engage in satisfactory sexual interaction (Meston and Stanton 2019). In a study, it was found that some women with a history of CSA may exhibit a learned stress response when they encounter erotic stimuli, which may negatively affect their physiological sexual arousal (Rellini et al. 2009). In another study, it was found that most women with a history of CSA were able to avoid close sexual interactions and had less common and compatible perceptions of sexuality with a sexual partner (Rellini 2008). In different studies, it has been reported that sexual avoidance, negative attitudes towards sexuality and sexual intimacy, difficulty in establishing satisfactory sexual relations, and feelings of anger, shame and guilt about sexuality were higher in women with a history of abuse (Berlo and Ensinck 2000, DiLillo 2001). Mechanisms proposed to explain the correlation between CSA and sexual dysfunctions include sexual cognitive status, sexual self-schemas, sympathetic nervous system activation, body image and esteem, shame, and guilt (Pulverman et al. 2018).

However, there is a need for further studies on the effects of CSA history features on sexual arousal.

CSA decreases sexual satisfaction in adult women (Kilimnik et al. 2018, Lacelle et al. 2012, Pulverman et al. 2018, Rellini 2008) and some features of CSA (vaginal penetration, fear at the time of abuse, familial bond with the perpetrator, and persistence of abuse) are associated with satisfaction level (Rellini and Meston 2007). In this study, only two studies which evaluated sexual satisfaction in women with and without CSA were found, and the results of these studies were not suitable for meta-analysis. In addition, the findings of this study supported the results of the study, which reports that there is no standard definition of CSA in studies, researchers often focus on the effects of severe CSA, and non-contact experiences are not considered as CSA (Mathews and Collin-Vézina 2019, Pulverman et al. 2018). These findings suggest that further studies are needed to draw consistent conclusions about the effect of CSA on sexual satisfaction.

In our systematic review and meta-analysis, the strengths of this study include using a comprehensive research strategy, revealing the current situation on the subject and determining the analyzed results with reliable methods. The findings of this study are limited to the results of the study with a relatively small sample including young women living in the United States and Israel. A limited number of studies included in this study and the fact that the I^2 value was above 50% in some of the results included in the meta-analysis suggest that there is a significant heterogeneity in some of the included results (lubrication, orgasm, general sexual function and sexual distress). This may be a factor that may weaken the strength of the evidence. On the other hand, heterogeneity was controlled by using random effects model while performing meta-analysis in this study (Higgins and Green 2011). Since it is known that statistical power does not always increase even if the number of studies increases (Cohn and Becker 2003), it is thought that reliable results can be obtained with a small number of studies in cases where this model is used in meta-analysis. In addition, when the number of studies in the meta-analysis was less than 10, publication bias was not evaluated in this study because the success and power of the tests used to evaluate publication bias were low (Hoffman 2015). However, there is a general tendency to publish studies with significant results in academic journals. The inclusion of theses in this study can be considered as a factor that increases the power of the study in terms of inclusiveness and can reduce publication bias.

CSA is common in almost every society. Strong evidence is needed to demonstrate the association of CSA with adverse health outcomes (Barth et al. 2013, Hailes et al. 2019). This study can be considered as a beginning in understanding the deficiencies in the literature and determining the research needs. When interpreting the findings of this study, it should

be taken into account that the characteristics and quality of the included studies and the results of the studies are based on self-reported findings.

CONCLUSION

Further studies are needed to evaluate the correlations between CSA and sexual health outcomes in different cultures and age groups. Healthcare professionals (such as psychiatrists, clinical psychologists, family physicians, nurses, midwives) should definitely question the history of CSA in the evaluation of sexual health and should be aware that women with a history of CSA may have worse sexual functions and higher sexual distress. When planning the diagnosis and treatment of sexual problems in women with a history of CSA, the participation of different disciplines should be ensured, and women should be appropriately supported concerning treatment according to their needs.

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Description: *This study was presented as an oral presentation at the 5th International 6th National Midwifery Congress held in 11-14 November 2021.*

Neuroleptic Malignant Syndrome Concurrent with COVID-19 Infection: A Case Report



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ABSTRACT

Neuroleptic malignant syndrome (NMS), which most often occurs after the use of antipsychotics, is a rare but life-threatening condition. In this article, a 56-year-old male patient with a diagnosis of bipolar affective disorder (BPD) who developed NMS after a COVID-19 infection will be presented. The patient had been brought to the emergency room with high fever, fatigue, and slowness of movements that had been going on for two days. The examination revealed tachycardia, tachypnea, lethargy and rigidity. Upon further investigation the COVID-19 test came out positive and the serum levels of creatine kinase were considerably high. He was admitted to the psychiatric ward with diagnoses of COVID-19 infection and NMS. COVID-19 infection might have been a risk factor for NMS in this patient. Especially in patients who are taking antipsychotic drugs, if COVID-19 is present, the risk of NMS should be taken into consideration.

