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Information for Authors

Turkish Journal of Clinical Psychiatry includes researches, reviews, brief reports, and letter to the editor reports in the fields of Psychiatry, Clinical Psychology, Psychopharmacology and psychiatry issues of neurology. The journal, published four times a year, accepts Turkish and English articles.

For submitted articles; submission, evaluation, publication at any stage of the fee is not requested.

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The referees are unaware of the identity of the authors and the authors are unaware of the referee's identity.

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The abbreviations should be internationally accepted, clearly marked in the place where they are first used, and displayed in abbreviated form in parentheses. Abbreviations should not be included in the summary. Footnotes should not be used in manuscripts, descriptions should be given in writing.

The articles can only be submitted via the online article uploading and evaluation system of the journal at www.klinikpsikiyatri.org. Articles sent from other circles will not be evaluated.

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The research articles should consist of the following subheadings: Introduction, Methods, Results, Discussion and Conclusion. The research articles should consist of headings in Turkish and English abstracts, Objectives, Method, Results, Conclusion.

The articles should be prepared in accordance with ICMJE-Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals. Ethical principles should be observed in research. Ethics committee decisions and case approval forms should be attached to the article and should be indicated in a sentence that the ethical principles are followed.

The limitations, barriers and inadequacies of original research should be mentioned in the "Discussion" section before the conclusion section.

Review and Case Report

In the case of review and case report types, the main writing scheme above should be followed. After the summary page, it should be taken in accordance with the type of the article, and the number of references in the collections should not exceed 50. In reviews, one of the writers must have published three or more original researches on the subject. Review authors should have accumulated expertise on the topic, as international literary publications and citations. Authors who meet these criteria can be invited by the Editorial Board to write review articles.

The introduction and discussion parts of the case reports presentations should be concise and the number of references should be limited. These articles should include the subheadings "Introduction", "Case Report" and "Discussion".

Brief Report

Brief reports should contain abstracts, be short-core, and have limited references. Brief report (except title page, resources, table / figure / picture) must not exceed 2500 words.

Letter to editor

Letter to editor section should be short-concise, non-abstract, and limited in references, in order to bring criticism, contribution or information that was not prepared or prepared as an original work in the journal.

Tables, Figures and Pictures

Tables, Figures and Pictures should be numbered and indicated in the order of transitions in the text. The title or subheadings should be added to the article, each page being prepared on a separate page. FIgures should be sent in quality to which photographic film can be taken. The charecters, numbers or symbols in the figure should be clear and legible.

Tables should be added to the main file, presented after the reference list, numbered according to the transition order in the main text. Descriptive headings should be placed on the tables and the expansions of the abbreviations in the table should be defined under the table. Tables should be prepared in a Microsoft Office Word file using the "Insert Table" command and should be easily readable. The data presented in the tables should not be a repeat of the data presented in the main text; they must be of a supporting nature in the main text.

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When cited, the latest and most recent publications should be preferred. DOI numbers of earlier cited online articles must be provided. The authors are responsible for the correctness of the references. Journal titles should be abbreviated in accordance with journal abbreviations in Index Medicus / Medline / PubMed. All author names should be listed in the references. Arabic numbers should be used in parantheses when referring to references in the main text.

An example of the notation in the text:

Many studies emphasize the importance of the couple's unconscious identification process as a principal mediator of couple's marital satisfaction and even argue that the activation of projective identification process is one of the underlying sources of conflicts that distress couples (1,2,3,4,5,6).

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Abedi MR, Bahrami F, Etemadi O, Fatehizadeh M, Ghasemi V. Personality types and marital satisfaction. Interdiscip J Contemp Res in Bus 2012; 4:372-383.

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Boyce P, Parker G, Barnett B, Cooney M, Smith F. Personality as a vulnerability factor to depression. Br J Psychiatry 1991; 159:106-114.

Zinbarg RE, Barlow DH, Liebowitz M, Street L, Broadhead E, Katon W, Roy-Byrne P, Lepine J-P, Teherani M, Richards J, Brantley PJ, Kraemer H. The DSM-IV field trial for mixed anxiety-depression. Am J Psychiatry 1994; 151:1153-1162

An additional number of journal,

Beskow J. Depression and suicide. Pharmaco-psychiatry 1990; 23 (Suppl 1): 3.

Burrows GD, Norman TR, Judd FK, Marriott PF. Short-acting versus long-acting benzodiazepines: discontinuation effects in panic disorders. J Psychiatr Res 1990; 24 (suppl 2): 65-72.

If the reference is a book,

Beahrs JO. The Cultural Impact of Psychiatry: The Question of Regressive Effects, in American Psychiatry After World War II: 1944-1994. Edited by Menninger RW, Nemiah JC. Washington, DC, American Psychiatric Press, 2000, pp. 321-342.

If the reference is the translation book,

Saddock BJ, Saddock VA. Klinik Psikiyatri. Aydın H, Bozkurt A (Çeviri Ed.) 2. Baskı, Ankara: Güneş Kitabevi Ltd. Şti., 2005, 155-157.

If the reference is thesis,

Yılmaz B. Ankara Üniversitesindeki Öğrencilerin Beslenme Durumları, Fiziksel Aktiviteleri ve Beden Kitle İndeksleri Kan Lipidleri Arasındaki İlişkiler. H.Ü. Sağlık Bilimleri Enstitüsü, Doktora Tezi. 2007.

For the articles in the press,

Cai L, Yeh BM, Westphalen AC, Roberts JP, Wang ZJ. Adult living donor liver imaging. Diagn Interv Radiol 2016; 24. doi: 10.5152/dir.2016.15323. [In press].

For congress notification,

Yumru M, Savas HA, Kalenderoglu A, Bulut M, Erel O, Celik H. İkiuçlu bozukluk alt tiplerinde oksidatif dengesizlik. 44. Ulusal Psikiyatri Kongresi Bildiri Kitabı 2008; 105.

For references from the internet,

World Health Organization. Depression. http://www.who.int/mediacentre/ factsheets/fs369/en/. Erişim tarihi: Ağustos 22, 2016.

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Disasters, Psychiatry and Mental Health

Afetler, Psikiyatri ve Ruh Sağlığı

M. Hamid Boztaş[1], Ejder Akgün Yıldırım[2]
[1]Prof. Dr.,Bolu Izzet Baysal University, Department of Psychiatry, Bolu, Turkey, https://orcid.org/0000-0001-6541-0666
[2]Prof. Dr.,Bakırköy Prof. Mazhar Osman Mental Health Training and Research Hospital, Department of Psychiatry, İstanbul, Turkey, https://orcid.org/0000-0002-8620-1254

Turkey has a long history of disasters and human-induced traumas. This situation, in addition to increasing the traumatic effect in the society, also led to the formation of an experienced mental health staff. Although Turkish psychiatry tries to respond more strongly in every new disaster, the impact of the February 6 Kahramanmaraş earthquake is felt heavily both in the earthquake zone and in Turkey due to intense out-migration. While the 3rd week of the earthquake is almost over, there is still no water, electricity or tents in many regions. Access to healthcare continues to be a problem in many regions. Insecurity, uneasiness, uncertainty, and secondary traumas experienced every day aggravate the psychological impact caused by the earthquake. Although the number of dead due to the earthquake has approached 50 thousand for now, it is expected that both the number of dead and social damage will be much higher.

Psychiatry Association of Turkey (PAT) decided to establish a new unit to prepare for the Istanbul earthquake, which is expected to be a massive destruction, and other disasters, and on July 23, 2022, the association estabilished Disasters Preparedness and Intervention Unit (DPIU), which will have central and local organizing, develop national diasaster preparation plans and create intervention teams (1). While the trainings to increase the response capacity by the unit's executive had just begun, the earthquakes of February 6 took place, and on the morning of the first earthquake, the Central Executive Board and the DPIU executive convened to form the Disaster Crisis Management. We psychiatrists should demand and pioneer a very comprehensive multidisciplinary mental strategy program to reduce the psychological impact, performing psychosocial interventions, try to continue the treatment of chronic mental problems, loss of limbs after surgical interventions, experiences of severe loss, children without parents, mental health problems for those who can not support their relatives in multi-actor, multi-factor, fast-moving variability which is reminiscent of war zones in some places.

Messages of solidarity and support come from many parts of the world. The solidarity effort of poor people, mass organizations and professional associations once again gives hope to the affected and volunteers. However, after all the earthquakes and disasters that have been experienced and lessons to be learned, there are still things that should not happen. Among these, lack of general coordination affecting all services, late and inadequate rescue intervention, disorganization of social support, approaches that are far from community-based and preventive/protective mental health principles, uncertainty of responsibilities and authorities, insufficient coordination of mental health employees with each other, a disappearing response teams, the harmful practices of unauthorized, untrained, incompetent groups are coming (2).

At a time when history is accelerating, there are questions that every mental health professional should ask him/herself, such as what to do, how and with whom, and for what period of time, in 11 provinces, especially in Hatay, Maraş and Adıyaman, and across the country.

We know that the effects of earthquakes, migrations and secondary traumatic processes will last for many years (3-6). One of the most valuable tools in determining what to do is field evaluation reports (7). Although the reports prepared by PAT-DPIU in accordance with national experiences and international standards (8,9) during the 6 February earthquakes partially reveal the answers to the

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questions, we still have a long way to go. We will walk this path together with the great family of humanity, especially healthcare professionals and volunteer citizens, who have been making efforts in the field from the first day in our country with science, ethics and solidarity.

Not only the management of mental difficulties and mental disorders such as loneliness, insecurity, uneasiness, grief, depression, and traumatic stress reactions, but also a working order that will ensure a safe future in order to be healthy and prevent these difficulties from happening again, awaits us mental health workers.

Correspondence address: Prof. M. Hamid Boztaş, Bolu İzzet Baysal University, Department of Psychiatry, Bolu, Türkiye, boztashamid@yahoo.com

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Afetler, Psikiyatri ve Ruh Sağlığı

Disasters, Psychiatry and Mental Health

M. Hamid Boztaş[1], Ejder Akgün Yıldırım[2]
[1]Prof. Dr.,Bolu Izzet Baysal Üniversitesi, Psikiyatri AD, Bolu, Türkiye, https://orcid.org/0000-0001-6541-0666
[2]Prof. Dr.,Bakırköy Prof. Dr. Mazhar Osman Ruh Sağlığı ve Sinir Hastalıkları Eğitim ve Araştırma Hastanesi, Psikiyatri Kliniği, İstanbul, Türkiye, https://orcid.org/0000-0002-8620-1254

Türkiye afetler ve insan kaynaklı travmalar açısından yüklü bir tarihe sahip. Bu durum toplumdaki travmatik etkilenmeyi artırmak yanında deneyimli bir ruh sağlığı kadrosunun da oluşmasına neden oldu. Türkiye psikiyatrisi her yeni afette daha güçlü yanıt vermeye çalışsa da 6 Şubat Kahramanmaraş depreminin etkisi hem deprem bölgesinde hem de yoğun bölge dışı göç nedeniyle tüm Türkiye'de ağır biçimde hissedilmektedir. Depremin 3. haftası nerdeyse bitmek üzereyken hala bir çok bölgede su, elektrik, çadır bulunmamakta. Birçok bölgede sağlığa erişim sorunları devam ediyor. Güvensizlik, tedirginlik, belirsizlik, hergün yaşanan ikincil travmalar depremin neden olduğu ruhsal etkilenmeyi daha da ağırlaştırmakta. .Deprem nedeniyle şimdilik açıklanan ölü sayısı 50 bine yaklaşmış olsa da hem ölü sayısının hem de sosyal hasarın çok daha fazla olacağı beklenmekte.

Türkiye Psikiyatri Derneği (TPD) Mayıs 2022'de kitlesel yıkım beklenen İstanbul Depremi'ne ve diğer afetlere hazırlık amacı ile yeni bir birim oluşturma kararı almış, 23 Temmuz 2022 tarihinde merkezi ve yerel örgütlenmesi olacak ve ulusal afet hazırlık planları ve müdahale kadroları oluşturacak Afetlere Hazırlık Müdahale Birimi'ni (AHMB) kurmuştur (1). Birim yürütmesince müdahale kapasitesini artırma eğitimleri henüz başlamışken 6 Şubat depremleri olmuş, ilk deprem sabahı Merkez Yönetim Kurulu ve AHMB yürütmesi toplanarak Afet Kriz Yönetimini oluşturmuştur. Çok aktörlü, çok etmenli, hızlı ilerleyen, kimi yerlerde savaş bölgelerini andıran bir değişkenlik içerisinde ruhsal etkilenmeyi azaltmak, psikososyal müdahaleyi yapmak, kronik ruhsal sorunların tedavisini sürdürmeye çalışmak, cerrahi müdahaleler sonrası yaşanan uzuv kayıpları, ağır kayıp yaşantıları, ebevenysiz çocuklar, yakınlarına yetemeyenlere yönelik ruhsal destek programlarını oluşturmak için biz psikiyatristler ulusal ölçekte çok kapsamlı ve multidsipliner bir ruhsal strateji programını talep etmeli ve öncüsü olmalıyız.

Dünyanın birçok yerinden dayanışma mesajları ve destekler gelmekte. Yoksul insanların, kitle örgütleri ve meslek derneklerinin dayanışma çabası bir kez daha etkilenenlere ve gönüllülere umut olmakta. Bununla birlikte yaşanan ve dersler alınması gereken bunca deprem ve afetten sonra hala olmaması gerekenler var. Bunların başında tüm hizmetleri etkileyen genel koordinasyonda eksiklik, geç ve yetersiz kurtarma müdahalesi, sosyal desteğin dezorganize oluşu, toplum temelli ve önleyici/koruyucu ruh sağlığı ilkelerinden uzak yaklaşımlar, sorumlulukların ve yetkilerin belirsizliği, ruh sağlığı ile ilişkili çalışanlarının birbirleri ile yeterince koordineli olamaması, bir görünüp bir kaybolan müdahele ekipleri, yetkisiz, eğitimsiz, yetersiz grupların zarar verici uygulamaları gelmekte. Ruhsal sağlık ve psikososyal müdahale ilkelerinin bilinmesi bu açıdan hayati bir önem arzetmektedir (2).

Tarihin hızlandığı bir dönemde her bir ruh sağlığı meslek mensubunun kendisine sorması gereken sorular var, başta Hatay, Maraş ve Adıyaman olmak üzere 11 ile ve ülke geneline yayılan etkilenmiş nüfusa ne yapmalı, nasıl ve kiminle ve hangi zaman süresince olmalı gibi.

Biliyoruz ki depremlerin, göçlerin, ikincil travmatik süreçlerin etkisi uzun yıllar sürecek (3-6). Yapılacakları belirlemede en kıymetli araçlardan biri saha değerlendirme raporları (7). 6 Şubat depremlerinde TPD-AHMB tarafından ulusal deneyimler ve uluslar arası standartlara göre hazırlanan raporlar (8,9).soruların yanıtlarını kısmen ortaya koysa da önümüzde uzun bir yol var. Bu yolu bilim, etik, dayanışma ile ülkemizde ilk günden itibaren alanda çaba sarfeden başta sağlık mensupları v egönüllü yurttaşlarımız olmak üzere büyük insanlık ailesi ile birlikte yürüyeceğiz.

Sadece yalnızlık, güvensizlik, tedirginlik, yas, depresyon, travmatik stres tepkileri gibi ruhsal zorlanma ve ruhsal bozuklukların yönetimi değil,

sağlıklı olma ve bu zorlukların bir daha yaşanmaması adına geleceği güvenli kılmayı sağlayacak bir çalışma düzeni biz ruh sağlığı çalışanlarını bekliyor.

Yazışma Adresi: Prof. Dr. M. Hamid Boztaş, Bolu İzzet Baysal Üniversitesi, Psikiyatri AD, Bolu, Türkiye, boztashamid@yahoo.com

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Does chronobiological preference affect the clinical appearance of obsessive-compulsive disorders?

Kronobiyolojik tercih, obsesif-kompulsif bozuklukların klinik görünümünü etkiler mi?

Ayşe Sakallı Kani[1], Uzay Dural[2], Volkan Topçuoğlu[3], Kemal Sayar[3]
[1]Assist. Prof., [3]Prof. Marmara University School of Medicine, Department of Psychiatry, Istanbul, Turkey, https://orcid.org/0000-0002-7391-8221, https://orcid.org/0000-0002-4006-7520, https://orcid.org/0000-0001-6909-3012
[2]Assist. Prof., Istanbul Medeniyet University, Faculty of Arts and Humanities, Department of Psychology, Istanbul, Turkey, https://orcid.org/0000-0003-1578-6686

SUMMARY

Objective: There is a growing body of evidence supporting the involvement of circadian rhythm abnormalities in the psychopathology of obsessive-compulsive disorder. However, the effects of chronotype preference on the clinical features of this disorder are elusive. The aim of this study is to investigate how chronobiological predispositions of people with obsessive compulsive disorder affect obsessive compulsive disorder symptomatology, age of onset, course of the disease and accompanying comorbid conditions. **Method:** Within this cross-sectional study, 76 participants with mean age of 32.53, who have been under treatment with a diagnosis of obsessive-compulsive disorder, were evaluated. Sociodemographic and clinical data form, Yale-Brown Obsessive Compulsive Scale, Morningness and Eveningness Questionnaire, Hamilton Depression Rating Scale, and Hamilton Anxiety Scale were applied to the participants. **Results:** 65.8% (n=50) of the participants consisted of women. Mean age of onset is 18.74 ± 9.36 years. Most of the patients were reactive type (n=47, 61,8 %). Most common obsession type was contamination (n=53, %69,74), the most common compulsion type was cleaning/washing (n=52, %68,42). There was no significant correlation between morningness and eveningness scale scores and obsession and compulsion types. No significant correlation was found between morningness and eveningness scale scores and OCD onset age. There was no significant difference between morningness and eveningness scale scores according to the OCD type of the patients and the presence of accompanying clinical diagnoses. **Discussion:** Morningness or eveningness chronotype tendencies did not have a significant impact on the clinical appearance of OCD.

Key Words: chronotype, obsession compulsion type, clinical features

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ÖZET

Amaç: Obsesif kompulsif bozukluğun psikopatolojisinde sirkadiyen ritim anormalliklerinin rol oynadığını destekleyen kanıtlar giderek artmaktadır. Ancak kişilerin kronotip farklılıklarının bu bozukluğun klinik özelliklerini nasıl etkilediği henüz bilinmemektedir. Bu çalışmanın amacı, obsesif kompulsif bozukluk tanısı olan bireylerdeki kronotip farklılıklarının obsesif kompulsif bozukluk semptomatolojisi, hastalığın ortaya çıkış yaşı, klinik seyri ve eşlik eden komorbid durumları etkileyip etkilemediğini araştırmaktır. **Yöntem:** Bu çalışmada obsesif kompulsif bozukluk tanısı ile tedavi gören yaş ortalaması 32,53 olan 76 katılımcı değerlendirilmiştir. Katılımcılara sosyodemografik ve klinik veri formu, Yale-Brown Obsesyon Kompulsiyon Ölçeği, Sabahlılık ve Akşamlılık Ölçeği, Hamilton Depresyon Derecelendirme Ölçeği ve Hamilton Anksiyete Ölçeği uygulanmıştır. **Bulgular:** Katılımcıların %65,8'i (n=50) kadınlardan oluşmaktadır. Ortalama başlangıç yaşı 18.74 ± 9.36 yıldır. Hastaların çoğu reaktif tiptir (n= 47, %61,8). En sık obsesyon tipi kontaminasyon (n=53, %69,74), en yaygın kompulsiyon tipi temizlik/yıkama (n=52, %68,42) olarak saptanmıştır. Sabahlılık ve akşamlılık ölçeği puanları ile obsesyon ve kompulsiyon tipleri arasında anlamlı bir korelasyon yoktur. Sabahlılık ve akşamlılık ölçeği puanları ile OKB başlangıç yaşı arasında herhangi anlamlı bir korelasyon saptanmamıştır. Hastaların OKB tipi ve eşlik eden klinik tanıların varlığına göre sabahlılık ve akşamlılık ölçeği skorları arasında anlamlı bir farklılık yoktur. **Sonuç:** Obsesif kompulsif bozukluk tanısı olan bireylerde, sabahlılık ve akşamlılık kronotip eğilimlerinin hastalığın klinik görünümü üzerinde anlamlı bir etkisi olmadığı gözlenmiştir.

Anahtar Sözcükler: kronotip, obsesyon kompulsiyon tipi, klinik özellikler

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INTRODUCTION

Like other psychiatric disorders, obsessive-compulsive disorder (OCD) is diagnosed based on clinical evaluation rather than laboratory and imaging assessments. Cardinal features of OCD are the presence of either obsessions or compulsions that are time-consuming (> 1 hour per day), distressing or impairing daily function, and are not the direct result of a medical condition or substance use (1). Despite the defining criteria having been unchanged since DSM- III, the classification of OCD in a novel diagnostic class in DSM-5 has led to the arguments regarding the nosology of the disorder and pushed experts to reconsider the phenotypic features of this disorder (2, 3).

Individuals with OCD have a wide variety of symptom profiles (subtypes/ symptom dimensions) as well as comorbid conditions and outcomes (4). Symptom dimensions most reliably identified include contamination/cleaning, doubt about harm/checking, symmetry/ordering, and unacceptable thoughts/mental rituals (5). Many studies in the literature examined the relationship of different clinical subtypes with prognosis or investigated the reflection of comorbidities on the clinical course and phenomenology (4). For instance, in a study, hoarding obsessions and compulsions were found to be a predictor of poor treatment response (6). In another study, it was found that the patients with comorbid bipolar disorder have a more episodic course, and these patients exhibit more aggressive/impulsive, sexual, religious, and pathological doubt obsessions and compulsions of checking, hoarding, and ordering (7). A study examining the relationship between OCD symptom dimension and suicidality revealed that violent obsessions have a specific role in suicidality beyond the influence of depressive symptoms (8). Finally, a recent study showed that OCD patients with symmetry dimension symptoms have more severe depressive symptoms compared to other dimensions (9). In addition to these, studies have shown that different psychopathologic processes and different neuroimaging symptom profiles are present within different symptom dimensions of OCD (10, 11). Defining the factors which affect the symptom dimension, clinical presentation, and course of the OCD; and recognizing the factors underlying the heterogeneity of the disease, will guide the next clinical classifications and studies that will enable us to understand the etiopathogenesis of the disease.

Natural tendencies regarding an individual's circadian preference for sleeping or performing everyday activities while alert and energetic are referred to as chronotypes. According to circadian typology, evening types are characterized by the later bed and rising times, more irregular sleep-wake-up habits, ascending evening energy, and a preference for nocturnal activities; morning types have an earlier bed and rising times, greater morning energy, and a preference for diurnal activities. Those people without a clear preference are termed as intermediate or neither type (12). Measures of individual differences in diurnal activity rhythms are thought to reflect the underlying circadian system (13). There is a substantial body of evidence showing that evening chronotype is a consistent risk factor for various mental health problems, such as mood disorders, attention deficit and hyperactivity disorder, anxiety, alcohol dependence, antisocial behavior, and suicide. Underlying these associations various genetic factors and neurobiological mechanisms have been postulated to be involved. But in addition to these, psychological studies suggest that eveningness chronotype is related to impulsivity, cognitive bias toward negative stimuli, slower extinction of conditioned fear, and rumination (14). Finally, later circadian rhythms are also found to be associated with poorer executive function and behavioral inhibition (14, 15).

Recently, based on the findings suggesting that circadian rhythm disruptions might also play a role in the pathogenesis of OCD (16) and the studies showing hormonal dysregulation and delayed sleep phase in patients with severe OCD (17, 18); chronobiology studies gained importance in OCD patients. However, while there is evidence regarding eveningness chronotype may be related to increased OCD symptoms, the results of the studies are contradictory (19) and the effect of chronotype differences on the symptom dimensions and clinical features of OCD is lacking in the literature.

With this study, we aimed to examine the effect of chronotype preference on the clinical appearance of OCD and to compare the patients with different chronotypes in terms of clinical course and concomitant clinical features. We hypothesized that chronotype differences might make a difference in terms of the emerging type of obsessions/compulsions, age of onset, disease course, and accompanying tic/trichotillomania and other comorbidities. Especially, due to the evidence regarding the relationship between eveningness chronotype and impulsivity cited above, we expected patients with eveningness chronotype would have more impulse related symptoms. Also, since there is a strong connection between eveningness chronotype and mood disorders, we proposed that there would be fluctuating symptom course and more depression-related symptoms, mentioned above, in patients who have eveningness tendency.

METHOD

Setting and Sample

This study was conducted on OCD patients who presented to Istanbul University Cerrahpaşa School of Medicine's Psychiatry Department between 2013 and 2014. The sample consisted of 76 patients (50 women, 65.8%) aged 18-60, who had been under treatment for at least 12 weeks with a minimum effective SSRI dose accepted for OCD treatment (20) with or without antipsychotic medication. The exclusion criteria for the participants included a history of neurological disorder, head trauma, mental retardation, and psychotic disorders. Furthermore, patients who were diagnosed primarily with bipolar disorder comorbid with OCD were not included in the study. The study was approved by the Istanbul University School of Medicine's Ethics Committee, and all participants provided written informed consent.

Measures

A semi-structured interview, which lasted approximately one hour, was conducted on the patients to evaluate their sociodemographic and clinical characteristics, and then survey scales were applied to the patients.

Sociodemographic and Clinical Data Form: After the sociodemographic data of the patients such as age, gender, marital status, and educational status was recorded, the phenomenological variables and clinical characteristics of obsessive-compulsive disorder were evaluated through a clinical data form prepared by the research team. Through this data form, the age of onset of the disease, the type of obsession (contamination, pathological doubt, somatic, symmetry, aggressive, sexual, religious, other), and compulsion (checking, washing/cleaning, mental compulsions, ordering/arranging, repeating rituals, other); obsessive-compulsive disorder type (autogenous, reactive, mixed) and the course of the disease was recorded. Also, the information about having any history of druginduced hypomanic/manic switch, comorbid diagnoses of tic disorder, trichotillomania, panic disorder, generalized anxiety disorder, eating disorder, and body dysmorphic disorder was also obtained.

Yale-Brown Obsessive-Compulsive Scale (Y-BOCS): Developed by Goodman et al. (1989) it is a semi-structured scale administered by an interviewer who knows psychopathology to measure the type and severity of obsessivecompulsive symptoms in patients with OCD (21). It consists of 19 items in total, but only the first 10 items are used to measure the symptom severity. In scoring the Y-BOCS, obsessions and compulsions are scored separately with five items, and each item is scored out of four points, the sub-total scores of obsessions and compulsions and finally, a total score of over 40 points is obtained. According to the scores obtained from the scale, the severity of the OCD is classified into four categories (0-7 subclinical; 8-15 mild; 16-23 moderate; 24-31 severe OCD). The scale was translated into Turkish by Uluğ and Savaşır, and the validity and reliability study was carried out by Karamustafalıoğlu et al. in 1993 (22).

Hamilton Depression Rating Scale (HAM-D): It is a test administered by the clinician to people with depressive symptoms, to measure the level of depression and the change in severity. (23) In this test, which includes 17 questions in total, each question is graded between 0 and 4, and the score obtained from the scale is between 0 and 53. Higher scores on the scale are associated with greater symptom severity of depression. The vali-

dity and reliability study of the Turkish form was made by A. Akdemir et al. (24).

Hamilton Anxiety Rating Scale (HAM-A): The HAM-A scale was developed by Hamilton in 1959 to determine the level and symptom distribution of anxiety and to measure the change in severity. The validity and reliability study of the Turkish form was carried out in 1998. (25, 26). The test is used to assess the anxiety level within 72 hours, it contains a total of 14 questions. Each question is scored between 0 and 4, and the total score is obtained by adding the score obtained from each item. The total score of the scale varies between 0 and 56.

Morningness and Eveningness Questionnaire (MEQ): The MEQ is a 19-item self-rated questionnaire providing an assessment of habitual waking and bedtimes, preferred times of physical and mental performance, and subjective alertness after rising and before going to bed. (27). It is the tool most frequently used to assess chronotype, both in healthy individuals and in patients. The MEQ yields scores ranging from 16 to 86. Higher scores indicate greater morningness, and lower scores indicate greater eveningness. MEQ classifies participants who score between 59 and 86 as morning types, those who score 42–58 as neither types and those who score 16–41 as evening types. The psychometric properties of the Turkish version of the MEQ were tested by Agargun et al. (2007); its validity and reliability were found to be as high as the original version (28).

Statistical Analyses

We performed statistical analyses with SPSS Version 20.0. Before analyses, all dichotomous variables (i.e., gender, marital status, the presence of obsessive symptoms, the presence of compulsive symptoms, the presence of comorbidity, and the history of other mental disorders) were dummy coded. We conducted Pearson Correlation Coefficient Analyses and SpearmanBrown Correlation Analyses to examine the relationship between variables. Kruskal Wallis test was used for the comparison of OCD type, OCD course, and the type of medication in terms of chronotype scores. Multiple regression analyses were performed to test whether chronotype predicts YBOCS scores controlling for depression level and anxiety level of patients. We calculated effect sizes by Cohen's f^2 via G*Power 3.1 (29, 30). We also performed post-hoc power analyses via G*Power 3.1 to test whether we had sufficient sample size for our statistical inferences by taking alpha level of .05 and estimated effect sizes Cohen's f^2 was calculated for effect size analyses via G*Power 3.1 (29, 30). The alpha level is .05 for all analyses.

