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What do the amendments to the associate professorship exam regulation mean?

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For many years, the discussions we have been having are still alive, and at the forefront of topics where both determinations and criticisms maintain their currency are the academic promotion criteria applied in universities and the Associate Professorship exam or appointment criteria organized by the Turkish Interuniversity Board. Today, most research are produced for academic promotion and mainly to achieve a quantitative level, consisting of master's, doctoral, and specialization thesis studies that find identity in this context (1). These research are done to complete an academic stage rather than reaching original results aimed at changing life, the world, and science. These research, which cannot always gain the quality of national and international publications, create a data and article landfill after a while. Labor and value loss are just the tip of the iceberg. One of the most significant triggers of this process is the quantitative evaluation of scientific studies in the academic promotion process in today's scientific world, the haste of the research, and their values as a number. Another significant reason is that the standards defined by the Council of Higher Education (CHE) and the Turkish Interuniversity Board (TIB) in academic promotions lead to the production of research that responds to the needs of the West, the USA and Europe's developed countries, in other words, international capitalism, without any economic burden on these countries, rather than researches that will meet Turkey's needs and make the events, phenomena, and developments experienced in the country understandable. We can say that this process has particularly increased the number of mostly biologically based research guided by the pharmaceutical and medical technology industry (1).

TIB updates the academic appointment and promotion criteria, as well as the associate professorship conditions at regular intervals. The associate professorship regulation was previously updated in 2016, and significant changes were made. Looking at the changes made during that period, a scoring system had been established that provided a significant advantage to being the sole author, aside from determinations regarding the number of publications that needed to be included in the scanning indexes determining the international publication category. Furthermore, all activities and endeavours conducted throughout academic life, including book authorship, editorship, patents, citations, consultancies, projects, meetings, and educational activities, were somehow included in this scoring. These changes were viewed positively. However, one of the most significant shortcomings was the overemphasis on international publications while not sufficiently supporting national publications. This tendency carried the potential to create an impact that would lead to fewer studies and research addressing the country's needs in the national field, thus reducing productions in this area (2). This prediction has largely come true.

Although we see that relatively more points are given to the research listed in the TR Index in the new criteria we are discussing today, we observe that national scientific publishing has not developed since 2016, many domestic scientific journals have closed, changed hands, a significant portion stopped publishing articles in Turkish, some national journals only accept articles in English, and many journals publish articles by charging authors with very high fees. It seems that this trend has not slowed down with the latest amendments and

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changes made in 2023. It is extremely difficult to say that the new criteria, which are stated to be implemented from 2024 onwards, bring an innovation that allows overcoming this problem.

A while after the 2016 amendments, it should be remembered that the oral exam, which was an extremely important phase to overcome in the process of becoming an associate professor, was abolished, and the title of associate professor began to be granted only through a review of the scientific dossier. Previously, the obligatory requirement to teach a lesson for associate professorship, which was an important evaluation criterion in making the decision to become an associate professor, had also been abolished. These changes have been highly criticized for disabling the competency of the faculty member, whose primary duty definition is education and teaching, followed by the responsibility for scientific research and health service, to provide education, its testing and responsibility, and for being a decision inflicting damage to university education, while the subsequent removal of the requirement for oral exams indicates that this qualitative erosion is growing. After educational competence, clinical competence was also excluded from the assessment, and an associate professorship assessment dominated the process, only through the "scientific" studies whose framework I outlined above. The oral exams, which were conducted earlier, were problematic as a practice that doomed the candidate's associate professorship process to arbitrariness, with its characteristic of not aiming to test clinical interview skills, and being prone to unethical guidance, evaluating more knowledge and to a lesser extent attitudes. Therefore, while it was desired to enhance the quality of the oral exams, its complete abolition initiated a destructive change that sterilized education. It should not be considered an empty claim to say that the changes made in 2023 aim to conceal this erosion, this sterilization with quantitative and publication criteria, and that an effort is being displayed in this direction.

So, what do the amendments made in 2023 encompass? These amendments include:

1. Taking into account the Web of Science Quartile category for journals within the scope of SCIE or SSCI.

2. Abolishing the field index definitions, and in their place, implementing scoring for articles published in AHCI, ESCI, and Scopus covered journals, introducing a minimum limit purported to enhance quality in the relevant category.

3. Increasing the score for national articles published in journals under the TR Index.

4. Introducing a requirement of at least one single-authored publication for each fundamental field, increasing the number where they exist, and raising the main author number from one to three.

5. Utilizing the WoS Book Citation Index as a reference for books and book chapters, while categorizing others separately.

6. Instituting restrictions which have become one of the most debated alterations regarding editorships in other international/national book chapters.

7. Renewing the citation category within the scope of Web of Science, giving more weight to citations made in journals under the TR Index, and assessing other citations under the "other" title.

8. Awarding points for completed thesis supervisions across all basic fields.

9. Introducing a completion requirement for all projects, with role definitions in these projects being fundamental in scoring.

10. Using the Web of Science Conference Proceedings Citation Index as a reference for scoring publications in all fundamental fields, categorizing others as "other."

11. Renewing the clause titled "Educational/Teaching activity."

12. Adding a "Patent/Utility Model" clause, an "Award" clause, and an "Other" clause (WoS h-

index, overseas research/teaching activity) to all fundamental fields, with the amendments updating and expanding the scope of patent definitions and patent/utility model specifications.

When all these changes are examined, it indicates the formation of academic criteria allowing both the orientation of scientific research and academic production towards generating content required by neoliberal capitalism, and the shaping of a scientific knowledge production and educational model that meets the needs of political power. The objectives, which have been gradually becoming more evident since the first associate professorship regulation, indicate this trend. Although the president of CHE states that these changes were made with the aim of improving quality (4), the perception that the alterations fundamentally aim to foster an academic competition environment oriented towards the needs of national and international capitalism is shared in many circles (5,6,7). For instance, one of the new criteria, which necessitates scholars to be “a professor registered in the YÖKSİS system and have permission from their affiliated university” to be able to become an editor for a book, clearly disregards freedom of speech and thought, eliminates scientific freedom, and showcases a tendency that submits scientific production to the direct control of the political power. Science is being reduced to an activity that can only be conducted under the supervision and scrutiny of a “professor” who has “official permission from the university” (6). Additionally, criticisms are being raised that CHE condemns researchers to these establishments because it refers to internationally centralized WOS (Web of Science) Book Citation Index (BKCI), WOS Journal Index, and WOS Conference Proceeding Index for scoring scientific works (articles, books, reports, etc.). These scanning indexes are commercial entities; they are international organizations directing scientific publishing with the main objective being to achieve high profits. It is claimed that these decisions push all scientific production in the country, scholars, those dealing with scientific publishing, individuals, and professional organizations organizing scientific congresses, into a global capital group, forcing them to succumb to the dominance of these organizations and creating a ground that does not allow for overcoming this (5,7). Especially labour and professional organizations emphatically underline that academic education and production will be harmed and suffer permanent damage with these new criteria (5,7).

The imposed condition requiring all sections of the published book to be "related" to the scientific field applied for associate professorship is expected to cause confusion, creating ambiguities such as whether a book written on political psychology will be included in political science or the field of psychology, and generating uncertainties about the boundaries of science and who will draw them. It is said that this situation will render interdisciplinary studies impossible, and it will deem academics who "perform editorial duties without permission from the university and are not considered authorized" worthless. These criteria have left out candidates who have given/give lectures in associate degree programs by imposing the condition of "having given undergraduate and postgraduate courses” and scored the lecture-giving activity as the least valuable academic activity. Moreover, there are ambiguities that can create rights violations for those who make their initial applications for associate professorship and are forced to wait for three terms (5).

The scoring assigned to the roles undertaken in projects makes the effort of young academics, who have a significant contribution to bringing the projects to life, invisible and valueless, given the high proportion allocated to project coordinators. This situation implies that the hierarchy here will make the advantages stemming from status and managerial positions determining, and that all the gains of a teamwork, of a collective production will be credited to a single individual. The obligation of single-author research is also likely to produce the same results.

Especially the addition of the clause regarding patents and awards, the definitions of patents and utility patents, and the increase in the number of items in certain fundamental fields, make the basic ideological and class preferences in this direction more visible with the aim of encouraging academic education oriented towards the requirements of national and international capitalism that has been

emphasized through the university-industry collaboration until today.

In conclusion, the principles and criteria for academic promotion will continue to be debated historically along with the new associate professorship assessment criteria. While determining these criteria, CHE and TIB make regulations with the demands and directives of the political power without consulting the professional organizations, scientific institutions and organizations, and competent academics in the field. Particularly, what organizations like the Turkish Medical Association and specialty associations, as well as educational and professional organizations, should do in this context is not to remain silent, to conduct comprehensive studies, to publish reports, to form pressure groups, and to force CHE and TIB to make arrangements based on science, ethics, and solidarity that develop academic production that meets the needs of the society.

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Decreased serum levels of glial markers and their relation with clinical parameters in patients with schizophrenia

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SUMMARY

Objective: The neurodevelopmental hypothesis of schizophrenia suggests that alterations of glial fibrillary acidic protein (GFAP) and glial cell line-derived neurotrophic factor (GDNF) functions may play a role in the pathogenesis of schizophrenia. However, there is limited information about the relationship of these molecules with the clinical features of schizophrenia. In this study, it was aimed to compare patients with schizophrenia and healthy controls in terms of serum GFAP and GDNF levels and to investigate the effects of clinical parameters on serum levels of molecules in patients with schizophrenia.

Method: 37 patients with schizophrenia followed in the psychosis unit and 37 age- and sex-matched healthy controls without a history of psychiatric disease were recruited in study. The patients evaluated through the Turkish version of positive and negative syndrome scale. On the other hand, sociodemographic question form was applied to both the patients and the healthy controls.

Results: Serum GDNF and GFAP levels of patients with schizophrenia were significantly lower than those of healthy controls. Furthermore, serum GDNF levels were negatively correlated with general and negative syndrome scales (PANSS) in these patients.

Conclusion: It has been observed that there is a relationship between PANSS and changes in the GDNF levels of schizophrenia patients. However, larger clinical studies in which these markers are also measured in cerebrospinal fluid are needed to understand the biological mechanisms underlying these associations and to understand whether glial markers could be useful as biomarkers for the diagnosis of schizophrenia.

Keywords: Schizophrenia, Neurodegeneration, GFAP, GDNF, Glial Markers, PANSS Scores

INTRODUCTION

Synaptic, metabolic and inflammatory dysregulations were documented in schizophrenia and bipolar disorder, leading to speculation that astrocyte dysfunction occurs in these disorders (1). Accordingly, in great number of investigations carried out on astrocytes in schizophrenia and bipolar disorder, glial fibrillary acidic protein (GFAP) was used as a marker (2). Astrocytes are the most prevalent cell types in human brain; and they serve for a range of functions including regulation of neuronal metabolism, modulation of central nervous system inflammation, conducting direct and indirect roles in synaptic transmission (2, 3). It was reported that regional and antigen-specific downregulation of GFAP protein in orbitofrontal cortex in schizophrenia and bipolar disorder may be related to disease mechanisms of psychosis (4). It was determined that there is increasing GFAP protein expression in prefrontal cortex of patients with psychotic illness indicating a role for this protein in the pathophysiology of psychosis (2). GFAP and glutamine synthetase in subregions of prefrontal cortex in schizophrenia and mood disorders were studied by some researchers, and an increase in GFAP immunoreactivity in area 9 in schizophrenia was detected, and the case was stated to be a conse-

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quence of chronic antipsychotic medication (4). However, decreased GFAP immunoreactivity in area 11/47 in schizophrenia and bipolar disorder was observed and it was suggested that this could not be attributed to drug treatment (4). Besides pathological findings of GFAP pathology, serum study results also differed. When compared to healthy controls, lower serum GFAP levels were determined in patients with schizophrenia, (5) while Steiner at al. could not found this (6).

It was suggested that neurotrophic factors such as nerve-growth factor and brain-derived neurotrophic factor have significant parts in pathophysiology of schizophrenia (7). On the other hand, glial cell line-derived from neurotrophic factor (GDNF) is one of the strongest trophic factors for dopaminergic neurones within the central nervous system of the mammalian (8). Functionally, GDNF is thus potentially related to the dopaminergic and neurodevelopmental hypothesis of schizophrenia. GDNF and its related genes are integrated with the pathophysiology of neurodegenerative and neuropsychiatric disorders, for example; addiction of drug, (9) Parkinson's disease, (10) Alzheimer's disease, (11) mood disorders, (9,12,13) stress vulnerability and schizophrenia (14, 15). Focusing on schizophrenia, although there are studies with no significant association with GDNF genes, it was reported by a study that there is nominally positive interaction between GDNF family receptor genes and schizophrenia (10,16,17). Serum GDNF investigations on patients with schizophrenia were performed by Niitsu et al. (17) and Tunca et al. (14). Niitsu et al. (17) found no difference between serum GDNF levels of schizophrenia patients and healthy controls, although it may be associated with working memory in healthy controls and the pathophysiology of attention deficits in schizophrenia. Tunca et al. (14) on the other hand, found that patients with schizophrenia have had significantly lower GDNF levels. Furthermore, the therapy of rat C6 glioma cells in an artificial environment with not just typical (haloperidol) but also atypical (quetiapine and clozapine) antipsychotic drugs proved to change GDNF (18) which happened with phencyclidine, a drug producing symptoms similar to schizophrenia in healthy humans (19,20).

Considering these aspects, it is understood that the structural and/or functional modifications in the brain associated with astrocyte and synaptic functions may be involved in pathogenesis of schizophrenia (4, 6, 14, 16). On the other hand, few studies studying astrocytic and trophic factors including GDNF and GFAP serum levels in patients with schizophrenia are available. Moreover, there is a considerable uncertainty about the clinical characteristics such as the number of hospitalizations, type of antipsychotic and positive and negative syndrome scale (PANSS) on the serum levels of these molecules in patients with schizophrenia. Therefore, we aimed to compare control and patient groups in terms of serum levels of GFAP and GDNF, and also to investigate their clinical characteristic effects on serum levels with the help of these parameters in patients with schizophrenia.