Keyword: COVID-19, Neuroleptic Malignant Syndrome, Risperidone, Antipsikotik, Enfeksiyon

INTRODUCTION

Coronaviruses are known as viruses that have an affinity to the nervous system (van Vuren et al. 2021). During the pandemic, there have been different peripheral and central neurological symptoms seen in COVID-19 patients. These symptoms have varied from loss of smell/taste and headaches to delirium and impaired consciousness (Mao et al. 2020). There have been different studies put forward during this period, which claim that the COVID-19 infection has effects on the central nervous system thus causing neurologic and psychiatric symptoms.

Neuroleptic malignant syndrome is a neurological emergency involving the central nervous system. We believe that COVID-19 infection might make patients who are using antipsychotics susceptible to the development of NMS. To our knowledge, five similar cases have been reported so far (Kajani et al. 2020; Soh et al. 2020; Burad and Kodange 2021; Espiridion et al. 2021). In this study, we present a COVID-19 patient with neuroleptic malignant syndrome (NMS).

CASE

A 56-year-old male patient with a diagnosis of bipolar affective disorder and a treatment history of about 10 years was brought to the emergency department due to altered consciousness. The patient was reported to be using 6 mg/day of risperidone and 1000 mg/day of valproic acid. Due to the history taken from the relatives, he had not experienced mood changes within the year and there had been no changes in his medications in the last three months. The patient was under regular follow-ups in our hospital. According to previous patient records and the history taken from his relatives, it was found out that he has not experienced any adverse effects of the extrapyramidal system before.

He had been experiencing high fever, fatigue, and slowing of movements for the last two days. The first assessment of vitals showed a fever of 40.5 °C while his blood pressure was 100/50 mmHg and his sPO2 was 95%. Tachycardia and tachypnea were observed. During the physical evaluation, it had been detected that the patient had confusion, somnolence (drowsiness), short incoherent responses to sound, and rigidity of all four limbs.

Received: 28.02.2022, Accepted: 07.06.2022, Available Online Date: 02.11.2023

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Laboratory results showed that the blood levels of creatine kinase were 1947 IU/L; d-dimer was 2347 µg/L; white blood cells were 2690/mm³ with lymphopenia and thrombocytopenia, and CRP was 98 mg/L. A combined nasopharyngeal swab test for COVID-19 was performed via PCR and it turned out to be positive. Chest CT revealed consolidation in the middle lobe of the right lung and ground-glass opacity in the lower lobe of the right lung.

Fever, altered mental status, and autonomic instability were interpreted to be related to the COVID-19 disease. However, additional creatine kinase increase and rigidity led to the consideration of neuroleptic malignant syndrome.

According to Levenson Criteria (Baltacıoğlu and Hocaoglu 2019), the patient had 3 major (fever, high serum levels of creatine kinase, and rigidity) and 4 minor (altered consciousness, tachycardia, changes in blood pressure, and tachypnea) criteria of neuroleptic malignant syndrome. The diagnoses of COVID-19 disease and neuroleptic malignant syndrome were concluded and due to his autonomic instability and altered mental status, the patient was admitted to the Intensive Care Unit.

Broad-spectrum antibiotics (piperacillin-tazobactam, Moxifloxacin) and faripiravir were started for the empirical treatment of COVID-19 and pneumonia. Support treatments (dopamine, enoxaparin sodium, hydration, PPIs) and lorazepam were also given to the patient. Lorazepam was started with a dosage of 6 mg/day and the dosage was gradually reduced. There was no need for tracheal intubation due to sufficiently-high saturation follow-ups. Intermittent

non-invasive mechanical ventilation with a nasal cannula (and reservoir mask when needed) was administered. During the observation and investigation period, starting drug therapy for NMS (bromocriptine, dantrolene) had not been necessary. With supportive therapy, the creatine kinase (CK) values began to decrease, and the patient's rigidity considerably improved on the third day of hospitalization (3rd day CK levels: 1245 U/L, 7th day CK levels: 566 U/L). Renal failure had not developed. Favipiravir treatment was completed in the hospital. Antibiotic therapy was stopped on the 10th day. The patient gained full consciousness, the clinical condition improved and he was discharged on the 12th day of hospitalization with informed consent.