RESULTS

Sociodemographic characteristics of the study population are presented in Table 1. The average age of the population was 32.53 and 65.8% (n=50) of the participants consisted of women. The mean age of onset is 18.74 ± 9.36 years. There was no statistically significant difference between genders in terms of age of onset. Most of the patients were reactive type (n= 47, 61,8%). Most of the patients were on selective serotonin reuptake inhibitor (SSRI) treatment during assessment (n=35, 46 %). While pathological doubt, contamination, and religious obsessions were the most common obsession types; the detailed clinical features of the participants are presented in Table 2. The most common obsession type was pathological doubt in male group (n=19, % 73,1), in females the most frequent obsession type was contamination (n= 39, % 78). Regarding compulsions, the most common compulsion types were repeating rituals and cleaning/washing in males (n= 14, %53,8) however, in females the most common type was cleaning/washing (n=38, %76). Concerning comorbidities: seven patients reported manic switch history (%9,2), 23 patients (%30,3) had general anxiety disorder, three patients had panic disorder (%3,9), and 28 patients had tic disorder (%36,8), 10 patients had trichotillomania (%13,2). Three patients had eating disorders

Table 1: Socio-demographics of patients

		Frequency	Percent
Gender	Female	50	65.8
	Male	26	34.2
Marital status	Married	26	34.2
	Single	43	56.6
	Others (divorced etc.)	7	9.2
		Mean	Std. Deviation
Age (year)		32.53	11.10
Education level (year)		10.72	3.76

Table 2. Clinical background of patients

			Mean	Std Dev.
Age of onset			18.74	9.36
			f	%
OCD type	Autogenous		4	5.26
	Reactive		47	61.84
	Mixed		25	32.89
OCD course	Chronic without any change in symptoms		17	22.37
	Chronic with worsening symptoms		24	31.58
	Episodic with partial remission		23	30.26
	Episodic with full remission		11	14.47
Type of medication	SSRI		35	46.05
	Clomipramine		7	9.21
	SSRI+AP		18	23.68
	Clomipramine+ AP		8	10.53
	SSRI+ Clomipramine+ AP		1	1.32
Type of obsessions	Contamination	Yes	53	69.74
		No	23	30.26
	Pathological doubt	Yes	50	65.79
		No	26	34.21
	Somatic	Yes	4	5.26
		No	72	94.74
	Symmetry	Yes	14	18.42
		No	62	81.58
	Aggressive	Yes	66	86.84
		No	10	13.16
	Sexual	Yes	9	11.84
		No	67	88.16
	Religious	Yes	17	22.37
		No	59	77.63
	Other types	Yes	9	11.84
		No	67	88.16
Type of compulsions	Checking	Yes	30	39.47
		No	46	60.53
	Cleaning, washing	Yes	52	68.42
		No	24	31.58
	Mental compulsions (praying, counting, repeating words)	Yes	15	19.74
		No	61	80.26
	Repeating rituals	No	43	56.58
		Yes	33	43.42
	Ordering and arranging	No	63	82.89
		Yes	13	17.11

SSRI: selective serotonin reuptake inhibitors AP: antipsychotic

(%3,9) and two patients (%2,6) had a body dysmorphic disorder history. There was no statistically significant difference in terms of comorbidities among genders and finally, no difference was detected between genders in terms of disease course type.

The relationship between Socio-Demographic Characteristics and Chronotype Tendency of OCD Patients

We examined the relationship between chronotype tendencies of OCD patients and their sociodemographic features. The analyses revealed that patients' gender (0 = male, 1 = female; r = .08), marital status (0 = single, 1 = married; r = .09), age (r = .08) and education level (r = -.02) did not have statistically significant correlations with chronotype tendencies.

The relationship between the chronotype scores and OCD symptom dimensions

We correlated the presence of obsessive symptom types and the presence of compulsive symptom types with chronotype scores (see, Table 3). The analyses yielded that patients who had morningness or eveningness tendencies did not statistically have significant correlations with the presence of contamination obsessions (r = -.043, n.s.), pathological doubt obsessions (r = .111, n.s.), somatic obsessions (Spearman ρ = -.108, n.s.), aggressive obsessions (Spearman ρ = .140, n.s.), sexual obsessions (Spearman ρ = .104, n.s.), religious obsessions (Spearman ρ = .081, n.s.), or other types of obsessions (Spearman ρ = -.063, n.s.). Similarly, morningness or eveningness tendencies did not significantly correlate with compulsive symptoms, i.e., checking (r = .176, n.s.), cleaning/washing (r = .003, n.s.), mental compulsions (Spearman ρ =

Table 3. Pearson correlation coefficients among chronotype score, YBOCS scores, Hamilton depression rating scale score, and Hamilton anxiety rating scale scores

	Mean	Std. Deviation	YBOCS, obsession sub-score	YBOCS, compulsion sub-score	YBOCS, insight sub-score	Chrono type score	Hamilton depression scale score	Hamilton anxiety scale score
YBOCS, obsession sub-score	9.83	5.055	-	.836**	.275*	-.205	.679**	.615**
YBOCS, compulsion sub-score	9.66	5.341		-	.301**	-.158	.639**	.572**
YBOCS, insight sub-score	.50	.887			-	-.098	.158	.097
Chronotype score	47.75	9.146				-	-.128	-.156
Hamilton depression scale score	10.39	6.753					-	.768**
Hamilton anxiety scale score	13.59	9.839						-

**p<.05; **p<.01.*

Table 4: Results of Multiple Regression Analyses

Outcome Variable: YBOCS Obsession Sub-Scale	Unstandardized Coefficients		Standardized Coefficients				
	B	SE	Beta	t	R^2	F	Cohen s
(Constant)	8.051	2.372		3.395**	.513	25.31***	.99
Depression	.358	.089	.478	4.013***			
Anxiety	.133	.061	.259	2.181*			
Chronotype	-.079	.046	-.142	-1.722			
Outcome Variable: YBOCS Compulsion Sub-Scale	**Unstandardized Coefficients**		**Standardized Coefficients**				
	B	SE	Beta	t	R^2	F	Cohen s
(Constant)	6.909	2.678		2.579*	.444	19.14***	.99
Depression	.367	.101	.464	3.646**			
Anxiety	.124	.069	.229	1.804			
Chronotype	-.058	.052	-.099	-1.121			
Outcome Variable: YBOCS Insight Sub-Scale	**Unstandardized Coefficients**		**Standardized Coefficients**				
	B	SE	Beta	t	R^2	F	Cohen s
(Constant)	.692	.587		1.180	.033	.81	.28
Depression	.023	.022	.177	1.051			
Anxiety	-.003	.015	-.036	-.217			
Chronotype	-.008	.011	-.084	-.720			

**p<.05. **p<.01. ***p<.001.*

.190, n.s.), repeating rituals (r = -.100, n.s.) or ordering/arranging (Spearman ρ = -.045, n.s.).

The relationship between the chronotype scores and age of onset, disease course, current or previous comorbidities

We further examined the relationship between other OCD characteristics of patients and their chronotype scores. Chronotype score of patients did not have statistically significant correlations with the onset age of OCD (r = .17), the presence of medication-induced manic shift (r = .09, n.s.), the history of trichotillomania (r = -.06, n.s.), the history of tic disorder (r = -.17, n.s.), the history of eating disorder (r = -.10, n.s.), the comorbidity of panic disorder (r = .01, n.s.) or the comorbidity of generalized anxiety disorder (r = .12, n.s.). When the chronotype scores of the groups with different disease courses were compared, no statistically significant difference was found. Similarly, Kruskal Wallis tests revealed that chronotype tendencies did not significantly relate with OCD type [H (2) = 1.66, n.s.] and OCD course [H (3) = 1.88, n.s.].

The Relationship between chronotype scores and YBOC-S, HAM-D and HAM-A scores

Pearson correlation coefficient analyses yielded that chronotype tendencies did not statistically correlate with YBOC-S scores (obsessions sub-score, compulsion sub-score, insight sub-score), scores on Hamilton depression or anxiety rating scales (see, Table 4).

Does the chronotype score of patients predict OCD characteristics when depression and anxiety are controlled?

We finally tested whether and to what extent chronotype scores of OCD patients predicted obsessive or compulsive tendencies controlling for depression and anxiety levels. As seen in Table 5, we conducted several multiple regression analyses. In the first analysis, we regressed chronotype score, Hamilton depression rating scale score, and Hamilton anxiety rating scale score on YBOCS total score. The predictors explained 44.7% variance in Y-BOCS total score, and the model was statistically significant, F = 19.27, p < .001. Controlling for the depression level and anxiety level, chronotype did not significantly predict Y-BOCS total score (β=-.104, t=-1.184, n.s.). In subsequent analyses, chronotype, depression, and anxiety levels of patients explained 51.3% of the variance in the Y-BOCS obsession sub-scale score, 44.4% of the variance in Y-BOCS compulsion scores, and 3.3% of the variance in Y-BOCS insight score. Like findings in YBOCS total, chronotype did not predict Y-BOCS obsession score, compulsion score, or insight score at a significant level.

The effect sizes – i.e., Cohen's f^2- of these multivariate analyses ranged from .28 to .99. Posthoc power analyses revealed that with an alpha of .05 and the given effect sizes, sample size of 76 is sufficient for achieving power of .80 for all multiple regression analyses (ranging from .81 to .98).

DISCUSSION

Despite tremendous progress in the research of OCD, key problems about the disorder's proper diagnostic classification and clinical heterogeneity remain unanswered (4, 31). Previous studies suggest that circadian abnormalities and particularly eveningness chronotype may contribute to the psy-

chopathology of OCD via different mechanisms (16, 32), furthermore, several studies indicate that delayed bedtimes are associated with increased obsessive-compulsive symptoms (33) and treatment resistance (34). Finally, a recent study revealed that chronotype causes a fluctuation in OCD symptom severity and OCD patients were more likely to experience peaks in symptom severity during nonoptimal times based on their chronotype (35). Although there is inconsistent and limited evidence in the literature, taken together it is recommended to examine the role of circadian rhythms for future OCD research (19).

Our main hypothesis of this study was that the chronotype preference would make a difference in OCD symptom dimensions, but on the contrary, morningness or eveningness tendencies did not statistically have significant correlations with the presence of any types of obsessions and compulsions. Findings of a recent meta-analysis revealed that two discrete OCD groups of "washers" and "checkers" significantly differ in neuropsychological functioning and checkers were more impaired than washers in executive functions which is proposed to be associated with later circadian phases (36). Eveningness chronotype is associated with poor behavioral inhibition and plays a role in compulsive behaviors. In our study, we hypothesized that compulsive behaviors would be more present in participants with eveningness tendency compared to patients who have morningness tendency. In terms of obsessions, we expected to find more doubt obsessions accompanied by checking compulsions (which are thought to be related to poorer executive functions) in patients who have an eveningness tendency. But we did not detect any difference in symptom presentation between the two chronotype tendencies.

According to our knowledge, there is no study in literature investigating the phenomenological features of different chronotypes to make a comparison with our findings. But we speculate the results of the index study may arise for several reasons. In nearly all participants, more than one type of obsessions and compulsions were present together in our study. Grouping patients into certain domains as doubt obsessions-checkers, symmetry obsessions-ordering, and cleaning obsessions-washing would be more comparable. Another major point was that the number of participants who has eveningness and morningness chronotype preferences was limited. Instead of investigating the correlation between symptom frequencies and chronotype tendencies, comparing chronotype preferences in patients with different symptom dimensions or comparing symptom dimensions of patients with different chronotypes in sizeable and clinically well-characterized sample, would provide more precise information. Lastly, psychotropic medications are known to have adverse influences on sleep and circadian rhythms broadly (37, 38). In our study, we did not question the current bedtime and wake-up times while evaluating the chronotype preference of our participants. Considering that the participants have been under treatment for at least 3 months, although it is stated that they should answer the questions about chronotype by considering their whole life, there may be shifts in their circadian rhythms as a result of chronic psychotropic use, and this may have affected the answers given to the questions. Involving drug-naïve OCD patients or assessing circadian rhythm changes after pharmacological treatment would provide more accurate information.

Secondly, we hypothesized that chronotype tendencies would affect the clinical features of OCD. In terms of the onset of OCD, there was no significant correlation between chronotype tendencies and onset age of the disease. Similarly, the chronotype score of patients did not differ with a history of any psychiatric comorbidity and chronotype scores did not differ between the different course types of the disease. In literature, there are only two recent studies investigating the chronotype in tic disorders. However, the number of these studies is scant, both studies similarly revealed increased eveningness chronotype in individuals with tic disorders (39, 40).

Furthermore, increased tic severity predicted greater eveningness (40). In our study, we expected to find greater eveningness in patients with comorbid tic disorders but contrary to our expectation, neither tic disorders nor other comorbidities rose to statistical significance in their associations with chronotype tendencies. This might be related again to small sample size and having a limited number of

eveningness chronotype in our sample.

Finally, controlling for the depression level and anxiety level, chronotype did not significantly predict total or sub-scores of Y-BOCS. This finding is contradictory with studies showing that the eveningness chronotype increases OCD severity (33, 34).

While interpreting our findings, several points should be noted. Our sample might have limited the validity of our findings. First, our sample might limit the generalization of our findings to the OCD population. We recruited our participants from the only outpatient clinic and this might have restricted the range of representation of all OCD patients. Furthermore, our sample size (n=76) might be relatively small, given that effect size analyses demonstrated small power for analyses on chronobiology scores. However, note that we obtained high effect sizes for analyses on depression and anxiety (one exception is the YBOCS-insight sub-scale). The lack of significant relationship between chronobiology and OCD symptoms, therefore, may be valid to some extent and we recommend future studies to retest our hypotheses with a more representative sample of OCD patients. Secondly, we did not categorize and compare the patients as morningness and eveningness groups, since most of the participants were in intermediate chronotype (n=50, %65, 8) and the number of patients with morningness and eveningness chronotype is limited (morningness n=9, %11.8; eveningness n= 17, % 22.4). Therefore, we compared the patients according to their MEQ scores: higher scores indicate greater morningness, and lower scores indicate greater eveningness. However, this usage of this instrument is supported in the literature and investigators suggest that the morningnesseveningness dimension could be considered as a continuum between two extremes (41). Finally, evaluating current or past comorbidities via psychiatric questioning merely, without using SCID, may be another study limitation that the readers should keep in mind.

In summary, the results of our study showed that chronotype tendency was not a significant factor determining the comorbidity, the age of onset, disease course, either OCD type, or a variety of obsessions and compulsions.

CONCLUSION

For the first time, this study revealed that chronotype tendency doesn't have a significant impact on the OCD symptom diversity and concomitant clinical features. Since we aimed to examine the effect of chronotypes on symptom dimensions and phenomenology of OCD, we did not consider recruiting healthy controls for the study. But investigating the presence and type of obsessions and compulsions in non-clinical individuals with different chronotype preferences would be valuable for understanding the effect of chronobiology. Also, despite our negative findings, we recommend researchers conduct prospective studies in larger clinical samples to understand the effect of chronotype preference on OCD clinical presentation. Understanding the impact of chronotype preferences on OCD presentation may affect current treatment options and can lead to a change in the clinical approach to different OCD dimensions.

Conflicts of interest: The authors declare that they have no conflict of interest.

Correspondence address: Assist. Prof. Ayşe Sakallı Kani, Marmara University School of Medicine, Department of Psychiatry, İstanbul, Türkiye akanisakalli@gmail.com

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Are the consequences of substance use disorder more severe than schizophrenia?: Effects on the mothers and the patients

Madde kullanım bozukluğunun sonuçları şizofreniden daha şiddetli olabilir mi ?: Annelere ve hastalara olan etkileri

Meltem Saraçoğlu[1], Demet Atlam[2], Betül Akyel Göven[3], Zeki Yüncü[4]
[1]M.D., Bursa Provincial Health Directorate, Bursa, Turkey, https://orcid.org/0000-0001-9575-6000
[2]Res. Assist., Ege University Institute on Drug Abuse, Toxicology and Pharmaceutical Science, Department of Drug Addiction, Izmir, Turkey, https://orcid.org/0000-0002-8279-4531
[3]Res. Assist., Ege University Research and Application Center of Child and Adolescent Alcohol Drug Addiction, Izmir, Turkey, https://orcid.org/0000-0002-0098-1254
[4]Prof. Dr., Ege University Faculty of Medicine, Department of Child and Adolescent Psychiatry, Izmir, Turkey, https://orcid.org/0000-0002-8893-6449

SUMMARY

Objective: The aim of this study is to examine the effects of mental disorders on patients with schizophrenia and their mothers. Also, it was aimed to evaluate the patients in terms of internalized stigma, and their mothers' in terms of beliefs about the illness and their mental status as hopelessness, depression, and burnout levels. **Method:** Participants with SUD (n=30), SCH (n=30), control group (CG) (n=30) and all their mothers (n=90) were included in the study. Pearson chi-square, t test, ANOVA, Dunnet's C post hoc and Scheffe post hoc tests, effect size test eta squared (η2) and Pearson correlation tests were used. **Results:** The internalized stigma of patients was similar and different from CG. Depression and burnout levels of mothers of patients with SUD were higher than in other groups. The depression levels of mothers were significantly different and had a large effect. Hopelessness was higher in mothers of SUD patients than in mothers of CG. A relationship was found between SUD patients' mothers' depression, hopelessness, burnout and their negative beliefs toward MI. **Discussion:** It is seen that the presence of MI has a huge impact on the self-stigmatization of the patient and depression, burnout and hopelessness in their mothers. SUD effects on the mother are more severe. The mental health of the mothers affects their perspectives on MI.
Key Words: Substance use disorder, Schizophrenia, Internalized stigma, Mother, Depression, Burnout

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ÖZET

Amaç: Bu çalışmanın amacı, ruhsal bozukluğun, şizofreni olan hastalar ile madde kullanım bozukluğu olan hastalar ve anneleri üzerindeki etkilerini incelemektir. Ayrıca hastaların içselleştirilmiş damgalanma düzeylerinin, annelerinin hastalığa ilişkin inançlarının, annelerin ruhsal durumlarının umutsuzluk, depresyon, tükenmişlik düzeyleri açısından değerlendirilmesi amaçlanmıştır. **Yöntem:** Madde kullanım bozukluğu (n=30), şizofreni (n=30) ve kontrol (n=30) gruplarından oluşan katılımcılar ile anneleri (n=90) çalışmaya dahil edildi. Pearson ki-kare, t testi, ANOVA, Dunnet's C post hoc ve Scheffe post hoc testleri, etki büyüklüğü testi eta kare (η2) ve Pearson korelasyon testleri kullanıldı. **Bulgular:** Hastaların içselleştirilmiş damgalanmaları, kontrolden farklı, hasta grubunda benzerdi. Madde kullanım bozukluğu olan hastaların annelerinin depresyon ve tükenmişlik düzeyleri diğer gruplara göre daha yüksekti. Annelerin depresyon düzeyleri anlamlı derecede farklıydı ve etkisi büyüktü. Madde kullanım bozukluğu hastalarının annelerinde umutsuzluk, kontrolün annelerine göre yüksekti. Bu grubun annelerinde depresyon, umutsuzluk ve tükenmişlikleri ile hastalığa olumsuz bakış açıları arasında ilişki bulundu. **Sonuç:** Ruhsal hastalığın varlığının hastanın kendini damgalamasında ve annelerinde depresyon, tükenmişlik ve umutsuzluk üzerinde büyük etkisi olduğu görülmektedir. Madde kullanım bozukluğunun anneler üzerindeki etkileri daha şiddetlidir. Annelerin ruhsal durum, ruhsal hastalığa bakış açılarını da etkilemektedir.

Anahtar Sözcükler: Madde kullanım bozukluğu, şizofreni, içselleştirilmiş damgalama, anne, depresyon, tükenmişlik

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INTRODUCTION

Substance use disorder (SUD) and schizophrenia (SCH) are mental illnesses (MI) that affect relationships and cause mental stress and harm for individuals and their families. Patients lose their productivity and can not fulfil their own and family needs. In this case, the burden on patients' families increases and their family role distribution reshapes. SCH faces extensive caregiving challenges that can deteriorate family functioning. SUD can cause family destruction and disturbed relationship (1,2).

Stigma towards SCH and SUD is more severe among MIs (3,4). Dysfunctions (movement, speech, etc), and unusual and inappropriate behaviours of some patients attract attention in society. This situation creates unrest, fear and anxiety in society. Individuals with MI are mostly labelled as "dangerous", "unpredictable", "unstable", and "damaging to the environment" and excluded from social groups. This is how the MI stigmatization process generally takes place in society (5,6). In the presence of a family member with a mental illness, stigma is an important factor affecting individuals and their families, as well as the increasing burden on the family (7). Stigma could cause mental distress in families. Family members (FM) of those with MIs also live a process of self-stigma and experience shame, and social rejection (3). FM also hide the patient and illness to cope with shame and anxiety caused by society's approach (7).

Society's prejudiced and negative attitudes towards people with MI lead to internalized stigma (IS). IS causes shame, anger, fear, worthlessness, hopelessness, loss of social status, social exclusion, marginalization, and social isolation (8,9). Stigmatized individuals have difficulties in finding a job, owning a home, receiving treatment support, and establishing interpersonal relationships. Stigma can lead to depression and a decrease in quality of life (8,10). It is reported that 22-36% of individuals with MI experience IS (11).

Parents mostly experience frustration, guilt, denial, surprise, anger, shame, fear, embarrassment, abandonment, and hopelessness in the face of their children's substance use. Individuals who use substances cannot fulfil their responsibilities, and experience legal and financial problems. These situations create economical, judicial and psychological difficulties in the family environment. In addition, society's negative attitude, avoidance of treatment, failure to quit substance use, and failure to fulfil promises lead to hopelessness and helplessness in families (12,13,14). It has been reported that depression, anxiety and stress are common in the families of individuals with SUD (13,15).

SCH is a chronic psychiatric disorder that seriously affects family life and causes burnout in relatives of patients. In particular, it has been reported that patients' positive and negative symptoms provoke burnout in the family (16). SCH patients' families have emotional responses such as anxiety, fear, guilt, stigma, frustration, anger, and sadness (17).

This study includes the comparison of people with SCH and SUD, which are considered to be important in terms of IS and its effects on mothers. The study is aimed to evaluate the IS levels of the patients, their mothers' beliefs about MI and addiction, and mothers' hopelessness, depression and burnout levels. In addition, the relationship between patients' IS scores and their mothers' beliefs about the disease was evaluated.

METHOD

It is a case-control study that examines individuals with SUD and SCH and their mothers by comparing them with CG.

Participants

The sample of this study consisted of 30 adult male patients with SUD and their mothers (n=30); 30 adult males with SCH and their mothers (n=30), and 30 healthy controls and their mothers (n=30). The control group was matched for age, sex and marital status with patient groups. In the healthy control group, the exclusion criteria included also substance use and the presence of present or past neurological and psychiatric disorders. The sample

consisted of 6 groups and 180 people.

Instruments

Demographic Information Form: Two separate forms were prepared for individuals with MI and their mothers. Socio-demographic information and MI characteristics (substance use, and SCH) were asked of adult males. Socio-demographic information and information about their children's illnesses were also asked of their mothers.

Internalized Stigma of Mental Illness (ISMI): It is a 29-item Likert-type self-report scale developed by Ritsher et al. (2003) to assess IS (18). The scale consists of five sub-scales as stereotype endorsement, alienation, stigma resistance, discrimination experience and social withdrawal.

Addiction Belief Inventory (ABI): The 5-point Likert-type scale, which evaluates beliefs and attitudes towards addiction, was developed by Luke in 2002. The scale has eight factors that are the inability to control, chronic disease, reliance on experts, responsibility for actions, responsibility for recovery, genetic basis, coping, and moral weakness (19).

Belief toward Mental Illness Scale (BMI): The scale developed by Hirai and Clum (2000) was created to determine the positive and negative beliefs of people with different cultural characteristics regarding MI (20). The sub-dimensions of the scale are “shame”, “dangerousness” and “helplessness and deterioration in interpersonal relations”.

Beck Depression Inventory (BDI): The inventory developed by Beck (1961) aims to objectively quantify the degree of depression by evaluating the vegetative, cognitive, emotional and motivational symptoms observed in depression (21).

Maslach Burnout Inventory (MBI): The 22-item 3-dimensional scale, which was developed by Maslach and Jackson (1986) aims to evaluate burnout (22). The scale consists of emotional exhaustion, depersonalization and personal accomplishment.

Beck Hopelessness Scale (BHS): The scale developed by Beck et al. (1974) to evaluate the level of hopelessness (23). It is a self-report scale consisting of 20 items. The scale has three factors: feelings about the future, loss of motivation and expectations.

Procedures

This study was conducted at two treatment agencies as Alcohol and Substance Addiction Treatment and Training Center (ASATTC) for people with SUD and Community Mental Health Centers (CMHC) for SCH patients. The study was approved by the Human Research and Ethics Committee of Ege University, Turkey.

A total of 30 male patients diagnosed with SCH and 30 patients with SUD according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) were included in the study. Additionally, mothers of patients who volunteered to participate in the study were invited to the ASATTC and CMHC. Healthy controls were 30 males without substance use and any psychiatric diseases who matched for sex, age and marital status of the patients. Controls and their mothers participated in the study voluntarily. Written informed consent was obtained from all subjects following detailed explanations of the protocol of the study.

Data analysis

In statistical analysis, Pearson chi-square, t-test, one-way analysis of variance (ANOVA), and Pearson correlation tests were used. Dunnet's C post hoc and Scheffe post hoc tests were used as advanced tests to compare the 3 groups and to reveal the differences between the groups. $P < 0.05$ level was considered statistically significant. Effect size test for ANOVA was used, eta squared (n^2) values were determined according to effect size $0.06 < n^2 < 0.14$ medium ; $0.14 < n^2$ large effect.

RESULTS

The sociodemographic characteristics of the subjects in the patient and control groups are listed in

Table 1. Demographic features of the participants

Group features	SCH	SUD	CG		
SCH,SUD and CG Groups	% (n)	% (n)	% (n)	p	Test value
Marital Status					
Single	100 (30)	96.7 (29)	100 (30)	0.364	x^2:2.002
Divorced	0	3.3 (1)	0		
Educational level					
Primary school	6.6 (2)	10.0 (3)	0		
Secondary school	26.7 (8)	43.3 (16)	0	0.0001*	x^2:48.044
High school	66.7 (20)	43.3 (13)	46.7 (14)		
University	0	3.3 (1)	53.3 (16)		
Employment Status	16.7 (5)	40.0 (12)	36.7 (11)	0.108	x^2:4.459
History of psychiatric illness of FM	16.7 (5)	13.3 (4)	0	0.075	x^2:5.185
Regular medicine use	86.7 (26)	30.0 (9)	-	0.0001*	x^2:19.817
	Mean – SD	Mean – SD	Mean – SD	p	Test value
Age	25.0 – 4.2	24.9 – 4.6	23.7 – 3.8	0.387	F=0.95
FM numbers	4.03 –1.1	4.0 – 1.2	3.33 – 0.8	0.022*	F=4.00
Disease onset age	17.73 – 3.9	17.76 – 5.0	-	0.977	t=-0.28
Disease duration year	7.3 – 4.0	7.2 – 4.9	-	0.955	t= 0.57
Hospitalization numbers	3.1 – 2.4	0.9 – 1.1	-	0.0001*	t= 4.30
Mothers Group	% (n)	% (n)	% (n)	p	Test value
Age	51.8 – 6.4	50.0 – 6.3	48.7 – 6.1	0.181	F=1.74
Marital Status					
Married	90.0 (27)	93.3 (28)	90.0 (27)	0.135	x^2:7.024
Divorced	10.0 (3)	0	10.0 (3)		
Widow	0	6.7 (2)	0		
Educational level					
<Primary school	10.0 (3)	20.0 (6)	0		
Primary school	63.3 (19)	63.3 (19)	30.0 (9)	0.001*	x^2:25.680
Secondary school	16.7 (5)	10.0 (3)	26.7 (8)		
High school	6.7 (2)	3.3 (1)	16.7 (5)		
University	3.3 (1)	3.3 (1)	26.7 (8)		
Employment Status					
Worker	26.7 (8)	26.7 (8)	43.3 (13)	0.280	x^2:2.544
Housewife	73.3 (22)	73.3 (22)	56.7 (17)		

Notes: * p<0.05 **Abbrevations:** FM, Family Member; SD, standart deviation; F, F test in analysis of variance; x^2,Pearson's chi-squared test; p, p value; SCH, Schizophrenia; SUD substance use disorder; CG, control group

Table 1. There were no significant differences in age and marital status among the 3 groups (p> 0,05). In terms of patient groups, the education levels of SCH and SUD patients were similar (p=0.225 χ2:5.675), but the working status was different (p=0.045). Employment status in SUD patients (40%) was higher than in SCH patients (16.7%) and was similar to CG (36.7%). Family members (FM) were close among SCH and SUD groups (p=0.913 t=0.109), different from CG (p=0.022 F=4.00). A history of psychiatric disorders among FM was similar in the patient groups (p=0.718 χ2:0.131). There were no differences in the mean age of onset and duration of MI in the patient groups (p>0.05). The hospitalization number (p=0.0001) was higher in SCH than in SUD patients. There were no significant differences in age, marital status, employment and income between mother groups (p>0.5). Mothers of CG had a higher education level than patient groups (p=0.001), educational levels of mothers of SCH and SUD groups were similar (p=0.76) (Table 1).