METHOD

Participants and procedures

This study was performed in psychotic disorders unit of department of psychiatry of Cerrahpaşa Medicine Faculty of Istanbul University between January 2015 and August 2015. There were 37 patients with schizophrenia, who were followed by psychotic disorders unit and were consecutively included in the study. The patients met the DSM-5 criteria for schizophrenia, and they were all under drug treatment (21). Exclusion criteria for all participants included mental retardation, history of neurological disease, clinically significant head injury and active substance abuse or dependence. In addition, patients with co-morbid psychiatric illness were excluded. The healthy controls consisted of 37 (age and gender matched) volunteers from hospital staff or their relatives with no psychiatric history, neurological disorder and alcohol and substance dependence.

The research protocols were approved by the Ethics Committee of Cerrahpaşa Faculty of Medicine at Istanbul University and were therefore performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. The study was carried out according to the principles of the Helsinki

Convention on Human Rights and good clinical practice. Participants were informed that the study was confidential, anonymous and voluntary. Consent forms were confirmed by both patients and healthy controls after they were explained the complete description of the study. In addition, before the consent forms were taken from the patients, both the patients and their first-degree relatives, accompanying them in the hospital during the examination, were informed about the purpose and scope of the study in detail. Turkish version of PANSS was applied to patients, while sociodemographic form was applied to both the patients and control groups (22).

Determination of serum GDNF and GFAP levels

Laboratory measurements were accomplished in microbiology laboratory of Istanbul University Medicine Faculty. Blood samples were drawn by the venepuncture technique and transferred into three different tubes without anticoagulant. This sample collection task was conducted for both patient and control groups after an overnight (≥12 h) fast. Afterwards, blood specimens were allowed to clot for 30 minutes. And then, they were centrifuged at 4000 rpm for 10 min as usual. Thus, blood cells and all large particles in blood samples were precipitated. Yellow and clear serum samples were selected for the study. Both haemolysed and lipemic blood samples were removed. The aliquots of serum samples were kept at −70 °C for measurement of GDNF and GFAP concentrations. Measurements of glial markers serum levels were made after all samples were frozen and completed.

Serum concentration of GDNF and GFAP were determined by Enzyme-Linked Immuno Sorbent Assay (ELISA) test. These kits (SUNRED Biotechnology, Shanghai / Catalog Number is 201-12-0123 for GDNF and is 201-12-2095 for GFAP) use a double-antibody sandwich ELISA to assay the level of human GDNF and GFAP in samples. Procedures were performed as follows; 50µl standards were added into standard solution wells, 40µl serum samples and 10µl GDNF and GFAP antibodies were added into sample wells. Then 50µl streptavidin-HRP was added to each well except blank well and the plate was covered with seal plate membrane. Plate was shaken gently so that it would mix and then it was let to be incubated at 37 0C for 60 minutes away from light. The plate was washed carefully four times and then it was blotted. 50µl chromogen reagent A was added to each well, then 50µl chromogen reagent B was added to each well and plate was incubated for 10 minutes at 37 0C away from light for colour development.

Finally, 50µl stop solution was added to each well. The optical density (OD) of each well was measured under 450 nm wavelength within 10 minutes after having added stop solution. According to standard concentrations and corresponding OD values, the linear regression equation of the standard curve was calculated and GDNF and GFAP concentration of samples were determined as Intra-Assay CV<10% and Inter-Assay: CV<12% for both parameters. Assay ranges were 0.1 ng/ml→20 ng/ml for GDNF and 0.1 ng/ml→15 ng/ml for GFAP. A measurement result for each molecule belonging to different patients exceeded the limit values during the measurement; and the result of this patient was not included in the statistical analysis.

Data analysis

All statistical analyses were performed using the IBM SPSS Statistics 22.0 package program (IBM Corp., Armonk, New York, USA). Chi-square and Fisher Exact Tests were applied to compare the categorical variables. Kolmogorov–Smirnov test (K–S test) was used; and histogram and q-q plots were examined to assess the data normality. A two-sided Mann-Whitney test was applied to compare the differences between groups for continuous variables. Effect Size analysis was performed with GPower software 3.1 (Düsseldorf University, Germany). Binary correlations and multiple regression analysis were performed between the parameters. Data were expressed as frequencies, median (min-max), and mean ± standard deviation. The value of $p<0.05$ denoted statistical significance.

RESULTS

The number of participants with schizophrenia was 37 and there were also 37 healthy individuals in the

Table 1. Clinical characteristics and pharmacological treatment of patients with schizophrenia

Patients (n=37)		
Parameters		Results
Disease Onset Age		24.4–5.7
Duration of Illness		15.1–9.3
Number of Hospitalizations		3.29–2.3
Psychiatric History in Family		14(37.8%)
Medication Use	Typical antipsychotics	17(45.9%)
	Atypical antipsychotics	35(94.5)
PANSS	Total	70.8–27.1
	Positive	15.3–8.4
	Negative	22.6–9.9
	General	39.5–16.9

Data are expressed as number for categorical variables and mean–SD for continuous variables.

Table 3. Correlation between glial markers and clinical characteristics levels in patients with schizophrenia

	GDNF		GFAP	
Parameters	rho	p	rho	p
Number of Hospitalizations	0.308	0.063	0.362	0.030
Duration of Illness	0.405	0.016	0.300	0.080
PANSS Total	-0.177	0.301	-0.015	0.932
PANSS Positive	-0.062	0.713	-0.070	0.685
PANSS Negative	-0.485	0.002	-0.220	0.197
PANSS General	-0.378	0.021	-0.088	0.609

*rho = Spearman correlation coefficient

study. When groups were compared in terms of sociodemographic and clinical characteristics: There were not any significant differences across the groups in terms of gender (p=0.816), age (years, p=0.375), marital status (p=0.278), smoker (p=0.482), number of siblings (p=0.177), duration of marriage (p=0.617), number of children (p=0.335), number of cigarettes (p=0.961). Yet, the duration of education was higher in control group (16 years for controls and 12 years for patients with schizophrenia; p=0.001) and there was a difference between the groups in terms of employment status (Employed / Unemployed, 20/17 for controls and 31/6 for patients with schizophrenia).

Clinical characteristics and pharmacological treatments of patient group are given in Table 1. Mean age for first psychotic episode was 24.4±5.7. Duration of illness was 15.1±9.3, and patient's mean number of hospitalization was 3.29±2.3 (Table 1).

Serum GDNF and GFAP levels for both of the groups, smokers and non-smokers are given in Table 2. Serum GDNF and GFAP levels of patients with schizophrenia were significantly lower than those of healthy controls (p<0.001). There was not any gender difference within the patients and between groups. There was no significant difference between smokers and non-smokers in groups in terms of glial marker levels (p<0.05).

There was no significant relationship between sociodemographic parameters and serum levels in the control group. On the other hand, in patients with schizophrenia, the number of hospitalizations was positively correlated with GFAP levels (rho=0.362, p=0.030). Duration of illness was positively correlated with GDNF and GFAP (rho=0.405, p=0.016 and rho=0.300, p=0.080; respectively, Table 3). Serum GDNF levels were negatively correlated with PANSS Negative (Figure 1) and PANSS General (rho=-0.485, p=0.002 and rho=-0.378, p=0.021; respectively) in the patients. We did not observe any relationships between other clinical parameters such as medication use, psychiatric history in family and disease onset age with serum levels of GDNF and GFAP in patients with schizophrenia.

DISCUSSION

Results of our study revealed that serum GFAP and GDNF levels in patients with schizophrenia were significantly lower than those of healthy controls. In patients with schizophrenia, GFAP levels were positively correlated with the number of hospitalizations. Moreover, serum GDNF levels were negatively correlated with PANSS Negative and PANSS General in patients with schizophrenia.

While Niitsu et al. (17) found no differences between serum GDNF levels of patients with schizophrenia and healthy controls, Tunca et al. (14) found that patients with schizophrenia had significantly lower GDNF levels. To our best knowledge, our study is the first study searching serum

Table 2. The comparison of the study groups in terms of the glial markers

			95% CI			
Parameters	Controls (n=37)	Patients (n=37)	L	U	P Values	Effect Size
GDNF (ng/ml)	11.49(2.56-18.7)	3.95(0.80-9.63)	5.2736	8.9821	<0.001	3.2681
GFAP (ng/ml)	7.12(1.70-10.2)	3.67(0.89-9.64)	1.9624	9.0046	<0.001	1.3526

Data are expressed as median (min-max) for continuous variables.

levels of both GFAP and GDNF, which are two important markers for astroglial function and neurotrophy in patients with schizophrenia.

A significant increase was found in GFAP levels in the post-mortem dorsolateral prefrontal cortex of patients with schizophrenia and bipolar disorder, which indicates the role of this protein in the pathophysiology of psychosis (2). Several possibilities were suggested as to why GFAP expression may increase in the absence of changes in other astrocyte-associated proteins. It is plausible that GFAP proteins are malfunctioning by leading to protein accumulation (2, 23). Lower serum GFAP levels in our study, when compared to healthy controls, can be explained with the proposal of protein accumulation resulting from lower serum levels of the molecules. However, factors influencing GFAP production and/or breakdown could also be altered in psychosis. For example, the RNA-binding protein quaking, which is downregulated in schizophrenia, has recently been found to be regulating GFAP mRNA expression (24, 25). Furthermore, GFAP is a cytoskeletal protein; and a growing body of evidence supports the role of cytoskeletal pathology in patients with schizophrenia and bipolar disorder (26,27). Increases in GFAP were most pronounced when cases were divided into psychotic and non-psychotic cohorts suggesting that increased GFAP may be associated with psychotic symptoms (2). Positive correlation between the number of hospitalizations and serum GFAP levels in our study also might be related with the cytoskeletal pathology of the illness.

Perhaps one of the most important findings of our study is that the demonstration of GFAP levels was positively correlated with the number of hospitalizations, while serum GDNF levels were negatively correlated with PANSS Negative and PANSS General in patients with schizophrenia.

The Positive and Negative Syndrome Scale is one of the most widely used methods for standardized measurement of core symptoms of schizophrenia (28). It is a well-known phenomenon that negative symptoms tend to increase with the duration of illness (6). In our study, correlation between serum GDNF levels with PANSS Negative in patients with schizophrenia is consistent with correlation between serum GDNF levels with PANSS General in in patients with schizophrenia. Moreover, in our study, it has been found that astrocyte and synaptic function deficiency can change the severity of schizophrenia.

While GFAP and GDNF are typically regarded as intracellular protein, they have, however, been discovered to be normally present in extracellular biological fluids, including human cerebrospinal fluid (CSF) and blood plasma (6,11,13,29). The CSF is in touch with the brain interstitial fluid directly; therefore, great likely it supplies a more accurate assessment than surrounding blood of GFAP and GDNF metabolism. However, the constant yielding of CSF entails that it should depart the subarachnoid space circumambient of the brain; and possibly, as CSF flows down the subarachnoid granulations into the venous circulation, products set free from the brain into the CSF could be carried into blood when CSF goes into the venous circulation (30). As a result, serum levels of GFAP and GDNF may cast back the intracellular level of these molecules.

The association between serum levels of GDNF and attention deficits in schizophrenia was studied, and it was demonstrated that GDNF serum levels showed no differences between patients with schizophrenia under treatment and healthy controls (17). According to these results, researchers suggest that GDNF serum levels may be utilized unsuitably as biomarkers for schizophrenia (23). Contrary to this research, our study revealed that lower serum GDNF levels in patients with schizophrenia are compatible with the results of Tunca et al. (14) who found that patients with schizophrenia had significantly lower GDNF levels. Another important finding is that higher serum levels of GDNF were associated with better performances on the digit span in healthy controls, yet greater severity of attention deficits in patients with schizophrenia (17).

In a previous study, GDNF was found to be increased after the phencyclidine subchronic administration and it was proposed that subchronic phencyclidine may modulate the function of the GDNF system (31). Another study showed that

serum levels of GDNF gradually increased during antipsychotic therapy and it was suggested that stimulation of GDNF release from glial cells by antipsychotic drugs might underlie some of their neuroprotective properties in situ. Furthermore, a negative association between GDNF levels following pharmacotherapy and disease duration in subjects with schizophrenia could be observed (32).

In the correlation analysis, we did not observe any relationships between typical antipsychotics and medication use with serum levels of glial markers in patients with schizophrenia.

Since GDNF signaling regulates neural activity, reduced expression of GDNF levels implicated neuronal damage, it was stated that antipsychotic medications stimulated C6 glioma cells to secrete GDNF in experimental and clinical reports (33). On the other hand, Xiao et al. proposed that the length of illness was positively correlated to glial cells and the number of neurons impairments, which led to perturbed GDNF synthesis (32). Although lifetime chlorpromazine dose and duration of illness correlated positively with GFAP levels, these correlations were no longer significant when age at death was controlled for (34). Rats exposed to antipsychotics did not display significant differences in any astrocytic protein, proposing that elevated GFAP levels in schizophrenia is not ascribable to antipsychotic treatment. Elevated levels of GFAP may imply that astrocyte numbers are unaffected but astrocytes are partially activated, or may demonstrate a dysregulation of GFAP (2).

In a longitudinal survey, it was expressed that during both manic and depressive episodes of bipolar disorder, patients showed lower serum levels of GDNF compared with healthy controls. In the same study, it was found that after the pharmacotherapy lasted for eight weeks, these levels rose with those of healthy controls (35).

Limitations

On the other hand, this study has some limitations including a small sample size and absence of CSF GFAP and GDNF levels, and absence of neuroimaging. However, if we could compare patients as first episode psychosis and chronic, undertreated psychotic patients, results might be more precise. Lastly, drug doses and chlorpromazine equivalant could increase the power of this study. For these reasons, results of this study need to be replicated by future studies.

The decrease of serum GFAP and GDNF may provide evidence for relationship between schizophrenia and changes of glial cells. We suggest that the negative correlation between GDNF with PANSS Negative and PANSS General and between GFAP levels with the number of hospitalizations may reveal that patients with schizophrenia may be affected by astrocyte and synaptic functions. It will be of great contribution to determine other potential causes of decrease in the serum GFAP and GDNF, and to clarify their usefulness in the clinical practice of serum GDNF as a biomarker in diagnosis for schizophrenia. Moreover, comparison of the patients as first episode psychosis and chronic, undertreated psychotic patients might be more precious and deserves further investigation.

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Ethical statement The research protocols were approved by the Ethics Committee of Cerrahpaşa Faculty of Medicine at Istanbul University and consent forms were confirmed by both patients and healthy controls after they were explained the complete description of the study.