DISCUSSION

NMS is associated with the use of antipsychotics, especially at high doses. There are various criteria for the diagnosis of NMS (i.e. Levenson, Lazarus, and Nierenberg).

According to Levenson criteria, at least 3 major criteria or 2 major and 4 minor criteria need to be present to make an NMS diagnosis (major criteria: hyperthermia, rigidity, high serum CK levels; minor criteria: altered mental status, tachycardia, changes in blood pressure, tachypnea, diaphoresis, leukocytosis).

Lazarus' criteria include "taking antipsychotic drugs in the last 7 days", while Nierenberg's criteria have "recent use of antipsychotic drugs". DSM-5 criteria indicate that during the last 72-hour period before the symptoms start, the patient needs to have taken a dopamine antagonist (Baltacıoğlu

Table 1. Neuroleptic Malignant Syndrome Diagnostic Criteria

Levenson Criteria	Lazarus Criteria	Nierenberg Criteria	DSM-5 Criteria
Major criteria -Hyperthermia -Rigidity -Elevated serum CPK (>1000 IU/L) Minor criteria -Altered consciousness -Tachycardia -Changes of blood pressure -Tachypnea -Diaphoresis -Leukocytosis	Major criteria -Treatment with neuroleptics within 7 days of onset (2-4 weeks for depot neuroleptics) -Hyperthermia -Rigidity Minor criteria -Altered consciousness -Tachycardia -Changes of blood pressure -Tachypnea -Elevated serum CPK or myoglobinuria -Leukocytosis	Essential criteria -Receiving or recently received an antipsychotic drug -Receiving another dopamine antagonist drug -Recently stopped therapy with a dopamine antagonist Major criteria -Hyperthermia (>38°C) -Muscular lead-pipe rigidity -Elevated serum CPK levels (>3 times normal) -Autonomic dysfunction -Altered consciousness Minor criteria -Other manifestations of autonomic dysfunction (e.g., urinary incontinence, arrhythmia or one of tachycardia, sweating, elevated or decreased blood pressure) -Leukocytosis -Other signs of EPS -Respiratory problems	-Exposure to dopamine antagonist within 72 hours prior to the beginning of the symptoms -Hyperthermia -Diffuse muscular lead-pipe rigidity and other neurological symptoms that are non-responsive to anti-Parkinson drugs -Elevated serum CPK levels (>4 times normal limit) -Altered consciousness -Tachycardia -Diaphoresis -Hypertension -Urinary incontinence -Tachypnea -Leukocytosis
Diagnosis: 3 major criteria or; 2 major + 4 minor criteria	Diagnosis: All three major criteria + 3 minor criteria	Diagnosis: 4 major criteria or; 3 major+3 minor criteria	

(Baltacıoğlu and Hocaoglu 2019). DSM-5: The Diagnostic and Statistical Manual of Mental Disorders.

and Hocaoglu 2019). It was determined that according to Levenson, Nierenberg, and Lazarus criteria, the patient had NMS (Table 1).

To our knowledge, five cases of NMS in COVID-19 patients have been reported so far. In the first patient presented by Soh et al., (2020) midazolam and fentanyl were seen as the causative agents, and these drugs were discontinued. In the second case, risperidone, which had been the causative agent, was discontinued and the deterioration of the condition was prevented. In the case report of Kajani et al., (2020) the patient was using haloperidol decanoate. In the study of Burad et al., (2021) the patient who had been observed for COVID-19 developed NMS after they were started on quetiapine. In the case study of Espiridion et al. (2021), a patient who had already been taking clozapine and risperidone developed NMS during their COVID-19-followed hospitalization. In our patient, we had seen the risperidone taken in regular daily doses by the patient as the risk factor and we stopped the risperidone use. Soh et al., (2020) also detected a connection between elevated CK levels and favipiravir treatment in influenza so they pointed out that favipiravir might be causing rhabdomyolysis. They underlined the possible connection between the use of favipiravir and NMS. On the other hand, in the case report of Kajani et al., (2020) the COVID-19 infected patient was not taking favipiravir, so they indicated that the effect of COVID-19 on the central nervous system might make patients more susceptible to the development of NMS. Other than these five cases, there was also a patient with ongoing quetiapine use who reportedly developed NMS after the COVID-19 vaccine, so the researchers warned the readers about the possible future adverse effects of the vaccine (Alfishawy et al. 2021).