According to the 3 group results, ISMI total scores of SCH and SUD patients were higher than CG (p=0.0001, F=36.87). A similar difference was seen in the sub-dimensions of ISMI as "alienation", "stereotype endorsement", "discrimination experience", and "social withdrawal" (p=0.0001). According to the Dunnet C post hoc test, the difference was due to the control group and had a large effect (0.14 >η2) (Table 2). In terms of SCH and SUD groups; there was no difference in ISMI total scores (p=0.303 t=1.040); alienation (p=0.152 t=1.452), stereotype endorsement (p=0.317 t=1.009), discrimination experience (p=0.336 t=0.971), social withdrawal (p=0.245 t=1.175) and stigma resistance (p=0.157 t=-1.433). When the relationship between disease characteristics and self-stigmatization had examined, a linear relation-

Table 2. ISMI results of the groups

ISMI	SCH (Mean – SD)	SUD (Mean – SD)	CG (Mean – SD)	p	F	n^2
ISMI Total	71.00 – 14.87	67.07 – 14.42	45.30 – 6.23	0.0001*	36.87	0.459***
Alienation	15.13 – 4.38	13.50 – 4.34	7.30 – 1.51	0.0001*	38.19	0.467***
Stereotype endorsement	16.17 – 4.19	15.10 – 3.99	11.37 – 2.62	0.0001*	14.15	0.245***
Discrimination experience	12.80 – 4.09	11.80 – 3.89	6.70 – 1.80	0.0001*	27.44	0.387***
Social withdrawal	14.93 – 4.35	13.60 – 4.44	7.60 – 1.99	0.0001*	32.22	0.425***
Stigma resistance	11.97 – 2.36	13.07 – 3.48	12.33 – 2.78	0.334	1.11	0.025

Notes: F: One Way ANOVA p<0.05 , n^2 :effect size *Difference between the groups Dunnet s C post hoc test
*ISMI Total: SCH, SUD>CG *Alienation: SCH, SUD>CG
* Stereotype endorsement: SCH, SUD>CG * Discrimination experience: SCH, SUD>CG
* Social withdrawal: SCH, SUD>CG *** 0.14 >n^2 : large effect size
Abbrevations: ISMI, Internalized Stigma of Mental Illness; SCH, Schizophrenia; SUD substance use disorder; CG, control group; SD, standart deviation; F, F test in analysis of variance; p, p value ; n^2 , eta squarred

Table 3. Addiction Belief Inventory, Belief toward Mental Illness, Depression, Burnout, Hopelessness Results of mothers

Mothers Group	SCH (Mean – SD)	SUD (Mean – SD)	CG (Mean – SD)	p	F	n^2
Addiction Belief Inventory (ABI)						
Inability to control	10.83 – 2.61	11.13 – 2.50	9.97 – 2.90	0.222	1.53	0.034
Chronic disease	15.10 – 2.06	16.23 – 1.55	15.43 – 2.74	0.121	2.16	0.047
Reliance on experts	13.00 – 1.17	13.43 – 1.14	13.60 – 1.43	0.166	1.83	0.040
Responsibility for actions	8.80 – 1.90	8.43 – 2.57	10.07 – 2.33	0.018*	4.22	0.088**
Responsibility for recovery	10.93 – 1.80	12.40 – 2.04	10.87 – 2.81	0.015*	4.41	0.092**
Genetic basis	8.13 – 1.87	7.37 – 1.81	7.20 – 2.46	0.181	1.74	0.039
Coping	17.03 – 3.07	17.13 – 3.49	17.30 – 4.71	0.963	0.04	0.001
Moral weakness	19.03 – 2.46	19.23 – 2.05	18.80 – 3.74	0.840	0.18	0.004
Beliefs toward Mental Illness (BMI)	64.67 – 16.24	66.30 – 9.58	57.80 – 18.97	0.083	2.56	0.056
Dangerousness	26.50 – 6.17	28.36 – 5.03	25.87 – 7.45	0.284	1.27	0.029
Helplessness and deterioration in interpersonal relations	36.10 – 10.12	35.67 – 5.34	30.70 – 12.06	0.059	2.93	0.063**
Shame	2.07 – 2.20	2.27 – 1.60	1.23 – 1.55	0.068	2.77	0.060**
Beck Depression (BDI)	10.07 – 7.67	19.00 – 9.47	5.43 – 3.87	0.0001*	26.19	0.376***
Maslach Burnout Index (MBI)						
Emotional exhaustion	7.30 – 5.69	14.43 – 6.75	4.90 – 3.74	0.0001*	24.09	0.356***
Depersonalization	1.53 – 1.87	4.0 – 2.95	1.57 – 1.57	0.0001*	12.29	0.220***
Personal accomplishment	24.33 – 4.88	20.20 – 5.80	28.00 – 3.19	0.0001*	20.24	0.318***
Beck Hopelessness Scale (BHS)	4.90 – 4.30	6.87 – 4.37	2.77 – 2.64	0.0001*	8.50	0.163***
Feelings about the future	0.83 – 1.51	1.37 – 1.38	0.33 – 0.88	0.01*	4.85	0.100**
Loss of motivation	2.77 – 1.87	3.73 – 1.91	1.60 – 1.45	0.0001*	11.10	0.203***
Expectations	1.30 – 1.70	1.77 – 1.89	0.83 – 1.15	0.087	2.52	0.055

Notes: One Way Anova p<0.05 * Difference between the groups Dunnet s C post hoc test (BDI, MBI)
* Difference between the groups Scheffe post hoc test (ABI, BHS) * ABI Responsibility for actions: CG>SUD
* ABI Responsibility for recovery: SUD> SCH, CG * BDI: SUD> SCH>CG
* MBI Emotional exhaustion: SUD> SCH, CG * MBI Depersonalization: SUD> SCH, CG
* MBI Personal accomplishment: CG> SCH>SUD * BHS Total: SUD> CG
* BHS Feelings about the future: SUD> CG * BHS Loss of motivation: SUD, SCH> CG
** 0.06 <n^2< 0.14 : medium effect size *** 0.14 >n^2 : large effect size
Abbrevations: SCH, Schizophrenia; SUD substance use disorder; CG, control group; SD, standart deviation; F, F test in analysis of variance; p, p value; ABI, Addiction Belief Inventory; BDI, Beck Depression; BMI, Beliefs toward Mental Illness; MBI, Maslach Burnout Index; BHS, Beck Hopelessness Scale; n^2, eta squarred

ship was found between ISMI and hospitalization number among SCH patients (p= 0.018 r=0.430).

In terms of the mothers' group about beliefs towards addiction, there were statistical differences in "responsibility for actions" (p=0.018) and "responsibility for recovery" (p=0.015). The results of the Scheffe post hoc test showed that the scores of "responsibility for actions" in mothers of the CG group were higher than the mothers of the SUD group. A medium effect size was found between CG and SUD (η2=0.08). According to the Scheffe post hoc test, "responsibility for recovery" subscale scores were statistically higher in the mothers of the SUD group than in the other two groups. A medium effect size was found between the SUD and the other groups (η2=0.09). There were no significant differences in BMI total point and subscales as dangerousness (p=0.131), helplessness and deterioration in interpersonal relationships (p=0.059), and shame (p=0.068) (Table 3).

Depression, burnout and hopelessness levels of mothers were also evaluated. It was determined that the depression levels of mothers were significantly different and had a large effect (0.14<η2). According to the Dunnet C post hoc test, the BDI score of mothers of the SUD group was higher than mothers of the SCH group; mothers of the SCH group were higher than mothers of the CG. In terms of mothers' burnout scores, "emotional exhaustion" and "depersonalization" scores were found to be higher in mothers of the SUD group than in SCH and CG (p=0.0001). It was found that mothers' "personal achievement" scores of CG were higher than those of mothers of the SCH group. The scores of mothers those with SCH were higher than mothers of the SUD group (p=0.0001). Evaluating to hopelessness scores of mothers; according to the Scheffe post hoc analysis, mothers of the SUD group have significantly higher scores on "hopelessness" and "feelings and expectations about the future" compared to CG and had a large effect (p=0.0001). It was determined that the "loss of motivation" of mothers of the SUD group and SCH group were higher than CG (p=0.0001). (Table 3)

The relationship between mothers' mental health and their beliefs toward MI and addiction was evaluated. A correlation was found between MBI depersonalization and stigma toward MI in mot-

Table 4. Correlation between mental scores and beliefs toward mental illness (BMI) / addiction (ABI) of the mothers of patients

Mothers	Depression	Hopelessness	(MBI) Emotional exhaustion	(MBI) Depersonalization	(MBI) Personal accomplishment
SCH group					
BMI	p=0.076 r=0.329	p=0.128 r=0.284	p=0.234 r=0.224	p=0.020* r=0.424	p=0.187 r=-0.247
ABI- Chronic disease	p=0.233 r=0.225	p=0.280 r=0.204	p=0.744 r=0.062	p=0.287 r=0.201	p=0.914 r=-0.021
ABI- Responsibility for actions	p=0.037* r=-0.382	p=0.133 r=-0.281	p=0.011* r=-0.456	p=0.030* r=-0.396	p=0.111 r=0.297
ABI- Coping	p=0.488 r=0.132	p=0.326 r=0.186	p=0.360 r=0.173	p=0.457 r=0.141	p=0.842 r=-0.038
SUD group					
BMI	p=0.009* r=0.469	p=0.020* r=0.423	p=0.0001* r=0.622	p=0.155 r=0.266	p=0.002* r=-0.532
ABI- Chronic disease	p=0.008* r=0.478	p=0.420 r=0.153	p=0.037* r=0.383	p=0.358 r=0.174	p=0.268 r=-0.209
ABI- Responsibility for actions	p=0.057 r=-0.352	p=0.070 r=-0.336	p=0.047* r=-0.365	p=0.021* r=-0.419	p=0.030* r=0.396
ABI- Coping	p=0.129 r=0.284	p=0.040* r=0.377	p=0.206 r=0.238	p=0.062 r=0.345	p=0.149 r=-0.270

MBI: Maslach Burnout Index; ABI, Addiction Belief Inventory; BMI, Beliefs toward Mental Illness p=0.0001

hers of SCH patients (r= 0.424). There was a relationship between ABI-responsibility for actions and depression (r=-0.382); emotional exhaustion (r=-0.456); depersonalization (r=-0.396) in mothers of SCH patients. A correlation was found between stigma toward MI and depression (r=0.469), hopelessness (r=0.423), emotional exhaustion (r=0.622), and personal accomplishment (r= -0.532) among SUD patients' mothers. In terms of beliefs toward addiction, there was a relationship between belief in chronic disease and depression (r=0.478); emotional exhaustion (r=0.383). A correlation was between responsibility for actions and emotional exhaustion (r=-0.365); depersonalization (r=-0.419); personal accomplishment (r=0.396) (Table 4).

The relationship between patients' IS and their mothers' beliefs about MI was evaluated. No statistically significant correlation was found between the ISMI scores of the SCH patients and the BMI scores of their mothers (p>0.05). There was a correlation between the SUD group's "alienation" scores of ISMI and their mothers' "inability to control" scores of ABI (p=0.024 r=0.41). That is, as SUD individuals' self-alienation increases, their mothers' belief in their "inability to control" the disease increase.

DISCUSSION

In this study, SUD and SCH patients were evaluated about internalized stigma and their mothers were evaluated in terms of their beliefs toward MI and addiction; mothers' depression, hopelessness and burnout levels. Our study pointed out that IS among SCH and SUD patients were higher than CG. This situation could be interpreted as the presence of MI playing a huge impact on the self-stigmatization of a person. It is stated that individuals living with MI face two major problems such as illness and stigma (11). Nevertheless, the results of the study showed that IS levels of SCH and SUD patients were not different. One study found that internalized stigma of SUD and SCH patients did not differ from as our study (24). The same study also showed that SUD patients' IS scores were significantly higher than those with bipolar disorder and anxiety disorder. We can say that the burden of these two diseases on the patient could be similar. We also found a linear relationship between hospitalization number and IS scores in patients with SCH. This situation can be interpreted in two ways. Hospitalization increases self-stigma or self-stigma complicates the recovery processes and increases hospitalization. This linear relationship was also shown in another study conducted in Turkey (25).

Stigma towards MI constitutes a serious problem in the processes of managing mental health. It has been revealed that 61% of society, 19% of family members, 11% of spouses/relatives and 14% of friends stigmatize individuals with psychiatric disorders (26). This indicates that the general population and family members approach psychiatric disorders differently. In this study, we noticed that mothers of patient groups had more negative beliefs about the diseases. Especially, SUD patients' mothers were more stigmatized toward

MI. Even though this situation revealed the difference in scores between the groups, it was not at a significant level. It was determined that the mental status of the mothers played a role in the negative evaluation of the illness. This research showed an association between MI stigmatization and depression, hopelessness, emotional exhaustion, and personal accomplishment in mothers of SUD patients. MI stigmatization was also associated with their depersonalization to the disease in terms of mothers of SCH patients. Exhaustion also negatively affects the ability to cope with the disease. It was found that when caregivers of SCH patients perceived that they were not coping with their patients' symptoms, there was an increase in their critical/hostile behaviour (27).

This study showed that mothers were different in their beliefs about addiction. Mothers of SUD patients hold addicted people more responsible for their actions. This evaluation could be associated with the mental status of the mothers. Depression and emotional exhaustion of the mothers affect them to see addiction as a more chronic and unending process. In addition, the relationship between burnout of the mothers and the responsibilities of SUD patients for their own actions came to the fore. Since substance use is perceived as one's own choice by society, individuals are held responsible for their disease (28). This factor also leads to a more negative evaluation of addiction than other MIs in society (29).

Family members both provide care and experience the spillover effects of MI (30). In a qualitative study, MI patients' families stated that they experience depression, apathy, pain, confusion, isolation, anger, destruction, helplessness, hopelessness, denial, disappointment, uncertainty, blame, and chronic sadness (31). An essential result of our study is that the depression levels of the mothers of those with SUD are higher than the mothers of those with SCH. In the study conducted with caregivers of SCH patients, distress, worry, shame, guilt, stigma, depression, grief, anxiety levels and somatic complaints were found at high levels (32). In a study conducted among adolescents with SUD, mood disorder was observed in 43.2% of the mothers (33). The most frequent disorder was found depression (40.5%), and anxiety disorder (21%) among SUD patients' caregivers (13). It is stated that the caregiver burden was more severe in the SUD population (34). Increased levels of burden cause depression, exhaustion, and sleep disturbance among caregivers of people with SUD (35). In our study, it was concluded that emotional exhaustion and depersonalization were higher in mothers of SUD patients compared to SCH and CG. Caregivers of individuals with SUD have difficulty in solving their problems because they receive little support from the social environment, and some families experience emotional exhaustion (36). According to our study, mothers of SUD people were more hopeless than mothers of CG. In particular, it has been reported that parents experience frustration, guilt, denial, surprise, anger, shame, fear, expectation, hopelessness and helplessness due to their children's substance use (12,13,14). It was stated that up to five people in the family of a person with SUD can be negatively affected by the disease (28). So we can point out that SUD, which is one of the mental illnesses, has more severe effects on mothers.

In this study, we focused on controlling two demographical variables age and marital status when matching the groups. The limitation of this study is that the education level of CG was higher than the patient groups.

CONCLUSION

This study provided a more detailed evaluation of individuals with SUD and SCH, especially their mothers. The study revealed that the self-stigmatization of individuals with SCH and SUD is similar, but that having a mental illness imposes a separate burden on self-stigmatization. So therapy models related to the reduction of self-stigma should be developed. This study provided that the effect of SUD on mothers is more devastating and may affect the mental health of the mothers. In addition, in this study, the relationship between the mental states of SUD mothers and their perspectives on the disease was revealed. It was seen that as the mental state of the mothers deteriorated, they began to have a more negative perspective on their children's illnesses. On the other hand, we can look at this situation from a different perspective.

We can also say that the process of children's illness affects their evaluation of the disease and their mental health begins to deteriorate. In addition, depression, emotional exhaustion and depersonalization were more severe in mothers of SUD patients than in mothers of SCH patients. Hopelessness and loss of motivation were both seen at high levels among mothers of SUD patients and mothers of SCH patients. In light of our findings, it is seen that having a child with SUD and the effect of substance use problem on the mother is more severe. In particular, the mental status of mothers should be evaluated and individual therapy opportunities should be offered. We can add that mother-oriented therapies can change their perspective on the disease and contribute to the recovery process of the patient.

Ethical Considerations

All the participants, both patients, and caregivers gave written informed consent before the test and all the ethical procedures were performed. The study was approved by the Human Research and Ethics Committee of Ege University (No.18-4.1/43).

Conflicts of interest: The authors declare that they have no conflict of interest.

Correspondence address: PhD Demet Atlam , Ege Üniversitesi Madde Bağımlığı, Toksikoloji ve İlaç Bilimleri Enstitüsü Bornova İzmĩr - Türkiye, demet.havaceligi@gmail.com

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Screening for cognitive impairment in schizophrenia: A comparison between the Mini-Mental State Examination and the Montreal Cognitive Assessment Test

Şizofrenide bilişsel bozulma taraması: Kısa Kognitif Muayene ve Montreal Bilişsel Değerlendirme Ölçeğinin karşılaştırılması

Selma Ercan Doğu[1], Ahmet Kokurcan[2]

[1]Asst. Prof., University of Health Sciences, Faculty of Hamidiye Health Sciences, Department of Occupational Therapy, Istanbul, Turkey, https://orcid.org/0000-0003-3276-8041

[2]Assoc. Prof., University of Health Sciences Dr. Abdurrahman Yurtaslan Ankara Oncology Training And Research Hospital, Department of Psychiatry, Ankara, Turkey, https://orcid.org/0000-0002-5763-2506

SUMMARY

Objective: Cognitive impairment is a core feature affecting social and occupational functionality in schizophrenia. The aim of this study is to compare the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA) in screening for cognitive impairment in individuals diagnosed with schizophrenia and to examine the relationship between neurocognitive functions and clinical symptoms. **Method:** The study included 135 individuals with schizophrenia followed in Ankara Dışkapı Community Mental Health Centre. Sociodemographic Data Form, Brief Psychiatric Rating Scale (BPRS), The Scale for The Assessment of Positive Symptoms (SAPS), Negative Symptoms Assessment Scale (SANS), MMSE and MoCA were administered. **Results:** The mean MMSE score was 25.64 ± 2.72, and the mean MoCA score was 17.91 ± 3.83. There was a high positive correlation between the MMSE and MoCA scores (r=0.667). The MMSE and MoCA tests showed a substantial difference in the assessment of cognitive functions; and MoCA was found more sensitive than the MMSE in determining cognitive impairment. Moreover, the MMSE and MoCA scores showed a negative correlation with the BPRS, SANS, and SAPS scores. **Discussion:** These findings indicate that MoCA may be used as a more useful screening test for cognitive impairment in people with schizophrenia.

Key Words: Schizophrenia, cognitive tests, MoCA, MMSE, psychopathology

ÖZET

Amaç: Bilişsel bozulma, şizofrenide sosyal ve mesleki işlevselliği etkileyen temel bir özelliktir. Bu çalışmanın amacı, şizofreni tanısı olan bireylerde bilişsel bozulma taramasında Kısa Kognitif Muayene (KKM) ile Montreal Bilişsel Değerlendirme Ölçeği'ni (MOBID) karşılaştırmak ve nörobilişsel işlevler ile klinik belirtiler arasındaki ilişkiyi incelemektir. **Yöntem:** Çalışmaya Ankara Dışkapı Toplum Ruh Sağlığı Merkezinde takip edilen 135 şizofreni tanısı olan birey dahil edildi. Sosyodemografik Veri Formu, Kısa Psikiyatrik Derecelendirme Ölçeği (KPDÖ), Pozitif Belirtileri Değerlendirme Ölçeği (SAPS), Negatif Belirtileri Değerlendirme Ölçeği (SANS), KKM ve MOBID uygulandı. **Bulgular:** Ortalama KKM puanı 25.64 ± 2.72 ve ortalama MOBID puanı 17.91 ± 3.83 idi. KKM ve MOBID skorları arasında yüksek pozitif korelasyon vardı (r=0,667). KKM ve MOBID testleri, bilişsel işlevlerin değerlendirilmesinde önemli bir farklılık gösterdi ve MOBID'in bilişsel bozulmayı belirlemede KKM'den daha duyarlı olduğu bulundu. Ayrıca, KKM ve MOBID puanları, BPRS, SANS ve SAPS puanları ile negatif korelasyon göstermiştir. **Sonuç:** Bu bulgular, MOBID'in şizofreni tanısı olan bireylerde bilişsel bozulma için daha yararlı bir tarama testi olarak kullanılabileceğini göstermektedir.

Anahtar Sözcükler: Şizofreni, bilişsel testler, KKM, MOBID, psikopatoloji

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INTRODUCTION

Cognitive impairment is one of the prominent clinical features of individuals with schizophrenia and it has negative effects on the functionality of individuals (1). Although not included in the diagnostic criteria of schizophrenia, cognitive impairment is common in individuals with schizophrenia. It is estimated that 61–78% of patients with schizophrenia have cognitive problems (2). The cognitive impairment in schizophrenia is especially marked in executive functions, attention, and memory areas (3,4). Cognitive impairment is highly associated with poor functionality in schizophrenia. Especially, impairment in information processing speed, working memory and cognitive flexibility are strongly associated with lower daily functioning. Deficits in those cognitive areas make it difficult for individuals to follow task-oriented jobs and maintain their social relationships (2). Although cognitive impairment has negative effects on patients, it has been largely ignored in the treatment of schizophrenia.

Previous studies have shown improvement in cognitive functions through cognitive rehabilitation programs in patients with schizophrenia (5-7). Screening cognitive impairment in patients with schizophrenia and addressing the impaired cognitive domain in the rehabilitation program can provide better outcomes (8). Thus, it is important to assess the cognitive functions of patients with schizophrenia for applying for a proper rehabilitation program and increasing participation in daily living. There are various instruments for evaluating the cognitive functions of individuals with schizophrenia. There is not any standard, easily administered test battery in the assessment of cognitive impairment in patients with schizophrenia. Many paper-pencil tests and individual neuropsychological tests or batteries were developed for patients with schizophrenia, such as the MATRICS Consensus Cognitive Battery (MCCB), and Brief Assessment of Cognition in Schizophrenia (BACS) (8,9). The MATRICS battery is a valid and reliable cognitive assessment tool for schizophrenia and it includes 10 tests to measure a wide range of cognitive domains. However, it takes almost 60- 90 minutes for administration. The BACS was developed to evaluate the most damaged cognitive areas and assesses five different domains of cognitive functions through six tests (9). Administration of the BACS takes about 30–35 minutes in patients with schizophrenia. These comprehensive neuropsychological batteries have many benefits and provide detailed information; however, administration of the batteries requires trained testers and a longer time to administer (10).

A shorter cognitive test may be preferred for ease of completion and tolerability by patients in busy clinical settings (9). The MMSE and MoCA scales were used to assess cognitive dysfunction in patients with schizophrenia in some previous studies (11,12,13). Both the MMSE and the MoCA were developed to make a differential diagnosis between mild cognitive impairment and dementia and to detect dementia at an early stage. Although they are not specialized tests for cognitive impairment in schizophrenia, both tests are easy and practical to implement in daily practice. Some studies compared those tests and MoCA was found to be better at earlier detection of cognitive impairment in patients with schizophrenia (14). It will be important to assess the cognitive functions more frequently to achieve rehabilitation goals and to determine proper scales for screening cognitive impairment in schizophrenia.

There is not a certain relationship between the severity of clinical symptoms and the level of cognitive impairment in schizophrenia (15,16,17). Many studies demonstrated a significant but modest association between the severity of negative symptoms and cognitive impairment level, despite that, there was no association between cognitive impairment level and severity of positive symptoms in most of the studies (16,17,18,19). The severity of positive symptoms was associated with more cognitive impairment, especially in memory and attention areas in a previous study (20). In another study, schizophrenia patients with severe psychotic symptoms showed a greater cognitive impairment across multiple tests compared with the patients with mild or moderate clinical symptoms (21). There is not a simple and linear relationship between the severity of clinical symptoms and cognitive impairment level in schizophrenia. Therefore, future studies are needed to assess the relationship more clearly (18,19).

In summary, there is no study comparing the MMSE and MoCA tests for cognitive impairment in schizophrenia in Turkey. Also, there is a paucity of research regarding the administration of the MMSE and MoCA tests in outpatients with severe mental illness. Screening for cognitive impairment and referring for a further neuropsychological assessment will help detect cognitive deterioration in patients with schizophrenia. From this point of view, it was aimed to compare the MMSE and MoCA tests for screening cognitive impairment in schizophrenia and to assess the relationship between cognitive functions and clinical symptoms in this study.

METHOD

Participants

The present study was carried out in a Community Mental Health Center (CMHC) of the University Hospital in March 2020-June 2020 in Turkey. A total of 135 patients who were followed up with the diagnosis of schizophrenia in CMHC were included in the study. The inclusion criteria were having at least five years of education, being aged 18-59 years old, and not being hospitalized in the last six months. The participants were excluded if they had a comorbid diagnosis of intellectual disability, organic brain disease, or alcohol/substance abuse.

All subjects received information about the content of this study and signed a written consent form before participating. All procedures complied with the Declaration of Helsinki and were approved by the Clinical Research Ethics Committee of the University Hospital (Ethics Committee Decision Date-Number: 17.02.2020-82/10).

Instruments

Sociodemographic Data Form: Sociodemographic data included age, gender, marital status, education, employment status and duration of illness.

Mini-Mental State Examination (MMSE): The MMSE is developed by Folstein et al. (22). MMSE is scored on a 30-point scale, with items assessing orientation (temporal and spatial: 10 points), memory (registration and recall: 6 points), attention/concentration (5 points), language (verbal and written: 8 points) and visuospatial function (1 point). MMSE lasts about 5-10 minutes. Turkish validity and reliability study of the MMSE was done by Gurgen et al. (23). It was found that MMSE is valid and reliable in the diagnosis of mild dementia in Turkish society. A score of 24 on the MMSE is defined as the cut-off score in the Turkish population.

Montreal Cognitive Assessment (MoCA): The MoCA is used as a screening test to detect Mild Cognitive Impairment (MCI). MoCA is scored on a 30-point scale, with items assessing delayed word recall (5 points), visuospatial/executive function (7 points; includes clock drawing), language (6 points), attention/concentration (6 points) and orientation (6 points). MoCA lasts approximately 10-15 minutes and is a valid and reliable scale in the diagnosis of mild-stage dementia and MCI (24). Turkish validity and reliability study of the MoCA was performed by Selekler et al. (25). A score of 21 on the MoCA is defined as a cut-off score in the Turkish population.

Brief Psychiatric Rating Scale (BPRS): The BPRS is a scale aiming to assess the severity of clinical symptoms, such as depressive, psychotic, and negative symptoms (26). The BPRS consists of 18 items and each item is scored between 0 (none) and 6 (very severe) points. The minimum score that can be obtained from the scale is 0 and the maximum score is 108. The Turkish validity and reliability study of the scale was done by Soykan (27).

The Scale For The Assessment of Positive Symptoms (SAPS): The Scale for the Assessment of Positive Symptoms was developed by Andreasen (28) to measure the severity of positive symptoms. It is a clinician-administered questionnaire and includes 34 items. Each item is rated between 0 (absent) and 5 (severe) and the test includes four subscales (hallucinations, delusions, bizarre behaviour and formal thought disorder). A reliability study of the Turkish form was done by Erkoç et al. (29).

The Scale for the Assessment of Negative Symptoms

(SANS): The Scale for the Assessment of Negative Symptoms was developed by Andreasen (30) to measure the severity of the negative symptoms of schizophrenia. The SANS consists of 25 items representing 5 scales: Affective flattening or blunting, alogia, avolition-apathy, anhedonia-asociality and inattention. Each item is individually graded between 0 and 5. A reliability study of the Turkish form was done by Erkoç et al. (31)

Procedure

Sociodemographic Data Form, Brief Psychiatric Rating Scale (BPRS), Scale for The Assessment of Positive Symptoms (SAPS), Scale for the Assessment of Negative Symptoms (SANS), Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment Scale (MoCA) were administered to the individuals. The MMSE and MoCA were conducted by a psychologist (first author) who had training in neuropsychological testing and who has a clinical experience in the psychosocial rehabilitation of people with schizophrenia. The clinical assessments were conducted by a psychiatrist (second author). The tests were administered and scored as instructed by the relevant instruments.

Statistical analysis

Data analyses were conducted using SPSS version 22 (SPSS Inc., Chicago, USA). First, the skewness kurtosis tests and histogram were used to check normal distribution. Continuous variables were expressed as mean ±standart deviation and categorical variables were expressed as frequencies. Collected data was analyzed via independent samples t-test, chi-square test, and Pearson correlation analysis. The level of significance was accepted at 0.05.

RESULTS

135 patients completed the MMSE and MoCA tests in our study. The mean age of participants was 39.43±9.07. Most of the participants were men (66.7%) and single (50.4%). There was a high rate of unemployment (79.3%) while 44.4% of the patients graduated from high school. The duration of the disorder was 14.66±6.90 years. Table 1 summarizes the sociodemographic and clinical variables of the patients.