Conflicts of interest There are no conflicts of interest

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The frequency of OPRK1 G36T and OPRM1 A118G opioid receptor gene polymorphisms in heroin-dependent individuals and non-dependent healthy subjects in Turkey

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SUMMARY

Objective: Polymorphisms of the Mu opioid receptor (MOR) gene (OPRM1), which encodes for the primary action site of heroin, have also been found to be associated with heroin addiction. The aim of this study was to investigate the relationships between heroin addiction and G36T OPRK1 and A118G OPRM1 receptor gene polymorphisms in a male population in Turkey.

Method: 102 male patients with heroin use (without any other drug use) and 82 subjects without any history of opioid use were evaluated. The A118G and G36T SNPs on the MOR and Kappa opioid receptors (KOR) genes were assessed via TaqMan 5'-exonuclease allelic discrimination assays.

Results: The mean duration of heroin use was 4.6±1.9 years. The G36T polymorphism and heterozygous genotype were both found to be more frequent in the patient group (OPRK1 gene). In the patient group, 79 (77.5%) patients had wild-type genotype and 23 (22.5%) patients had mutant genotype. In the control group, 76 (92.7 %) subjects had wild-type genotype and 6 (7.3 %) subjects had mutant genotype (p=0.005). Wild type allele frequency was determined to be 0.894 and mutant type allele frequency was 0.105. With regard to the A118G polymorphism, we found that there was no difference between groups in terms of genotype.

Discussion: Our findings support a considerable role for OPRK1 in opioid addiction; however, in conflict with most studies, we did not determine a relationship with A118G in Turkish subjects. We suggest that further stu-dies should be conducted to ascertain the clinical implications of opioid gene polymorphisms in Turkey.

Key Words: Genetic, Dependence, Opioid, Polymorphism

INTRODUCTION

Addiction is a chronic relapsing condition caused by short- and long-term adaptations in the dopaminergic system, leading to all manners of change in epigenetic, mRNA, neuropeptide, neurotransmitter and protein levels (1). Heroin dependence (HD) is a chronic disease with medical, social and economic burden (2). It has been reported that the number of people using heroin has increased by 62.5% from 2002 to 2013 in the USA. The number of deaths related to high dose heroin use has dramatically increased by 285% in the same period (3). Turkey is geographically located in a region between drug producing and consuming countries, making it a transit country and a target for drug dealers.

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Heroin directly interacts with opioid receptors (3). The opioid system is comprised of 3 types of G protein coupled receptors, mu (μ), kappa (κ) and delta (δ) (2). Single nucleotide polymorphisms (SNPs) in the opioid system have been shown to have significant effects on the tendency to develop addiction, and their frequencies change from population to population (4,5). There have been several studies showing that SNPs may influence HD and addictive characteristics. For instance, polymorphisms of the kappa receptor were associated with alcohol use and symptoms of withdrawal among recipients of methadone treatment (6,7). Kappa opioid receptors (KOR) play a modulatory role in the reward system by regulating dopaminergic activity. Whereas, presynaptic Mu opioid receptor (MOR) activity has been demonstrated to decrease Gamma aminobutyric acid (GABA) levels that inhibit the dopamine pathway (2,8). Chronic use of addictive drugs causes an upregulation in the KOR/dynorphin system, and the presence of the G36T SNP (located in exon-2) has been shown to be associated with addiction-related findings in humans and voluntary alcohol-drinking behavior in experimental animals (1,6). However, despite literature reviews yielding a high number of studies that found associations with the proclivity for dependence, there is also strong evidence to the contrary from different populations (9,10), which indicates the need for further population-based research on this subject.

Polymorphisms of the MOR gene (OPRM1), which encodes for the primary action site of heroin, have also been found to be associated with heroin addiction (11-14). In the OPRM1 gene, the presence of A118G SNP (located in exon-1) demonstrates a 3-fold increase in the affinity of MOR to beta endorphin; thus, A118G has gained interest due to its role in affinity, demonstrated by both in vivo and in vitro analyses (6). Furthermore, the rapid activation of MOR by heroin and/or analogues results in a euphoric effect, contributing to the development of drug addiction in humans, as suggested by previous studies (15).

In the light of this knowledge, our hypothesis is that heroin dependence is related to genes such as OPRM1 and A118G, and that genetic is a predictor for addiction.

Taken together, due to the lack of concrete data on this topic (whether or not these polymorphisms are indeed associated with dependency) and the apparent need for assessments in different populations (due to conflicting results), the aim of this study was to investigate the relationships between heroin addiction and G36T OPRK1 and A118G OPRM1 receptor gene polymorphisms in an outpatient population of the Alcohol and Substance Addiction Research, Treatment and Education Center (AMATEM) in Turkey. As far as we know, our study has the feature of being the first study to examine two different polymorphisms in the Turkish population after the reference study (16).

METHODS

Study Samples

In this study, 102 (55.4%) unrelated male patients who used only heroin were diagnosed with opioid use disorder according to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) criteria were included. Patients were recruited from the AMATEM clinic of Pamukkale University Department of Psychiatry. Approximately 500 patients applied to the AMATEM clinic between September and November 2019, when the data of the study were collected. Excluding non-heroin users, multiple substance users (excluding nicotine use), those who did not agree to participate in the study, female patients, and those with chronic psychiatric disorders (eg, mental retardation, psychosis, bipolar disorder…), the remaining 102 patients were included in the study. The inclusion criteria were as follows for the patient group: providing written informed consent, being aged older than 18 years, and recei-ving addiction therapy during the course of the study. No sampling method was used in the study, and all patients who were treated in the relevant clinic at the time of the study and who met the inclusion criteria and accepted to participate in the study were included in the study. Additionally, an age- and ethnicity-matched control group of 82 (44.6%) subjects without any history of opioid use were included. The control group was recruited from the same university employees. Declare that they have not used any substance in their lifetime

(excluding nicotine use), providing written informed consent, being male, being aged older than 18 years were the inclusion criteria for the control group. Participants with chronic psychiatric disorders (eg, mental retardation, psychosis, bipolar disorder…) were also excluded. All participants were resided in the same geographical area. They did not receive any monetary compensation for study inclusion and agreed to participate in the study voluntarily. Two Independent Proportions (Null Case) Power Analysis were performed on PASS 11 (Hintze, J. (2011). PASS 11. NCSS, LLC. Kaysville, Utah, USA. www.ncss.com.). According to the power analysis, there should be minimum of 106 patients to detect the difference between the polymorphism rate of 75% and 59% with 0.05 alpha error and 80% power.

A questionnaire was used to record the sociodemographic and clinical characteristics of patients and controls. Opioid use disorder was diagnosed according to DSM-5 diagnostic criteria.

This study was carried out in accordance with the Helsinki Declaration and approved by Pamukkale University Medical Faculty Clinical Trials Ethical Committee (approval number: 10.09.2019/15). All subjects provided written informed consent before study inclusion.

DNA Isolation and Genotyping

Whole blood samples taken into ethylenediaminetetraacetic acid-treated tubes were used for DNA extraction with a commercially available kit (QIAamp DNA Blood Mini Kit Qiagen, Germany) according to the manufacturer's protocol. The DNA concentration was determined using a NanoDrop spectrophotometer (Thermo-Scientific, USA) and samples were stored at -20 °C until polymerase chain reaction (PCR) was performed.

The primers and the probes used in PCR were designed for the rs1051660 polymorphic region of OPRK1 gene and the rs1799971 polymorphic region of the OPRM1 gene. The gene sequence was found on https://www.ensembl.org/index.html database and primers were designed using the Primer 3 program. The sequences of designed primers were controlled with BLAST program (https://www.ncbi.nlm.nih.gov). Genotyping was carried out using the TaqMan 5'-exonuclease allelic discrimination assays (Bioline, SensiFAST™ Lo-ROX Genotyping) and Real-Time PCR system for the following variants: rs1051660 (G/T) in the OPRK1 gene and rs1799971(A/G) in the OPRM1 gene.

Statistical Analysis

All statistical analyses were conducted with the Statistical Program for Social Sciences (SPSS) for Windows (version 20.0) computer program. The Pearson's Chi Square and Fisher's Exact test were used to compare the distribution of categorical variables among groups. The results were evaluated with a 95% confidence interval (CI), and statistical significance was noted at a p-value of less than 0.05 ($p < 0.05$). Goodness of fit X2 test was used to assess deviations from the Hardy–Weinberg equilibrium (HWE) in the control group.

RESULTS

Sociodemographic Characteristics of the Sample

The study was completed with the participation of a total of 184 subjects, 102 patients with opioid use disorder and 82 healthy controls. All subjects were male and had a mean age of 23.4 ± 4.4 (18–40) years. Seventy-five patients (75%) were single, 22 (22%) were married and three (3%) were divorced/widowed. Three (3.2%) patients were illiterate, 19 were (20.4%) primary school graduates, 48 (51.6%) were secondary school graduates, 22 (23.7%) were high school graduates and one (1.1%) was a university graduate (Table 1).

Substance Use Releated Characteristics of the Patients

The substance use characteristics of the patients showed that 58 (56.9%) patients used heroin with inhalation, 42 (41.1%) used inhalation and intravenous injections (IV), and two (2%) used only intravenous injection. The average duration of drug use was 4.6 ± 1.9 (1–11) years. Anti-HCV

Table 1: Distribution of sociodemographics and heroin use-related characteristics in patients

	Variables	Patients	
		n	%
Marital status	Single	75	75
	Married	22	22
	Divorced/widowed	3	3
Education	Illiterate	3	3.2
	Primary school	19	20.4
	Secondary school	48	51.6
	High school	22	23.7
	University	1	1.1
Heroin Use	Inhalation	58	56.9
	Inhalation and intravenous injection	42	41.1
	Intravenous injection	2	2
Anti-HCV	Positive	17	16.7
	Negative	85	83.3
Treatment compliance during follow-up	Regular	30	29.4
	Irregular	28	27.5
	Lost to follow up	44	43.1

positivity was detected in 17 (16.7%) patients. Thirty (29.4%) of the patients visited the hospital regularly for follow-up studies, 28 (27.5%) visited irregularly and 44 (43.1%) patients never showed-up for follow-up (Table 1). Additionally, all patients were being treated with buprenorphine-naloxone.

OPRK1 G36T and OPRM1 A118G Opioid Receptor Gene Polymorphisms

The G36T polymorphism and heterozygous genotype were both found to be more frequent in the patient group (OPRK1 gene). In the patient group, 79 (77.5%) patients had wild-type genotype and 23 (22.5%) patients had mutant (heterozygous or homozygous) genotype. In the control group, 76 (92.7%) subjects had wild-type genotype and 6 (7.3%) subjects had mutant genotype (p=0.005) (Table 2). Wild type allele frequency was determined to be 0.894 and mutant type allele frequency was 0.105.

With regard to the A118G polymorphism, we found that there was no difference between groups in terms of genotype (Table 3).

In addition, polymorphisms (OPRK1 and A118G) in the patient group were compared according to anti-HCV, heroin use (inhalation and IV/inhalation) and treatment compliance during follow-up, and no significant difference was found (p>0.05).

DISCUSSION

Our results suggest an association between opioid addiction and the presence of G36T polymorphism in the OPRK1 gene; however, the A118G polymorphism results do not demonstrate any relationships, which is somewhat conflicting with previous studies. Nevertheless, it is apparent that various studies showing a relationship between drug addiction and OPRK1 gene polymorphisms (17-19) are supported by our findings. To our knowledge, this is one of the pioneering study investigating the association between heroin addiction and opioid gene polymorphisms (OPRK1 rs1051660 (G36T), OPRM1 rs1799971 (A118G)) in Turkey. Turkan et al. conducted a 103 patients included study which had investigated OPRM1 A118G polymorphism (rs1799971) in a Turkish population. They found that this polymorphism was associated with opioid and other substance addiction (16).

Since the function and features of opioid receptors make them obvious targets for addiction-related research, numerous studies have sought to identify

Table 2: Distribution of the rs1051660 (G36T) polymorphism in OPRK1 gene

	Patients		Controls		Overall		p*
	n	%	n	%	n	%	
Mutant (heterozygous+homozygous)	23	22.5	6	7.3	29	15.8	0.005
Wild-type (normal)	79	77.5	76	92.7	155	84.2	
Total	102	100	82	100	184	100	

*Pearson Chi-Square test, patients versus controls.

Table 3: Distribution of rs1799971 (A118G) polymorphism in OPRM1 gene

	Patients		Controls		Overall		p*
	n	%	n	%	n	%	
Mutant (heterozygous+ homozygous)	8	7.8	4	4.9	12	6.5	0.418
Wild-type (normal)	94	92.2	78	95.1	172	93.5	
Total	102	100	82	100	184	100	

*Pearson Chi-Square test, patients versus controls.

their exact roles via experimental and human-based investigations. Although exact mechanisms remain to be identified due to the complex relationships between the effects and overall functions of these receptors (20), all 3 types of receptors in the opioid system appear to have significant roles in addiction, be it through genetic, epigenetic or post-translational characteristics or adaptations. In this context, KOR seems to be a regulatory receptor due to its profound relationship with MOR effects (21), as well as demonstrating pro-addictive properties in the presence of anxiety and stress (22). For these properties, KOR has been suggested as a target for therapy in patients with addiction, especially in the presence of mood-related disorders (23). Although concluding any direct relationships with SNPs and the predisposition to HD would be far-fetched to say the least, our findings might be interpreted as being supportive in this context. That is, the presence of the G36T polymorphism in KOR may result in functional or efficacy-related changes in the receptor, possibly alleviating or eliminating its anti-MOR properties in patients with HD, which could explain the higher frequency of the G36T mutation in the patient group compared to controls. This hypothesis may find some support from the results of previous studies demonstrating a higher frequency of the G36T polymorphism in patients with HD (24,25). Furthermore, other alterations in the OPRK1 gene have also been associated with drug or alcohol abuse (26,27), indicating that further research must be performed to ascertain the mechanistic relationship between KOR and MOR in terms of addiction development (and its treatment).