Some patients with COVID-19 infection present with neurological and psychiatric symptoms. It is suggested that the SARS-CoV-2 virus causes neurological symptoms using Angiotensin Converting Enzyme (ACE2) receptors located in the nervous system. In addition, psychiatric disorders were thought to be related to COVID-19-caused biological stress. It was also claimed that a pre-existing psychiatric disease or psychotropic drug use might increase the risk of a COVID-19-related psychiatric condition (van Vuren et al. 2021).

Our patient had a bipolar disorder diagnosis and was using risperidone when he developed NMS. The patient had experienced fever, rigidity, alteration in consciousness, autonomic instability, and they had high serum CK levels. These symptoms were present before the favipiravir use. As

seen in our patient, we believe that COVID-19 infection makes patients more susceptible to NMS development because of the infection's central effects.

The first step of the NMS treatment is to cease the predisposing antipsychotic drugs in time. After that, the treatment follows a supportive care and supportive pharmacotherapy (Pleggi and Cook 2016). In the case we presented, even the cessation of the antipsychotic drug, which was possibly the cause, was enough to improve the condition with some supportive treatment. NMS is a rare but highly mortal adversity of antipsychotics (Ware et al. 2018). For adequate measurements, NMS needs to be recognized fast (Ware et al. 2018). Therefore, when antipsychotic treatment is needed during any infection, especially in COVID-19, the risk of NMS should be taken into consideration when making psychiatric treatment choices for conditions such as agitation or delirium.

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Transient Fever Response After ECT in a Patient with Catatonic Schizophrenia: A Case Report



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ABSTRACT

Electroconvulsive therapy (ECT) is an effective and safe treatment method for many psychiatric disorders. In general medical practice, ECT may cause side effects as most other treatment methods do. Headache, myalgia, nausea, vomiting, confusion, anterograde amnesia are common side effects of electroconvulsive therapy. Fever; in addition to general medical conditions such as infection, malignancy, connective tissue diseases, drug treatments, malignant hyperthermia, convulsions, it can also occur due to conditions such as neuroleptic malignant syndrome (NMS), serotonin syndrome, catatonia, malignant catatonia, which are frequently encountered in psychiatry clinics. In the literature, transient fever response due to electroconvulsive therapy application have been described, albeit rarely. Although there are many proposed mechanisms for the emergence of a fever response, regardless of its cause, it is still not understood why some fever responses occur. In this article, we present the differential diagnosis of the fever response, possible causes, and the mechanisms that may reveal the secondary fever response to electroconvulsive therapy in a case with a diagnosis of catatonic schizophrenia, who developed a fever response during electroconvulsive therapy sessions and no fever response was observed at times other than electroconvulsive therapy sessions. In this case, postictal benign fever response associated with electroconvulsive therapy was considered after excluding other medical conditions that may cause a fever response after electroconvulsive therapy.

Keywords: ECT, Fever, Catatonia, NMS

INTRODUCTION

Electroconvulsive therapy (ECT) is currently used effectively and safely in many psychiatric diseases such as mood disorders, psychotic disorders, and catatonia syndrome (Kellner et al. 2020). The most common and recognized side effects of ECT are headaches, anterograde amnesia, confusion and muscle pain (Andrade et al. 2016). Fever or hyperthermia are not among the commonly reported side effects of ECT. In the literature, a transient fever response after ECT has been reported in only a few case reports (Antosik-Wojcinska et al. 2014, Bation et al. 2012, Bryson et al. 2012, Lau et al. 2015, Majeske et al. 2013).

In this article, it was aimed to discuss possible differential diagnoses for a patient with a transient fever response observed four times during acute ECT sessions.

CASE

A 25-year-old male patient, who was being followed-up with the diagnosis of schizophrenia, applied to the emergency department of our hospital with complaints of not speaking, staring, and aggression. After he had been evaluated in the emergency room, he was admitted to our inpatient service due to the catatonia symptoms such as staring, mutism, catalepsy, waxy flexibility, withdrawal, automatic obedience, mitgehen, ambitendency, and posturing.

His psychiatric complaints started when he was 18 years old, with social withdrawal and paranoid thoughts that there were people trying to poison him. He had auditory hallucinations of voices saying that his mother was not his real mother and he also had aggressive behavior.