Table 1 Sociodemographic and clinical characteristics of the patients

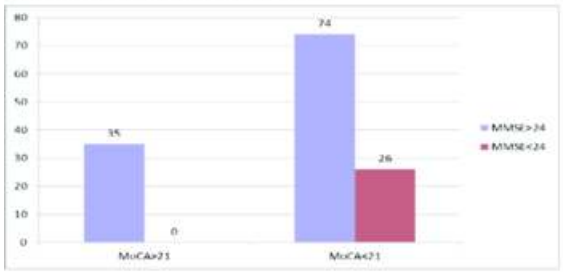
Characteristics		Total Sample (n=135)
Age (Mean–SD)		39.43–9.07
Duration of illness (Mean±SD)		14.66–6.90
Gender (n,%)	Female	45 (33. 3%)
	Male	90 (66.7%)
Marital status (n,%)	Married	68 (50.4%)
	Single	55 (40.7%)
	Divorced	12 (8.9%)
Education (n,%)	Primary	23 (17%)
	Secondary	29(21.5%)
	High school	60 (44.4%)
	University	23 (17%)
Employment (n,%)	Employed	28 (20.7%)
	Unemployed	107 (79.3%)
Mean SANS score		33.96–13.43
Mean SAPS score		22.53–11.85
Mean BPRS score		13.46–6.43
Mean MMSE score		25.63–2.71
Mean MOCA score		17.91–3.82
MMSE ≥24		109 (80.7%)
≤ 23		26 (19%)
MOCA ≥ 21		35 (25.9%)
≤ 20		100 (74.1%)

Standardized Mini Mental Test (MMSE); Montreal Cognitive Assessment Scale (MoCA); Brief Psychiatric Rating Scale (BPRS); Scale for The Assessment of Positive Symptoms (SAPS); Scale for the Assessment of Negative Symptoms (SANS)

There was a positive correlation between the MMSE and MoCA scores ($r=0.667$, $p<0.01$). The mean score of the MoCA scale was 17.91±3.82 (range 8 to 27) while the mean score of the MMSE scale was 25.63±2.71 (range 18 to 30) (Table 1). In addition, 80.7% (n =109) of the patients had 24 points (normal range) or higher on the MMSE scale. All of the patients who had a score of 21 or higher in the MoCA got 24 points or higher in the MMSE test, indicating the sensitivity of MoCA as 100% according to the MMSE test. However, 35 patients who had a score of 24 or higher in the MMSE got 21 points or higher in the MoCA test, and thus, the sensitivity of MMSE was 25.9% according to the MoCA test (Figure 1). The comparison of MMSE and MoCA tests according to cut-off values showed a statistically significant difference in the chi-square independence test ($x^2=11.271$, $p<0.01$).

The subdimension scores of the scales were given in Table 2. The patients had the highest score at the orientation subdimension in both tests. The mean orientation score was 5.79±0.58 (range 0 to 6)in the MoCA and 9.61±0.75 in the MMSE tests.

Figure 1 Comparison of the MMSE and MoCA tests



Data; number of cases, Standardized Mini Mental Test (MMSE), and Montreal Cognitive Assessment Scale (MoCA)

Attention-concentration subtest scores were 3.68±1.53 (range 0 to 6) in the MoCA and 3.06±1.64 (range 0 to 5) in the MMSE tests. The mean language score was 3.30±1.00, out of 6 points while it was 7.68±0.63 out of 8 points in the MMSE. There was only one item for visuospatial function in the MMSE and more than half of the patients (52.5were was not successful in drawing the geometrical shape. The MoCA had a combined visuospatial-executive dimension and the mean score was 3.60±1.66 out of 7 points. The patients had the lowest scores in the memory-delayed word recall domain (1.54±1.16, range 0 to 5) in the MOCA test whereas it was 4.82±0.95 out of 6 points in the MMSE.

The relationship between sociodemographic variables, clinical symptoms, and cognitive functions was assessed in the study. The results were reported in the correlation matrix in Table 3. Both MMSE and MoCA scores were not correlated with age (p>0.05). Despite that, the duration of the disorder showed a negative correlation with both the MMSE and MoCA scores (r=-.272, p=.001; r=-0.237, p=.006). Gender and education level showed a significant association with the MMSE score (x^2=4.02 p<0.05; x^2= 12.99, p<0.05, respectively). Increased education level was associated with higher MMSE scores while male patients had a higher MMSE score compared to females. However, the MMSE score was not associated with marital status and employment status (p>0.05). The mean MoCA score did not show a significant difference according to gender, marital status or employment status (p>0.05). Despite that, increased education level was associated with higher MoCA scores (x^2=20.97; p<0.05). The mean MMSE score was negatively correlated with mean BPRS, SANS, and SAPS scores (r=-.368, p<0.01, r=-.257, p<0.01, and r=-.199, p<0.05, respectively). In addition, the mean MoCA score also showed a moderate negative correlation between the BPRS, SANS, and SAPS scores (r=-.466, p<0.01, r=-.501, p<0.01, and r=-.401, p<0.01, respectively).

Table 2 Descriptive statistics of subtests of MoCA and MMSE

MoCA items/maximum score (n=135)	Minimum	Maximum	Mean±SD
Visuospatial-executive function/7	1	7	3.60–1.66
Language/6	1	6	3.30–1.00
Attention-concentration/6	0	6	3.68–1.53
Orientation/6	3	6	5.79–0.58
Memory (delayed word recall)/5	0	5	1.54–1.16
Total/30	8	27	17.91–3.83
MMSE items/maximum score (n=135)	Minimum	Maximum	Mean±SD
Visuospatial function/1	0	1	0.47–0.50
Language/8	6	8	7.68–0.63
Attention-concentration/5	0	5	3.06–1.64
Orientation/10	7	10	9.61–0.75
Memory/6	2	6	4.82–0.95
Total/30	18	30	25.63–2.71

tandardized Mini Mental Test (MMSE); Montreal Cognitive Assessment Scale (MoCA)

DISCUSSION

Most patients with schizophrenia have a significant cognitive impairment, and cognitive impairment negatively affects their daily life and treatment adherence. Although cognitive impairment is related to poor functionality, it has been largely neglected in the treatment of schizophrenia (32). However, cognitive difficulties severely affect the social and occupational lives of the patients, and therefore, cognitive impairment also should be assessed in addition to the treatment of clinical symptoms in schizophrenia. Comprehensive neuropsychological batteries take too much time during clinical evaluation and it is difficult for individuals with schizophrenia to finish a prolonged clinical battery. Shorter, less time-consuming and

Table 3 Correlations between scores of age, duration of illness, MMSE, MoCA, BPRS, SANS, SAPS

Variable	Age	Duration of illness	MMSE	MoCA	BPRS	SANS	SAPS
Age	1	.853**	-.159	-.094	-.120	-.121	-.154
Duration of illness		1	-.272**	-.237**	.140	.102	.080
MMSE			1	.667**	-.368**	.257**	-.199*
MoCA				1	-.466**	-.501**	-.401**
BPRS					1	.679**	.651**
SANS						1	.567**
SAPS							1

Standardized Mini Mental Test (MMSE); Montreal Cognitive Assessment Scale (MoCA); Brief Psychiatric Rating Scale (BPRS); Scale for The Assessment of Positive Symptoms (SAPS); Scale for the Assessment of Negative Symptoms (SANS)

more effective assessments are needed for screening cognitive deficits in patients with schizophrenia. From this point of view, it was aimed to compare the MMSE and MoCA tests for screening cognitive impairment in schizophrenia and to assess the relationship between cognitive functions and clinical symptoms in this study.

The mean MoCA score was lower than the cut-off level in the current study, despite that, the mean MMSE score was higher than the cut-off level. The mean MMSE score of the patients indicates no cognitive impairment whereas the mean MoCA score of the patients indicated moderate cognitive impairment. Furthermore, eighty per cent of the patients showed no cognitive impairment according to the MMSE scale while only one-fourth of the patients did not demonstrate a cognitive impairment according to the MoCA. Using the cut-off scores of the tests, 74.1% of the sample displayed a cognitive impairment in the MoCA while it was 19% in the MMSE test. According to our findings, cognitive impairment was shown in four domains of the MoCA test, while only one domain showed a clear impairment in the MMSE test. Therefore, MoCA was more sensitive in detecting cognitive impairment compared to the MMSE in the current study. Our findings were consistent with previous literature as the MoCA test showed a high sensitivity for the detection of cognitive impairment in long-term psychosis patients (33,34,35). Fiskevoic et al. (11) examined the clinical usability of MoCA in 30 patients with schizophrenia and compared the degree of sensitivity of the MoCA and MMSE. In that study, the sensitivity of MMSE was 41.7% compared to the MoCA test. Although the sensitivity of the MMSE according to the MoCA was higher in that study compared to our study, the sensitivity of the MMSE was also low for detecting cognitive impairment (11,34,36). Previous studies also demonstrated the superiority of the MoCA over the MMSE in the screening of cognitive functions in schizophrenia (11,12,35). On the other hand, the mean MoCA score of the participants in our study (17.9±3.8) was slightly lower than the mean MoCA scores of other studies. Participants had a mean MoCA score was 22.5±3.9 in the study of Rademeyer and Joubert (12). In addition, the MoCA mean score was 19.9±5.1 in the study of Fiskevoic et al. (11). Rodríguez-Bores et al. (37) stated that the mean MoCA score was 23.0±3.9. Lower mean scores in our study might be related to different sociodemographic and clinical variables of the patients and the duration of the disorder.

In the current study, the participants had the highest score at the orientation subdimension in both MMSE and MoCA tests. In other words, the orientation subtest was correctly answered by nearly all participants in both tests. Previous studies showed that participants had higher scores on the orientation subtest (33,35,38). Similarly, it is reported that orientation is not mostly impaired in schizophrenia (39). The items of the language subtest in the MMSE test were correctly answered by nearly all participants in the current study, contrarily, the patients showed impairment in the language area in the MoCA. The items of short memory and naming are more difficult in the MOCA rather than the MMSE, and that difference might be the reason for the better screening in those areas. In addition, the language (naming) and orientation subtests form 60% of the MMSE scale. There is no specific assessment for executive functions in the MMSE and there is only one item for visuospatial function in the MMSE. That is a big failure of the MMSE in the cognitive assessment of patients with schizophrenia (38). The participants had the lowest score at the visuospatial-executive subdimension in the MoCA test, one of the core cognitive impairment areas in schizophrenia. The MoCA contains specific subtests addressing abstraction and problem-solving which are core cognitive impairments in schizophrenia (40). As a result, the cognitive impairment of the patients can be assessed better with the MoCA compared with the MMSE and it can be suggested that the major difference among these instruments lies in the assessment of executive functions. Therefore, the MMSE does not seem appropriate for the cognitive assessment of patients with schizophrenia, and more patients who would benefit from psychosocial interventions can be determined with the MoCA test.

Another aim of the current study was to examine the relationship between sociodemographic variables, clinical symptoms, and cognitive impairment. Although age did not show a significant correlation with the mean MMSE and MoCA scores, the duration of the disorder showed a mild negative corre-

lation with the MMSE and MoCA scores. That result was shown in previous studies and it was revealed that cognitive impairment occurs gradually in schizophrenia. Considering that, screening cognitive functions during the course of the disorder and administering psychosocial and cognitive rehabilitation when needed is a substantial issue for the patients. The mean MMSE and MoCA scores were correlated with higher education levels. Some studies did not find a significant relationship between MoCA scores and education level while some others found a significant correlation between total MoCA scores and education level (13,33,34,35). Education level is a factor affecting the scores on cognitive scales, however, it showed a partial impact on the clinical scores in the present study. There is no definite cut-off point according to education level, and follow-up of cognitive functions during the disorder will be better at detecting cognitive impairment. Male patients had a higher MMSE score compared to females in the study, however, there was no significant difference between male and female patients in the MoCA. The reason for these different results might be due to the different clinical populations involved in those studies and there is still no definite relationship between gender and cognitive scores in the current literature (13,33). In literature, the relationship between sociodemographic variables (i.e., age, marital status, education level) and cognitive scales are incongruent, and our study also did not show a significant association between marital status, employment, and MMSE/MoCA scores.

Both the MMSE and MoCA scores showed a negative correlation with the BPRS, SAPS, and SANS scores. Current findings showed that the higher the scores on the BPRS, SAPS and SANS, the lower the score in the cognitive scales, indicating that the severity of clinical symptoms was related to more severe cognitive impairment. There was a moderate correlation between the severity of clinical symptoms and the MMSE while the MOCA score showed a high negative correlation with the clinical symptoms. MoCA was found to show a stronger relationship with the severity of psychotic symptoms compared to the MMSE in the current study. Wu et al. (35) examined the relationship between the MoCA and PANNS scales in 121 patients with schizophrenia and schizoaffective disorder. The authors found that the MoCA score was related to PANNS negative subscale score, but not to the positive or general subscale scores. Current study findings demonstrated that the severity of negative symptoms was associated with MMSE and MoCA scores, consistent with previous studies. Severe negative symptoms were related to cognitive slowing, worse verbal memory, visual memory, and attention and processing speed in previous studies (19,41). Therefore, psychosocial rehabilitation should be applied earlier to patients with resistant negative and cognitive symptoms. A negative relationship was found between the severity of positive symptoms and MMSE and MoCA scores in the current study and the evidence of that relationship was conflicting in the current literature (21). Davidson et al. (42) found that there was not a significant correlation between the severity of positive symptoms and the MMSE score. On the other hand, Talreja et al. (20) demonstrated that the severity of positive symptoms was associated with more cognitive impairment, especially in memory and attention areas. In addition, the lowest score was found in the visuospatial-executive area in the MoCA test, similar to previous studies. In another study, schizophrenia patients with severe psychotic symptoms showed a greater cognitive decline in the memory domain compared to the patients with mild or moderate symptoms (21). Therefore, although the relationship between positive symptoms and cognitive functions is controversial, our study findings suggest that treatment adherence and treatment follow-up will contribute positively to cognitive skills in individuals with schizophrenia.

Our study has some limitations. First, the sample size was modest, and we could not use a comprehensive neuropsychological battery to compare with the MMSE/MoCA. There was a disproportionate number of male patients (66.7%). There was not any control group. On the other hand, assessing the relationships between clinical symptoms and cognitive impairment is a strength of our study as clinical symptoms affect cognitive functions. To the best of our knowledge, this was the first study to compare the scores of the MMSE and MoCA scales in patients with schizophrenia in the Turkish population. The present study contributes to the literature in terms of testing the cognitive functions of patients with schizophrenia in a diffe-

rent culture and language. In particular, cognitive impairment in schizophrenia is one of the factors that hinder participation in daily life. On the other hand, cognitive impairment may be ignored because of focusing on psychiatric symptoms. In addition, comprehensive neuropsychological batteries are very time-consuming and challenging for people with schizophrenia during clinical assessments. Early cognitive assessment is quite important for rehabilitation planning and the social participation of individuals. Therefore, shorter, less time-consuming and more effective assessments are needed to screen for cognitive difficulties in patients with schizophrenia. The aim and findings of our study provide valuable contributions to the literature due to the limited number of studies in this respect. In addition, including outpatients with schizophrenia followed at a community mental health centre regularly and assessing the relationship between cognitive functions and clinical symptoms are the differences of the study.

CONCLUSION

MoCA was more sensitive in detecting cognitive impairment compared to the MMSE in that study, consistent with previous literature. Considering its ease of use, short administration time, and relevance to clinical practice, clinicians may consider using the MoCA in screening cognitive impairment in schizophrenia in daily practice. Incorporating MoCA as a brief screening tool in follow-up examinations of individuals with schizophrenia may improve the detection of cognitive impairments and may facilitate treatment and rehabilitation planning. It will be important to compare the MoCA with a comprehensive neuropsychological battery in future studies.

Conflicts of interest: The authors declare that they have no conflict of interest.

Correspondence address: Asst. Prof. Selma Ercan Doğu , Sağlık Bilimleri Üniversitesi Hamidiye Sağlık Bilimleri Fakültesi Ergoterapi Bölümü Selimiye Mah. Tıbbiye Cad. No: 38 34668 Üsküdar İstanbul 34668 İstanbul - Türkiye selmaer@yahoo.com

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Predictability of depression by plasma low-grade inflammatory markers in the background of pediatric celiac disease

Pediatrik çölyak hastalığı zemininde plazma düşük dereceli inflamatuvar belirteçlerle depresyonun öngörülebilirliği

Ayşegül Efe[1], Ayşegül Tok[2]
[1]M.D., University of Health Sciences, Dr. Sami Ulus Maternity, Children's Health and Diseases Training and Research Hospital, Department of Child and Adolescent Psychiatry, Ankara, Turkey, https://orcid.org/0000-0003-4507-6511
[2]M.D., University of Health Sciences, Dr. Sami Ulus Maternity, Children's Health and Diseases Training and Research Hospital, Department of Child Hepatology, Gastroenterology and Nutrition, Ankara, Turkey, https://orcid.org/0000-0002-7095-8121

SUMMARY

Objective: Previous hypothesis on the predictability of either psychopathological or chronic metabolic disorders by complete blood count (CBC)-derived, low-grade peripheral inflammatory indicators should be considered with caution given the discrepancies in earlier findings. We aimed to examine the predictability of depression with low-grade inflammatory indices in a background of celiac disease (CD) and the association with gluten-free diet compliance by a case-control study in a pediatric sample.**Method:** A total of 59 children with a biopsy-proven CD were mainly compared with 40 controls in terms of depression and anxiety symptoms, as well as global functionality and CBC-derived indices which the previous studies focused on. Laboratory findings and psychiatric symptoms were examined through subgroups by either depression or gluten-free diet (GFD) compliance. **Results:** Prevalence of depression was 34% in the celiac group and there was a perpetual association of depression with CD. However, none of the CBC-derived indices investigated in earlier studies of either depression or CD was found to be differed by the presence of CD, depression, or status of GFD compliance. **Discussion:** Despite the presence of strong evidence for the role of inflammation on the prevalent comorbidity of depression with CD, the impact of inflammation on the depression-CD relationship was not demonstrated on these subjected markers which have been previously recommended as good indicators of systemic inflammation, however, with a low level of evidence and contradictory findings on predicting inflammation. The predictability of psychiatric and metabolic outcomes based on chronic inflammatory conditions with these CBC-derived indices requires further investigation.

Key Words: celiac disease, depression, neutrophil/lymphocyte ratio, PLR, MPV, inflammatory markers

ÖZET

Amaç: Kronik inflamasyonla seyreden tıbbi durumlara ikincil depresyonda, tam kan sayımına dayalı düşük-dereceli periferik inflamatuvar belirteçlerin tanısal öngörü niteliğine yönelik öncül hipotezleri inceleyen çalışmalarda çelişen bulgular saptanmıştır. Bu doğrultuda, düşük dereceli inflamatuvar belirteçlerin depresyon ve glütenden-kısıtlı diyetle olan ilişkisini çölyak hastalığı zemininde değerlendirerek belirteçlerin öngörülebilirliğinin araştırılması amaçlanmıştır. **Yöntem:** Biyopsi ile kanıtlanmış Çölyak hastalığı tanılı 59 çocuk ve genç, önceki çalışmaların odaklandığı düşük dereceli inflamatuvar indekslerin yanı sıra global işlevsellik düzeyleri, depresyon ve anksiyete semptomları açısından yaş ve cinsiyet bakımından eşleştirilmiş 40 kontrolle vaka-kontrol deseninde alt-grup analizleri ile karşılaştırılmıştır. **Bulgular:** Çölyak grubunda depresyon prevalansı %34'idi. Depresyon veya çölyak hastalığıyla ilgili daha önceki çalışmalarda odaklanılan düşük dereceli inflamatuvar belirteçlerin hiçbirisinin çölyak varlığı ve/veya depresyon komorbiditesi veya glütensiz diyet uyumu açısından değişkenlik göstermediği bulunmuştur. **Sonuç:** Çölyak hastalığı ile depresyonun yaygın komorbiditesi üzerinde inflamasyonun rolüne ilişkin güçlü kanıtlar bulunmasına rağmen, inflamasyonun depresyon-çölyak ilişkisi üzerindeki etkisi, önceki çalışmalarda düşük kanıt düzeyi ve çelişkili bulgulara rağmen sistemik inflamasyonun iyi göstergeleri olarak önerilen bu belirteçler üzerinden güncel bulgularla gösterilememiştir. Bahsi geçen belirteçlerin metabolik hastalıkların psikopatolojik sonuçlarını öngörme potansiyellerine yönelik düşük kanıt düzeyine işaret eden bulgular desteklenmiştir. Düşük dereceli inflamatuvar indekslerin kronik inflamatuvar koşullara dayalı psikiyatrik ve metabolik sonuçları öngörülebilirliğine yönelik daha fazla araştırma gerektiği görülmüştür.

Anahtar Sözcükler: Çölyak hastalığı, depresyon, nötrofil/lenfosit oranı, PLR, MPV, inflamatuvar belirteçler

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INTRODUCTION

Celiac disease (CD) is a chronic inflammatory condition of the small intestine induced by an immune reaction against dietary gluten in individuals with a genetic predisposition. However, it is a multisystem disorder with not only gastrointestinal but also extra-intestinal manifestations such as further hematological, endocrinological, immunological, and several neuropsychiatric consequences. Higher rates of major depression, suicide, anxiety disorders, and eating disorders were reported in earlier studies of either adult or pediatric CD (1-3). The vast majority of present evidence is particularly concentrated on depression and anxiety comorbidities in youth with CD, as well as amelioration with good adherence to the gluten-free diet (GFD) (4, 5). However, previous studies of CD have reported prevalence rates of depression with a wide variability of 6-69% (2, 5). Furthermore, the detection of similar rates of depression and anxiety comorbidities in inflammatory bowel disease as in CD (6) raises a debate as to whether the pathophysiological relationship between different psychiatric disorders and chronic inflammation is nonspecific.

Based on the data regarding chronic stress-associated disturbances in the central nervous system and immune system, an increase in plasma neutrophil-to-lymphocyte ratio (NLR) has been widely recommended as a useful index of ongoing systemic inflammation and relevant immune alterations in recent studies of several chronic metabolic and oncologic disorders, including CD and lymphoma (7, 8). Not only NLR, but also several other complete blood count (CBC)-derived indices such as platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), red blood cell distribution width-to-lymphocyte (RDW/L), etc. have previously been reported in the literature of CD (8, 9). Moreover, some of the subjected CBC-derived indices have also been recommended as potential biologic indicators of the low-grade inflammatory process in several psychiatric conditions such as ADHD, suicidal behavior, schizophrenia, bipolar disorder, and opioid use disorder, as well as major depression and anxiety disorders (10-17).

The aforementioned indicators have been widely investigated in terms of their nonspecific diagnostic value on systemic inflammation and dietary compliance in CD. However, to the best of our knowledge, there is no data regarding the association of CBC-derived low-grade inflammatory biomarkers such as MPV, NLR, PLR, etc. with celiac-related prevalent psychiatric outcomes, especially such as depression, which may best exhibit their real predictability of either psychiatric or metabolic disturbances, potentially based on ongoing inflammation and relevant immune alterations. In this study conducted with a pediatric sample, we hereby aimed to investigate the aforementioned hypothesis regarding the predictability of psychiatric outcomes of chronic inflammation and relevant immune alterations with those CBC-derived, low-grade peripheral inflammatory indices, via examining the relationship of these biological parameters with depression comorbidity in the background of a chronic inflammatory condition such as CD. Additionally, we further investigated the cross-sectional impact of GFD compliance on both depressive symptoms and CBC-derived indices to examine the previous evidence on the ameliorative potential of psychopathological outcomes with GFD status.

METHOD

Study design and sample collection

A total of 78 children with biopsy-proven CD (8-18 years old) who were newly diagnosed or had been followed up in the pediatric gastroenterology outpatient clinic were referred to child and adolescent psychiatry for psychiatric screening within the last season (during autumn 2021), in line with legal custodian's and self-consent. Diagnosis of CD was verified by duodenal biopsies compatible with Marsh-destructive type (Marsh-type 3) in clients with positive celiac-related autoantibodies. The patients were excluded according to criteria such as having additional medical or psychiatric disorders other than CD and depression; a known previous hematological abnormality in the complete blood count (CBC) like anemia/polycythemia, lymphopenia/lymphocytosis, neutropenia/neutrophilia, or thrombocytopenia/thrombocytosis; any use of medication within last three months

before blood sampling; obesity [body mass index (BMI) > 30 kg/m^2]; and a history of smoking. Some of the patients with CD (n: 19) were excluded from the study after referral to psychiatry for reasons which could affect the laboratory results, such as having additional systemic disorders or previous psychiatric diagnoses and current use of any medication in the last three months. As a result, 59 children with CD were included in the study as the 'celiac group' and compared with opponents (n: 40) in the 'control group', who had neither a systemic nor a psychiatric disorder. The groups were primarily compared in terms of demographic features, scale-scores of depression and anxiety symptoms, as well as the aforementioned hematological indices and relevant ratios being recommended as low-grade inflammatory markers including MPV, NLR, and PLR, as the first step of the analysis (Table 1 and 2).

Psychiatric assessments consisted of a semi-structured clinical interview and child-self-reports. The presence or absence of psychiatric symptoms was hereby verified by a face-to-face clinical interview with both children and their parents to determine each participant's inclusion or exclusion. The psychiatrist then prepared a narrative summary report describing individual psychiatric symptoms and DSM-5 diagnoses with the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version, DSM-5 November 2016, Turkish Version (K-SADS-PL-DSM-5-T). In the second step of the analysis, the patients in the 'celiac group' were allocated according to the existence of depression comorbidity based on the clinical interview. The patients with depression (celiac+depression group) were compared in terms of hematological indices and relevant inflammatory markers with the patients without depression (celiac-depression group) and with the control group (Table 3). In the third step of the analysis, the patients in the 'celiac group' were allocated according to their diet compliance. The patients with higher anti-tissue transglutaminase (anti-tTg) IgA and anti-tTg IgG, as well as those reporting poor adherence to GFD (as if the transgression number was > 2 per month) within the last three months were determined as 'GFD- group', whereas the patients with lower antibodies and good adherence were determined as 'GFD+ group'. In between-group analyses, depression and anxiety scores, as well as inflammatory markers, were compared between each subgroup and the control group (Table 4).

Laboratory procedures

The current hematological and celiac-related nutritional parameters [including complete blood count (CBC), C-reactive protein (CRP), vitamin B12, vitamin D, folate, iron, ferritin, and thyroid function tests (TSH and sT4)] were recorded for all patients as part of their routine clinical management. The acute phase reactants (CRP and ferritin) were especially included in this study to exclude an acute infection that may affect whole blood cell counts. Blood samples were drawn without stasis in the early morning hours, following fasting for more than 12 hours and abstinence of any heavy exercise in the previous 3 days, within last autumn 2021. CBC and other biochemical tests were determined from venous blood samples using a Beckman Coulter Gen S hematology analyzer. CD patients and controls were checked for serum celiac-related autoantibodies, including anti-tTg IgA, anti-tTg IgG, and IgA. As for the verification of CD at the first diagnosis process, the patients with CD also underwent an upper gastrointestinal endoscopy process with multiple biopsies, both from the bulb and distal duodenum. Duodenal lesions were reported according to the Marsh-Oberhuber classification, and a vast majority of the cases had commonly destructive type lesions (Marsh 3b).

Measures

Demographic data, including psychiatric and medical history of both children and parents, were all reported by parents using a form designed by the authors. Socioeconomic status (SES) was determined due to the Hollingshead-Redlich Index (HRI) which allows the social status of each individual to be determined by categorizing their occupation and education into three main categories, such as low (HRI: 0-22), moderate (HRI: 23-44) and high SES (HRI: 45-66).

The K-SADS-PL-DSM-5-T, which is a semi-structured clinical interview, was administered individu-

ally to screen psychiatric diagnosis and comorbidities. The Clinical Global Impression Scale-Severity Score [CGI-S (scoring from '1/normal' to '7/extremelly ill')] and the Children's Global Assessment Scale [C-GAS (scoring from '0/severe impairment' to '100/superior functioning')] were administered by clinicians routinely for a global assessment of the current functioning of the clients.

Children's Depression Inventory (CDI); which is a 27-item, self-rated inventory with each item scored on a 3-point scale (total score: 0-54), was used to determine the severity of depressive symptoms of all participants in this study. The CDI has been designed to measure the assessment of cognitive, affective, and behavioral symptoms of depression in children and adolescents aged between 7 and 17 years. The cut-off score for depression was reported as 19.

Screen for Child Anxiety and Related Disorders (SCARED) – Child Form, which is a 41-item, self-rated inventory with each item scored on a 3-point scale from 0 to 2 (total score: 0-82) and provides a multidimensional assessment for different types of anxiety disorders with a cut-off score of 25 and above, was used to screen the anxiety symptoms in this study. Patients with a diagnosis of any anxiety disorder were excluded from the study according to diagnosis based on clinical interviews.

Current anthropometry with weight and height was evaluated and we obtained the body-mass index (BMI).

Ethics

The research protocol was approved by the local ethics committee (ethics committee decision date: 26.07.2021, decision number: 116/23) and was in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants and their parents/legal custodians prior to the beginning of data collection.