It has been well established that MOR is the primary action site for opium derivatives (morphine, heroin, fentanyl and methadone) (4). Therefore, the gene encoding for human MOR is the main focus point of studies investigating the potential association between endogenous opioid system genes and alcohol and drug use (or addiction). The two common SNPs of the MOR gene (C17T and A118G), as well as the (CA)n repeat polymorphism have been studied in different ethnic, cultural and geographical populations (28). Ahmed et al. have shown a significant association between the A118G polymorphism and opioid addiction in Pakistanis (29). Tan et al. have demonstrated a significant difference between the allele frequencies of A118G SNP in an Asian population (30). The A118G SNP affects the β-endorphin binding affinity of MOR. Nucleotide 118 is the first base in codon 40 of the human MOR, and the A118G variant predicts an Asn-to-Asp change in amino acid residue 40 of the receptor (N40D) (31). It should also be noted that a remarkable study by Kumar et al. reported that the likelihood of both heroin and alcohol addiction were increased in the presence of A118G; whereas OPRK1 the three OPRK1 SNPs (rs16918875, rs702764 and rs963549) did not show any particular effect one way or the other. However, greater than 2-fold increases in the odds of having heroin and alcohol addiction was identified in the presence of specific alterations in OPRK1 (rs16918875) and OPRM1 (A118G) (27). This latter finding indicate an underlying relationship between the two receptors that could translate to increased susceptibility to opioid addiction.

A number of studies conducted on different populations have revealed a significant difference in the allele frequency of A118G polymorphism. As listed above, various studies report that OPRM1 gen polymorphisms are relevant to opioid dependence, but it is important to note that conflicting studies in different populations also exist, and their results are similar to ours. Although conflicting results on this topic are reported throughout the world (6,32,33), authors often suggest caution in the assessment and generalization of their results, since it is apparent that ethnic and racial differences may alter not only the frequency of SNPs, but also the exact effects/relationships they have with HD or other types of addiction.

In the patient group, both polymorphisms were found to be similar when compared according to anti-HCV positivity, using heroin intravenously or by inhalation and treatment compliance. In the literature, no data were found about the polymorphisms and hepatitis C in patients using opioids. OPRM1 and A118G were examined in terms of the effectiveness of methadone and buprenorphine

treatment, it was found that the efficacy was regulated in an allele-specific manner (34). In our study, all patients were using buprenorphine treatment. No difference was found in terms of treatment compliance compared to polymorphisms. In the study of Turkan et al. (16), alleles were found to be similar according to the history of psychiatric illness. In our study, chronic psychiatric diseases were excluded, but comorbid diseases such as depression, anxiety, attention deficit hyperactivity disorder were not considered.

There are several limitations of this study that must be discussed. The primary limitation is the lack of analysis for other established polymorphisms of the target genes; however, we were limited by available funding in this respect. Secondly, our study group was comprised of individuals who had sought treatment for HD; therefore, baseline characteristics of the participants may not be directly representative of the population of individuals with HD. The absence of substance use in the control group was accepted based on their statement and was not confirmed by any test (urine, etc.). Although the number for each group was 106 in the power analysis, the number of those who agreed to participate in the control group was 82. Lastly, genetic studies –and the relationships shown therein– must be supported by further analyses that demonstrate the alteration in protein levels and subsequent characteristics of patients –which is a limitation for all similar studies, as mentioned above.

To conclude, we showed that the OPRK1 (G36T) polymorphism frequency is significantly higher in heroin-dependent individuals compared to healthy control subjects comprised of males. It is critical to note that previous studies have suggested a role for sex-related differences in the function of these receptors (35,36); thus, it is inadvisable to predict similar findings among females. The OPRM1 (A118G) polymorphism frequency was not found to be at a higher frequency among heroin-dependent individuals in our study. It is recommended that future studies be planned with a larger sample size and to include the relationship of polymorphisms with treatment strategies, so that data can be correlated to the clinic practice.

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Evaluation of substance induced and substance free first-episode psychosis in terms of inflammatory whole blood count parameters

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SUMMARY

Objective: Substance use is known to trigger psychotic episodes in individuals predisposed to psychosis. Recently, the importance of inflammatory processes in psychotic disorders has been increasingly emphasized. This study aimed to examine the manner in which inflammatory whole blood count (WBC) parameters change in substance-induced first-episode psychosis (siFEP) and substance-free first-episode psychosis (sfFEP).

Method: The present study included 32 patients with siFEP, 48 patients with sfFEP, and 80 healthy controls. For the comparison of inflammatory WBC parameters between the three groups, age and sex were considered as covariates when MANCOVA was applied; further, LSD post hoc test was performed. The relationship between clinical variables and inflammatory WBC parameters was analyzed using Pearson's correlation analysis.

Results: Monocyte levels were higher in patients with siFEP than in those with sfFEP and healthy controls, and platelet-to-lymphocyte ratio values were lower in patients with siFEP than in healthy controls. Furthermore, a moderately significant relationship between duration of illness and monocyte levels was found in the siFEP group.

Discussion: The fact that inflammatory WBC parameters differ among the siFEP, sfFEP, and healthy control groups suggests that inflammatory processes contribute to psychotic disorder. However, the data from the present study are still insufficient to support the use of these parameters in clinical practice.

Key Words: First-episode psychosis, substance-induced first-episode psychosis, substance-free first-episode psychosis, inflammatory whole blood count parameters

INTRODUCTION

Psychotic disorder is a condition that has cognitive and behavioral components and causes significant impairment in functionality and quality of life. As interventions in the early stages of the disorder are believed to have a positive impact on the prognosis, follow-up of patients from the first psychotic episode is of great importance (1,2). Substance use has been reported to precipitate psychotic symptoms in individuals predisposed to psychosis. 7-25% of individuals who have had a psychotic episode for the first time are diagnosed with substance-induced psychotic disorder (3), especially having a family history of alcohol and substance use disorder is a risk for developing this condition (4). Notably, a previous study reported that substance-induced psychosis is associated with a high risk of transforming into schizophrenia (4). In addition, a family history of psychotic disorder is believed to be an important risk factor in the transformation of the disease into schizophrenia (4). Substance-induced first-episode psychosis (siFEP) and substance-free first-episode psychosis (sfFEP) may differ in terms of some clinical features. It is known that forensic events and history of trauma are more common, insight is better, and anxiety and hostility are more pronounced in siFEP than in sfFEP (5). Furthermore, the fact that patients with siFEP have shorter treatment processes and that they are not preferentially enrolled in treatment programs represents an obstacle for them to receive appropriate

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treatment (6). In cases of siFEP and sfFEP, in addition to clinical features, the presence of practical clinical markers, which can provide information about the differential diagnosis and prognosis of the disease, may help such patients to receive treatment at the right time with appropriate dose.

With recent studies in the relevant literature, the importance of inflammatory processes in the neurobiology of psychosis has been increasingly emphasized (7-9). Moreover, the number of studies using inflammatory whole blood count (WBC) parameters has steadily increased because of the readily available, inexpensive, and practical use of these markers. To date, these parameters have been reported to be affected in many systemic diseases, such as malignancies and cardiovascular diseases (10,11). In addition, inflammatory WBC parameters, such as neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), and systemic immune inflammation index (SII), vary in many psychiatric disorders (e.g., bipolar, depressive, attention-deficit hyperactivity, and substance and alcohol use disorders) (12-16). Although these parameters are not considered to be disease-specific, they are important for elucidating the underlying inflammatory processes and for monitoring the disease progression.

Most of the studies showed that patients with psychotic symptoms (schizophrenia or bipolar disorder) have increased NLR, PLR, MLR values and decreased lymphocyte levels (12, 17-19). In addition, these inflammatory markers change according to the stage of the illness (e.g., remission or relapse) (17). On the other hand, studies on patients with first-episode psychosis revealed conflicting results (20-23). To date the only study evaluating inflammatory WBC parameters on patients with substance-induced and substance-free first-episode psychosis showed that patients sfFEP have increased leukocyte, neutrophil, monocyte levels and NLR, MLR values compared to healthy controls while patients with siFEP showed differences only on leukocyte, monocyte levels and MLR values (24).

Markers that clinically distinguish siFEP from sfFEP can be useful for the appropriate diagnosis, follow-up, and treatment. Therefore, the present study aimed to compare inflammatory WBC parameters of patients with siFEP, patients with sfFEP, and healthy controls. In this study, it was hypothesized that patients with siFEP, patients with sfFEP and healthy controls would differ from each other in terms of inflamatory WBC parameters.

METHODS

This is a retrospective observational study. The records of a total of 1599 patients who were hospitalized at Maltepe University, Faculty of Medicine, Department of Psychiatry between January 2013 and October 2022, were reviewed. After excluding other psychiatric diagnostic groups and readmissions, it was found that 191 patients who had acute psychotic spectrum diagnoses admitted for the treatment. The first psychotic episode was defined as the Diagnostic and Statistical Manual of Mental Disorders-5-based diagnosis of psychotic disorders or bipolar disorder (manic episode with psychotic features) in patients who admitted to a healthcare service following the manifestation of psychotic symptoms started for the first time within the past 1 year. Patients who had recurrent psychotic episodes, or comorbid medical illness were excluded from the study. Patients with insufficient data were not included in the study. As a result, a total of 80 patients (siFEP (n=32) and sfFEP (n=48)) were eligible for inclusion.

80 healthy controls were randomly selected from individuals with no history of psychiatric disorders and substance use who had applied to Maltepe University Faculty of Medicine for health screening or obtaining medical board report between 2020 and 2022.

Patients aged 17–50 years were included in the present study. Blood samples from patients admitted to the psychiatric unit for siFEP or sfFEP were collected within the first 24 hours. Participants with concomitant hypertension, diabetes mellitus, heart disease, inflammatory or autoimmune diseases, cancer, and active infection and those taking immunosuppressive drugs were excluded from the study. For sfFEP group, patients with a history of

substance use were excluded from the study. Moreover, for healthy control group, individuals who were considered to have an acute or lifelong psychiatric disease based on a psychiatric interview were not included. This study was approved by the Maltepe University Faculty of Medicine Clinical Research Ethics Committee (Number: 2022/900/02; Date: 19.01.2022).

Statistical Analysis

IBM SPSS Statistics 23.0 (Chicago IL, USA) was used for all statistical analyses. Categorical variables were compared using the chi-square test. The Kolmogorov–Smirnov test was used to determine whether the continuous data corresponded to the normal distribution, and appropriate transformations were performed for data that did not correspond to the normal distribution. In addition, paired group comparisons were performed using the Student's t-test. Moreover, ANOVA and Bonferroni post hoc test were used for multiple group comparisons. For the comparison of inflammatory WBC markers between the diagnostic groups, age and sex were used as covariates when MANCOVA was applied, and LSD post hoc test was performed. Furthermore, the relationship between clinical variables and inflammatory whole blood parameters was analyzed in both patient groups separately using Pearson's correlation analysis. A p-value of < 0.05 was considered statistically significant. The power analysis is performed by G Power 3.1.

RESULTS

A comparison of the demographic and clinical characteristics between the study groups is presented in Table 1. No significant difference was found between the patients and healthy controls in terms of age, but a significant difference was found between the study groups in terms of sex ($p< 0.001$).

When comparing inflammatory WBC parameters between the study groups using age and sex as covariates, monocyte levels were significantly higher in patients with siFEP than in patients with sfFEP ($p = 0.004$) and healthy controls ($p= 0.022$). In addition, PLR values in patients with siFEP were significantly lower than those in healthy controls ($p = 0.006$). Notably, no significant difference was found between the groups in leukocyte, neutrophil, lymphocyte, platelet, NLR, MLR, and SII values (Table 2).

In the correlation analyses between age at onset of substance use, duration of substance use, age at onset of disease, duration of, and inflammatory WBC parameters, a moderately significant association between disease duration and monocyte levels was found in the siFEP group ($p=0.021$, $r=0.435$). Power analysis conducted by calculating effect size and sample size has resulted in a power of 0.69 for the study.

DISCUSSION

In the present study, patients diagnosed with siFEP and sfFEP and healthy controls were compared in terms of inflammatory WBC parameters. Monocyte levels were higher in patients with siFEP than in those with sfFEP and healthy controls, and PLR values were lower in patients with siFEP than

Table 1. Comparison of sociodemographic and clinical characteristics between the study groups

	siFEP (n=32)	sfFEP (n=48)	HC (n=80)	Test statistic F/x^2	p
Age	28.38 (8.20)	29.54 (9.75)	27.83 (6.68)	0.691	0.503
Sex (n, %)				27.058	**<0.001**
Female	2 (6.2)	24 (50)	12 (15)		
Male	30 (93.8)	24 (50)	68 (85)		
Duration of illness (month)	5.63 (4.13)	4.75 (4.66)	-	0.910	0.366
Age of illness onset	27.00 (8.80)	29.13 (9.94)	-	1.059	0.294
Age of first substance use	20.00 (8.35)	-	-		
Duration of substance use (month)	94.96 (74.98)	-	-		
Substance type (n, %)		-	-		
Cannabinoid	11 (34.38)				
Cocaine	3 (9.38)				
Polysubstance*	18 (56.25)				

siFEP: Substance-induced first-episode psychosis; sfFEP: substance-free first-episode psychosis; HC: Healthy control *Number of patients and type of substance used for polysubstance users: Cannabinoids (n=17), stimulants (n=17), opioids (n=3), sedatives (n=1)

Table 2. Comparison of inflammatory whole blood parameters between the study groups

	siFEP (n=32)	sfFEP (n=48)	HC (n=80)	Test statistic F	p
Leukocyte (/mm^3)	7873 (1712)	7044 (17949	7335 (1473)	1.863	0.159
Neutrophil (/mm^3)	4132 (1412)	3838 (1402)	3983 (1095)	0.484	0.618
Lymphocyte (/mm^3)	2757 (625)	2461 (716)	2508 (624)	2.092	0.127
Monocyte (/mm^3)	706 (207)	567 (198)	604 (158)	4.395	0.014 siFEP>sfFEP p=0.004 siFEP>HC p=0.022
Platelet (/mm^3)	224372 (48135)	231498 (46639)	244411 (51483)	2.805	0.064
NLR	1.59 (0.76)	1.69 (0.80)	1.67 (0.59)	0.530	0.590
MLR	0.27 (0.09)	0.24 (0.09)	0.25 (0.07)	0.522	0.595
PLR	84.61 (25.31)	101.47 (36.32)	103.00 (31.99)	3.939	0.021 HC> siFEP p=0.006
SII	357852 (181051)	394494 (216801)	411603 (178721)	1.639	0.198

siFEP: Substance induced first episode psychosis; sfFEP : substance-free first-episode psychosis; HC: Healthy control; NLR: Neutrophil-to-lymphocyte ratio; MLR: Monocyte -to-lymphocyte ratio; PLR: Platelet -to-lymphocyte ratio; SII: systemic immune inflammation index

in healthy controls.