Received: 08.10.2021, **Accepted:** 26.01.2022, **Available Online Date:** 05.30.2023

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He was hospitalized in the psychiatry ward with these complaints twice. Despite the use of olanzapine, risperidone, amisulpiride and clozapine treatments for a sufficient duration and in effective doses, his complaints did not improve. For this reason, eight sessions of bitemporal effective ECT has been administered in addition to the antipsychotic drug treatment. He did not benefit from this treatment either. It was found out that his complaints reduced only with 100 mg once-monthly long-acting injections of paliperidone palmitate in the past, but the patient's insight into his disease was still weak and his treatment compliance was low. It was found out that his positive psychotic symptoms exacerbated and his catatonic symptoms reappeared after he had interrupted the paliperidone palmitate 100 mg once-monthly maintenance injection treatment.

Complete blood count (CBC), liver function tests (LFT), kidney function tests (KFT), serum electrolyte levels, electrocardiography (ECG), posterior-anterior chest X-ray, complete urinalysis were within normal limits. Brain magnetic resonance imaging (MRI) was performed for the etiology of catatonia. Brain MRI revealed volume loss in the cavum septum pellicidum et vergae, inferior vermis and cerebellar folia, enlargement pointing to arachnoid cysts in the posterior fossa, enlargement in the perirolandic sulci, cerebellopontine and prepontine cisterns. Lorazepam 5 mg/d treatment was started for catatonic symptoms and increased up to 10 mg/d. After lorazepam was increased to 10 mg/d, the patient's symptoms of catatonia such as refusal to eat, urinary incontinence, catatonic stupor, and catatonic combativeness improved and the Bush-Francis Catatonia Rating Scale (BFCRS) score decreased from 32 to 19. However, immobility, staring, catalepsy, grimace, automatic obedience, mitgehen, ambitendency, withdrawal, waxy flexibility, rigidity, verbigeration persisted. In addition to lorazepam treatment, it was decided to start ECT twice a week. During the ECT sessions, 150 mg of propofol was used as a general anesthetic agent, 50 mcg rocuronium as a muscle relaxant, and 200 mg of sugammadex and 0.2 mg of flumazenil were used. The patient had a fever of 38.6°C six hours after the seventh ECT session. In order to investigate the etiology of fever, CBC, KFT, LFT, serum electrolyte levels, ECG, posterior-anterior chest X-ray, complete urinalysis, urine-blood and stool cultures, sedimentation rate, C-reactive protein (CRP), procalcitonin, serum total creatinine-kinase (total CK) tests were performed. Except for borderline elevation of CK (185 U/L, reference value: <171 U/L) and mild leukocytosis (13,800 /mCL; reference value: 4,300-10,300 /mCL), no abnormal laboratory findings were detected. The Covid-19 PCR test was negative. It was observed that the patient's fever returned to the normal limits within two hours after 500 mg oral paracetamol was administered, and the leukocyte count and

total-CK values also returned within twelve hours after the fever response. The department of infectious diseases was consulted and it was stated that the fever was not due to an infection as a result of the examination, the laboratory tests and the fact that the fever subsided easily with paracetamol within two hours and did not reappear in the following days. The patient's fever response was not accompanied by autonomic instability, altered consciousness, rigidity, or any other clinical symptoms.

During the follow-up, the patient's BFCRS score decreased to 10. Signs of waxy flexibility, catalepsy, staring, automatic obedience, and ambitendency persisted. Lorazepam 10 mg/d and two sessions of ECT per week were continued. Although there was no change in the symptoms of catatonia in the follow-up of the patient, it was observed that he was more talkative and communication with the environment being better. 150 mg of paliperidone palmitate monthly injections was added to the treatment of the patient who had persecutory thoughts and auditory hallucinations.

The patient, whose ECT was continued, had fever responses in the range of 38.4-39.1°C in three different sessions, approximately six hours after the completion of the procedure. In order to investigate the etiology of fever, CBC, KFT, LFT, serum electrolyte levels, ECG, posterior-anterior chest X-ray, complete urinalysis, urine, blood and stool cultures, sedimentation rate, C-reactive protein (CRP), procalcitonin, and total creatinine kinase (total CK) level tests were performed at the time of fever. No abnormal findings were detected except neutrophilia, leukocytosis and mild total CK elevation. Mild leukocytosis and total CK elevation spontaneously regressed to normal limits within twelve hours in the follow-up. The patient's fever decreased within approximately two hours after 500 mg oral paracetamol was administered. On days when ECT was not applied, the patient never had a fever, his vital values were normal, and no leukocytosis or neutrophilia was observed.