Data Analysis

All statistical analyses were performed with the Statistical Package for the Social Sciences (SPSS), Version 22.0 (SPSS Inc., Chicago, IL, USA). The Shapiro-Wilk test was performed to assess the normality of the distribution of continuous data. Descriptive statistics were presented as numbers and percentages [n (%)] or mean ± standard deviation, which demonstrated the demographic and clinical characteristics and laboratory findings. A Pearson chi-square test (x^2) was performed on categorical variables, while a Mann-Whitney U-test (Z) or Kruskal-Wallis (KW) test was performed on continuous variables to explore group differences. Post hoc tests were also used to identify differences among multiple groups, along with a Bonferroni correction for each test to reduce type I errors. The Bonferroni adjustments in the between-group analysis were demonstrated as 'p^1, p^2, and p^3' for the analysis according to groups by depression and 'p^a, p^b, and p^c' for the analysis according to groups by GFD compliance (look at footnotes of Table 3 and 4). In the post hoc analysis, the '$p \leq 0.017$' indicates statistical significance after the Bonferroni adjustment. The p-values were based on two-tailed tests with $\alpha = 0.05$.

RESULTS

The findings regarding the comparison of demographic and clinical data between the patients in the celiac group (n: 59) and control group (n: 40) were summarized in Table 1. The mean age of the entire sample was '12.5 ± 0.36 years', with adolescents (≥ 12 years old) constituting the vast majority (approximately 61%). There was no difference between celiac and control groups in terms of age,

Table 1. Demographic data of celiac and control groups.

Variables	Celiac Group (n: 59)	Control Group (n: 40)	Chi-Square (df) or Z	*p*
Age (month)	149.98 – 4.28	151.68 – 4.81	- 0.225	0.822
Age group [Child group (< 12-year-old)]	26 (44.1)	12 (30)	1.99 (1)	0.158
Gender [male]	23 (39)	10 (25)	2.09 (1)	0.148
Education:			0.26 (2)	0.879
-Primary school	10 (16.9)	6 (15)		
-Secondary school	25 (56.8)	19 (47.5)		
-High school	24 (40.7)	15 (37.5)		
Family structure:			0.002 (1)	0.967
-Nuclear family	43 (72.9)	29 (72.5)		
-Others:				
Extended family	12 (20.3)	1 (2.5)		
Separated /Divorced parents	4 (6.8)	4 (10)		
Death parent(s)	0 (0)	6 (15)		
SES (HRS):			12.56 (2)	0.002
-Low (HRS ?22)	34 (57.6)	11 (27.5)		
-Moderate (HRS 23-44)	22 (53.7)	19 (47.5)		
-High (HRS ?45)	3 (5.1)	10 (25)		
Mothers				
Age (year)	38.2 – 0.61	39.8 – 0.77	-1.4	0.164
Education (year)	8.24 – 0.4	12.1 – 0.44	-5.48	<0.001
Fathers				
Age (year)	42.3 – 0.87	43.1 – 0.9	-1.2	0.233
Education (year)	9.8 – 0.4	12.1 – 0.47	-3.9	<0.001
History of parents psychiatric disorders	11 (18.6)	4 (10)	1.38 (1)	0.239
History of parents physical disorders	21 (35.6)	10 (25)	1.24 (1)	0.265

Note: n (%): number of the participants with frequencies in parenthesis, SES: socioeconomic status, HRI: Hollingshead-Redlich Index.
Data presented as mean – SD, or the number of clients along with frequencies. Mann Whitney U (Z) and Chi-Square Tests for comparison of groups. Values in parenthesis indicate degrees of freedom (df).
$p < 0.05$: statistically significant and the significant values are in bold.

age-groups (child or adolescent), gender, education, or family structure. The only notable findings in the demographic data were the differences in SES and the education levels of each parent; all of them were prone to be lower in the celiac group than the controls.

There was no difference between the celiac- and control groups in terms of prominent inflammatory markers such as NLR, PLR, and MPV, as well as most other hematological indices (Table 2). The BMI was lower in the celiac group, without supporting the existence of malnutrition. The data regarding the between-group analysis of the psychiatric scales are summarized in Table 2. The most notable findings were the higher scores of CDI and poor global functioning in the celiac group than opponents.

According to the structured clinical interview, depression was diagnosed in 34% (n: 20) of the celiac group. The comparison of clinical data among three groups, consisting of the CD patients with depression comorbidity, the depression-free CD patients, and the controls, was summarized in Table 3. While there was no difference in the comparison of the ages and age groups, there was a difference in gender distribution (p = 0.03). The female prevalence (80%) was higher in patients with celiac and depression. The groups differed only in TSH (KW: 7.2, df: 2, p = 0.027) and neutrophil levels (KW: 6.1, df: 2, p = 0.047) in terms of laboratory findings. However, the difference between each group disappeared after the Bonferroni adjustment in either TSH (p^2 = 0.095, p^3 = 0.058) or neutrophil levels (p^3 = 0.05). According to the comparison of psychiatric scales, the global functioning was detected as being in a worse state and particularly affected by the presence of depression comorbidity (G-GAS: p^1 = 0.011, p^2 < 0.001, and p^3 < 0.001; CGI-S: p^1 < 0.001, p^2 < 0.001, and p^3 = 0.855). Both of the depression (CDI: p^1 < 0.001, p^2 < 0.001, and p^3 = 1.00) and anxiety (SCARED: p^1 < 0.001, p^2, = 0.002 and p^3 = 1.00) scores were significantly higher in the patients with comorbid depression, even when the patients with any anxiety disorder were excluded.

When the patients with CD were assessed due to their cross-sectional status of GFD compliance based on self-reports, parent-proxy-reports, and current levels of antibodies, two sub-groups consisted of the patients with good adherence to GFD (n: 36) and the others with less adherence to GFD (n: 23). The groups did not differ in terms of age, age groups, and gender (Table 4). The patients without GFD compliance had lower levels of hemoglobin (KW: 8.33, df: 2, p = 0.016) and hematocrit (KW: 8.9, df: 2, p = 0.011). However, the differences between groups disappeared after the Bonferroni correction in post hoc analysis (p^a = 0.019 and p^b = 0.045 for hemoglobin; p^a = 0.011 and p^b = 0.053 for hematocrit). Moreover, the three groups did not differ in terms of iron and fer-

Table 2. Laboratory findings and psychiatric parameters of celiac and control groups

Variables	Celiac Group (n: 59)	Control Group (n: 40)	Chi-Square (df) or Z	*p*
Body mass index (BMI, kg/m2)	19.16 – 0.57	20.82 – 0.62	-2.13	0.033
C-GAS	46.27 – 2.25	79.5 – 1.63	-7.68	<0.001
CGI-S	2.69 – 0.25	1.28 – 0.07	-4.025	<0.001
CDI	14.78 – 1.65	7.78 – 0.91	-2.594	0.009
SCARED	9.5 – 1.25	6.83 – 0.86	-0.934	0.35
Celiac-related autoantibodies				
Anti-Tt IgA (U/mL)	79.5 – 14.5	1.87 – 0.25	- 6.44	<0.001
Anti-Tt IgG (U/mL)	25.1 – 7.65	2.48 – 0.34	- 3.5	<0.001
IgA (U/mL)	134.85 – 8.36	134.68 – 11.95	- 0.66	0.507
Acute-phase reactants				
C-reactive protein (CRP, mg/L)	1.98 – 0.11	1.79 – 0.17	- 1.09	0.274
Ferritin (ng/mL)	27.88 – 8.07	26.96 – 4.2	- 0.82	0.414
Serum vitamin levels				
Vitamin B12 (pg/mL)	384.71 – 16.41	351.63 – 15.24	- 1.39	0.163
Vitamin D (pg/mL)	16.15 – 0.81	18.7 – 1.15	- 1.9	0.057
Folate (pg/mL)	12.8 – 1.4	10.9 – 0.78	-0.67	0.500
Serum iron (mol/l)	75.9 – 4.44	77.17 – 5.86	- 0.09	0.923
Zinc (pg/mL)	755.77 – 31.87	681.24 – 61.51	- 1.47	0.142
Thyroid function tests				
Thyroxine (t4)	1.182 – 0.02	1.18 – 0.021	- 0.12	0.906
TSH	2.44 – 0.13	2.05 – 0.2	- 2.67	0.007
Complete blood count (CBC)				
Hemoglobin (g/dL)	13.58 – 0.15	13.8 – 0.16	- 0.93	0.352
Hematocrit (%)	40.35 – 0.38	41 – 0.46	- 0.72	0.471
White blood cells (/ L)	6.87 – 0.23	7.84 – 0.34	- 2.32	0.02
Neutrophil (/ L)	3.7 – 0.22	4.52 – 0.29	- 2.43	0.015
Lymphocyte (/ L)	2.46 – 0.1	2.6 – 0.13	-0.75	0.454
Platelet (/ L)	297.24 – 10.53	283.55 – 8.79	-1.03	0.304
Mean platelet volume (fL)	11.4 – 1.48	10.16 – 0.14	-0.84	0.399
Basophil (/ L)	0.052 – 0.017	0.041 – 0.001	-2.29	0.022
Eosinophil (/ L)	0.167 – 0.021	0.137 – 0.014	-0.354	0.724
Monocyte (/ L)	0.611 – 0.089	0.541 – 0.029	-0.61	0.524
CBC-related ratios				
NLR (neutrophil / lymphocyte ratio)	1.81 – 0.21	1.92 – 0.17	-1.54	0.123
PLR (platelet / lymphocyte ratio)	133.015 – 8.743	118.65 – 6.25	-0.88	0.377
BLR (basophil / lymphocyte ratio)	0.024 – 0.009	0.017 – 0.001	-1.75	0.08
MLR (monocyte / lymphocyte ratio)	0.267 – 0.034	0.226 – 0.016	-0.25	0.803
ELR (eosinophil / lymphocyte ratio)	0.078 – 0.014	0.053 – 0.004	-0.834	0.404

Note: CGI-S: Clinical Global Impression Scale Severity Scores, C-GAS: Children s Global Assessment Scale, CDI: Children s Depression Inventory, SCARED: Screen for Child Anxiety and Related Disorders. Anti-Tt IgA: Tissue transglutaminase immunoglobulin A antibody level, Anti-Tt IgG: Tissue transglutaminase immunoglobulin G antibody level, Ig A: Immunoglobulin A level, TSH: Thyroid-stimulating hormone.
Data presented as mean – SD. Mann Whitney U (Z) and Chi-Square Tests for comparison of groups. Values in parenthesis indicate degrees of freedom (df).
p < 0.05: statistically significant and the significant values are in bold.

Table 3. Comparison of clinical data, notable laboratory findings, and psychiatric parameters between the celiac+ depression, celiac-depression, and control groups.

Variable	Celiac+depression Group (n: 20)	Celiac-depression Group (n: 39)	Control Group (n: 40)	Chi-Square or KW (df)	p
Age (month)	152.35 – 6.9	148.77 – 5.5	151.68 – 4.81	0.31 (2)	0.854
Age group [Child group]	7 (35)	19 (48.7)	12 (30)	3 (2)	0.218
Gender [male]	4 (20)	19 (48.7)	10 (25)	7 (2)	0.03
BMI (kg/m2)	18.34 – 0.78	19.57 – 0.76	20.82 – 0.62	5.45 (2)	0.066
C-GAS	32.75 – 2.75	53.21 – 2.46	79.5 – 1.63	67,4 (2)	<0.001
CGI-S	4.95 – 0.27	1.54 – 0.15	1.28 – 0.07	55.4 (2)	<0.001
CDI	30.55 – 1.8	6.7 – 0.64	7.78 – 0.9	46.4 (2)	<0.001
SCARED	16.8 – 2.7	5.74 – 0.8	6.83 – 0.86	17.4 (2)	<0.001
Anti-Tt IgA (U/mL)	85.5 – 22.9	76.4 – 18.7	1.87 – 0.25	42.7 (2)	<0.001
Anti-Tt IgG (U/mL)	28.1 – 15.2	23.5 – 8.7	2.48 – 0.34	12.48 (2)	0.002
MPV (fL)	14.35 – 4.35	9.89 – 0.15	10.16 – 0.14	1.28 (2)	0.526
NLR	2.02 – 0.51	1.69 – 0.2	1.92 – 0.17	2.4 (2)	0.298
PLR	135.8 – 18.9	131.57 – 9.2	118.65 – 6.25	0.78 (2)	0.676
BLR	0.016 – 0.003	0.027 – 0.014	0.017 – 0.001	3.5 (2)	0.171
MLR	0.275 – 0.049	0.26 – 0.045	0.226 – 0.016	0.16 (2)	0.922
ELR	0.075 – 0.021	0.08 – 0.019	0.053 – 0.004	0.72 (2)	0.697

Note: CGI-S: Clinical Global Impression Scale Severity Scores, C-GAS: Children s Global Assessment Scale, CDI: Children s Depression Inventory, SCARED: Screen for Child Anxiety and Related Disorders, BMI: Body mass index, Anti-Tt IgA: Tissue transglutaminase immunoglobulin A antibody level, Anti-Tt IgG: Tissue transglutaminase immunoglobulin G antibody level, Ig A: Immunoglobulin A level, MPV: Mean platelet volume, NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio, BLR: basophil/lymphocyte ratio, MLR: monocyte/lymphocyte ratio, ELR: eosinophil/lymphocyte ratio.
n (%): number of the participants with frequencies in parenthesis. Data presented as mean – SD. Kruskal-Wallis (KW) and Chi-Square Tests for comparison of groups. Values in parenthesis indicate degrees of freedom (df). **p <** 0.05: statistically significant and the significant values are in bold.
When the p-value was found to be smaller than the adjusted p-value (0.017) by the Bonferroni correction in post hoc analysis, it was considered to be significant. p,: p-values of the difference between celiac+depression and celiac-depression groups, p†: p-values of the difference between celiac+depression and control groups, p‡: p-values of the difference between celiac-depression and control groups after the Bonferroni adjustment.

Table 4. Comparison of clinical data, notable laboratory findings, and psychiatric parameters between GFD-, GFD+ and control groups

Variable	GFD- group (n:23)	GFD+ group (n:36)	Control group (n:40)	x^2 or KW (df)	*p*
Age (month)	140.9 ± 7.2	155.8 ± 5.15	151.68 ± 4.81	3.44 (2)	0.178
Age group [Child group]	12 (54.5)	14 (37.8)	12 (30)	3.623 (2)	0.163
Gender [male]	8 (34.8)	15 (41.7)	10 (25)	2.4 (2)	0.302
BMI (kg/m2)	16.8 ± 0.5	20.7 ± 0.8	20.8 ± 0.6	16.9 (2)	<0.001
C-GAS	42.6 ± 3.06	48.6 ± 3.1	79.5 ± 1.63	59.9 (2)	<0.001
CGI-S	2.96 ± 0.38	2.53 ± 0.33	1.28 ± 0.07	18.6 (2)	<0.001
CDI	17.43 ± 3.3	13.08 ± 1.7	7.78 ± 0.91	6.85 (2)	0.033
SCARED	10.52 ± 2.44	8.83 ± 1.35	6.83 ± 0.86	1.3 (2)	0.518
Anti-Tt IgA (U/mL)	195.04 ± 20.6	5.68 ± 0.89	1.87 ± 0.25	65 (2)	<0.001
Anti-Tt IgG (U/mL)	54.14 ± 18.06	6.55 ± 1.7	2.48 ± 0.34	23 (2)	<0.001
MPV (fL)	13.3 ± 3.8	10.2 ± 0.12	10.16 ± 0.14	4.8 (2)	0.091
NLR	1.83 ± 0.44	1.79 ± 0.21	1.91 ± 0.17	2.59 (2)	0.273
PLR	146.7 ± 15.1	124.2 ± 10.5	118.65 ± 6.25	2.15 (2)	0.342
BLR	0.04 ± 0.023	0.013 ± 0.001	0.017 ± 0.001	6.03 (2)	0.049
MLR	0.26 ± 0.041	0.274 ± 0.049	0.226 ± 0.016	0.27 (2)	0.871
ELR	0.075 ± 0.02	0.08 ± 0.02	0.053 ± 0.004	0.8 (2)	0.667

Note: CGI-S: Clinical Global Impression Scale – Severity Scores, C-GAS: Children's Global Assessment Scale, CDI: Children's Depression Inventory, SCARED: Screen for Child Anxiety and Related Disorders, BMI: Body mass index, Anti-Tt IgA: Tissue transglutaminase immunoglobulin A antibody level, Anti-Tt IgG: Tissue transglutaminase immunoglobulin G antibody level, Ig A: Immunoglobulin A level, MPV: Mean platelet volume, NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio, BLR: basophil/lymphocyte ratio, MLR: monocyte/lymphocyte ratio, ELR: eosinophil/lymphocyte ratio.
n (%): number of the participants with frequencies in parenthesis. Data presented as mean ± SD. Kruskal-Wallis (KW) and Chi-Square Tests (x^2) for comparison of groups. Values in parenthesis indicate degrees of freedom (df). $p < 0.05$: statistically significant and the significant values are in bold.
When the p-value was found to be smaller than the adjusted p-value (0.017) by the Bonferroni correction in post hoc analysis, it was considered to be significant. p^a: p-values of the difference between GFD- and GFD+ groups, p^b: p-values of the difference between GFD- and control groups, p^c: p-values of the difference between GFD+ and control groups after the Bonferroni adjustment.

ritin levels, as well as other vitamin levels, which may show the absence of iron deficiency or malnutrition in the patients with poor diet adherence. TSH levels tended to be higher in the patients of the GFD- group (KW: 7.6, df: 2, p = 0.022), despite the fact that the clients having thyroid function abnormalities were excluded from the study, however without considering the subclinical thyroid-related disorders. The difference in TSH disappeared after Bonferroni adjustment (p^a = 1.00, p^b = 0.036, p^c = 0.112), as being also in the comparison of platelet levels (KW: 6.6, df: 2, p = 0.036, p^a = 0.041, p^b = 0.055, p^c = 1.00) and basophile levels (KW: 7.8, df: 2, p = 0.02, p^a = 0.322, p^b = 1.00, p^c = 0.017). BMI scores were different between groups even after Bonferroni adjustment (p^a = 0.001, p^b < 0.001, p^c = 1.00).

As for the comparison according to psychiatric scales; CGAS (p^a = 0.955, p^b < 0.001, p^c <0.001) and CGI-S (p^a = 0.371, p^b =0.012, p^c <0.001) levels were differed between groups, however similar between GFD- and GFD+ groups. As for the most notable point in Table 4, CDI (p^a = 1.00, p^b = 0.074, p^c = 0.094) scores differed among the three groups, however, the difference disappeared between the two-group-analysis with Bonferroni correction.

DISCUSSION

The role of inflammation in the etiology of major depression has been investigated in numerous studies conducted in both children and adults, and many inflammation biomarkers were found to be significantly higher in the depressed group, which was also associated with the severity of depression. In this context, NLR, PLR, and MPV were found to be the most studied markers (17-25). These markers have been recommended as useful in the evaluation of inflammation and relevant immune alteration in chronic disorders due to their low cost and high diagnostic power. Therefore, investigating the plausible role of inflammation in the underlying pathogenesis of depression, via an assessment using the subjected peripheral inflammatory markers in the background of a chronic inflammatory condition such as CD in a pediatric sample, was planned with the current study.

The most prominent findings of the intergroup analysis were the perpetual association of depression with having CD, however no association with either CBC-derived, low-grade inflammatory indices or the status of GFD compliance. Depression was found at a rate of 34% in the celiac group with the structured diagnostic interview, and a significant relationship was observed between celiac disease and depression-severity (CDI) scores compared to the controls. However, previous evidence about a triple link mediated by inflammatory/immune processes on the CD-depression association could not be affirmed by investigating the impact of inflammation and related-immune alterations on the common pathogenesis of CD and

depression through the subjected low-grade inflammatory indices. Many other CBC-derived inflammatory parameters examined in previous studies were also included in this study. However, none were found to be changing with the presence of CD, depression, or poor GFD compliance.

The depression scores (CDI) were found to be higher in the group of patients with poor GFD compliance, but intergroup differences disappeared in post hoc analysis. Therefore it can be stated that the GFD compliance status did not affect the celiac-depression relationship. However, several contrary pieces of evidence on the impact of diet adherence were demonstrated in previous studies. In a recent longitudinal examination regarding the impact of GFD on altered inflammatory markers in CD, a significant increase in neutrophil, MPV, and NLR values with GFD after one-year follow-up was reported, and the authors indicated that NLR may be a promising marker in predicting GFD compliance in patients with CD (26). However, the GFD compliance status we examined in the present study was evaluated by a cross-sectional way, and it would be better to look at it with a longitudinal study design to fully understand its clinical and psychological implications.

In a recent clinical survey (nationwide and population-based cohort) on psychiatric disorders in CD (27), it was stated that childhood CD is associated with an increased risk of subsequent psychiatric disorders, which persists into adulthood, and the authors emphasized the importance of the integration of mental health surveillance in the care of CD (27, 28). The authors reported that psychiatric disorders were more common before the diagnosis of CD, and the overall risk for psychiatric disorders was highest in the first year after the diagnosis of CD, which might be associated with excess inflammation (27). Moreover, the majority of the patients presented with psychiatric diagnoses before the diagnosis of CD that might be related to systemic inflammation initiating before CD (1,27,28). Despite the presence of strong evidence for the role of chronic inflammation in the underlying mechanisms of the prevalent comorbidity of depression with CD, we could not affirm the subjected evidence by examining the impact of chronic inflammatory processes and relevant immune alterations through CBC-derived indices such as NLR, PLR, and MPV, which have been persistently suggested as diagnostic or prognostic biological indicators of variable psychiatric and chronic metabolic disorders.

Given the significant evidence from a twin-family study (29), demonstrating the wide variation of NLR and PLR due to the effects of age, sex, and environmental factors such as seasonal conditions and lifestyles, as well as heritability, discrepancies in the findings regarding the association of each marker with medical or psychiatric disorders make sense. On the other hand, in a recent study investigating NLR, MPV, and PLR in adolescents with depression (23), a significantly higher NLR, with no difference in PLR comparison, than those of the controls was demonstrated, even after adjusting for other covariates such as age, sex, BMI, and the severity of depression. However, no findings regarding acute phase reactants were demonstrated in that study, confirming the exclusion of any other systemic inflammation.

As for more evidence regarding depression-related alterations in the peripheral inflammatory process and cellular immunity, a significant relationship (even a positive correlation in some) between depression severity and different types of subclinical inflammatory markers such as NLR, PLR, MLR, MPV, etc. was reported in several recent studies (17-25). Other psychiatric disorders such as obsessive-compulsive disorder (19,30), bipolar disorder (25,31), anxiety disorders (32), etc. are other psychiatric conditions where the aforementioned low-grade inflammatory markers have been investigated. On the other hand, the wide range of associations between these markers and a variety of psychiatric conditions may also demonstrate the non-specificity of those relationships. It should be noted that the acute-phase reactants were not included in the majority of the studies on the subject; simply a statement about the exclusion of the inflammatory diseases was instead reported in most of their methods. Additionally, there were some other limitations in previous investigations, such as not controlling results for covariates that could influence inflammatory status, such as menstrual cycle, eating habits, physical activity, etc. The positive relationship between the inflammatory markers

indicated in these studies and the lack of these parameters makes it hard to be sure that systemic inflammation from other causes has been properly ruled out.

Besides all these, the CD is defined as a common cause of various hematological disorders such as anemia, including either iron, folate, or pernicious types in children. Hematological abnormalities may be associated with CD-based nutritional deficiency of folate, vitamin B12, and copper (33). These hematological changes, which have been explained by a variety of factors related to the natural course of the disease in CD, make it difficult to investigate the effects of inflammation-related mechanisms in the psychopathological tendencies of the celiac background and may explain the discrepancies in the literature. All these differences in our findings may be due to sample composition. Current findings may contribute a shed of distinct evidence to the literature regarding the conflicting place of the qualitative use of these CBC-derived low-grade inflammatory indices in demonstration of the impact of systemic inflammation and related immune alterations on the underlying mechanisms of psychopathologies in chronic systemic disorders.

Besides several beneficial contributions and strong sides of the study design, such as verification of psychiatric diagnosis by structural interview, the inclusion of acute-phase reactants for demonstration of proper exclusion of any acute inflammation based on other sources; controlling the covariates which would potentially influence the findings of indices such as age and sex match between study groups; collecting blood samples by fixing several individuals (starving or exercise status) and conditional (in the same season and similar early morning times); as well as high results in power analysis (G-power), the findings should be considered in the context of the following limitations. First, the inclusion of only clinically referred clients with CD limited the generalizability of the interpretation of the findings. Second, the cross-sectional design is limited to evaluating the real implications of diet-compliance on depressive symptoms, so further longitudinal evaluation on the alterations in depressive symptoms and severity could be better for investigating the real influences of GFD status. And last, another limitation is that ancillary markers to examine the role of inflammation were not included.

CONCLUSION

Despite the presence of strong evidence for the role of inflammation in the prevalent comorbidity of depression with CD, we could not confirm the impact of inflammation on the depression-CD relationship through those markers which have been widely recommended as good indicators of systemic inflammation, however, with a low level of evidence and contradictory findings on predicting inflammation. Further investigations, including other more proven biomarkers of chronic inflammation such as cytokines, etc., would be beneficial to compare with the findings relevant to subjected CBC-derived indices.

Conflicts of interest: The authors declare that they have no conflict of interest.

Correspondence address: M.D. Ayşegül Efe, Beştepeler Neigh., Alparslan Türkeş Street, No: 27, 06560 Ankara, Turkey
aysegulboreas@gmail.com

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RESEARCH ARTICLE

Intimate partner violence during the COVID-19 pandemic: An online survey

COVID-19 pandemisi sırasında yakın partner şiddeti: Çevrim içi bir araştırma

Ekin Sönmez Güngör[1], İmran Gökçen Yılmaz Karaman[2], Burcu Rahşan Erim[3], Hasibe Rengin Güvenç[4], Ceylan Ergül[5], Kerem Laçiner[6], Gamze Akçay Oruç[3], Fatmagül Dikyar Altun[3], Arzu Erkan[7], Gamze Erzin[8], Ebru Toprak[3], Yıldız Akvardar[9]

[1]M.D.,Department of Psychiatry, Erenköy Mental Health and Neurological Diseases Training and Research Hospital, Turkey, https://orcid.org/0000-0002-2874-4306
[2]Assist. Prof., Department of Psychiatry, Eskişehir Osmangazi University School of Medicine, Turkey, https://orcid.org/0000-0003-2821-7749
[3]M.D., Private Practice, Turkey, https://orcid.org/0000-0003-4145-8969, https://orcid.org/0000-0002-2444-6192, https://orcid.org/0000-0003-4753-5080
[4]M.D., Department of Psychiatry, Balıklı Greek Hospital, Turkey, https://orcid.org/0000-0002-4645-5479
[5]Assist. Prof., Department of Psychiatry, Üsküdar University School of Medicine,Turkey, https://orcid.org/0000-0001-6635-5195
[6]M.D., Department of Psychiatry, Sivas Numune Hospital, Turkey, https://orcid.org/0000-0001-8253-7933
[7]Assist. Prof., Department of Psychology, İstanbul Kültür University, Turkey, https://orcid.org/0000-0002-4127-7503
[8]Assoc. Prof., Department of Psychiatry, Dışkapı Training and Research Hospital, Turkey, https://orcid.org/0000-0001-8002-5053
[9]Prof. Dr., Department of Psychiatry, Marmara University School of Medicine, Turkey, https://orcid.org/0000-0002-9195-7371

SUMMARY

Objective: Intimate partner violence (IPV) against women is a human rights violation and a public health concern. The incidence of IPV increases in mass events such as epidemics. The aim of this study was to assess the nature and the extent of IPV among women in Turkey; to identify the associated factors, and mental health outcomes during the COVID-19 pandemic. **Method:**The study has a cross-sectional, descriptive design. An online self-report survey, based on World Health Organization guidance on epidemiological studies to assess IPV, was conducted among women between 09.01.2021 and 09.02.2021. The survey had 69 questions which covered sociodemographic characteristics, relationship history, types of violence and mental well-being. Inclusion criteria were being over the age of 18, and having a spouse/partner during the pandemic. Participation was on voluntary basis. 1372 women were included in the analysis. **Results:**Around a third (30.7%) of participants were exposed to any type of violence before the pandemic, with most common form being emotional violence, and this rate remained unchanged during the pandemic, despite the time spent with partners were expected to increase due to isolation measures. 61 women (4.4%), mostly university graduates living in cities, reported being subject to violence for the first time during the pandemic. 31.2% of them were cases of digital violence. Lower level of education, younger age and partner's alcohol and substance use was associated with IPV, and IPV was associated with poorer mental well-being. **Discussion:**Despite the public health measures taken during the pandemic (e.g. lockdowns), where women would have spent more time isolated with their partners, rates of IPV did not change from pre-pandemic to pandemic. This outcome needs to be compared with findings from other contexts. Strategies to prevent IPV is of utmost importance for the protection of mental well-being of women and the society during and after the pandemic.