Although studies in the relevant literature have reported increased NLR, PLR, MLR values and decreased lymphocyte levels in schizophrenia and bipolar disorder (12, 17-19), there are conflicting results in studies conducted during the first episode of psychosis (20-23). One large sample sized study found that patients with first episode psychosis have increased NLR, MLR, and PLR values compared to healthy controls (23), while other did not (22). In a previous study that compared patients diagnosed with a substance-induced psychotic disorder to patients diagnosed with a substance-free psychotic disorder in terms of inflammatory WBC parameters (24) - leukocyte, neutrophil, monocyte, and MLR values were found to be higher in patients diagnosed with siFEP and sfFEP than in healthy controls. In contrast, that study reported that compared with healthy controls, NLR values were higher only in patients diagnosed with sfFEP. Consistent with this study, our results showed that monocyte levels increase in patients diagnosed with siFEP compared to healthy controls. However, we did not find any differences in leukocyte, neutrophil levels or MLR values. The absence of differences in some of the inflammatory WBC parameters, between patients with first psychotic episode and healthy controls in our study may indicate that the inflammatory burden, which becomes clear in the later stages of psychosis, does not become evident in the early stages of the illness. Notably, to the best of our knowledge, the finding of monocyte levels being higher in patients diagnosed with siFEP than in those diagnosed with sfFEP reported in our study has not been reported in any studies till date. It is known that monocytes play an important role in the immune system by transforming into macrophages, secreting acute phase reactants, phagocytosing foreign molecules, and presenting these molecules to lymphocytes (25). Moreover, in the study by Orum et al., it was found that monocyte levels and MLR values were significantly higher in cannabis users than in opioid users (26). Cannabis was the substance used by almost all of the individuals who were using polysubstance in this study. Notably, patients with cannabis and polysubstance use in the siFEP group constituted a large proportion of the sample. Accordingly, monocyte levels may have been higher in patients diagnosed with siFEP than in those diagnosed with sfFEP and healthy controls owing to the effect of substance used and the type of substance.

Similarly, there are no definitive results regarding the direction of changes in inflammatory WBC parameters in substance use disorder. There are studies that report an increase in NLR and PLR values among opioid users compared with healthy controls (13,27,28). On the other hand, a previous study found no difference in NLR values (29), and some studies reported a decrease in MLR and PLR values (26,29). To the best of our knowledge, this is the first study to report that PLR values are lower in patients with siFEP than in healthy controls. In the study by Onur et al., no difference was found between patients with first-episode psychosis and healthy controls in terms of PLR values (24). Notably, platelets are known to play an important role in inflammation and immune response (30). In addition, they secrete many mediators that are not involved in hemostasis, and some of these media-

tors modulate leukocyte and endothelial responses to a variety of inflammatory stimuli. In contrast, in a meta-analysis by Miller et al., they demonstrated that lymphocyte counts were higher in patients with first-episode psychosis than in healthy controls, and these counts decreased in recurrent episodes (31). In chronic disease, elevated cortisol levels and chronic inflammatory processes cause apoptosis in lymphocytes as well as lymphopenia (32,33). Based on the abovementioned findings, it can be reported that PLR values in patients diagnosed with siFEP are lower than those in healthy individuals owing to the acute course of the disease. However, based on the results of the limited number of studies conducted to date, it is still too early to make a definitive judgment on how PLR levels are affected in siFEP and sfFEP.

In the present study, a moderately significant relationship was found between disease duration and monocyte levels in the siFEP group. Although inflammatory WBC parameters have been reported to be associated with various clinical features, particularly the disease prognosis, in various systemic diseases in the literature (10,11,34), the number of studies on psychotic disorders remains limited. Monocyte levels have been found to affect pulse pressure—an important cardiovascular risk marker—in patients with first-episode psychosis (20). Although there are also studies that found no association between disease duration and NLR levels in patients diagnosed with schizophrenia (18,19), no study has examined the association between monocyte levels and disease progression.

This study has some limitations. First, this was a retrospective study. All participants were retrospectively screened from hospital records. Second, based on the information obtained from the hospital records, the fact that the diagnosis of the first episode psychosis was made by different physicians is an important limitation of the study. Third, the relatively small number of people in the patient groups may have introduced a type 2 error. Fourth, patient groups included different types of psychotic conditions such as patients with psychotic disorders or bipolar disorder (manic episode with psychotic features). This is an important issue to keep in mind when interpreting the findings, as it can lead to diagnostic heterogeneity among patient groups. Fifth, this study included different type of substances which may also cause heterogeneity in inflammatory WBC parameters in siFEP group. In the study by Orum et al., it was shown that the levels of monocytes and MLR values increased while PLR values decreased in patients with cannabinoid use disorder compared to those with opioid use disorder (26). Sixth, smoking, which is thought to be an important factor affecting inflammatory WBC parameters (35), could not be controlled in this study. Finally, other limitation of the study is that lifestyle differences, dietary preferences, body mass index, and previous treatments with psychotropic drugs were not included in the evaluation.

In conclusion, although most studies in the relevant literature report that inflammatory WBC parameters are elevated in patients with psychiatric disorders compared with healthy controls, some studies report the opposite conclusion or find no significant difference. These results may be an indicator that there is not a unidirectional change in these parameters throughout the course of the illness. Based on this perspective, it can be reported that there is insufficient evidence to support the use of inflammatory WBC parameters in clinical practice for the differential diagnosis of siFEP and sfFEP. On the other hand, these parameters are of great importance in demonstrating the underlying inflammatory burden of both siFEP and sfFEP. Understanding the direction of changes in these parameters throughout the follow-up process from the onset of the illness will be helpful in elucidating the etiology of the disease. To understand the clinical importance of these parameters, studies with a longitudinal design, large sample size, and common inclusion criteria are needed.

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Does the coexistence of attention deficit hyperactivity disorder and sluggish cognitive tempo affect the treatment response in children?

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SUMMARY

Objective: We aimed to evaluate treatment response in children with sluggish cognitive tempo and attention deficit/ hyperactivity disorder.

Method: Child Behavior Checklist and Barkley Child Attention Scale were used to define SCT symptoms. Parents and teachers completed Turgay DSM-IV-Based Screening Scale for Disruptive Behavior disorders, severity and improvement were eva-luated via Clinical Global Impressions Scale- Severity and CGI- Improvement. Methylphenidate responses were evaluated retrospectively by patient charts.

Results: SCT + ADHD group was rated as more inattentive by their parents while teachers rated children with ADHD as more hyperactive/ impulsive ($p<0,01$; $p<0,01$, respectively). Symptom reduction was significantly greater for teacher rated hyperactivity/ impulsivity in the ADHD group and children with SCT+ ADHD were still rated as more inattentive by their parents after treatment. The sole predictor of treatment response in the SCT+ ADHD group was treatment duration ($p=0.012$).

Discussion: Longer treatment duration seemed to be more effective in the SCT group.

Key Words: Sluggish cognitive tempo, methylphenidate, attention deficit hyperactivity disorder, treatment response, treatment duration

INTRODUCTION

Attention Deficit/ Hyperactivity Disorder (ADHD) is among the most common neurodevelopmental disorders of childhood characterized by developmentally inappropriate and impairing symptoms of inattention, hyperactivity and/ or impulsivity (1). Impairing symptoms of ADHD may persist in up to of adults diagnosed in childhood (1). Currently accepted subtypes of ADHD include inattentive (IA), hyperactive/ impulsive (HIP) and combined (C) presentations which are classified according to dominant symptoms (1,2).

A subgroup of children among those with ADHD may present with mental confusion (i.e., "fogginess"), slow behavior and thinking and excessive daydreaming and they were classified as having "Sluggish Cognitive Tempo" (SCT) (3). Although initially thought to be a subgroup within the ADHD- inattentive type, a series of studies and meta-analyses have established the SCT as a clinical entity partially overlapping with ADHD (3–7). In addition to ADHD, it may accompany other neurodevelopmental disorders and lead to further impairment especially by increasing social problems and internalizing symptoms (7,8). According to population-based studies, up to a third of child-

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ren with ADHD may also have SCT (9).

Recent studies have advanced our knowledge on the psychiatric, neuropsychological, neurophysiological, and neurobiological correlates of SCT. Children with ADHD and comorbid SCT symptoms may display elevated levels of autistic traits, mind-wandering/ rumination, emotional dysregulation, symptoms of anxiety and depression and eveningness chronotype (8,10-14). Also, there are recent findings that children with SCT may be impaired in orienting attention and memory (15,16). SCT accompanying ADHD may further impair executive functions (17). SCT may also be associated with greater behavioral inhibition and pronounced autonomic system reactivity in social situations and slower processing speed especially with elevated motor demands (10, 18-19). A specific allele of the DRD4 gene (i.e., 7R) may be associated with SCT and children with SCT may also display changes in internal capsules, cerebral peduncles and fornices bilaterally (20,21).

Despite better characterization of SCT symptoms and comorbidity, the effects of SCT comorbidity in ADHD on treatment response is relatively less studied (22,23). Froehlich and colleagues (22) reported that increased SCT- sluggish/ sleepy symptom scores were associated with methylphenidate (MPH) non-response/ placebo response and with lower MPH responses to parent and teacher –rated IA symptoms. Fırat and colleagues (23) reported that MPH treatment improved SCT-total and SCT-daydreaming scores at home and school while SCT-sluggish scores were improved only at school. In this study, older age predicted treatment response in SCT symptoms while pretreatment SCT and ODD symptoms predicted lower MPH treatment response. McBurnett and colleagues (24) found that treatment with atomoxetine (ATX) may improve SCT symptoms among children with ADHD and dyslexia and that this effect was independent of inattentive symptoms. In a recent case report, Tahillioglu and Ercan (25) suggested that ATX may be more beneficial for SCT, and subthreshold ADHD compared to MPH. Additional preliminary evidence suggests that children with SCT may also respond less to behavioral interventions which was posited to be related to memory problems (26).

Therefore, the aims of this study were;

a. To evaluate the difference in treatment response among Turkish children with ADHD with (ADHD + SCT) or without SCT (ADHD) symptoms under naturalistic treatment;

b. To determine the predictors of MPH treatment response (according to clinician evaluations) in ADHD+SCT group.

METHODS

Study center, sampling, and ethics

This naturalistic study was conducted at Duzce University Medical Faculty Department between February 2016 and December 2019. Children who applied to the department of Child and Adolescent Psychiatry and were diagnosed with ADHD according to DSM-5 based clinical interviews were eligible for enrollment. Children diagnosed with ADHD were screened for SCT symptoms at baseline with Child Behavior Checklist (CBCL) and those scoring 1.5 standard deviations above the mean of the ADHD group in the SCT index of CBCL (8th, 17th, 80th, 102nd items) were further evaluated with parent-completed Barkley Child Attention Scale (BCAS). Inclusion criteria for patients with ADHD were being diagnosed with ADHD according to DSM-5 based clinical interviews and receiving at least two months of treatment with MPH. Intellectual disability (ID, as evaluated by Wechsler Intelligence scale for Children-Revised Turkish version), a history of head trauma causing loss of consciousness, presence of chronic neurological/ medical disorders requiring treatment, comorbid bipolar disorder, autism spectrum disorder (ASD), psychosis and substance use disorders were criteria for exclusion.

Briefly; 434 patients were eligible for potential enrollment while 25, 30 and 62 Patients were excluded due to ID, history of head trauma and chronic neurological/ medical disorders requiring treatment; respectively. Thirteen patients had comorbid ASD while 38 had comorbid specific learning disability.

Two of the patients were excluded due to comorbid bipolar disorder while none were excluded due to comorbid psychosis. Among patients with ADHD fifteen were initiated ATX and were excluded from the present sample. Ten patients did not attend follow-up interviews and were excluded leading to a final sample of 241 patients with ADHD.

Parents and teachers completed Turgay DSM-IV-Based Screening Scale for Disruptive Behavior disorders at baseline and after at least two months of treatment, disorder severity and improvement were evaluated by clinicians via Clinical Global Impressions Scale- Severity (CGI-S) and CGI-Improvement (CGI-I). Methylphenidate responses were evaluated retrospectively by patient charts. The daily equivalent dose was calculated according to clinician toolkits of Utah Academy of Child and Adolescent Psychiatry (https://www.uacap.org/_files/ugd/1da6d0_55267f5b04204cb58bcc848398c0286f.pdf) as well as product sheets. IRB approval for study was granted by Duzce University Medical Faculty Ethics Committee (No: 2019/ 259). Written informed consent of parents/ guardians were procured as well as verbal assent of children prior to participation. All the study procedures were in accordance with the Declaration of Helsinki as well as local laws and regulations.

Measures

Sociodemographic Data Form: The form was prepared to collect information about sociodemographic characteristics of children and parents. It consisted of questions examining child's age, gender, grade, family structure, parent's age, marital status, family history of medical and psychiatric illnesses and it was completed by the clinician.

Turgay DSM-IV- Based Screening Scale for Disruptive Behavior Disorders (T-DSM-IV-S): This Scale was used to evaluate severity of symptoms of ADHD, ODD and Conduct Disorder (27. The items in the scale are identical to the list of symptoms described in the DSM-IV criteria for ADHD, ODD and CD and are scored by assigning a severity estimate for each symptom on a 4-point Likert-type scale. The T-DSM-IV-S was developed by Turgay (1994) and translated and adapted to Turkish by Ercan and colleagues (28).

Child Behavior Checklist (CBCL/ 6-18): The CBCL is a broad-band scale to evaluate problematic behaviors in children and adolescents from 6 to 18 years old according to parent or teacher reports. The problematic behaviors are evaluated in 113 3-point Likert type items (0 to 2) according to their frequency in the past six months. Apart from a total problem score, the CBCL provides internalizing (anxious/ depressed, withdrawn/ depressed, somatic complaints), externalizing (rule breaking and aggressive behavior), attention and thought problem scores29. The Turkish translation, validity and reliability was established previously (30,31). In this study the SCT index (8th, 17th, 80th, 102nd) of the parent version of the Child Behavior Checklist (CBCL) was used to differentiate probable SCT comorbidity (i.e., those with a score above 1.5 standard deviations above the ADHD group (17, 21, 32). The mean SCT index score in our patients with ADHD was 2.0 (S. D=1.3) which led to a cut-off score of 4.0 similar to previous studies (17,21).