After the 21st ECT session, the patient had disorientation and confusion, fever response was not observed in this session, and the patient's confusion completely resolved after 72 hours. ECT was discontinued because the patient's catatonic symptoms didn't improve and BFCRS score did not decrease after the twelfth session. The patient's treatment was arranged as lorazepam 10 mg/d, paliperidone 150 mg monthly long-acting injection and biperiden 2 mg/d. Clinical and laboratory findings accompanying ECT sessions in which fever response is observed are shown in Table-1.

DISCUSSION

Infection, malignant catatonia, malignant hyperthermia, neuroleptic malignant syndrome (NMS) could be considered

Table 1. A Table Showing the Pattern of Fever Response and Other Clinical and Laboratory Findings Accompanying ECT Sessions in Which Fever Response is Observed

ECT Sessions	Application Dates	Fever (max, C)	Total-CK (U/L)	Rigidity Sign	Leukocyte (/mCL)	Control Leukocyte Value Within 24 Hours (/mCL)	Confusion	Autonomous instability	Time to Onset of Fever After ECT (hours)	Duration of Fever Response (hours)	Paliperidone Long-acting Injection Application Dates
7. ECT	16 November 2020	38.6	185	-	13800	6900	-	-	6	2	20 November 2020 (first initiation)
13. ECT	25 December 2020	38.4	225	-	12400	6200	-	-	6.5	1.5	27 December 2020 (first maintenance)
20. ECT	22 January 2021	38.4	200	-	12200	6000	+	-	6	1.5	24 January 2021 (second maintenance)
21. ECT	25 January 2021	39.1	168	Cogwheel	11300	9700	+	-	6.5	2	

Not-1: Hacettepe University Hospital Laboratory reference range for Total-CK:<171 U/L.

Not-2: Hacettepe University Hospital Laboratory reference range for leukocyte values: 4300-10300/mcL.

Not-3: 150 mg of propofol, 50 mcg of rocuronium, 200 mg of sugammadex and 0.2 mg of flumazenil were administered during all sessions, including ECT sessions in which there was no fever response.

in the differential diagnosis of fever observed after ECT sessions of this patient who was being followed-up for the diagnosis of catatonic schizophrenia and received antipsychotic treatment.

Possibility of infection was excluded by the Department of Infectious Diseases because the patient's fever response lasted only two hours, there was no growth in cultures, and there were no other accompanying physical examination findings.

Neuroleptic malignant syndrome (NMS), known as an idiosyncratic drug reaction, with four cardinal symptoms such as fever, autonomic instability, altered consciousness, and lead pipe rigidity, should be considered in the differential diagnosis of the patient (Velamoor 2017). Some authors also classify NMS as a severe subtype of catatonia (Mathews and Aderibigbe 1999). It was reported that blood-brain barrier (BBB) permeability increases temporarily after ECT (Bolwig et al. 1977, Zimmermann et al. 2012) and increased penetration of psychotropics into the brain tissue with increased permeability may lead to NMS symptoms (Zimmermann et al. 2012). In this case, the patient was not taking antipsychotic medication during the ECT session, in which the fever response first occurred. Also, considering the time of long-acting antipsychotic injection, no fever response was observed in ECT sessions with the highest levels of paliperidone in the plasma. The occurrence of fever response in ECT sessions when paliperidone is in the lowest levels in the plasma weakens this possibility.

It was stated that the disruption of the integrity of BBB with ECT might lead to a mild cerebral edema, and that some molecules leaching into the brain due to loss of integrity might interrupt the normal functioning of neurons for a short time (Andrade and Bolwig 2014). This mechanism is

suggested to cause the associated cognitive adverse effects of ECT, though it has not been verified for certain. (Andrade and Bolwig 2014).

Another disorder that should be excluded in the differential diagnosis is malignant (lethal) catatonia which is a syndrome that progresses with clinical and biochemical changes similar to NMS, occurs on the basis of a neuropsychiatric disorder or a general medical condition, and can result in coma and then death when left untreated. In addition to behavioral disorders and psychotic symptoms, dehydration, blood pressure changes, hyperthermia, rigidity, marked increase in muscle enzymes, leukocytosis, electrolyte imbalances can be seen in malignant catatonia (Oldham et al. 2015, Özkul et al. 2010). The patient's fever regressed within two hours after paracetamol, CK values increased slightly (176-200 U/L), and CK elevation and leukocyte elevation resolved spontaneously within 24 hours. Beside all these, there is a time-wise relationship between this finding to ECT. The fact that ECT is effective in the treatment of NMS rather than being a factor that will trigger NMS reduces the possibility of the patient having NMS or malignant catatonia.