Key Words: Women`s Health, Sexual Abuse, COVID-19, Domestic Violence, Intimate Partner Violence

ÖZET

Amaç: Kadınlara yönelik yakın partner şiddeti (YPŞ), bir insan hakları ihlali ve bir halk sağlığı sorunudur. YPŞ insidansı, salgın hastalıklar gibi toplumsal olaylarda artmaktadır. Bu çalışmanın amaçları, Türkiye'de COVID-19 pandemisi sırasında kadınlara yönelik YPŞ'nin niteliğini ve boyutlarını değerlendirmek; YPŞ ile ilişkili etkenleri ve ruh sağlığı açısından sonuçlarını belirlemektir. **Yöntem:** Kesitsel, tanımlayıcı desende bir araştırma planlanmıştır. Kadınlara yönelik YPŞ'yi değerlendirmek için Dünya Sağlık Örgütü'nün epidemiyolojik çalışmalara ilişkin rehberlerine dayanarak hazırlanan, çevrimiçi öz bildirime dayanan bir anket 09.01.2021 ve 09.02.2021 tarihleri arasında uygulanmıştır. Ankette sosyodemografik özellikler, ilişki geçmişi, şiddet türleri ve ruhsal iyilik halini kapsayan 69 soru bulunmaktadır. Çalışmaya dahil edilme kriterleri, 18 yaşından büyük olmak ve pandemi sırasında bir eş/partner sahibi olmak olarak belirlenmiş, katılım gönüllülük esasına dayandırılmıştır. Analize dahil edilen katılımcı sayısı 1372'dir. **Bulgular:** Katılımcıların yaklaşık üçte biri (%30,7) pandemi öncesinde herhangi bir tür YPŞ'ye maruz kaldığını belirtti. Bu oranda önlemler nedeniyle kadınların partnerleri ile daha fazla zaman geçirmeleri beklenen pandemi sırasında anlamlı bir değişiklik olmamıştır; ancak üniversite mezunu, şehirde yaşayan 61 (%4.4) kadının ilk kez pandemi döneminde YPŞ'ye maruz kaldığı görülmüştür. Bunların %31,2'si dijital şiddet olgularıdır. En sık YPŞ türü duygusal şiddet olarak bildirilmiştir. Düşük eğitim düzeyi, genç yaş ve partnerin alkol/madde kullanımı YPŞ ile ilişkili bulunmuştur. YPŞ'nin, düşük ruhsal iyilik hali skoru ile ilişkili olduğu belirlenmiştir.**Sonuç:** Bu araştırmada, karantina ve benzeri önlemler nedeniyle kadınların partnerleri daha fazla izole zaman geçirmeleri beklenen pandemi sırasında, YPŞ oranının pandemi öncesine göre değişkenlik göstermediği saptanmıştır. Bu sonucun diğer çalışmalardan elde edilen bulgularla karşılaştırılması gerekmektedir. YPŞ'yi önleme stratejileri, pandemi sırasında ve sonrasında kadınların ve toplumun ruh sağlığının korunması için büyük önem taşımaktadır.

Anahtar Sözcükler: Kadın Sağlığı, Cinsel İstismar, COVID-19, Ev İçi Şiddet, Yakın Partner Şiddeti

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INTRODUCTION

Intimate partner violence (IPV) against women is a human rights violation and a public health concern, although its prevalence and presentations vary across countries (1). IPV is responsible for a quarter of all serious attacks on women and accounts for a third of all murders of women (2). IPV occurs when a partner tries to control the other partner physically or psychologically (3).

Interpersonal violence targets women and men alike. However, IPV predominantly targets women of all ages. IPV differs from other interpersonal violence acts because it emerges in private rather than public spaces. IPV perpetrators and survivors have a close relationship. That comes along with the chronicity of violence. Additionally, societal factors like gender-unequable norms becloud the awareness of violence, complicate the legal process, and finally result in violations of women's human rights (2, 4).

Violence against women can occur in all parts of the world. Moreover, it has been shown that rates of IPV increase in mass events such as epidemics and natural disasters (5). For example, a four-fold increase in violence against women has been reported among displaced women in Mississippi after Hurricane Katrina (6). After the 2004 Indian Ocean earthquake and tsunami (7) and the Black Saturday bushfires in Australia (8), violence against women has also increased rapidly.

Risk factors associated with a disaster, such as the deterioration of the social structure, economic difficulties, forced migration, increased tension of the perpetrator and impairment of psychological well-being were also present in the COVID-19 pandemic. Measures like border closures, staying at home, remote working, and school closures were taken to reduce the speed of transmission. Stay-at-home was the most common and effective worldwide measure, which was also implemented in Turkey. However, this preventive measure meant that women had to stay at home with aggressors or potential aggressors (9). Indeed, during the lockdown period, reports and news from all over the world, including countries such as Brazil, Spain, Cyprus, the UK and Italy stated that domestic violence was on the rise (10, 11). It was predicted that 31 million cases of violence against women will be increased if the lockdown period is extended by 6 months (12). In addition, it was reported a 75% increase in searches for IPV on the Google search engine during this process (13). The situation is not different in Turkey. Professional organizations and non-governmental organizations in Turkey have pointed out that violence against women has increased with home isolation and social distancing measures since the first coronavirus case was announced on 11 March (14, 15). According to the statement of the, We Will Stop Femicide Platform, following the isolation measures, the number of people calling hotlines increased by 55% in April 2020 and 78% in May 2020 compared to the previous months (16). According to the report of the Federation of Turkish Women's Associations, psychological violence increased by 93%, physical violence by 80%, and the demand for shelter by 78% in March 2020 compared to the previous year (17). Descriptive studies from different parts of Turkey also showed that during the pandemic, IPV was related to negative outcomes for women (18-20). Moreover, several NGOs from Turkey and the world reported that the number and accessibility of shelter houses were also diminished during the pandemic (21).

IPV is associated with poor mental well-being and psychiatric disorders including depression, anxiety, post-traumatic stress disorder, and sleep disorders (22-24). It is also linked with physical and reproductive health problems in women, which might gain chronicity (21, 25, 26). Descriptive studies from different parts of Turkey also showed that during the pandemic, IPV was related to negative outcomes for women (18-20, 27-29). It is necessary for all healthcare professionals, including doctors, nurses and community health staff who are at the forefront to assess the presence of IPV, to have accurate knowledge about the extent and impact of this growing and multifaceted problem (30).

In this study, we aimed to measure and compare the prevalence of IPV among a sample of women in Turkey pre- and during the pandemic. We also aimed to investigate the situation during the lockdown regarding the extent and forms of IPV

women are exposed to. Another aim of our research is to find out the factors associated with IPV during the COVID-19 pandemic and its relationship with women's mental well-being. We hypothesized that during the COVID-19 lockdown, IPV rates would increase. We also hypothesized that IPV would harm the mental well-being of women.

METHOD

An online cross-sectional survey was created and digitalized using the Qualtrics program. Given the pandemic-related contact restrictions during the time of the survey, the sample was created using the snowball sampling method. The web link and QR-code generated for the survey were distributed via social media servers (Twitter, Facebook and Instagram pages of relevant NGOs including that of the Psychiatric Association of Turkey and personal pages voluntarily) and communication applications (WhatsApp), so that each participant would share the link to other people if they preferred to. Before starting to fill out the questionnaire, the participants were asked to click a button indicating that they had read the consent information and agreed to participate anonymously, without any incentives. Once the button was clicked, the participants were directed to the first page of the survey questionnaire. Repetitive participation was avoided based on the system arrangements avoiding repetitive entries from the same IP numbers. The survey was implemented between 09.01.2021 and 09.02.2021.

Women who agreed to participate in the study, and who had a spouse/partner were included in the study. Exclusion criteria were being illiterate and/or not being able to follow the instructions on the webpage, not having a partner at the time of the study, and being under the age of 18.

The survey questionnaire was prepared by the authors based on previous studies in the field (24, 31, 32). It had a total of 69 multiple-choice questions and took approximately 15-20 minutes to complete. The first 25 questions are related to socio-demographic characteristics, age, education, working status, and alcohol and substance use of women and their partners. The remaining questions focused on the presence of awareness of intimate partner violence as well as the household conditions. The types and severity of violence were assessed based on the World Health Organization (WHO) guidance (33), which aims to estimate the prevalence of lifetime IPV against women and determine associations between IPV and health outcomes. The types of IPV that were evaluated were emotional, economic, physical (moderate and severe), sexual and digital violence. A study based on this guidance was carried out in 12 countries in 2005 (34), and the questionnaire of that study was adapted to Turkish society by the Ministry of Family and Social Policies (35). In our study, we included the fifth section of this instrument which questions the basic characteristics and behaviours of the partner, and the seventh section on the violence of the partner (see questions provided in Chart-1). The survey questionnaire ended with an information note for participants on details about relevant organizations', legal procedures, IPV hotlines, and shelter houses, to enhance awareness and support.

The survey was enriched with the WHO-5 index (36). The WHO-5 consists of 5 positive items about

Chart - 1

Types of violence and how they were questioned in the interview

Economic violence	Has or does your partner - prevent you from having or keeping a job although you wanted to? - control access to household money, although he had for other expenses? - take your paycheck, money or other valuable belongings against your will?
Emotional violence	Has or does your partner - ridicule or insult you? - humiliate you in public or private? - threaten to assault you or your relatives/friends? - threaten you with his words, looks, or by hitting household items?
Physical violence (moderate)	Has or does your partner - slap you in the face? - throw objects onto you that may hurt you? - pull your hair?
Physical violence (severe)	Has or does your partner - hit or punch you - push, shove or kick you? - bit, stab, burn or choke you? - threaten or hurt you with a weapon or knife?
Sexual violence	Has or does your partner - force sex with him? - force sex after beating or threatening beating, or made you have sex because you felt threathened? - make humiliating or crude remarks about you?
Digital violence	Has or does your partner - prevent you from access to telephone or internet? - listen to your conversations on the phone or read your messages against your will? - check your internet history against your will?

the feelings of the participants in the last two weeks. These are "I have felt cheerful and in good spirits.", "I have felt calm and relaxed.", "I have felt active and vigorous.", "I wake up feeling fresh and rested.", "My daily life has been filled with things that interest me". Each item is scored on a 6-point Likert-type scale between 0-5 with higher scores indicating better well-being and scores of less than 13 indicating probable depression. The reliability and validity study of the Turkish version of the WHO-5 for adults was done by Eser et. al (37).

The research project was approved by the XXX(blinded) University Non-Interventional Practices Ethics Committee (Approval number: 27.10.2020/ 248) following the Helsinki Declaration.

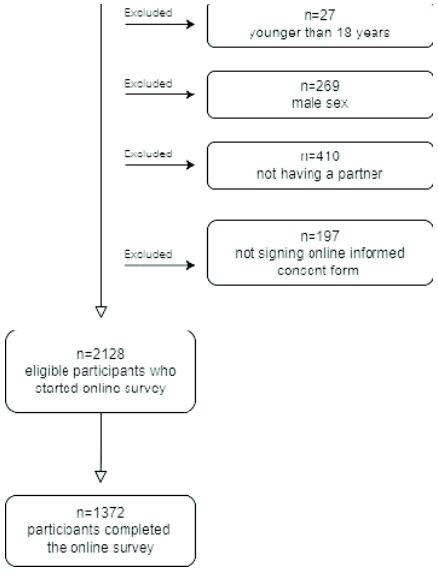
Responses, which were compiled anonymously via the Qualtrics program, were converted into numerical data, and statistical analyses were made by IBM SPSS v.21.0 (SPSS Inc., Chicago, IL, USA). Categorical variables were analysed with the chi-square and McNemar's tests. We used the Kolmogorov-Smirnoff test to determine if the continuous data were normally distributed or not. Statistical comparisons were analysed with the Student's T test when continuous variables were normally distributed, and the Mann-Whitney U test when they were non-normally distributed. We performed a logistic regression analysis to investigate the factors which determine exposure to any type of IPV. While exposure to any type of IPV was taken as the dependent variable, socioeconomic situation, time spent at home, changes during the pandemic, and individual's and partner's alcohol and substance use were taken as independent variables. The relationship between exposure to IPV and mental well-being scores was analysed using Student's T-test. The significance level was set at $p < 0.05$.

RESULTS

General characteristics of the sample

The study reached 3031 potential participants from 79 out of 81 cities in Turkey. The survey was programmed to control including criteria in the beginning. As a result, 2325 applicants were eligible participants for the present study: 18 years old or older, female, and had a partner. However, 197 of them did not sign the online informed consent form. 2128 women initialized the survey, and 1372 of them finished off. Thus, these 1372 women from 72 cities in Turkey were included in the statistical analysis (Figure 1).

Figure 1. Flowchart demonstrating the recruitment and exclusion of participants



The participants' mean age was 42.0 ±11.2 (19-75) years. 168 of them (12.2%) were single, and 1204 of them (87.8%) were either married or cohabitating. Most women (86.2%) lived in city centres. The duration of the relationship with the current partner was 10 years or more for 61.6% of the participants (n=844). 66% of women had one child or two children. 83.9% of them graduated from college (Table 1). 79.6% of the partners had graduated from college (Table 2).

While the number of women who were not working in a paid job before the pandemic was 195 (10.8%), this number increased to 241 (17.6%) during the pandemic period. Nine (0.65%) women lost their health insurance during the pandemic. The number of partners who did not have a paid job before the pandemic was 69 (5.0%), which increased to 112 (8.2%) during the pandemic.

During the pandemic, 86.4% of women (n=1185)

Table 1. Sociodemographic characteristics and mental well-being scores of the participants (n=1372)

Variable	Mean – standard deviation		min-max
Age	42.0 – 11.2		19-75
WHO-5 total score	17.9 – 0.7		6-18
			n (%)
Marital status	**Not married**		168 (12.2)
	Married or cohabiting		1204 (87.8)
Place of residence	**City centre**		1183 (86.2)
	County - town		171 (12.5)
	Village		18 (1.3)
Education	**Primary**		11 (0.8)
	Secondary		6 (0.4)
	High school		110 (8.0)
	Junior college		94 (6.9)
	College		1151 (83.9)
Duration of the relationship with the current partner	**10 years or more**		844 (61.6)
	<10 years		528 (38.4)
Number of children	**0**		404 (29.4)
	1		432 (31.5)
	2		473 (34.5)
	3 or more		63 (4.6)
Smoking	**Yes**		410 (29.9)
	No		962 (70.1)
If yes, increased smoking during the pandemic (n=410)	**Yes**		231 (56.3)
	No		179 (43.7)
Alcohol use	**Yes**	**Six standard drinks or less/week**	735 (53.6)
	Yes	**Seven standard drinks or more/week**	32 (2.3)
	No		605 (44.1)
	Yes		204 (26.6)
	No		563 (73.4)
	Yes		21 (1.5)
	No		1351 (98.5)
	Yes		12 (57.1)
	No		9 (42.9)
	Yes		1185 (86.4)
	No		187 (13.6)
	Yes		1078 (78.6)
	No		294 (21.4)
	Yes		511 (37.2)
	No		861 (62.8)
	Yes		434 (84.9)
	No		77 (15.1)
	Increased		412 (30.0)
	Decreased		705 (51.4)
	No change		255 (18.6)

reported spending more time at home with their partners. 84.9% said that the time they spent with the persons they cared for at home (children, elderly, sick) increased. 51.4% of women stated that they had been less able to spend time for themselves during the pandemic.

Table 2. Sociodemographic characteristics of the partners, as reported by women (n=1372)

Variable			n (%)
Education		**Primary**	20 (1.4)
		Secondary	29 (2.1)
		High school	149 (10.9)
		Junior college	82 (6.0)
		College	1092 (79.6)
Smoking		**Yes**	410 (29.9)
		No	962 (70.1)
If yes, increased smoking during the pandemic (n=528)		**Yes**	282 (53.4)
		No	246 (46.6)
Alcohol use	**Yes**	**Less than 14 standard drinks/week**	780 (56.9)
	Yes	**14 standard drinks or more/week**	86 (6.3)
	No		506 (36.8)
If yes, increased alcohol use during the pandemic (n=866)		**Yes**	251 (29.0)
		No	615 (71.0)
Illegal substance use		**Yes**	28 (2.0)
		No	1344 (98.0)
If yes, increased illegal substance use during the pandemic (n=28)		**Yes**	16 (57.1)
		No	12 (42.9)

Although it is observed that women mostly undertook unpaid domestic labour before and during the pandemic, during the pandemic, there was an increase in the rate of women who said, "we divide work equally" (29.8% vs 34.0%, p=0.020) or "my husband does more housework than me" (4.0% vs 6.5%, p=0.004).

Among those women who smoked or used illegal substances, the majority had increased use during the pandemic. For those who used alcohol, 26.6% reported an increase in their use during the pandemic (Table 1).

Regarding mental well-being, the WHO-5 mean score was 17.9 ± 0.7, and only 2 participants scored under the cut-off of 13 points (indicating probable depression).

Among the partners of participants, the majority of those who smoked or used illegal substances reported an increase during the pandemic, as reported by the participants. 29.0% of the partners who were reported to use alcohol increased their use (Table 2).

Table 3: IPV prevalence before and during the pandemic, the rates of medical, psychological and legal support

Variable		All participants (n=1372)		The subgroup who were exposed to IPV first time in the pandemic (n=61)
		Before the pandemic	During the pandemic	During the pandemic
		n (%)	n (%)	n (%)
Digital violence	Yes	148 (10.8)	147 (10.7)	19 (31.1)
	No	1224 (89.2)	1225 (89.3)	42 (68.9)
Economical violence	Yes	97 (7.1)	91 (6.6)	9 (14.7)
	No	1275 (92.9)	1281 (93.4)	52 (85.2)
Emotional violence	Yes	325 (23.7)	321 (23.4)	41 (67.2)
	No	1047 (76.3)	1051 (76.6)	20 (32.8)
Physical violence -moderate	Yes	138 (10.0)	99 (7.2)	5 (8.2)
	No	1234 (90.0)	1273 (92.8)	56 (91.8)
Physical violence - severe	Yes	44 (3.2)	30 (2.2)	1 (1.6)
	No	1328 (96.8)	1342 (97.8)	60 (98.4)
Sexual violence	Yes	47 (4.1)	36 (2.6)	0 (0.0)
	No	1325 (95.9)	1336 (97.4)	61 (100.0)
*Medical support (n=193)	Yes	16 (8.4)	8 (4.2)	0 (0.0)
	No	183 (91.6)	183 (95.8)	6 (100.0)
*Psychological support (n=490)	Yes	61 (12.37)	49 (10.2)	8 (13.1)
	No	429 (87.63)	431 (89.8)	53 (86.9)

*The questions with an asterisk were only asked to the participants who stated that they were exposed to any form of IPV.

Findings related to IPV

Before the pandemic, 30.7% of participants were exposed to any type of violence. Among them, emotional violence was 23.7%, digital violence 10.8%, moderate and severe physical violence was 10.0% and 3.2%, economic violence was 7.1% and sexual violence was 4.1% prevalent. During the pandemic, 29.6% of women reported being exposed to violence. Among these, emotional violence was 23.4%, digital violence 10.7%, moderate and severe physical violence was 7.2% and 2.2%, economical violence was 6.6% and sexual violence was 2.6% prevalent. To compare the rates of violence of the same sample before and during the pandemic, and given the non-normality of the distribution, McNemar's test for paired samples was used. It was found that the rate of physical violence decreased during the COVID-19 pandemic (McNemar's $\chi2 = 22.51$, $p<0.001$). The rate of sexual violence was also found to be decreased (McNemar's $\chi2 = 15.38$, $p=0.0001$). There was no difference between the rates of other subtypes of violence before and during the pandemic.

Participants who are exposed to IPV stated decreasing rates of seeking medical and psychological support from a healthcare professional (including doctors, nurses and community healthcare staff) during the pandemic (Table 3 – see the bottom section). WHO-5 well-being score was significantly lower among women who were exposed to violence, regardless of subtype ($p<0.001$), although the most distinct association was with severe physical violence ($p<0.001$).

Regarding the knowledge and awareness about IPV and available support systems, 58.7% (n=805)

Table 4. Logistic regression analysis of the IPV predictors

Variables		OR	%95 CI	z	p
Age of the participant	**<45**	ref			
	>45	0.76	0.59-0.98	-2.14	0.033
Education level of the participant	**Less than undergraduate degree**	ref			
	Undergraduate degree or more	0.71	0.51-0.97	-2.12	0.034
Employment	**No**	ref			
	Yes	0.74	0.51-0.97	-1.88	0.060
Having children	**No**	ref			
	Yes	0.78	0.44-1.37	-0.88	0.379
Alcohol use of the partner	**No**	ref			
	13 standard drinks or less/week	0.94	0.73-1.21	-0.48	0.634
	14 standard drinks or more/week	2.08	1.30-3.33	3.06	0.002

of the participants were aware of Law Nr. 6284 to Protect Family and Prevent Violence Against Women. 77.8% (n=1067) of them were informed of the governmental violence helpline "Alo 183", 68.2% (n=935) knew about the governmental phone application "KADES" which gives women the opportunity to click to call the police in case of violence and, 90.9% (n=1247) were aware of non-governmental organizations in the field of violence against women. Moreover, both before and during the pandemic, women stated that they had a friend or relative to ask for help in case of exposure to IPV (94.7% and 93.9%, respectively).

The ages of women did not have a normal distribution; therefore, the Mann-Whitney U test was used. No significant differences were found in terms of age between the survivors of IPV and the other participants. Women who were not married nor cohabiting with their partners were found to be exposed to sexual violence more frequently (5.4% vs 2.2%, $\chi 2 = 5.60$, $p=0.018$). IPV was more often in rural areas compared to city centres (35.5% vs 28.3%, $\chi 2 = 4.0014$, $p=0.045$). Graduate women were exposed to IPV less when compared to women with lower educational levels (28.0% vs 36.2%, $\chi 2 = 6.0524$, $p=0.014$). Job loss during the pandemic was not associated with a statistically significant difference in terms of exposure to IPV. Logistic regression analysis revealed a significant relationship between exposure to IPV during the pandemic and women's age, with being 45 or older and higher education level being protective (OR=0.76 and 0.71, respectively), and partners' risky alcohol use being a risk factor (OR=2.08) (Table 4).

The level of education of partners who committed and did not commit IPV was significantly different. The rate of university graduates among IPV aggressors was lower (72.7% vs. 82.6%, Pearson $\chi 2 = 17.4396$, $p<0.001$). The rate of aggressors among smokers and risky alcohol users was significantly higher than non-users (37.1% vs. 24.4%, $\chi 2 = 25.3438$, $p<0.001$; 45.4%, vs 27.3%, $\chi 2 = 12.2164$, $p=0.002$, respectively). Besides, during the pandemic, women whose partners had risky alcohol use were more likely to be exposed to IPV (OR=2.08) (Table 4). The frequency of sexual violence by partners using illegal substances was significantly higher compared to partners who did not use illegal substances (10.7% vs. 2.5%, $\chi 2 = 7.3223$, $p=0.007$).

During the pandemic, 58 partners were reported to have lost their jobs. Among them, 48.28% were IPV aggressors, while the rate of committing IPV was 28.46% among those who maintained their employment status ($\chi 2 = 10.526$ $p<0.01$).

Sixty-one women stated that during the pandemic they were exposed to IPV for the first time in their lives. The findings of this subgroup were analysed in detail. Their ages ranged from 19 to 66 years, with a mean of 20.38±10.84 years. They were statistically significantly younger (20.38 vs 25.17, $p<0.001$) and had a lower rate of being married/cohabiting (68.9% vs 88.6%, $p<0.001$) compared to the rest of the group. 89% of them lived in the city centres, 83.6% were university graduates, 36.1% had been in a relationship with their partner for ten years or longer, and 42.6% had no children. Among them, 67.2% have been exposed to emotional violence, 31.2% to digital violence, 14.8% to economic violence, and 9.8% to physical violence.

DISCUSSION

In this study, we hypothesized that there would be an increase in the incidence of IPV during the pandemic in Turkey, and we aimed to look for the relationship between the increase and factors such as job loss, economic difficulties, the increased workload at home, an increase in alcohol and substance use, and difficulties in reporting violence.

While the COVID-19 pandemic has become the focus of daily life and health systems, requiring a total reorganization since early 2020, the UN warned about the "shadow pandemic" of intensifying violence against women (38). Lockdown and other restrictive measures meant an increase in the time spent under the same roof with potential aggressors of IPV. Even before the pandemic, IPV was identified as a significant public health concern (39). The well-established links between intimate partner violence and mental health consequences (1, 21, 24) instruct that the extent and impact of violence during the COVID-19 pandemic should

be assessed and intervened upon by scholars and clinicians. To our knowledge, this is the widest nationwide study examining the extent of intimate partner violence during the COVID-19 pandemic in Turkey, following some initial studies (20, 40).

Our study demonstrates that the COVID-19 pandemic has resulted in negative changes in the socioeconomic status of women, whose household labour is already invisible, such as losing their formal job and/or insurance and spending more time at home, which may also hinder their access to health institutions or formal support in case of need. It is also of note that a higher percentage of women lost their jobs during the pandemic than that of partners (6.8% vs. 3.2%). Despite heterogeneity among countries, women have been shown to experience higher rates of job or income loss during the pandemic (41, 42). Moreover, during the pandemic, the time spent by children at home increased significantly with the closure of schools and daycare centres. The absence of helping maids during this period resulted in an increase in household-related responsibilities for people living together at home (43). Such differential socioeconomic transitions between men and women during the pandemic may lead to changes in relationship dynamics and create a risky environment for violence (21).

Despite our sample is not a representative one, the rate of exposure to violence in our sample is comparable to other local and national surveys conducted in Turkey within the past decade (31, 32, 44, 45), suggesting that in the general population, around 1 out of 3, women are subjected to violence. Among the member countries of the Organization for Economic Cooperation and Development (OECD), Turkey ranks first among the countries where violence against women is most common, with 38% of women being subjected to physical or sexual violence by their partners (46). According to the widest research conducted in Turkey between 2013-2014, the rate of women who stated that they were exposed to physical violence at any point in their lives was 36%, the rate of psychological violence was 44%, and the rate of economic violence was 30%. 12% of ever-married women stated that they were exposed to sexual violence at any point in their lives (32).

In our sample, emotional violence was the most frequently encountered form among different types of violence, which is estimated to be the most commonly perpetuated form in other studies (47). However, we noticed a change in the ranking of other forms of violence. Digital violence has become more common during the pandemic, surpassing the level of physical violence, especially among women who were exposed to IPV for the first time. We interpret this finding to be specific to the pandemic period, in which time spent at home and online has dramatically increased. Further discussion on this is provided below.

While time spent at home has increased, rates of physical and sexual violence have decreased, in contrast with expectations. Yet, this finding might be due to the largely underreported socioeconomic strata in our survey. Yılmaz Karaman and colleagues stated that during the COVID-19 pandemic; IPV survivors who applied to emergency departments were more likely to be without social insurance, to be severely injured and to be attacked at home, compared to the pre-pandemic period (27), which may indicate a selection bias in our study due to its methodology. Moreover, we asked for a comparison between their lifetime exposure to IPV and relatively recent exposure during the pandemic, which might explain the maintenance of the already high rate of violence (30.7%). Another survey conducted in Turkey during the pandemic found that emotional violence increased among literate women (20). Some other descriptive studies conducted in different settings pointed to increased rates of IPV (27, 29), while another study yielded a comparable result with a rate of IPV of 35.5% (19). On the other hand, a systematic review that has compiled studies from various countries also stated that evidence for changes in the prevalence of IPV is yet inconclusive (48). Hoehn-Velasco and colleagues found that domestic violence in Mexico declined during the lockdown and increased back to pre-pandemic levels after returning to daily life (49). Our study period did not include a complete lockdown, however, there were partial curfews(50). Besides, COVID-19 public vaccination did not start then (51). Several researchers argued that IPV might more frequently occur in psychological rather than physical form during the COVID-19 pandemic, a form of violence that is hard to detect

(52).

Regarding the related factors, we found that partner alcohol and substance use were associated with greater rates of violence, in line with the literature (53, 54). Moreover, it is reported that alcohol and substance use increased during the pandemic, due to increased levels of stress, anxiety, depression, and caregiving load, which might have exacerbated this situation (55, 56). Higher WHO-5 scores were associated with all types of violence and especially physical violence in our study, confirming the negative consequences of IPV on mental health as reported in the literature (1, 24, 57). Poorer mental well-being might also be related to the influence of some confounding factors, such as poorer socioeconomic status, lower level of education, and so forth, yet we believe IPV is a reflection of these negative psychosocial determinants, the visible tip of the iceberg.

The impact of age and education

We demonstrated that a lower level of education and younger age are two main predictors of IPV, a finding repeatedly shown in other studies, especially regarding recently encountered IPV (24, 32, 45, 58-61). A WHO study demonstrated that younger age is associated with greater recent experience of spousal violence (62). However, there are other studies indicating that older age is significantly associated with higher exposure to IPV (63). Our findings and findings from other studies signify that women are exposed to violence regardless of their education level, but the higher their education level is, the lower becomes their exposure to violence. It is argued that the level of education does not make a difference in women's exposure to violence, but that educated women are more successful in ending violence (64). We interpret that education is an important factor that helps women to develop their self-esteem and self-confidence, raising their awareness of new options and allowing them to make rational decisions. However, based on the distribution of our results, we believe it is important to note that vulnerable populations might not be reached via an online survey and that field still requires the attention of researchers.

Studies from a wide range of countries have shown that in the past year, factors related to IPV were exacerbated (65-67), lockdowns and quarantines were related to abusive situations, and there is an alarming trend of the increased rate of IPV (68-70). Up to a three-fold increase in cases of IPV is shared (71, 72). This trend is also highlighted in the 2020 report of UN Women (73). Besides, the routes of reaching out for help have become limited and studies have shown that the pandemic situation is associated with a delay in reporting IPV (74), a condition in which less than 40% of women who experience seek help from any sort (73). While in our study it was found that the rates of IPV did not increase, based on responses to dichotomous-type questions, the quality/severity of each type of IPV might have changed, which was not examined in our study.