Barkley Child Attention Scale (BCAS): The BCAS consists of 12- item four point-likert type scale evaluating two dimensions of SCT (i.e., sluggishness and daydreaming (33). The reliability and validity of the Turkish version was established by Fırat and colleagues (34). We used BCAS completed by the parents to evaluate SCT symptom severity in children above cut-off in the CBCL-SCT index.

Clinical Global Impressions Scale (CGI): The Clinical Global Impressions Scale (CGI) is a clinician rated scale developed by the National Institute of Mental Health to evaluate patients according to symptom severity and change with treatment (35). It consists of three sections in which disease severity, improvement and side effect severity are evaluated. We used the severity section before treatment, and the recovery section in the period after treatment.

Statistical analysis

The data were entered into a database prepared with Statistical Program for Social Sciences (IBM

Inc., Armonk, NY) Version 23.0. Qualitative variables were summarized in counts and frequencies while quantitative variables were summarized either as means and standard deviations or medians and inter-quartile ranges depending on assumptions of normality. Assumptions of normality were evaluated with Kolmogorov Smirnov test. Bivariate comparisons of nominal variables were conducted with chi square test (with Yates', Fisher's and Likelihood Ratio corrections as needed). Bivariate comparisons of quantitative variables were conducted with Mann-Whitney or Student's t tests. Logistic regression was used in evaluating the predictive value of SCT symptoms for ADHD treatment. Multivariate analyses of variance (MANOVA) were conducted to evaluate the effects group on baseline and end-visit ADHD symptoms. P was set at 0.05 (two-tailed).

RESULTS

Within the specified time period 241 patients (ADHD, n= 141, 58.5 %, ADHD + SCT, n= 100, 41.5 %) were enrolled in the study. Clinical and sociodemographic variables according to patient groups are illustrated in Table 1.

The groups were similar in terms of age, gender and clinician evaluated severity of symptoms at baseline while ADHD- IA type was significantly more common among children with SCT comorbidity.

Most common comorbid disorders in the SCT group were Oppositional Defiant Disorder (ODD, n= 20, 20.0 %), Learning Disorders (n= 18, 18.0 %), Conduct Disorder (CD, n= 10, 10.0%) and Anxiety Disorders (n= 7, 7.0 %). Most common comorbid disorders in the ADHD group were Learning Disorders (n= 32, 22.7 %), ODD (n= 28, 19.9 %), CD (n= 21, 14.9 %) and Anxiety Disorders (n=5, 3.5 %). The groups did not differ significantly in terms of comorbid disorders (Table 2).

Long-acting MPH formulations were the most common choice of treatment in both groups (ADHD, n= 73, 51.8 % vs. SCT, n= 49, 49.0 %) and the groups did not differ significantly in terms of MPH formulations selected for treatment (x^2= 0.36, dF= 2, p= 0.837, Likelihood ratio). Daily mean equivalent dose of MPH for SCT and ADHD groups were 26.0 (S.D.= 12.3) and 24.3 (S.D.= 12.4) milligrams, respectively. The groups did not differ significantly in terms of mean daily equivalent dose of MPH (t (239) = 1.1, p= 0.291, 95 % Confidence Interval= - 1.5- 4.9). Five patients in both groups received additional treatment with SSRIs while four patients in the SCT and nine in ADHD groups received atypical antipsychotics

Table 1. Clinical and sociodemographic variables of children with Attention Deficit/ Hyperactivity Disorder (ADHD) with or without accompanying SCT symptoms.

N, % or Median, IQR		SCT+ADHD (n= 100)	ADHD (n= 141)	x^2/ Z*	P**
Gender (male)		75 (%75.0)	113 (%80.1)	0.63	0.429
ADHD Type	IA	51 (%51.0)	40 (%28.4)	13.7	***0.001***
	HIP	4 (%4.0)	14 (%9.9)		
	C	45 (%45.0)	87 (%61.7)		
Age		9.0 (%4.0)	8.1 (%2.9)	- 0.89	0.372
CGI-S		4.0 (%1.0)	4.0 (%1.0)	-0.49	0.627

*: Mann-Whitney U test, **: Chi Square, IQR: Inter-quartile range, SCT: Sluggish Cognitive Tempo, ADHD: Attention Deficit/ Hyperactivity Disorder, E.S: Effect Size (Cramer s V), IA: Inattentive, HIP: Hyperactive/ Impulsive, C: Combined, CGI-S: Clinical Global Impression- Severity

Table 2. Comorbid disorders in children with Attention Deficit/ Hyperactivity Disorder with or without accompanying SCT

N, %	SCT+ADHD (n= 100)	ADHD (n= 141)	x^2	P*	O.R.
Learning Disorders	18 (%18.0)	32 (%22.7)	0.53	0.469	1.3 (0.7- 2.6)
Oppositional Defiant Disorder	20 (%20.0)	28 (%19.9)	0.00	1.000	1.0 (0.5- 1.9)
Conduct Disorder	10 (%10.0)	21 (%14.9)	0.85	0.356	1.6 (0.7- 3.5)
Anxiety Disorders	7 (%7.0)	5 (%3.5)	1.48	0.244	0.5 (0.2- 1.6)

*Chi Square Test (with Fisher and Yates corrections as needed), SCT: Sluggish Cognitive Tempo, ADHD: Attention Deficit/ Hyperactivity Disorder, O.R.: Odds Ratio (with 95 % Confidence Interval), E.S.: Effect Size

Table 3. Baseline symptom severity reported by parents and teachers in children with Attention Deficit/ Hyperactivity Disorder with or without accompanying SCT

Mean, S.D.	SCT (n= 100)	ADHD (n= 141)	F	P*	Partial n^2
T-DSM-IV-S- IA- P	19.2 (5.2)	16.4 (5.6)	*16.9*	***0.000***	*0.07*
T-DSM-IV-S- HIP- P	13.0 (8.3)	14.3 (7.3)	1.8	0.187	0.01
T-DSM-IV-S- ODD- P	10.2 (7.2)	9.7 (6.7)	0.3	0.585	0.00
T-DSM-IV-S- CD-P	3.6 (5.6)	3.8 (5.4)	0.1	0.780	0.00
T-DSM-IV-S- IA- T	17.9 (5.1)	17.0 (5.6)	1.9	0.174	0.01
T-DSM-IV-S- HIP- T	10.5 (8.3)	13.9 (7.8)	*10.7*	***0.001***	*0.04*
T-DSM-IV- S- ODD- T	8.2 (6.7)	9.0 (7.0)	0.9	0.357	0.00
T-DSM-IV-S- CD- T	2.7 (4.6)	3.7 (5.4)	2.2	0.141	0.01

*Univariate ANOVAs, S.D.: Standard Deviation, SCT: Sluggish Cognitive Tempo, ADHD: Attention Deficit/ Hyperactivity disorder, dF: degrees of freedom, CI: Confidence Interval, T-DSM-S: Turgay DSM-IV Based Screening Scale for Disruptive Behavior Disorders, IA: Inattention, HIP: Hyperactivity/ Impulsivity, ODD: Oppositional Defiant Disorder CD: Conduct Disorder, P: Parent, T: Teacher

Table 4. Parent and teacher reported symptoms at baseline and end point among children with ADHD + SCT (SCT) and those with ADHD only

Mean (SD)	SCT (n= 100)		ADHD (n= 141)	
	Baseline	End point	Baseline	End point
T-DSM-IV-S- IA- P	19.2 (5.2)	8.5 (4.5)	16.4 (5.6)	6.7 (3.6)
T-DSM-IV-S- HIP- P	13.0 (8.3)	4.3 (4.2)	14.3 (7.3)	5.2 (4.3)
T-DSM-IV-S- ODD-P	10.2 (7.2)	3.6 (4.2)	9.7 (6.7)	3.4 (4.0)
T-DSM-IV-S- CD-P	3.6 (5.6)	1.1 (2.5)	3.8 (5.4)	1.2 (2.6)
T-DSM-IV-S- IA- T	17.9 (5.1)	7.5 (4.1)	17.0 (5.6)	6.8 (4.2)
T-DSM-IV-S- HIP- T	10.5 (8.3)	4.0 (4.1)	13.9 (7.8)	4.8 (4.1)
T-DSM-IV- S- ODD-T	8.2 (6.7)	2.8 (3.5)	9.0 (7.0)	2.8 (3.5)
T-DSM-IV-S- CD- T	2.7 (4.6)	1.1 (2.3)	3.7 (5.4)	1.1 (2.1)

S.D.: Standard Deviation, SCT: Sluggish Cognitive Tempo, ADHD: Attention Deficit/ Hyperactivity disorder, T-DSM-S: Turgay DSM-IV Based Screening Scale for Disruptive Behavior Disorders, IA: Inattention, HIP: Hyperactivity/ Impulsivity, ODD: Oppositional Defiant Disorder, CD: Conduct Disorder, P: Parent, T: Teacher

(AAP) The groups did not differ significantly in terms of receiving additional treatment with SSRIs or AAPs (x^2=0.31, p=0.745 and x^2=0.65, p=0.566, both with Fisher's corrections).

Baseline symptom severity reported by parents and teachers were compared between groups with MANOVA. Covariance matrices were not equal (Box's M= 54.0, p=0.041) while error variances were equal for all subtests of T-DSM-IV-S (p> 0.05, Levene test); therefore Pillai's trace was used in analyses. Children with ADHD with and without SCT differed significantly in terms of baseline symptoms reported by parents and teachers (F (8.0, 232.0)= 5.1, p< 0.001, partial η^2=0.15). Follow-up univariate analyses are illustrated in Table 3.

SCT group were rated as significantly more inattentive by their parents at baseline (p=0.000, 95 % CI= 1.5- 4.3) while the ADHD group were rated as significantly more hyperactive and impulsive (p=0.000, 95 % CI= 1.4- 5.5) by their teachers.

Median duration of treatment for SCT and ADHD groups were 5.0 (IQR= 7.0) and 6.0 (IQR= 10.0) months; respectively with no significant difference across groups (Z= - 1.3, p= 0.183, Mann-Whitney U test).

After treatment most of the patients in both groups were rated by clinicians as "much" (SCT, n= 38, 38.0 % vs. ADHD, n= 67, 47.5 %) or "very much" improved (SCT, n= 30, 30.0 % vs. ADHD, n= 44, 31.2 %). Median CGI-I scores in SCT+ADHD and ADHD groups were 2.0 (IQR= 2.0) and 2.0 (IQR= 1.0); respectively with no significant difference (Z= -1.1, p=0.256, Mann-Whitney U test). MANOVA was used to evaluate the effects of group on treatment related change in parent and teacher reports (Table 4) .

Covariance matrices (Box's M= 61.4, p=0.009) were not equal while error variances except for parent reported change hyperactive/ impulsive symptoms (p=0.007, Levene test) were equal. The groups differed significantly in terms of parent and teacher reported change in ADHD symptoms (F (8.0, 232.0) = 3.0, p=0.004, partial η^2= 0.09, Pillai's trace). Follow-up univariate ANOVAs revealed that teachers rated hyperactive/impulsive symptoms of children with ADHD + SCT as less responsive to treatment (F= 9.2, p=0.003, partial η^2=0.04). Change in other symptom domains reported by parents and teachers did not differ across groups.

Afterwards, patients with CGI-I scores of "much" or "very much improved" were classified as treatment responders and logistic regression analysis was used to evaluate predictors of treatment response in children with SCT+ADHD. Gender, ADHD type, presence of any comorbidity, mean equivalent daily dose of MPH, duration of treatment, parent ratings of inattention and oppositionality, teacher ratings of hyperactivity/ impulsivity and BCAS sluggishness and daydreaming scores (dummy-coded according to median as significant/ not significant) were entered as predictors. The

Table 5. Predictors of treatment response in children with Attention Deficit/ Hyperactivity Disorder and Sluggish Cognitive Tempo according to logistic regression

Variable	O.R.	95 % Confidence Interval	p
Gender (Male)	0.6	0.2- 2.0	0.404
ADHD-IA	2.2	0.4-11.1	0.359
Comorbid diagnosis	0.4	0.1- 1.2	0.115
Mean daily equivalent dose of MPH	1.0	1.0- 1.1	0.598
Treatment duration (month)	1.1	1.0- 1.3	*0.012*
BCAS- daydreaming	0.5	0.2- 1.3	0.167
BCAS- sluggishness	1.3	0.5- 3.7	0.621
T-DSM-IV-S-P-IA	1.0	0.9- 1.1	0.718
T-DSM-IV-S-P- ODD	0.9	0.8- 1.0	0.149
T-DSM-IV-S-T-HIP	1.0	0.9- 1.1	0.911

O.R.: Odds Ratio, ADHD: Attention Deficit/ Hyperactivity Disorder, IA: Inattention, MPH: methylphenidate, BCAS: Barkley Child Attention Scale, T-DSM-IV-S: Turgay DSM-IV Based Screening Scale for Disruptive Behavior Disorders, ODD: Oppositional Defiant disorder.

model was significant (Hosmer- Lemeshow x^2 (8) = 6.6, p=0.582) and could explain 22.7 % of the variance in treatment response (Nagelkerke R2=0.227). The predictors could classify 86.8 % of treatment responders and 40.6 % of treatment non-responders in the SCT group for an overall accuracy of 72.0 % (Table 5). The sole predictor of treatment response was its duration.

DISCUSSION

This study aimed to evaluate the difference in treatment response in children with ADHD with or without SCT symptoms and to evaluate the predictors of MPH treatment response in ADHD+SCT group. We found that SCT was more frequently associated with ADHD- inattentive type. Parents rated children with SCT + ADHD as more inattentive by their parents while teachers rated children with ADHD as more hyperactive/ impulsive. Parent and teacher reported symptoms reduced significantly with treatment in both groups. However, reduction was significantly greater for teacher rated hyperactivity/ impulsivity in the ADHD group. The sole predictor of treatment response in the SCT+ ADHD group was treatment duration.