Neuroleptic malignant syndrome should also be excluded because of the presence of confusion and disorientation after the last ECT despite the absence of fever. The absence of fever, rigidity, and abnormal laboratory findings strengthened the possibility of postictal confusion associated with ECT. The sign of lead pipe rigidity had never been observed in the patient since the first occurrence of catatonic symptoms, including the period before and after lorazepam treatment. Mild cogwheel rigidity was a stable finding during the

antipsychotics use, and the severity did not change when fever and leukocytosis occur.

It was reported that the innate immune system members, IL-1beta, IL-6, and the proinflammatory cytokine TNF-alpha which are thought to be responsible for the fever response and increased in serum 3 hours after a single ECT session returned to their basal values within 24 hours after ECT (Fluitman et al. 2011, Guloksuz et al. 2014). It was determined that proinflammatory cytokines eotaxin-2, eotaxin-3, IL-5, IL-1beta, IL-6 decreased after repeated ECT sessions (Guloksuz et al. 2014, Rotter et al. 2013, Yrondi et al. 2018). In this case, fever response was observed after repeated ECT sessions, in contrast to previous findings showing that the inflammatory response gradually decreased.

Fever after ECT is a very rare condition and may be directly related to the seizure or anesthetic agents used in the procedure (Blossom et al. 2009, Yatabe et al. 2015). Propofol used during ECT was not reported to be associated with fever response after ECT until now, but there are some case reports presenting drug reactions related to propofol used in other surgical procedures (Blossom et al. 2009, Yatabe et al. 2015). One of the case reports which suggests fever response after propofol use declares continuous use of it for sedation after the surgical procedure (Yatabe et al. 2015). In another one, fever response has been stated to be present in 74 patients due to propofol used once for sedation (Blossom et al. 2009). The proposed mechanism for the propofol-induced fever response is that propofol is open to environmental microbiological contamination due to its lipid-based content (Blossom et al. 2009, Yatabe et al. 2015). In this case, propofol was administered as a single dose before the procedure, and fever response did not occur in other patients who were administered the same trademarked propofol on the same days.

Drugs used in anesthesia during ECT may cause a malignant hyperthermia reaction (Bation et al. 2012, Lau et al. 2015). Symptoms of malignant hyperthermia are tachycardia, tachypnea, muscle rigidity, rhabdomyolysis, myoglobinuria, arrhythmia, and it may be fatal (Larach et al. 2010). In this presented case, propofol was used for anesthesia induction, rocuronium was used for myorelaxant in all ECT sessions, inhaler drugs or depolarizing myorelaxants that could trigger malignant hyperthermia were not used.

In five cases, it has been reported that the transient fever response after ECT is associated with electrical stimulation (Antosik-Wojcinska et al. 2014, Bation et al. 2012, Bryson et al. 2012, Lau et al. 2015, Majeske et al. 2013). One of the hypotheses put forward to understand the underlying mechanism is that electrical stimulation in the preoptic area, the heat regulation center in the hypothalamus, triggers the transient fever response (Bation et al. 2012). In the

literature, it was suggested that the thermoregulatory center of the hypothalamus might be affected in the ictal period after electrical stimulation (Mraovitch and Calando 1999), and febrile reactions might occur after spontaneous seizures (Rossetti et al. 2007). In some studies, it was argued that the production of pyrogens which stimulated the natural immune system might increase (Lau et al. 2015, Turrin and Rivest 2004). It has been stated that ECT might cause neurochemical changes in the thermoregulation center and these changes might trigger the fever response after ECT. However, the underlying mechanism is not yet clearly known. (Lau et al. 2015).

We believe that post-ictal benign fever response was the main factor in the etiology of fever in this patient, since possible causes of fever response after ECT could be excluded in this particular case. In this case, unlike the previous ones, fever response occurred at a later period, not after the first ECT session, and was observed intermittently while ECT sessions were in progress. In addition, fever responses could be reduced more rapidly by paracetamol administration than other cases. However, it is not clear why fever occurs after some ECT sessions. It was reported that, side effects of ECT such as anterograde amnesia, headache and fever might occur with cumulative effects of ECT after later sessions and might be observed intermittently (Jo et al. 2021).

In this case report, possible mechanisms of transient fever response, which is a rare side effect that may occur within the first hours after ECT, and possible differential diagnoses are discussed. Since pathologies that may lead to fever after ECT may increase morbidity and mortality, differential diagnosis of post-ictal benign fever response should be made cautiously. Further studies are needed to understand the neurobiological mechanisms of this rare side effect.