A striking finding is that 61 women, mostly university graduates living in cities, reported being subject to violence for the first time during the pandemic. 31.2% of them were cases of digital violence. This is a new category of violence, which we believe requires special attention. The UN Women has released a special brief on the impact of information and communication technology facilitated violence (75), which can have many forms, including threats, trolling, stalking, harassment, and so forth. Increased digitalization was already a growing global trend and it has become inevitable during the COVID-19 pandemic, with up to 50-70% increase in the use of the internet (75). This phenomenon needs to be seen as a double-sided medallion. On the one hand, it poses risks of abuse, violence, privacy and security breaches. On the other hand, digital tools also have the potential of providing new ways of seeking help, delivering interventions or creating psychosocial support networks (71), such as the high level of awareness (90.9% of women) of the governmental digital application KADES we found, which may also be related to the high education level of participants.

The efforts to reduce the mental health consequences of intimate partner violence should have several dimensions, including prevention, intervention against risk factors, accurate reporting and reduction of violence (1). We note that Turkey has been among the countries with the lowest level of

income support throughout the pandemic (76), which might be related to an increased risk of future IPV cases. Another important factor in the development of violence is inequalities in various aspects of life, including economic, educational, political and so forth (21). The WEF Gender Gap Report states that Turkey has plummeted three steps down, from being ranked 130th to 133rd among all countries within the past year, indicating a widening in the gender gap (77). Unfortunately, recently after the completion of our online survey, the government in Turkey has withdrawn from the Council of Europe Convention on preventing and combating violence against women and domestic violence using a presidential decree, as addressed in the Official Gazette issue nr. 31429. Turkey was the first country to sign the convention in Istanbul; later, the convention was called as "Istanbul Convention." Many feminist activists from Turkey took part in the convention's development process. The convention and the related domestic law (Nr. 6284) have been in effect since 2014. The Istanbul Convention is not only about reducing harm after violence occurs; it also underlines gender equality, precautions for gender-based discrimination, and gender-based violence. After the withdrawal from the convention, women who applied to police stations due to domestic violence faced difficulties. Women reported that authorized persons did not act under the law numbered 6284(78). In 2021, 280 femicides and 217 suspected deaths of women occurred in Turkey (79). Gender inequality and domestic violence have many consequences; at the tip of the iceberg, they result in femicide. Before the withdrawal decree, 58% of the women in our survey responded that they knew about Law Nr.6284 to protect families and prevent violence against women, which can be considered moderate. We can expect a drop in this level and general awareness about legal protection measures in the future, which shall become an area of increased effort for all professionals in this field.

Limitations

Online surveys have been very helpful during the pandemic, enabling a real-time and rapid assessment of many issues related to the psychosocial health of individuals, despite being under restrictions. Since early 2020, there has been a plethora of online surveys. However, there are some limitations regarding the generalizability of the results from online surveys, inherent to the nature of the method, such as convenience sampling and responder selection bias (80). People without internet access for a variety of reasons, including those who are not familiar with digital technologies will have limited representation in the data set (81).

There are some recommendations to overcome these limitations, one of which is counting the complete responses in the analysis. In this regard, we have limited the analysis of our data to 1372 out of a total of 2128 responses, excluding the incomplete ones, aiming to increase the degree of robustness in the analysis. Still, the grossly skewed distribution of the educational level of survey participants, with around 4 out of every 5 being university graduates and 9 out of 10 having a paid job, is the main limitation of our data set. Based on the nationwide statistics conducted by the Turkish Statistical Institute (TurkSTAT), 17.5% of women over the age of 25 in Turkey are university graduates and 28.7% have a paid job (82). Among those who had a partner, the rate of those whose partners were university graduates was 79.5%, which is around 3 times more than the general rate of university graduation among males in Turkey (82). The rate of urban living in our sample was 86.3%, which is parallel to the rate of urban living in Turkey (93.0%) (83). We can interpret that our sample consists of relatively well-educated individuals living in urban conditions. Although this is a limitation to the generalizability of our results, the fact that violence is reported in a sample belonging to the upper strata of society is also important and worrisome. Moreover, our evaluation is based on a self-report measure, and detailed clinical assessments would be necessary to understand the real impact caused by IPV on women. There might also have been some reporting bias, including recall bias, particularly for the pre-pandemic period. The cross-sectional nature of the study also hinders the possibility of making causal interpretations. Given the limits of an online survey, the number of questions was limited to essential sociodemographic factors, and a thorough assessment of the relationship quality of our couple's adjustment characteristics before and during the pandemic was not made, which could have also impacted our results. A last limitation

might be that in our survey we included only women who had a partner at the time of the survey, so those who did not have an ongoing relationship but were exposed to violence are not reflected in our results.

CONCLUSION

To conclude, in this self-report online survey, we found that the prevalence and the most common form of violence (emotional) remained during the pandemic. However, there was a change in the ranking of other forms of violence. While life has become more digital during the pandemic, digital violence has become more common, surpassing the level of physical violence. Remarkably, a group of women were subjected to violence for the first time in their lives during the pandemic, with the most common form being digital violence. Our findings indicate the need to pay greater attention to this relatively new form of violence. Awareness, accurate reporting, and strategies to prevent and reduce intimate partner violence are of utmost importance for the protection of the mental well-being of women and society during and after the COVID-19 pandemic, and other natural and/or human-made disasters.

Conflicts of interest: The authors declare that they have no conflict of interest.

Correspondence address: M.D. Ekin Sönmez Güngör , 19 Mayıs Neigh. Kadıköy 34736 İstanbul - Türkiye
ekinsonmez88@gmail.com

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The relationship between internalized stigma and coping strategies in bipolar disorder

Bipolar bozuklukta içselleştirilmiş damgalanma ile başa çıkma tutumları arasındaki ilişki

Zeynep Çalışkan İlter[1], Sıdıka Baziki Çetin[2], Evrim Özkorumak[3], Ahmet Tiryaki[4], İsmail Ak[5]
[1]M.D.,Şanlıurfa Mehmet Akif İnan Education and Research Hospital, Turkey, https://orcid.org/0000-0002-4945-5896
[2]Assit. Prof., Şanlıurfa- Harran University, Faculty of Medicine, Department of Psychiatry, Turkey, https://orcid.org/0000-0002-4686-8214
[3]Prof. Dr., Karadeniz Technical University Department of Psychiatry, Turkey, https://orcid.org/0000-0002-0734-5437
[4]Prof. Dr., Medicana İnternational, Department of Psychiatry, Turkey, https://orcid.org/0000-0001-8923-6869
[5]Prof. Dr., Karabuk University, Karabuk Training and Research Hospital, Psychiatry Department, Turkey, https://orcid.org/0000-0002-0875-6377

SUMMARY

Objective: The aim of this study was to evaluate the relationship between internalized stigma and coping attitudes in patients in remission of bipolar disorder. **Method:** The study included 77 patients in remission who were diagnosed with bipolar affective disorder according to DSM-IV by applying the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I). Euthymia was established using the Young Mania Rating Scale and the Hamilton Depression Rating Scale. All patients were evaluated with a Sociodemographic Data Form, the Internalized Stigma in Mental Illness Scale (ISMI) and the Coping Attitudes Rating Scale (COPE). **Results:** The perceived discrimination subscale scores of patients living in towns/villages were found to be significantly higher than those living in urban areas (p=0.038). A positive correlation was found between the total number of episodes (10.0±10.8), the number of depressive episodes (3.7±4.8) and the history of depression with psychotic features and internalized stigma. Patients showing active coping, planning, use of useful social support, positive reinterpretation and development of coping styles were found to have lower internalized stigma scores and higher stigma resistance; moreover, patients using behaviorally disengaged coping styles had higher internalized stigma scores and lower stigma resistance. **Discussion:** According to the results of our study, active coping, planning, use of useful social support, positive reinterpretation and support of developmental coping attitudes, which are among the functional coping attitudes, and attempts to reduce the behavioral disregard of maladaptive coping attitudes can be targeted to reduce internalized stigma.

Key Words: Bipolar Disorder, Stigma, Coping Strategies

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ÖZET

Amaç: Bu çalışma ile bipolar bozukluk remisyon dönemindeki hastalarda içselleştirilmiş damgalanma ile başa çıkma tutumları arasındaki ilişkiyi ortaya koymak amaçlanmıştır.**Yöntem:** Çalışmaya psikiyatri polikliniğine ayaktan başvuran ve tedavisi devam etmekte olan, DSM-IV Eksen I Bozuklukları İçin Yapılandırılmış Klinik Görüşme (SCID-I) uygulanarak DSM-IV'e göre bipolar affektif bozukluk tanısı alan, remisyon dönemindeki 77 hasta dahil edilmiştir. Ötimi ölçütleri Young Mani Derecelendirme Ölçeği ve Hamilton Depresyon Derecelendirme Ölçeği kullanılarak belirlenmiştir. Tüm hastalar Sosyodemografik Veri Formu, Ruhsal Hastalıklarda İçselleştirilmiş Damgalanma Ölçeği (RHİDÖ) ve Başa Çıkma Tutumlarını Değerlendirme Ölçeği (COPE) ile değerlendirilmiştir. **Bulgular:** Kasaba/köyde yaşayan hastaların algılanan ayrımcılık alt ölçek puanları kentte yaşayanlara göre anlamlı düzeyde yüksek bulunmuştur (p=0,038). Toplam dönem sayısı (10.0±10.8), depresyon dönemi sayısı (3.7±4.8) ve psikotik özellikli depresyon öyküsü ile içselleştirilmiş damgalanma arasında pozitif yönde ilişki tespit edilmiştir. Başa çıkma tutumlarından aktif başa çıkma, plan yapma, yararlı sosyal destek kullanımı, pozitif yeniden yorumlama ve gelişme başa çıkma tutumlarını kullanan hastaların içselleştirilmiş damgalanma puanlarının daha az, direncin daha fazla olduğu, davranışsal olarak boş verme başa çıkma tutumunu kullanan hastaların içselleştirilmiş damgalanma puanlarının yüksek, dirençlerinin ise düşük olduğu belirlenmiştir. **Sonuç:** Çalışmamızın sonuçlarına göre işlevsel başa çıkma tutumlarından olan aktif başa çıkma, plan yapma, yararlı sosyal destek kullanımı, pozitif yeniden yorumlama ve gelişme başa çıkma tutumlarının desteklenmesi, uyumsuz başa çıkma tutumlarından davranışsal olarak boş verme tutumunun azaltılmasına yönelik girişimlerde bulunulması içselleştirilmiş damgalanmayı azaltmak için hedeflenebilir.

Anahtar Sözcükler: Bipolar Bozukluk, Damgalanma, Başetme Stratejileri

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INTRODUCTION

Stigma entails discrediting an individual, being seen as inferior to others and being vilified in a way that distinguishes them from others (1). Among all patients, those diagnosed with mental disorders are generally exposed to the negative consequences of the stigmatization the most. One of the biggest barriers to the diagnosis and treatment of mental disorders is stigmatization, prejudiced thinking/behaviour, stereotypical behaviours and discrimination against people with mental disorders (2). Internalized stigma is the individual's acceptance of negative stereotypes in society for themselves. As a consequence, the individual withdraws themselves from society with negative feelings such as worthlessness and shame (1). Bipolar disorder (BD) is relatively less recognized and stigmatized by society; nonetheless, the patients experience the feeling of stigma intensely, that is, they stigmatize themselves (3). Internalized stigma harms patients by worsening the symptoms of the disease and delaying recovery (4). There is an urgent need to address internalized stigma in the treatment process (2).

In the face of illnesses, an individual develops various coping attitudes to minimize and cope with the negative effects of the illness. Patients suffering from mental illnesses also apply certain coping attitudes to avoid or reduce rejection (5). Coping techniques that are used to alleviate or solve a perceived threat or problem can play an important role in adapting to challenging situations, protecting the individual against environmental, biological and cognitive factors, and maintaining functionality (6,7). However, while some of these coping efforts are likely to be effective, others may have significant adverse consequences. Coping attitudes generally serve to solve a problem and adapt to a situation by reducing mental stress; such attitudes, however, may also cause the stress response to gain a negative quality, making the solution difficult or impossible, thus increasing the mental distress caused by stress (6,8). Knowing the coping attitudes used by an individual may help in understanding the role of psychopathology, determining treatment goals and monitoring therapeutic effectiveness, as well as helping to prevent the occurrence of additional problems (9).

Several studies have been reported in the scientific literature on the relationship between schizophrenia and stigma; only a few studies have drawn attention to stigma in patients with bipolar disorder. The current study aimed to reveal the relationship between coping attitudes and internalized stigma in patients with BD in remission. To our knowledge, the current study is the first to explore the relationship between internalized stigma and coping attitudes in BD patients.

METHOD

Sampling

Participants were selected among patients; who applied to the Karadeniz Tecnichal University Faculty of Medicine Psychiatry Outpatient Clinic between July 2013 and April 2014, were diagnosed with bipolar disorder according to DSM-IV and were still under treatment. Only patients in remission were included in the study. Patients between the ages of 18-65, at least primary school graduates and those who agreed to participate in the study were included. The patients who were followed up with BD in the clinic were evaluated by the researcher for the diagnosis with a clinical examination before being included in the study. The remission status of the patients was evaluated by the clinician with the Hamilton Depression Rating Scale (HAM-D) and the Young Mania Rating Scale (YMRS). The patients with a HAM-D score of seven and a YMRS score of six and below were included in the study. The 8-week time required to use the definition of remission was determined by considering Perlis et al.'s (2007) study "Predictors of recurrence in bipolar disorder: primary results of the Systematic Treatment Development Program for Bipolar Disorder (STEP-BD)" (10). Approval for the research was obtained from the ethics committee of Karadeniz Technical University, Faculty of Medicine (01.10.2013, 2013/71)

Tools

DSM-IV Structured Clinical Interview-Clinical Version (SCID-CV): DSM-IV is a structured clinical interview scale used to diagnose Axis-I disorders. It consists of six modules and investigates 38

disorders in the DSM-IV Axis-I using diagnostic criteria and 10 disorders without the use of diagnostic criteria. Application of the scale takes about 25-60 minutes on average (11). The Turkish adaptation of the scale developed by First et al. (12) and its reliability study were reported by Özkürkçügil et al. (1999) (13).

Sociodemographic Data Collection Form: Data on age, gender, place of residence, marital status, level of education, income, diagnosis, age of onset of illness, family history of psychiatric illnesses, disease duration, the total number of hospitalizations, type of bipolar disorder, type of first and last episode, and the total number of episodes were collected. Information was obtained from patients' file records and through direct interviews with patients.

Hamilton Depression Rating Scale (HAM-D): HAM-D is used to measure the severity of depression. It is not a diagnostic tool; rather, it is used to monitor the course of depression. The original scale reported by Hamilton (1960) has 17 items and predominantly evaluates somatic complaints. A score of 0-4 is given for each item with the highest possible score of 53. Reliability and validity studies for the Turkish version of the scale were carried out by Akdemir et al. (14).

Young Mania Rating Scale (YMRS): YMRS is a scale developed by Young et al (15) to measure the severity and change of mania. The reliability and validity study of the Turkish version was performed by Karadağ et al. This scale consists of 11 items and each measures 5-stage symptom severity (16). A clinician obtains the data by marking it on the scale during an interview with the patients. The total score of the scale is obtained by summing the scores obtained from each item. YMRS is not used for diagnosis.

Internalized Stigma Scale in Mental Illnesses (ISMI): ISMI used to determine internalized stigma, was developed by Ritsher et al. (2003). It is a self-report scale consisting of 29 items. The scale evaluates the subjective stigmatization experiences of individuals within the framework of five subscales called “Alienation”, “Confirmation of Stereotypes”, “Perceived Discrimination”, “Social Withdrawal” and “Stigma Resistance ” (11). The items in ISMI are evaluated with a four-point Likert-type scale of “strongly disagree” (1 point), “disagree” (2 points), “agree” (3 points), and “strongly agree” (4 points).

Coping Attitudes Assessment Scale (COPE): COPE was developed by Carver and Scheier in 1989, aiming to evaluate the coping attitudes used by individuals who are faced with difficult or distressing events or problems in their daily lives. The scale was translated into Turkish by Agargün et al.in 2005 and its validity and reliability study has been conducted (7, 17). COPE is a self-report scale with 15 subscales and 60 questions. Each of these subscales gives information about a different coping attitude. As a result, the score obtained from each sub-scales indicates which coping attitude is used more by the individual (17). The sub-dimensions of the coping attitudes scale are as follows (6): Use of instrumental social support, active coping, restraint, suppression of competing activities, planning, positive reinterpretation and growth, religious coping, humour, acceptance, use of emotional social support, focus on and venting of emotions, denial, behavioral disengagement, mental disengagement, substance use. Each of the subscales provides information about a separate coping attitude. The total score of the first five of these subscales gives the "Problem-Focused Coping" score, the sum of the 6–10 subscale scores gives the "Emotional-Focused Coping" score and the total of the last five subscale scores gives the score of "Dysfunctional Coping". The high scores of the subscales allow commenting on which coping attitude is used more by the person (18).

Statistical analyses

In our study, as a result of the post-power analysis of the internalized stigma scale according to the coping strategies of the patients with bipolar disorder in remission; with 95% confidence (1-α), 81% test power (1-β), d=0.381 effect size, the number of samples to be taken was 72. Considering the withdrawal status of the patients, the study was conducted with 76 people. SPSS 13 for Windows was used for statistical analysis of the data obtained from the study. The data obtained by measurement were expressed as mean and standard deviation,

while qualitative data were expressed as numbers and %. Pairwise comparisons according to clinical characteristics were carried out with Student's t-test when the data were parametric and Mann Whitney U test when the data were non-parametric. ANOVA was used for data with normal distribution in comparisons of three or more groups (the Bonferroni test was used as a post hoc test). The Kruskal Wallis test was used for data that did not fit normal distribution (the Mann-Whitney U test was used as a post hoc test). The conformity of the data to a normal distribution was examined with the Kolmogorov-Smirnov test. Relationships between scales were determined by correlation analysis.

RESULTS

Clinical characteristics

Of the 77 BD patients who participated in the study, 29 (37.5%) were male and 48 (62.3%) were female. The age distribution of the patient group was between 18-64 years, and the mean age was determined as 38.8±12.1 years. The sociodemographic data of the patients are presented in Table 1.

Type I BD was diagnosed in 67 (87.0%) patients, while Type II BD was diagnosed in 10 (13.0%) patients participating in the study. The disease duration varied between 0.5 and 37 years, with a mean disease duration of 13.5±9.4 years. Other clinical features of the patients are presented in Table 2.

Assessment of Scales

The mean ISMI score was found to be 52.98±12.76 (min: 32, max: 92). The subscale mean scores are presented in Table 3. COPE, a multidimensional coping inventory, was used to evaluate the ways by which patients responded to stress. According to the COPE results, the total score of problem-focused coping varies between 25 and 72, with an average of 56.62±9.22. Emotionally focused coping total scores range from 27 to 79, with an average of 57.44±9.10. Dysfunctional coping scores range from 22 to 63, with a mean of 41.32±8.34.

Table 1: Sociodemographic Characteristics of the Patients

		n	%
Gender	Female	48	62.3
	Male	29	37,5
Marital status	Single	26	33,7
	Married	44	57,1
	Widowed/Divorced	7	9,0
Education level	Primary education	29	37,7
	High school	21	27,3
	High school over	27	35,1
Occupation	Unemployed	14	18,2
	Housewife	20	26,0
	Working	27	35,1
	Retired	8	10,4
	Student	8	10,4
Income level	Low	25	32,5
	Medium	45	58,4
	High	7	9,1
Co-habitants	Elementary family	67	87,0
	Extended family	10	13,0
Place of Residence	Urban	62	80,5
	Suburban/Country	15	19,5
Smoking	No	39	50,6
	Yes	38	49,4

According to the COPE results, it was found that the patients used problem-focused coping methods and emotionally-focused coping methods other than joking more, and they used dysfunctional coping styles such as denial, behavioral disengagement and substance use less.

Evaluation of the ISMI scale according to sociodemographic data such as age, gender, marital status, education level, job, financial situation, family, place of residence, smoking history, suicide history and the presence of another known medical disease indicated the presence of a significant relationship between the ISMI total score and the education level (p=0.013). ISMI total scores of patients with

Table 2: Clinical Characteristics of the Patients

	Mean– Standard Deviation	Min-Max Values
Disease duration (years)	13.5–9,4	0.5-37
Age of onset	25.0–9.9	12-60
Untreated time (years)	25.0–9.9	0-12
Number of hospitalizations	2.3–2.5	0-13
Duration after last hospitalization (years)	3.5–4.9	0-29
Time after last episode (years)	1.8–1.8	0.25-10.0
Total number of episodes	10.0–10.8	1.0-60.0
Number of manic episodes	3.3–4.2	0-26
Number of depressive episodes	3.7–4.8	0-30
Number of mixed episodes	0.16–0.44	0-2
Number of hypomanic episodes	2.5–7.2	0-50

Table 3: Distribution of ISMI Scale Scores

	Mean– Standard Deviation	Min-Max Values
Alienation	10.16–3.46	6-24
Confirmation of stereotypes	11.93–3.59	7-24
Perceived discrimination	8.97–3.26	5-20
Social withdrawal	10.57–3.30	6-19
Resistance to stigma	13.66–3.30	6-20
ISMI total	52.98–12.76	32-92

ISMI: Internalized Stigma Scale in Mental Illnesses

primary school education were found to be significantly higher than patients with a higher education level (p=0.042, Table-5).

Considering the relationship between disease characteristics and ISMI total score and subscale scores; A positive correlation was found between the age of onset of the disease and the confirmation of stereotypes. An inverse correlation was found between the time elapsed after the last period and the confirmation of stereotypes. A positive relationship was found between the total number of episodes and alienation, confirmation of stereotypes and total ISMI scores, a positive relationship was found between the number of depressive episodes and alienation and the total score, while a negative relationship was found between the number of mixed episodes and the scale scores of resistance to stigma. It was determined that the alienation and confirmation of stereotypes subscale scores of the patients were significantly different

Table 4: The Relationship Between Sociodemographic Data and ISMI Scale Scores

			ISMI	
		N	Mean– Standard deviation	p value
Age	18-38	39	50.7–12.2	p=0.119
	39-64	38	55.2–12.9	
Gender	Female	48	52.7–11.9	p=0.864
	Male	29	53.3–14.2	
Marital status	Single	26	52.5–12.0	p=0.216
	Married	44	55.4–12.0	
	Widowed / divorced	7	47.4–11.2	
Education level	Primary schol	28	58.3–11.5	**p=0.013**
	High school	21	53.2–9.0	
	Higher education	27	48.9–13.1	
Employment status	Active working	27	52.9–12.4	p=0.676
	Not working	50	54.1–11.9	
Financial status	Low	25	55.9–9.7	p=0.303
	Medium	45	53.1–13.3	
	High	7	48.1–10.2	
Co-habitants	Elementary family	67	52.7–12.3	p=0.710
	Extended family	10	54.4–15.7	
Smoking	No	39	54.8–12.7	p=0.185
	Yes	38	51.0–12.5	

ISMI: Internalized Stigma Scale in Mental Illnesses

Table 5: The Relationship Between Disease Characteristics and ISMI Scale Scores

	Alienation	Confirmation of stereotypes	Perceived discrimination	Social withdrawal	Resistance to stigma	ISMI total
Age onset	r=0.064 p=0.583	r=0.238 **p=0.037**	r=0.172 p=0.135	r=0.172 p=0.135	r=0.104 p=0.368	r=0.200 p=0.081
Time after last hospitalization	r=0.081 p=0.481	r=0.125 p=0.281	r=0.017 p=0.881	r=0.169 p=0.143	r=0.047 p=0.686	r=0.123 p=0.286
Time after last episodes	r=0.095 p=0.409	r=0.269 **p=0.018**	r=0.091 p=0.432	r=0.143 p=0.214	r=0.181 p=0.116	r=0.188 p=0.102
Total number of manic episodes	r=0.272 **p=0.017**	r=0.309 **p=0.006**	r=0.165 p=0.152	r=0.162 p=0.159	r=0.183 p=0.111	r=0.287 **p=0.011**
Total number of episodes	r=0.027 p=0.813	r=0.015 p=0.898	r=0.140 p=0.226	r=0.123 p=0.286	r=0.011 p=0.922	r=0.006 p=0.957
Number of depressive episodes	r=0.235 **p=0.040**	r=0.221 p=0.053	r=0.120 p=0.300	r=0.135 p=0.240	r=0.196 p=0.088	r=0.253 **p=0.027**
Number of mixed episodes	r=0.165 p=0.152	r=0.217 p=0.059	r=0.092 p=0.426	r=0.182 p=0.112	r=0.233 **p=0.042**	r=0.213 p=0.063

ISMI: Internalized Stigma Scale in Mental Illnesses

according to the type of the last period, and in the posthoc analyses, a significant difference was found between only the alienation subscale scores and those with depression or hypomania in the last stage. A positive correlation was found between a

Table 6: The Relationship Between ISMI and COPE Scale Scores

	Alienation	Confirmation of stereotypes	Perceived discrimination	Social withdrawal	Resistance to stigma	ISMI total
Problem-Focused Coping	0.134	0.056	0.597	0.075	**0.016**	**0.030**
Useful social support	0.078	**0.002**	0.181	**0.005**	0.104	**0.004**
Active coping	0.062	0.139	0.572	0.360	**0.006**	**0.044**
Restraint	0.482	0.315	0.498	0.478	0.759	0.362
Suppressing competing preoccupations	0.560	0.936	0.597	0.840	0.539	0.797
Planning	0.199	**0.021**	0.406	**0.016**	**0.002**	**0.008**
Emotionally focused coping	0.314	0.387	0.515	0.312	**0.041**	0.255
Positive reinterpretation and improvement	**0.001**	**<0.001**	0.524	**0.008**	**0.013**	**0.001**
Religious coping	0.298	0.201	**0.048**	0.206	0.868	0.082
Humor	0.892	0.838	0.726	0.540	0.205	0.763
Use of emotional social support	0.522	0.253	0.874	0.232	0.316	0.269
Acceptance	0.443	0.950	0.680	0.937	0.157	0.638
Dysfunctional Coping	0.480	**0.026**	0.358	0.084	0.068	**0.048**
Mentally disregard	0.684	0.102	0.197	0.304	0.465	0.330
Focusing on the problem and revealing	0.828	0.336	0.428	0.877	0.472	0.813
Denial	0.344	0.623	0.504	0.558	0.380	0.557
Behavioral disengagement	**0.027**	**0.021**	0.406	**0.028**	**0.009**	**0.004**
Substance abuse	0.551	0.077	0.599	0.149	0.258	0.074

ISMI: Internalized Stigma Scale in Mental Illnesses,COPE: : Coping Attitudes Assessment Scale

history of depression with psychotic features and confirmation of stereotypes, social withdrawal, and total ISMI scores. A positive correlation was found between the history of rapid cycling and the confirmation of stereotypes. Perceived discrimination scores were found to be significantly higher in patients with postpartum onset compared to those without.

Comparison of the subscale scores of alienation, approval of stereotypes, perceived discrimination, social withdrawal and stigma resistance with the same sociodemographic data indicated the presence of a statistically significant relationship between the perceived discrimination subscale score and the place of residence (city or town/village). The perceived discrimination subscale scores of patients living in towns/villages were found to be significantly higher than those living in urban areas ($p=0.038$, Table 5). No significant correlation was found between the other sociodemographic data and ISMI total and subscale scores.

A significant relationship was identified between the active coping scores under the problem-focused coping sub-dimension of the COPE scale and the total ISMI score ($p=0.044$). Additionally, a significant relationship was found between the stigma resistance score and active coping ($p=0.006$).

A significant relationship was also identified between the 'making a plan' scores and confirmation of stereotypes ($p=0.021$), social withdrawal ($p=0.016$), and total ISMI scores ($p=0.008$). A significant relationship was identified between the scores of stigma resistance and 'making a plan' ($p=0.02$). A significant negative correlation was found between the use of beneficial social support and the approval of stereotypes ($p=0.002$), social withdrawal ($p=0.005$) and total ISMI scores ($p=0.004$). The total score of the problem-focused coping sub-dimension of the COPE scale and the total score of ISMI ($p=0.030$) were negatively correlated while a significant positive correlation was identified between the stigma resistance score and problem-focused coping score ($p=0.016$).

A negative correlation was found between positive reinterpretation and development scores under the emotionally focused coping sub-dimension of the COPE scale and the total scores of alienation ($p=0.001$), confirmation of stereotypes ($p<0.001$), social withdrawal ($p=0.008$) and ISMI ($p=0.001$). Additionally, a positive correlation was identified between the scores of stigma resistance and the scores of positive reinterpretation and improvement ($p=0.013$).

A significant positive correlation was found between the scores of religious coping and the scores of perceived discrimination ($p=0.048$). A significant positive correlation between the total score of the emotionally focused coping sub-dimension of the COPE scale and the stigma resistance score ($p=0.041$) was found. A positive correlation was found between behavioural disengagement scores in the dysfunctional coping sub-dimension of the COPE scale and the total scores of alienation ($p=0.027$), confirmation of stereotypes ($p=0.021$), social withdrawal ($p=0.028$) and ISMI ($p=0.004$) while a negative correlation was identified between the behavioural disengagement and stigma resistance scores ($p=0.009$). A significant positive correlation was determined between the total score of the dysfunctional coping sub-dimension of the COPE scale and the total score of ISMI ($p=0.048$) and confirmation of stereotypes ($p=0.026$, Table 6).