In our study, the ADHD-I subtype ratio was higher in the SCT+ADHD group than the ADHD group. Although SCT symptoms are found to be distinct from the ADHD symptom dimensions and can be seen in both ADHD-combined (ADHD-C) and ADHD-inattentive types (ADHD-I), they display greater correlations with inattentive symptoms than hyperactive-impulsive symptoms (33). In a clinical sample study, Garner and colleagues found that SCT symptoms were higher in children with diagnosis of ADHD-I (36). In a randomized controlled trial to examine the association between SCT symptomatology and response to methylphenidate, Froehlich and colleagues (22) also found that children with SCT formed a greater proportion of cases with ADHD-I than ADHD-C subtype. Cevher, Binici and Kutlu (37) also reported that children with SCT symptoms were predominantly diagnosed with ADHD- IA. Therefore, our finding is consistent with studies reporting a partial overlap between inattention and SCT symptoms which may pose difficulties in accurate diagnosis. In the baseline symptom assessment, SCT+ADHD group in our sample were rated as significantly more inattentive by their parents but not by their teachers, while the ADHD group were rated as significantly more hyperactive and impulsive by their teachers. Various studies suggest that parent and teacher reported SCT symptom scores did not display significant correlations among children diagnosed with ADHD (22, 36). In contrast to our study, Garner and colleagues' study indicated that teacher ratings of SCT showed a clearer distinction between ADHD subtypes than parent ratings as the classroom could be a structured setting when compared to home. Cevher Binici and Kutlu (37 found that both parents and teachers rated children with SCT + ADHD as less aggressive and more withdrawn/ anxious while they rated children with ADHD as more aggressive and displaying greater behavioral problems. The difference in our results could be due to closer observations and greater academic expectations of parents or preferences of teachers for calm but inattentive pupils compared to hyperactive/ impulsive ones in the classroom. The manifestations and validity of SCT symptoms across the school and home settings and in differing cultures may be an important area for further research.

The clinicians rated symptom severities and improvement as similar across groups and parent and teacher reported symptom scores in both groups reduced significantly with treatment. Similar to our study, a retrospective naturalistic follow up study which evaluated the prognostic validity of SCT symptoms in MPH treatment response by comparing patients with inattentive ADHD (with and without SCT symptoms) also found no significant difference in ADHD total scores after a month of treatment (36). However, reductions in teacher-rated hyperactivity/ impulsivity symptoms were greater in the ADHD group among our sample. This may indicate a reduced response to MPH treatment among children with SCT and/ or IA symptoms. Supporting this position prior studies have suggested that children with the inattentive subtype of ADHD may show a less robust response to methylphenidate (38). Froehlich and colleagues (22) also reported that hyperactive-impulsive symptoms were more responsive to MPH treatment compared to inattentive/ SCT symptoms and

children with ADHD + SCT may respond to MPH treatment less. A recent study from Turkey also supports that SCT symptoms accompanying ADHD may signify reduced response to stimulant treatment (23. Although some studies suggest that children with ADHD + SCT may not differ in treatment response to those with ADHD alone, this difference may be due to dependence on parental reports alone (39. The reduction in sluggishness symptoms at school with treatment in our sample with ADHD + SCT may be interpreted as hyperactivity/ impulsivity by their teachers. We could not test this hypothesis due to our dependence on parent forms of BCAS completed at baseline. Further studies on treatment response among children with ADHD+ SCT may use repeated evaluations by BCAS completed by multiple informants to test this hypothesis. Also, as suggested by some recent studies, SCT symptoms accompanying ADHD may be more responsive to treatment with ATX (24,25). Future studies on treatment response among children with ADHD+ SCT may also evaluate the effects of non-stimulant treatments.

When we analyzed predictors of treatment response in children with the SCT+ADHD group, we found no relationship between SCT sluggish or daydreaming factors and treatment response with the sole predictor being treatment duration. This finding may suggest the relative resistance of SCT symptoms to MPH treatment and/ or the importance of cumulative dose of MPH received/ maturation in addressing symptoms of SCT. Partially supporting the importance of cognitive maturation in addressing SCT symptoms, Fırat and colleagues reported that MPH treatment may improve SCT symptoms especially among older children (23). Because of the preponderance of prepubertal children in our sample we could not evaluate the effects of cognitive maturation on MPH treatment for SCT symptoms accompanying ADHD. Further studies may enroll patients from varied age groups (i.e., prepubertal, early-mid-late adolescent) to determine the effects of cognitive maturation.

Limitations

Our results should be evaluated within their limitations. Firstly, the retrospective, single-center design of the study may affect our results and limit external validity. Secondly, we used a two-stage screening design to evaluate probable SCT (i.e CBCL-SCT index and BCAS) and this may have led to false negatives/ positives. Supporting this position, Wu and colleagues (17)reported that 10.8 % of their sample with ADHD were classified as having SCT symptoms while this increased to 30.0-60.0 % with BCAS. Third, addition of a placebo or atomoxetine arm could have enriched our results. Fourth we could not control for the effect of maturation on SCT symptoms. Fifth, we did not evaluate for the effects of autism spectrum disorder symptoms, anxiety and depression on treatment response among children with ADHD +/ - SCT.

Despite those limitations this naturalistic study may support the differing nature of inattentive symptoms in SCT and ADHD-IA. Also, longer treatment duration seemed to be more effective in the SCT group so randomized controlled studies with longer treatment duration with different dose regimes should be conducted to investigate validity of SCT symptoms across the school and home settings and the effect of different dimensions of SCT on MPH response.

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

Ethical Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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The effects of COVID-19 pandemic and lockdown on internet, smartphone use and emotional-behavioral problems in adolescents: A longitudinal study

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SUMMARY

Objective: Young people had adverse emotional and behavioral effects due to the pandemic and restricted measures, which caused social isolation, spending more time online with smartphones, tablets, and computers. We aimed to investigate adolescents' emotional/beha-vioral problems and internet/smartphone usage features during this pandemic and to compare the findings with the pre-pandemic features.

Method: The sample consisted of 57 adolescents (27 males, 30 females). Data were collected at two-time intervals: before the COVID-19 pandemic [T1] and during the COVID-19 pandemic [T2]. All participants fulfilled the Strengths and Difficulties Questionnaire (SDQ), The Young's Internet Addiction Test (IAT), Smartphone Addiction Scale-Short Version (SAS-SV).

Results: The results indicated that both internet and smartphone use duration significantly increased at T2($P < 0.001$). With regards to SDQ, emotional symptoms, hyperactivity problems, prosocial behaviors, and total difficulties subscales were significantly worse at T2 than T1 ($P < 0.05$). Additionally, significant correlations were found between IAT and SAS scores and SDQ behavioral problems, hyperactivity-inattention subscores, and total difficulties scores ($P<0.001$). Finally, according to regression analysis hyperactivity-inattention problems increased the risk of problematic internet use ($P < 0.05$).

Discussion: We objectively observed internet and smartphone use increase and relations with emotional and behavioral problems among adolescents during the outbreak of Covid-19. Therefore, these results should be carefully kept in mind while developing health policies for the long-term effects of the pandemic, whose duration is not yet known.

Key Words: Pandemic, internet addiction, smartphone addiction, emotional problems, behavioral problems

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INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has brought some challenges and difficulties to the lives of people around the world, including children and adolescents. The World Health Organization (WHO) declared the disease a pandemic on 11 March 2020. As a response to the pandemic, most countries immediately implemented some measures such as home quarantines, social restrictions, and school closures to slow down to spread of the infection. The mandated lockdowns keeping the social distance abruptly changed people's social lives and daily routines, along with the escalating use of digital gadgets and the internet (1). Although youngsters are less vulnerable to COVID-19, children and adolescents may experience more short and long-term side effects of the

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pandemic and measures, including lockdowns and school closures (2-4).

In recent years, the usage of technological communication devices (e.g., smartphones, tablets) has rapidly increased worldwide. With the restriction of outdoor activities due to lockdowns and school closures, participation in other activities (e.g., internet or smartphone use, exercise, watching television) may increase or decrease during the COVID-19 outbreak period. The pandemic induced an increase in internet usage, which may increase the risk of developing addictive behaviors in adolescents that persist throughout their lifespan (5). Furthermore, overuse of these devices and spending more time on the internet may lead to physical or mental problems (6-8). Previous researches have emphasized that in addition to excessive fear of being infected, social isolation and increasing digital consumption are also related to many mental health problems ranging from sleeping problems to emotional and behavioral problems among adolescents (9-12). Duan et al. (2020) has figured out the higher prevalence of anxiety and depression in adolescence during this global crisis, and it has been highlighted the positive correlation between internet/smartphone addiction and anxiety/depression levels (13).

During the pandemic, some children and adolescents may not be completely isolated due to their parents being at home. However, keeping in mind that social interaction with peers is a crucial part of psychosocial development, the social distance may force many adolescents to experience more loneliness (11). Additionally, previous studies have reported the impacts on mental and physical health during the pandemic (14). Since children and adolescents are more vulnerable to any type of addiction than adults, disasters such as epidemics and terrorist attacks may have increased addictive behaviors including smoking, excessive alcohol consumption, and internet addiction (15-17). In this case, children and adolescents may have increased spending more time on social media and the internet as a strategy to keep themselves busy and to cope with the feeling of loneliness, anxiety and depression (15,18,19). In the light of knowledge that adolescence involves immature coping strategies and resilience, it is not surprising that all the consequences of the pandemic could have a more compelling impact on adolescents' mental health.

Given the scope of the COVID-19 pandemic, it is essential to better understand impacts on the mental health of adolescents and behavioral changes. In this case, if related risk factors, mental health problems, and related factors are known, intervention methods can be developed accordingly during or after the pandemic. Based on current knowledge, we can guess that social isolation may increase screen time and internet use, but, in the literature, studies comparing the pre and during pandemic features of mental health, screen and internet usage have been limited. Because many previous studies have focused on the impacts of the pandemic on mental health, screen and internet usage time during this process comparing with the prepandemic data, which was obtained by asking in the same time with pandemic data. So that, the aims of this present study were 1) to investigate the emotional/behavioral problems and internet/smartphone usage features of adolescents during this pandemic and 2) to compare the findings with the pre-pandemic features.

METHODS

Participants and Study Design

Our study was first designed to investigate the smartphone and internet usage characteristics of adolescents who applied to Child and Adolescent Psychiatry outpatient unit due to any problem and their relationship with emotional/behavioral problems before the pandemic. Therefore, the first data of the study were collected between March and December 2019, Time 1 (T1). 126 adolescents (63 females, 63 males) aged 12-18 years participated in the first part of the study. Psychopathologies evaluated by clinical interviews and researchers collected data of participants via sociodemographic form including smartphone and internet usage time, online occupation areas (e.g. video gaming, social media, chat). All participants fulfilled the Strengths and Difficulties Questionnaire (SDQ), The Young's Internet Addiction Test (IAT), Smartphone Addiction Scale-Short Version (SAS-SV).

After March 2020, when the first COVID 19 case was diagnosed in our country, mandatory measures were started to be implemented in Turkey. As a result, school closures and lockdowns were imposed for a long time, as in many countries. Adolescents who participated in the first part were invited to the second part of study to fill out the questionnaires again in order to investigate the characteristics of the pandemic process. Fifty-seven adolescents (27 males, 30 females) of all participated in the second part of this study. The second data collection period was between September and December 2020, Time 2 (T2), a period that the schoolchildren in Turkey were not allowed to attend school. At T1, participants completed the study survey in the classroom setting, while at T2, students completed an online survey from home due to the COVID-19 restrictions.

Measures

The Socio-Demographic Measures

Gender, age, school grade, school achievement (self-perception), parental education statuses, family income, internet and smartphone usage areas (e.g., social media, video gaming, communication) were assessed.

Strengths and Difficulties Questionnaire (SDQ): SDQ has been developed by Goodman in 1997 to diagnose psychological problems in children and adolescents (20). The SDQ consists of 25 items, and responses are on a Likert-type scale of 0 to 2 (based on the following replies: "Not true", "Somewhat true", "Certainly true"). It has five subscales: conduct problems, hyperactivity-inattention, peer problems and prosocial behaviors, and emotional symptoms. All these scales, except prosocial behaviors, are added together to generate a total difficulty score. The total difficulty score ranges from 0 to 40; it can also be categorized as a total score 0–14 indicates normal, a total score of 16–19 indicates borderline, and 20–40 indicates an abnormal score (21). Turkish version of the scale was adapted and observed to be consistent and reliable, with the Cronbach's α: 0.70 (22).

The Young's Internet Addiction Test (IAT): Turkish version of The Young's Internet Addiction Test was used to assess internet addiction symptoms (23). It is a self-rated test with 20 items, and each item is scored on a scale of 1-5. According to Young et al.'s criteria (24), participants whose IAT total scores 70 or above were classified as addictive internet users (AIU). Participants with an IAT total score of 40-69 were classified as problematic internet users (PIU) who had encountered general life problems due to Internet use. Participants with an IAT score of 39 or below were classified as normal Internet users (NIU), who only had some or no problems controlling Internet use. Coefficient Alpha for the Turkish version of IAT equals 0.895 (23).

Smartphone Addiction Scale-Short Version (SAS-SV): SAS-SV was developed by Kwon et al. (2013) to measure the risk of smartphone addiction (25). Participants expressed their opinion for each item over a 6-point scale, ranging from 1 (strongly disagree) to 6 (strongly agree), with higher scores indicating a high risk of addiction. References to the previous studies, the cut-off value of this scale was defined by sex, precisely 31 for female and 33 for male, respectively (25). The internal consistency of the test was verified with a Cronbach's α of 0.90 in adolescents in Turkey (26).

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of Eskisehir Osmangazi University of Medicine School. (ethical approval references: Study One: 2018-231 Study Two: 2020-436). All participants provided written informed consent prior to completing the survey (computer-based, e.g., by clicking "yes").

Statistical Analysis

The Statistical Package for Social Sciences (SPSS) version 23.00 was used to analyze the data. Simple descriptive statistics were expressed as frequency and percentage for categorical variables, mean and standard deviation (SD) for continuous variables. The comparisons of the normal distribution of numeric variables were evaluated using Paired-samples t-test, and non-normally distributed numeric variables were evaluated using the Wilcoxon test in the study population before and during the COVID-19 lockdown. The McNemar test was used to compare the categorical before and

during the COVID-19 lockdown. A p-value lower than 0.05 was considered statistically significant.