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Turkish Journal of Psychiatry

Letter to the Editor

ARTIFICIAL INTELLIGENCE INNOVATIONS IN PSYCHIATRY: GLOBAL PERSPECTIVE FROM EARLY CAREER PSYCHIATRISTS

Dear Editor,

The editorial in the Spring 2023 issue of the Turkish Journal of Psychiatry highlighted a remarkable example of the key role played by artificial intelligence (AI) applications in the current era (Ayhan 2023). Inspired by both the content and writing method of this publication and the presented horizon, we, a group of early career psychiatrists from different parts of the world, offer our perspective on the integration of AI in psychiatry, along with some suggestions on how to navigate its potential challenges and needs.

Early career psychiatrists around the world face numerous challenges during their training, such as a growing shortage of mental health professionals, a growing demand for mental health care and services, and pressure to develop a diverse set of skills (Fiorillo et al. 2013).

The emergence of AI applications in psychiatry offers transformative solutions to help cope with these challenges (Torous et al. 2021). Possibilities include diagnostic support systems (using methods such as machine learning, deep learning, or natural language processing), improving diagnostic accuracy, reducing the risk of misdiagnosis, and providing treatment suggestions (Graham et al. 2019, Rush and Ibrahim 2018). AI can automate aspects of clinical diagnosis, increasing efficiency and acceptability, and provide support in decision-making, treatment suggestions, and the analysis of medical images, potentially helping to address the diagnostic challenges associated with traditional categorical diagnostic systems

(Graham et al. 2019). With respect to treatment, AI offers predictive modeling for treatment outcomes and personalized treatment recommendations based on patient characteristics, response data, and momentary assessments, leading to more effective and targeted interventions (Zhou et al. 2022). It can also provide Ecological Momentary Assessments and Just-In-Time Adaptive Interventions (JITAI), which may increase real-time benefit for patients (Nahum-Shani et al. 2018). AI applications can also significantly enhance the preventive role of psychiatrists (Lejeune et al. 2022).

These new possibilities also bring new challenges. Although medical education is not up to date with digital psychiatry globally, efforts are underway to equip it with the necessary skills and facilitate the relationship between digital technology and mental health professionals (Orsolini et al. 2021, Wisniewski et al. 2020). Key challenges include the need for proper training and addressing additional ethical and privacy concerns associated with the use of AI (Keskinbora 2019, McCradden et al. 2022) as well as the lack of a robust body of evidence for AI applications (Abd-Alrazaq et al. 2020, McCradden et al. 2022), as insufficient evidence can lead to serious prejudices and legitimate concerns for AI applications. Relevant training is essential for both psychiatrists and patients to effectively use these new applications (Hoffman et al. 2020, Torous et al. 2021). Additionally, given the rapid advancements in AI technology, traditional research methods may struggle to keep pace with these developments.

To help address these challenges, we offer some recommendations to researchers in the field of psychiatry here. First, incorporate artificial intelligence and machine learning methods more actively at different stages of research. Taking into account the growing availability of tools that can assist researchers, this includes reviewing the literature, collecting and analyzing data, and reporting results (Extance 2018, Chubb et al. 2022, Pinto da Costa

and Stewart 2023). Second, collaborate with data scientists and other professionals in the field to process large datasets more accurately (Barnett et al. 2018). Additionally, work with technology developers to validate new products and use them for data collection in research. Due to the patient-centered and ethical structure of medical and psychiatric training, these collaborations can also help address these concerns in the products. Thirdly, receive further training on how to use AI ethically and effectively, and use more remote research and monitoring techniques instead of in-person visits. This aims to expedite data collection, overcome logistical and financial barriers, and gather real-time data. Lastly, share data and routinely engage in collaborative studies.

In conclusion, as global early career psychiatrists, we recognize that AI holds valuable potential across various domains. Nevertheless, this technological advancement is not without its challenges. Addressing these challenges is crucial to fully harnessing the full potential of AI. In particular, we must devise effective methods to tackle the difficulties associated with training and ethical considerations, while also promoting further research to responsibly enhance AI's capabilities. Despite the persistence of these challenges, we believe that viable pathways exist to overcome them and pave the way for a more promising future enriched by AI.

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Received: 26.07.2023, **Accepted:** 06.10.2023, **Available Online Date:** 19.02.2024

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<https://doi.org/10.5080/u27384>