DISCUSSION

Relationship Between Sociodemographic Data and Internalized Stigma

The ISMI total scores of patients with primary school education were found to be significantly higher than patients with a higher level of education. Various studies have shown that stigma in general psychiatric patients was associated with a lower level of education, being unmarried or living alone, and being unemployed (19, 20, 21). Thus, the higher the education level, the lesser personal, social and biological reasons contribute towards the aetiology of the disease, providing greater optimism for recovery. In addition, since the increase in the level of education is likely to positively affect self-esteem, it can play a supportive role in reducing the level of internalized stigma (21,22). A sig-

nificant difference in the perceived discrimination subscale score was found between patients living in rural areas versus those living in a city in the current study. It has previously been reported that living in rural areas was associated with a greater perception of stigma, and individuals living in rural areas had greater stigma anxiety (22). No significant relationship was found between other sociodemographic characteristics such as age, gender, marital status, job, income level and internalized stigma.

Relationship Between Clinical Characteristics and Internalized Stigma

No significant relationship was identified between the age of onset of the disease and internalized stigma in the current study. However, a positive correlation was found between the subscale scores of confirming stereotypes and the age of onset of the disease. Patients whose disease was manifested at an early age approved the stereotypes less; as the age of onset of the disease increased, the stereotypes were approved more. We found an inverse correlation between the time elapsed after the last period and the confirmation of stereotypes. Previously, the absence of a significant relationship between internalized stigma and the last remission period has been reported (24). The most striking impression that emerges in patients at the end of a mood episode is that they have failed themselves and are unreliable because they have disappointed everyone. On the other hand, since BD patients mostly do not show any symptoms during the remission periods, their perception of stigma may also vary (22,24). An important finding of recent studies is that with the prolongation of the duration since an acute attack, psychosocial adjustment is improved and the general level of functioning is positively affected (25).

The current study showed a positive correlation between the total number of episodes and alienation, confirmation of stereotypes subscale scores, and total ISMI scores. It is well known that with each new episode, the risk associated with subsequent periods increases and the prognosis worsens (26). Similar to our study, Kamaradova et al. found a positive correlation between self-stigmatization and the number of hospitalizations, disease severity and depression episodes in a study they conducted with 332 patients with mental disorders (27). We observed a positive correlation between the number of depressive episodes, alienation and total ISMI score. A positive correlation was also found between a history of depression with psychotic features and confirmation of stereotypes, social withdrawal and total ISMI scores. Patients with end-stage depression were found to report more alienation than those with hypomania.

Patients with a history of rapid cycling recruited to the current study were found to be more likely to approve of stereotypes about the disease. A previous study has shown that internalized stigma was more common among patients with rapid cycling; moreover, the latter was predictive of internalized stigma (28). The fact that a process that is independent of life events or compelling can be observed clearly in rapid cycling takes the disease away from a reactive nature. Rapid cycling may enable the perception of the disease as a more structural or personal trait (22). Stigmatization was suggested to be aggravated due to the difficulty in distinguishing the disease from personality (33).

The Relationship Between Internalized Stigma and Coping Attitudes

In the face of illness, which is an important source of stress, the individual develops various coping attitudes to minimize and deal with various negativities caused by the illness. Such coping attitudes are considered to avoid or reduce rejection. However, while some of these coping efforts are likely to be effective, others may have significant adverse consequences. Knowing the coping attitudes used by patients may help in understanding the role of such attitudes in the psychopathology of the disease, determining treatment goals, monitoring therapeutic effectiveness and preventing the occurrence of other complications (7, 11). In a study investigating internalized stigma in patients with BD or depression, both groups of patients were determined to experience high levels of stigma; however, patients with BD felt more stigmatized than patients with depression. This difference between the experience of stigmatization and the

effects of stigmatization may be due to different coping attitudes in the two diseases. Thus, there is an urgent need for studies examining the coping attitudes used by patients with BD for stigma (30) since none of the studies in the published literature has examined internalized stigma and coping styles in BD patients. Such studies are important to increase functionality, identify coping attitudes that can be effective in preventing internalized stigma and support such patients.

Patients who used problem-focused coping styles were found to display less internalized stigma and more stigma resistance in the current study. Problem-focused coping attitudes play an important role in regulating stress, producing alternative solutions and including direct interventions that can change the relationship between the person and their environment (31). We found that patients who used problem-focused coping attitudes such as active coping, planning, and use of helpful social support were more resistant to stigma and therefore experienced less internalized stigma. We also observed that patients who used emotionally focused coping styles were more resistant to stigmatization. Emotionally focused coping styles are generally used together with problem-focused coping attitudes. Thus, it can facilitate the use of problem-focused attitudes by reducing stress in intensely challenging situations. However, emotionally focused coping can also restrict the individual and prevent problem-focused actions (32).

Patients in the current study who used positive reinterpretation and growth attitude, which is one of the emotionally focused coping styles, had less internalized stigma and more stigma resistance. Such a coping style has been shown to reduce anxiety, hopelessness, and suicidal thoughts (33). Coping here plays a role in reducing stress rather than dealing with the problem. It may help to reconstruct a challenging life event such as having a mental illness with positive terms and perspective, increase stigma resistance and reduce internalized stigma (34).

We observed a positive correlation between the use of dysfunctional coping attitudes and internalized stigma and a negative correlation between dysfunctional coping attitudes and stigma resistance. Patients who use dysfunctional coping styles of behavioral disengagement were found to feel more internalized stigma and have lower stigma resistance (7). Behavioural disengagement is a non-adaptive attitude that is based on giving up any struggles with the source of stress and also prevents adaptive coping. Behavioural disengagement has been reported to be associated with hopelessness and suicidal thoughts (35).

The current study has some limitations. Statistical analysis of some of the differences in scores of subscales did not reach significance most likely due to the number of patients included in the study. Additionally, a cause-effect relationship could not be established because of the cross-sectional design of the study. Studies with larger samples are needed to support and re-evaluate the data obtained from the current study.

CONCLUSION

Overall, the current study showed that active coping, planning, use of beneficial social support, positive reinterpretation and developmental coping strategies, as well as attempts to reduce behavioral disengagement can reduce internalized stigma and increase stigma resistance. The use of cognitive behavioral interventions may lead to a reduction in internalized stigma and increase psychosocial functionality (36, 37, 38, 39).

Conflicts of interest: The authors declare that they have no conflict of interest.

Correspondence address: Asst. Prof. Sıdıka Baziki Çetin, 63320 Şanlıurfa - Türkiye sdkabaziki@hotmail.com

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A case of adult-onset metachromatic leukodystrophy beginning with behavioral symptoms

Davranışsal belirtilerle başlayan yetişkin tip metakromatik distrofi olgusu

Cemile Hazan Tunalı[1], Süheyla Ünal[2], Ceren Acar[3], Emel Sağlar Özer[4]

[1]Assist. Dr.,Department of Psychiatry, Bursa Yuksek Ihtisas Training and Research Hospital, Bursa, Turkey, https://orcid.org/0000-0002-6498-8973

[2]Prof. Dr., Department Of Psychiatry, University of Health Science, Bursa Medical School, Bursa City Hospital, Bursa, Turkey, https://orcid.org/0000-0003-3266-6256

[3]Prof. Dr., Inonu University, Faculty of Science and Literature, Department Of Molecular Biology And Genetics, Malatya, Turkey, https://orcid.org/0000-0003-1842-9203

[4]Assoc. Prof., Hacettepe University, Department of Biology, Faculty of Science, Beytepe, Ankara, Turkey, https://orcid.org/0000-0002-8161-827X

SUMMARY

Metachromatic leukodystrophy is a rare inherited disorder of the nervous system with great clinical variability characterized by loss of both cognitive and motor functions upon extensive white matter damage by the accumulation of sulfatides. Although metachromatic leukodystrophy usually affects children, many cases of adult leukodystrophy have been reported in the literature in the last few years. Adult-onset leukodystrophy typically presents with a progressive syndrome that includes various combinations of cognitive impairment, spasticity, apraxia, ataxia, and upper motor neuron manifestations. In this article, we decided to present this case to draw attention to the fact that the adult form of metachromatic leukodystrophy, which presents with psychotic symptoms and behavioural problems, should be considered in the differential diagnosis of psychotic pictures. In a 48-year-old male patient who did not have any psychiatric or neurological problems before, symptoms such as meaningless shouting, running away from home, restlessness, and audio-visual hallucinations were added to the clinical picture that started with confusion and disorganized behaviour in a short time. MRI, plasma aryl sulfatase A level (ARSA) and gene analysis were performed for differential diagnosis in the patient. It is known that the patient has a sibling who died before the age of one, and two nephews diagnosed with an autism spectrum disorder. Heterozygous c.1283C>A (p P428Q) mutation was detected in the patient, which was not previously reported in the literature or mutation databases. The chromosomal region-22q13.33- in which the ARSA gene with this mutation is located is also a candidate region for autism. In this respect, it was thought that this mutation might be related to disorganized behavioural problems.

Keywords: adult metachromatic leukodystrophy, psychosis, neurologic symptoms, ARSA gene, mutation

ÖZET

Metakromatik lökodistrofi, sülfatidlerin birikmesiyle yaygın beyaz cevher hasarı oluşması üzerine hem bilişsel hem de motor fonksiyonların kaybı ile karakterize, büyük klinik değişkenliğe sahip, sinir sisteminin nadir görülen kalıtsal bir bozukluğudur. Metakromatik lökodistrofi genellikle çocukları etkilemekle birlikte son birkaç yılda literatürde birçok yetişkin lökodistrofi vakası bildirilmiştir. Yetişkin başlangıçlı genetik lökodistrofiler tipik olarak bilişsel bozulma, spastisite, apraksi, ataksi ve üst motor nöron belirtilerinin çeşitli kombinasyonlarını içeren ilerleyici bir sendromla kendini gösterir. Bu yazıda psikotik belirtiler ve davranış sorunları ile seyreden erişkin formu metakromatik lökodistrofinin psikotik tabloların ayırıcı tanısında düşünülmesi gerektiğine dikkat çekmek için bu olguyu sunmaya karar verdik. Daha önce herhangi bir psikiyatrik veya nörolojik sorunu olmayan erkek hastada, 48 yaşında konfüzyon ve dezorganize davranışlarla başlayan klinik tabloya kısa sürede anlamsız bağırmalar, evden kaçma, yerinde duramama gibi semptomlar ve görsel işitsel halüsinasyonlar eklendi. Hastada ayırıcı tanı için MR, plazma aril sülfataz A düzeyi (ARSA) ve gen analizi yapıldı. Hastanın bir yaşından önce ölen bir kardeşi ve otizm spektrum bozukluğu tanısı alan iki yeğeninin olduğu biliniyor. Hastada daha önce literatürde veya mutasyon veritabanlarında bildirilmeyen heterozigot c.1283C>A (p P428Q) mutasyonu saptandı. Bu mutasyona sahip ARSA geninin bulunduğu kromozomal bölge-22q13.33- aynı zamanda otizm için aday bir bölgedir. Bu açıdan bu mutasyonun dezorganize davranışsal problemlerle ilişkili olabileceği düşünülmüştür.

Anahtar Kelimeler: erişkin metakromatik lökodistrofi, psikoz, nörolojik belirtiler, ARSA geni, mutasyon

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INTRODUCTION

Metachromatic leukodystrophy (MLD) is a lysosomal autosomal recessive sphingolipid storage disorder caused by the deficiency of the arylsulfatase A (ARSA) enzyme (1). The ARSA gene is located on chromosome 22q13.33. It is the first enzyme in the pathway that degrades sulfatides (3-O-sulfogalactosylceramides), an essential component of ARSA myelin (2). Decreased ARSA activity causes sulfatide accumulation in the central nervous system (CNS), peripheral nervous system (PSS) and other internal organs (1). MLD is named from the presence of metachromatic granules in the affected cells, which are formed as a result of the accumulation of sulfatide and sphingolipids in myelin (3). Neurological and behavioural symptoms result from progressive myelin degeneration and loss of axons in the CNS and PSS (1).

The incidence of metachromatic leukodystrophy is approximately 1 in 100,000 live births in the European population (4). In general, MDL is divided into three different clinical forms: the late infantile form, the juvenile form, and the adult form. European studies show that approximately 40-50% of patients have the late infantile form, approximately 30-40% have the juvenile form, and approximately 18-20% have the adult form (4). In the adult form, the first symptoms often suggest a psychiatric illness, particularly schizophrenia, as psychotic symptoms and behavioural abnormalities often begin before or accompany the decline of intellectual capacities (4). In adults, the first symptoms may develop even after the age of 60 (5).

Since adult form MLD starts with psychotic and mental symptoms, a case report was decided to draw attention to the fact that it should be considered in the differential diagnosis. In addition, we aimed to bring the c.1283C>A mutation, which was detected in the heterozygous condition in our patient as a new mutation that has not been reported in the literature or mutation databases before, to the literature. We obtained informed consent from the relatives of the patients to publish the case in medical journals.

CASE HISTORY

A 49-year-old male patient presented with complaints of running away from home, shouting for no reason, and restlessness. His complaints started one year ago as confusing the way home, trying to go to work outside of work hours, talking to himself, pointing somewhere and saying "they are coming". The patient, who had a COVID-19 infection 10 months ago, was hospitalized for this reason. After he was discharged, he left the quality control job at the textile company due to complaints of aggression toward his surroundings, hiding food and belongings, meaningless shouting, and leaving the job before the end of the working hours. Donepezil 10 mg, olanzapine 10 mg, and acetylsalicylic acid treatment were started for the patient who was admitted to psychiatry at that time. The patient's complaints continued to increase and intensify. Risperidone 4 mg and escitalopram 10 mg were added to the treatment because of not being able to take care of himself, constant abusive speech, and the desire to move frequently.

Since the patient's complaints did not regress, he was admitted to the neurology service 2 months ago. During this period, urinary stool incontinence also started, the current medications of the patient were discontinued, and clozapine 12.5 mg was started and gradually increased to 75 mg. Clozapine was increased to 100 mg as the patient's disorganized behaviours, audio-visual hallucinations and running away from home continued during the follow-up. Olanzapine 10 mg and quetiapine XR 150 mg were added. During the sixth month of follow-up, the patient's visual auditory hallucinations continued, and there was a partial decrease in his mobility.

Because the patient's symptoms, which are not typical for psychosis, changed rapidly and the drugs used caused intolerable side effects, drug changes were frequently made to reach the appropriate treatment. A typical image for metachromatic dystrophy was obtained on MRI was taken to investigate organic aetiology in the patient who showed progressive deterioration with atypical symptoms and did not respond to different treatment agents. Thus, a definitive diagnosis was made approximate-

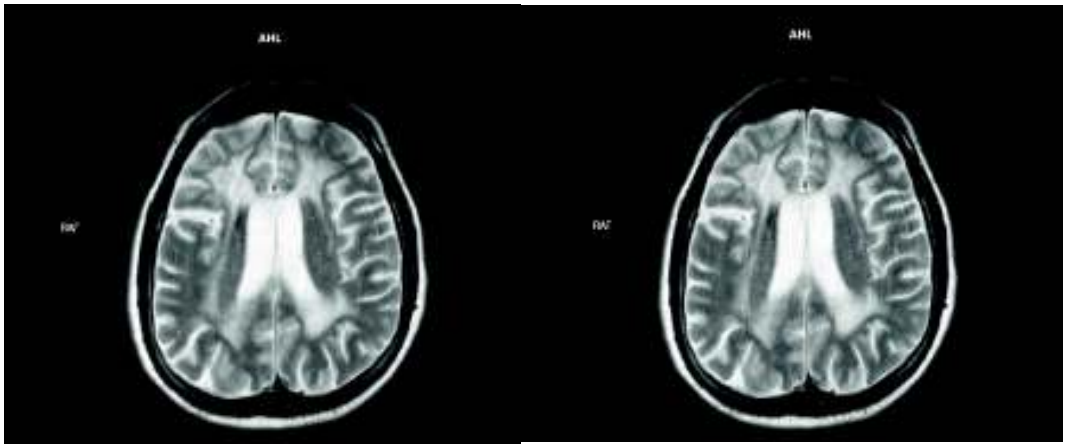

Fig.1. T2 FLAIR hyperintense diffuse lesions in the frontal subcortical deep white matter, periventricular white matter, and corpus callosum on MRI

ly one year after the onset of psychotic, disorganized behaviours in the patient.

His history of birth and childhood development was normal. There was no problem described in the school success of the patient who was a primary school graduate. He had no known history of chronic disease, except that he had been operated on for cystic kidney disease 22 years ago. He had completed his military service fully and on time. There was no history of trauma. There was no parental consanguinity in the family history. The patient had 6 living siblings. It was learned that one of his siblings died around the age of 1, and the cause of death was unknown. The patient's two nephews are diagnosed with autism.

In his neurological examination, he had significant spasticity and ataxia. In his mental state examination, he was conscious and had difficulty cooperating, and his orientation to place and time was lost. The amount of speech decreased; his speech was dysarthric. His affect was limited. There were audio-visual hallucinations. Neuropsychological tests, and nerve conduction studies such as VEP, and BAEP could not be performed because the patient could not cooperate.

Hemograms, biochemistry and sedimentation, thyroid function tests, and vitamin B12 and folic acid levels were within normal limits. HIV, syphilis, hepatitis B/C and tuberculosis tests performed to exclude treatable and acquired causes of white matter disease were negative.

CSF examination was normal. EEG was within normal limits.

In the evaluation of the supratentorial series in the MRI taken 1.5 months ago, confluent T2 FLAIR hyperintense diffuse lesions were observed in the periventricular white matter in the frontal subcortical deep white matter, which diffuses and thins the corpus callosum. More prominent enlargement of the hemispheric sulcus and fissures in the front and dilatation in the third and lateral ventricles were observed (Fig. 1).

A detailed investigation was initiated after the MRI result directed us to metachromatic leukodystrophy. The aryl sulfatase A level in the blood was found to be low (12 nmol/mg/17 hours; normal: 45-260 nmol/mg/17 hours). The change in p. Ser45Arg detected in the gene analysis to confirm the diagnosis is a variant that has been previously described and has been reported to be associated with metachromatic leukodystrophy in the Human Gene Mutation Database (HGMD). According to the American College of Medical Genetics (ACGM) criteria, it was evaluated as a “change of uncertain clinical significance”. In addition, the detected p. P428Q change has not been detected in any other disease before in the literature and was evaluated as “highly pathogenic” according to ACMG criteria.

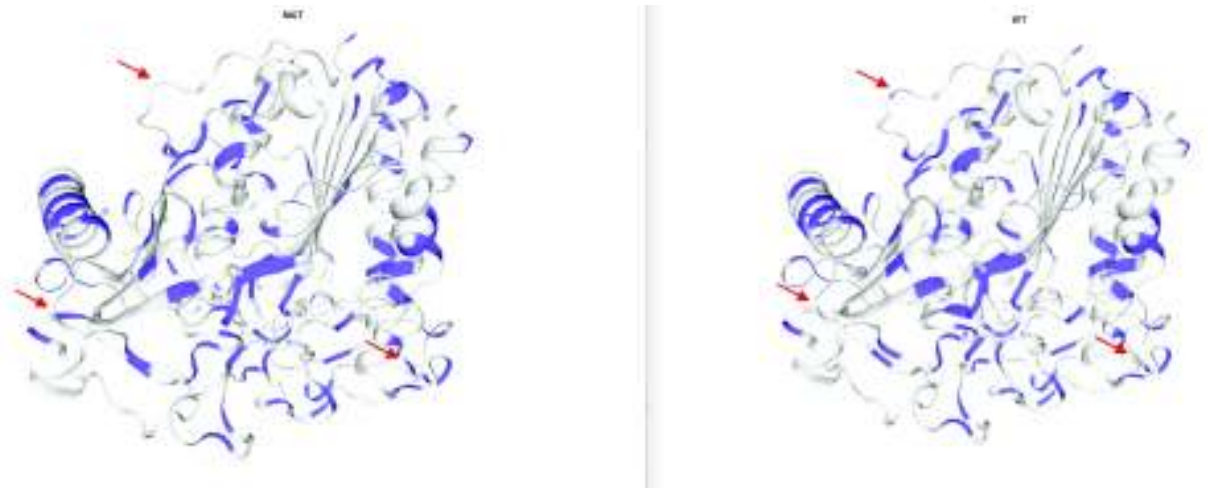

Figure 2. The molecular structure of the wild -type and mutant proteins according to their polarity (Mut on the left and wt-on the right). (http://swissmodel.expasy.org)

DNA Analysis

Genomic DNA was isolated from peripheral blood samples by using Next-generation sequencing. Whole-genome sequence analysis was performed by next-generation sequencing with an Illumina MiSeq instrument. Since the parents of the subject are not alive, the analysis could not be performed on them. However, from the family history, it is known that a sibling who died before the age of one and the two nephews of the subject have autism spectrum disorder. Comparisons of wild-type and mutant protein structures of ARSA were obtained with computational tools such as the Swiss Model (http://swissmodel.expasy.org).

Sequence analysis revealed the presence of 135C>A (p S45R) (p Ser45Arg)/c.1283C>A (p P428Q) (p. Pro428Gln) compound heterozygosity and the presence of the pseudo deficiency allele 1055A>G (p. N352S) in the heterozygous state. The changes in the protein structure are shown in Fig. 2.

The whole gene sequence analysis of the ARSA gene showed three sequence changes, 135C>A/1283C>A and pseudo deficiency mutation 1055A>G. Two of the mutations were previ-

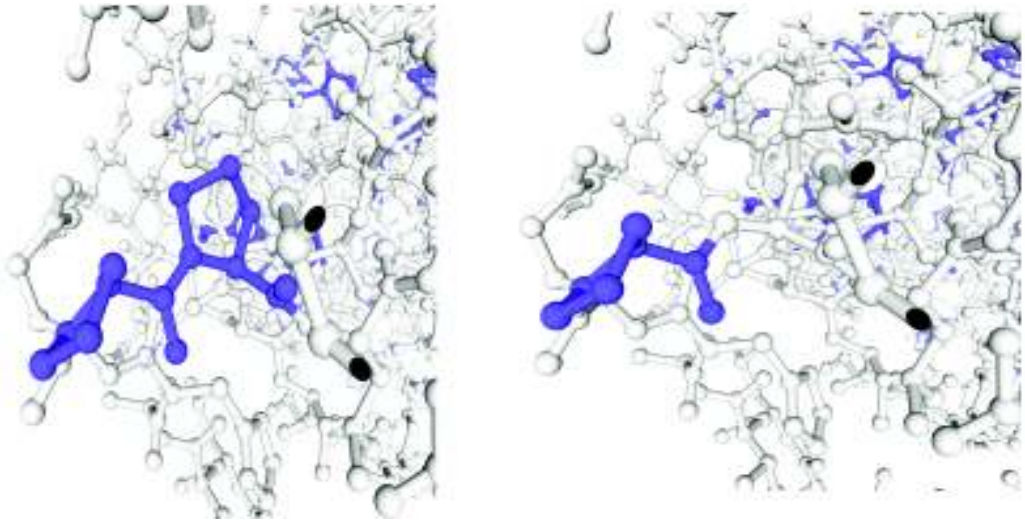

Fig. 3. Close caption of the newly found mutation P428Q. The left panel shows the wild type, and the right panel shows the mutant amino acid in the structure (http://swissmodel.expasy.org).

ously reported mutations, and one mutation was found in our subject and not reported in previous studies. Even though the pseudo deficiency allele 1055A>G, which causes the loss of an N glycosylation site, is found in patients and causes a great reduction in enzyme activity, patients show a clinically healthy phenotype. Therefore, the presence of the N352S mutation in the heterozygous state may not contribute to the disease phenotype of our patient (6).

On the other hand, the presence of 135C>A (p S45R)/c.1283C>A (p P428Q) compound heterozygosity is strongly suspected to cause the symptoms of the patient. The previously known S45R conversion was reported to be Disease-causing in different cases (7), and the c.1283C>A (p P428Q) mutation that was found at the heterozygous state in our patient is a new mutation that was not reported in the literature or mutation databases before. The newly identified C-to-A mutation causes a Pro-Gln conversion, and the localization of that amino acid in the protein's structure is in a region that is conserved among arylsulfatases PPLL (Pro-Pro-Leu-Leu) (8). It also resides in a region close to amino acid 424Glu, which participates in the regulation of dimer-octamer equilibrium by either protonation or deprotonation (9). Because of its position, this newly found mutation could be most likely pathogenic and may affect the activity of the enzyme. The structural changes at the molecular level as a result of the mutation are shown in Fig. 3.

DISCUSSION

Metachromatic leukodystrophy is an autosomal recessive disease caused by mutations in the ARSA gene located on chromosome 22q13.33 (5). More than 100 mutations causing MLD have been identified (4). In patients inheriting two mutant ARSA genes, sulfatides accumulate in microglia, oligodendrocytes and Schwann cells and cause extensive demyelination in the CNS and PSS.

Adult-onset leukodystrophies and genetic leukoencephalopathies include a diverse group of white matter neurodegenerative disorders with a broad age of onset and phenotypic spectrum. Patients typically present with the progressive syndrome that includes various combinations of cognitive impairment, spasticity, apraxia, ataxia, and upper motor neuron manifestations. Two distinct clinical presentations have been observed in adult MLD: patients with progressive motor or sensory deficits and patients with mental impairment. These two conditions may be caused by different specific mutations. It manifests itself with progressive gait disturbance mainly caused by spastic paraparesis or cerebellar ataxia in those with P426 L mutations from P426 L and I179S, the two most common mutations in late-onset MLD. It has been found that mental disturbance is insignificant at the beginning of the disease but becomes more pronounced as the disease develops. In contrast, the I179S mutation is manifested by schizophrenia-like behavioural abnormalities, social dysfunction, and mental regression; motor deficits are much less common (1).

We detected a heterozygous c.1283C>A (p P428Q) mutation in our patient, which has not been reported in the literature or mutation databases before. This new mutation is most likely pathogenic and may affect the activity of the enzyme. Analysis of the newly found P428Q mutation could not be performed because the patient's close relatives were not alive. However, it should be noted here that the nephews of the subject have autism spectrum disorder. The chromosomal region-22q13.33- in which the ARSA gene with this mutation is located is also a candidate region for autism. Individuals with 22q13.3 deletion syndrome, known as Phelan-McDermid syndrome (PMS), have autism-like behaviours. In a literature review covering 56 cases of PMS who showed signs of behavioural and neurological decompensation during adolescence or adulthood, one patient was found to have juvenile-onset metachromatic leukodystrophy, a severe demyelinating disorder caused by mutations in the ARSA gene at 22q13.33 (10). In this respect, it was thought that this mutation might be related to behavioural problems.

The definitive diagnosis of MLD requires a comprehensive evaluation based on a wide array of diagnostic procedures, including biochemical and molecular tests and neuroradiological (grey matter volume loss, white matter abnormalities) and neurophysiological evaluations (11). The most accu-

rate method in the diagnosis of hereditary genetic diseases is the detection of mutations by sequencing. However, since not all disease-associated mutations are currently identified, diagnosis can be made using MRI and determination of ARSA activity or sulfatide levels. Magnetic resonance imaging provides early detection of white matter damage. In the juvenile form, the central and periventricular white matter is primarily affected. As the disease progresses, subcortical structures of the white matter may also be affected. MRI findings consist of symmetric T2 hyperintensity in the frontal or periventricular white matter (12). Patients with adult-onset metachromatic leukodystrophy usually have frontal dominance. Loss of white matter volume causes brain atrophy in the late stages of the disease (13). The magnetic resonance imaging findings of our case were also in the form of frontal subcortical hyperintense with no contrast diffuse lesions in the white matter.

The adult form of MLD is characterized by nonspecific psychopathological symptoms. These include emotional lability, apathy, personality changes, schizophrenic disorder and dementia. The clinical course of the late-onset variant is slower (14). Psychiatric findings may be misdiagnosed as they may appear several years before neurological findings. Of the 129 MLD cases reported in the literature that started between the ages of 10 and 30, 53% had psychotic symptoms. Typical psychotic symptoms; auditory hallucinations, complex delusions, fragmentation of thought, inappropriate affect, bizarre behaviour and catatonic posture. Therefore, these initial statements may mimic schizophrenia (15). The later addition of motor signs, peripheral neuropathy and progressive loss of previously acquired abilities to the psychotic picture may help differentiate it from schizophrenia. In our case, the first complaints started with audiovisual hallucinations and bizarre behaviours.

Currently, there is no curative treatment method for metachromatic leukodystrophy. The positive results reported from different animal studies on hematopoietic stem cell transplantation (HSCT), gene therapy and enzyme replacement therapy have led to clinical trials investigating the efficacy of these approaches (16). Although HSCT is beneficial in some lysosomal storage diseases, the desired results could not be achieved in metachromatic leukodystrophy. Gene therapy is likely to be trialled in a limited number of patients in the near future (17).

In conclusion, we diagnosed our case with metachromatic leukodystrophy by examination, low blood arylsulfatase A level, imaging and gene analysis methods. Within the framework of this case, we wanted to emphasize that MLD, which is one of the metabolic diseases, can present with adult-onset psychotic symptoms by conducting a literature review regarding the diagnosis, clinical manifestations and treatment options of MLD.

Correspondence address: Assistant Cemile Hazan Tunalı , Kurtuluş Mahallesi Halide Edip Adıvar Caddesi Dörtçelik Ruh Sağlığı Hastanesi Nilüfer Bursa - Türkiye, hzancitlak@gmail.com

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