RESULTS

Sociodemographic characteristics

Of the 126 study participants (T1), 57 were included because they completed both times (T1 and T2) questionnaires. The mean age of adolescents was 15.1 ± 1.8 at baseline (T1). All participants were 5th grade to 12th-grade students at T1. At T2, 6 were university students, 9 were currently not attending school, and the rest were 6th to 12th-grade students. Table 1 shows the sociodemographic and additional data of participants during lockdowns.

Moreover, their time spent on smartphones at T2 (mean 6.4±4.7 h daily) was significantly longer than their time spent on smartphones at T1 (mean 3.9±2.7 h daily)(P < 0.001); time spent on the internet at T2 (mean 7.7±5 h daily) was significantly longer than their time spent on the internet at T1 (mean 4.5±3 h daily)(P < 0.001). With regards to SDQ, emotional symptoms, hyperactivity problems, prosocial behaviors, and total difficulties subscales were significantly worse at T2 than T1 (P < 0.05). In addition, when we evaluated the IAT and SAS scores, no difference was found between the scores in the two time periods (Table 2).

Table 1: Sociodemographic characteristics of the study population and frequency of Lock-Down-Related Ratings

	N (%)
Gender	
Female	30 (52.7%)
Male	27 (47.3%)
Marital status	
Married parents	45 (78.9%)
Divorced parents	9 (15.8%)
Widow parents	3 (5.3%)
Parents educational level	
Mother	
Primary school	28 (49.1%)
High School	15 (26.3%)
Graduation	14 (24.5%)
Father	
Primary school	18 (31.6%)
High School	21 (36.8%)
Graduation	18 (31.6%)
Psychiatric disorder at T1	
Depressive Disorders	9 (15%)
ADHD	9 (15%)
Anxiety Disorders	8 (14%)
Conduct Disorders	5 (8.8%)
Oppositional Defiant Disorder	1 (1.8%)
OCD	1 (1.8%)
Enuresis Nocturna	1 (1.8%)
None	23 (40.4)
School attendance	
Online	32 (56.1%9)
Online and in-person	17 (29.8%)
Not attending	8 (14%)
Meeting with friends	
No	22 (38.6%)
1-2 times a week	35 (61.4)
Smartphone usage areas	
Social media	48 (%84.2)
Game	28 (49.1%)
Communication	47 (82.5%)
Other	15 (26.3)
Academical performance	
Good	26 (45.6%)
Moderate-bad	31 (54.4%)

ADHD: Attention Deficiency Hyperactivity Disorder,
OCD: Obsessive-Compulsive Disorder

Tablo 2: Comparisons of daily hours and scale scores

	Time 1 Mean (95% CI)	Time 2 Mean (95% CI)	P-value
Internet use (hours/daily)	4.5–3	7.7–5	**< 0.001**
Smartphone use (hours/daily)	3.9–2.7	6.4–4.7	**< 0.001**
SDQ[a]-Emotional problems	3.3–2.1	4.3–2.5	**0.004**
SDQ-Behavioral problems	2.7–1.4	2.6–1.8	0.571
SDQ-Hyperactivity-inattention	4.8–2.1	5.5–2.0	**0.035**
SDQ-Peers problems	3.2–2.0	3.3–1.8	0.788
SDQ-Prosocial behaviors	8.2–1.9	7.5–2.1	**0.015**
SDQ-Total difficulty	14.1–4.8	15.9–5.0	**0.031**
IAT[b]	43.7–15.6	44.1–15.4	1.000
SAS-SV[c]	29.6–12.3	28.1–12.6	0.367

a: Strengths and Difficulties Questionnaire(SDQ) b: The Young s Internet Addiction Test (IAT),
c: Smartphone Addiction Scale-Short Version (SAS-SV)

Problematic internet users (PIU) were diagnosed based on the total score of the IAT. Participants who scored higher than 40 and more on the IAT were considered PIU. Table 3 reveals that PIU had poor behavioral problems, hyperactivity subscales and total scores of SDQ during lockdowns.

In addition, Table 4 shows the bivariate correlations of study variables. Statistically significant correlations were found between IAT and SAS scores and SDQ behavioral problems, hyperactivity-inattention subscores, and total difficulties scores.

According to the results of the regression analysis in Table 5, a 1- unit increase in hyperactivity-inattention subscores of SDQ led to increase the risk of problematic internet using (OR: 1.749, (P < 0.05).

DISCUSSION

To the best of our knowledge, although research on internet and smartphone use has increased recently, studies comparing pre-pandemic data with data during the pandemic are still limited. This study provides evidence of the adverse effects of the COVID-19 pandemic on internet and smartphone use and related risk factors. According to our findings, total daily time spent on the internet and

Table 3: Comparisons of SDQ scores between normal and problematic internet users

	PIU (n:31) mean–SD	Normal internet users (n:26) mean–SD	p
SDQ-Emotional problems	4.8–2.6	3.8–2.3	.117
SDQ-Behavioral problems	3.1–2	2.0–1.4	**0.045**
SDQ-Hyperactivity-inattention	6.4–1.8	4.5–1.7	**< 0.001**
SDQ-Peers problems	3.4–1.9	3.1–1.7	.524
SDQ-Prosocial behaviors	7.2–2.1	8–2.1	.127
SDQ-Total difficulty	17.9–4.4	13.5–4.7	**< 0.001**

PIU: problematic internet users, SDQ: Strengths and Difficulties Questionnaire

Table 4: Bivariate correlations of study variables.

Variable	1	2	3	4	5	6	7	8
1. SDQ[a]-Emotional problems	-							
2.SDQ-Behavioral problems	0.173	-						
3.SDQ-Hyperactivity-inattention	0.350**	0.214	-					
4.SDQ-Peers problems	0.023	0.224	-0.064	-				
5.SDQ-Prosocial behaviors	-0.007	-0.298*	-0.017	-0.147	-			
6.SDQ-Total difficulty	0.712**	0.621**	0.630**	0.441**	-0.174	-		
7.IAT[b]	0.244	0.343**	0.434**	0.083	-0.182	0.452**	-	
8.SAS-SV[c]	0.272*	0.424**	0.352**	-0.080	-0.198	0.402**	0.692**	-

* P < 0.05, ** P < 0.001, a: Strengths and Difficulties Questionnaire(SDQ) b: The Young s Internet Addiction Test (IAT), c:Smartphone Addiction Scale-Short Version (SAS-SV)

smartphone use has significantly increased during pandemic restrictions. This may be explained by the extensive usage areas of smartphones and internet. Pandemic restrictions have caused social isolation, lack of physical relationships, and contact with friends and relatives (8,27). In this case, the combined use of the internet and smartphones may have provided communication, games, entertainment, occupation, obtaining information, and coping with loneliness. Serra et al. (2021) have shown in their study that an increase in smartphone use because of its functions such as telephone calls, videos, online chats, and social networks (8). It is essential for adolescents to be a member of a group and connect with their peers (28). In support of this, in our study, it was determined that the most common use of smartphones was social media and communication. Thus, during the pandemic, adolescents provided the necessary communication and interactions for their psychosocial development through smartphones and the internet. Consistently, a previous study has reported high rates of social media and communication applications among adolescents during the pandemic (29). In addition, another study conducted in Turkey showed that problematic internet use was associated with loneliness (30).

Our study shows that the SDQ emotional, hyperactivity-inattention and prosocial subscores of adolescents are worse during the pandemic compared to pre-pandemic times. In the literature, although very few longitudinal studies, there are many studies investigating the impacts of the pandemic on mental health in many particular populations (13,31,32). Longitudinal studies have figured out an increase in depression, anxiety, and stress (33,34). Additionally, a meta-analysis has shown that depression and anxiety in adolescents increased by double (35). These results need to be interpreted from many perspectives. First of all, emotional and behavioral problems may have increased due to the direct effects of the pandemic, losses, diseases, social isolation, compulsory restrictions such as school closures (35-37). On the other hand, socioeconomic difficulties such as familial unemployment and economic problems caused by the pandemic may have contributed to the existing problems (35).

According to the results of our study, although behavioral problems did not change during the pandemic, the participants reported a significant increase in attention and hyperactivity problems. It was also reported that hyperactivity and attention problems increased in the follow-up study conducted with 1-month intervals at the beginning of the pandemic (34). These attention and hyperactivity problems might be associated with life changes, social isolation, online schooling-related concentration problems, and pandemic stress (36,38-40).

In addition, the findings of our study have shown that although the daily smartphone and internet usage times of the participants increased almost twice, there was no difference in IAT and SAS scores. One of the most important reasons why there was no difference in the scores despite the increase in the duration may have been that these uses did not cause a loss of functionality due to closures during the pandemic. Besides, contrary to the loss of functionality caused by addiction, it comes to mind that internet and smartphone use may contribute to functionality during the pandemic period. However, in a cohort study conducted with an interval of 2 months, it was reported that smartphone addiction increased (8).

Our findings showed that behavioral and hyperactivity-inattention problems were correlated to high-

Table 5: Multiple regression results on the effect of problematic internet users

	PIU OR	CI (95%) lower-upper	p
Gender (Male)	0.513	0.128-2.059	
SDQ-Emotional problems	1.000	0.762-1.312	0.999
SDQ-Behavioral problems	1.160	0.773-1.742	0.473
SDQ-Hyperactivity-inattention	1.749	1.181-2.589	**0.005**
SDQ-Peers problems	1.143	0.804-1.626	0.456
SDQ-Prosocial behaviors	0.848	0.613-1.174	0.320
SDQ-Total difficulty	1.090	0.782-1.520	0.610

SDQ: Strengths and Difficulties Questionnaire scores at T2

er IAT and SAS scores. In addition, regression analysis indicated that hyperactivity-inattention problems increased the risk of problematic internet use. This finding corresponded with other studies about this issue on adolescents (41,42). Furthermore, some studies have shown a significant correlation between psychiatric disorders (e.g. ADHD, MDD, anxiety disorders) and increased risk of internet addiction (43,44). In addition, similar to previous studies, the most common diagnoses we detected in T1 clinical evaluation were depressive disorder, ADHD, and anxiety disorders.

Interpretations of our findings should be taken with caution, and keep in mind the following limitations. First, as alluded to above, adolescents who applied to the outpatient clinic with any problem were included in our study. Therefore generalization to the whole population is restricted. Second, the psychiatric diagnosis interview was only made at T1; therefore, we cannot interpret cases' current diagnosis during the pandemic process. Further studies should conduct follow-up studies in order to clarify how psychiatric diagnoses have changed during the pandemic. Finally, the small sample size makes it difficult to interpret some data, so longitudinal studies with larger samples are needed.

In conclusion, the strength of our study is that T1 data were collected in the same population before the pandemic, and it allows objective comparison with the data during the pandemic process. Despite the small sample group, the results of our study revealed the negative impacts of the COVID 19 pandemic on the mental health and internet and smartphone usage features of adolescents. The current data do not yet give precise information about how long the pandemic will last. Therefore, this study suggests that while fighting the pandemic, both the pandemic and restrictive measures have negative effects on mental health, and this issue should be carefully kept in mind in the long-term fight against the pandemic.

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The effect of Sars-CoV2 pandemic on consultations of a child and adolescent emergency psychiatry clinic

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SUMMARY

Objectives: Our study aims to investigate how the pandemic has affected the emergency department (ED) visits and to assess whether COVID-19 pandemic changed the presentations of diagnoses /chief complaints of the patients across three years.

Method: This is a retrospective study. The study population was described as all patients who applied to our Pediatric Psychiatry ED from March to May of 2019, 2020 and 2021.

Results: The overall number of child and adolescent psychiatric emergency department visits declined by 49.5% in 2020 during pandemic period with implementation of COVID-19 related measures. From the corresponding period of 2021, the total number of ED visits have increased to a higher level than the same period of 2020 and even 2019. In 2020 and 2021, compared to 2019 (26.1%); there was a decrease of patients being admitted to the inpatient unit. We also found that the ratio of patients who were diagnosed with autism spectrum, mental retardation, depression, trauma and related, anxiety and obsessive-compulsive disorders got increased.

Conclusion: The immediate drop in visits to ED after the first pandemic restrictions may reflect people being more hesitant to hospitals at the beginning. But one year later, in the mid-pandemic period, the rise in visits to ED could have been because people got used to the pandemic or the need for acute psychiatric care cannot further be postponed. The decrease of admissions to the inpatient psychiatric unit may be a result of COVID-19 related measures as total number of beds got reduced due to restrictions.

Keywords: Child and adolescent psychiatry, COVID-19, emergency psychiatry, pandemic

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic and the restrictions associated with the pandemic are likely to have had a negative effect on the children and adolescents' mental health. Factors like school suspension, social isolation, not being able to access to social support such as friends and other activities, fear of contamination, economic problems and family distress may all cause long-term negative effects on children and adolescents.

Early reports of the pandemic reported that the COVID-19 outbreak caused an increased level of anxiety and depression in child and adolescent population (1, 2, 3). Besides stress factors, a deficit of psychiatric care during the pandemic was also considered a risk factor for increased mental health issues (4). Although several cross-sectional studies consistently showed high levels of depression and anxiety during the initial phase of the pandemic, less data is available about long-term effects on the child and adolescent's' mental health. A longitudinal study assessing psychopathological symptoms in adolescents after one year of the pandemic has found that anxiety and maladaptive behaviors such

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as self-harm ideation, self-harm behaviors, and aggressiveness scores tend to ascend at the follow-up interview. In contrast, there was no difference for depressive symptoms one year later (5). Another follow-up survey study reported an increased rates of depression, anxiety, self-harm and suicide attempts (6).

In Turkey after the first COVID-19 case was detected on 11th March 2020, the measurements and school closure were implemented immediately. During April and May 2020, the restrictions were still continued. One year later, during March to May 2021, schools were closed again. Long duration of school suspension in Turkey is expected to have detrimental effects on child and adolescent's mental health well-being as schools are not only crucial for education but they also serve as a preventative environment for the youth. Long duration of staying home may have led to an increased rate of abusive home. For example, in China, reports of domestic violence were tripled during the lock-down in February compared the previous pre-pandemic period (7).

Despite various reports across the world stating the early and late effects of pandemic on youth's mental health, up to our submission date, there is no study from Turkey which has evaluated the effect of the pandemic on child and adolescent psychiatric emergency admissions. Before the pandemic, visits to pediatric emergency departments (ED) had been increasing over the last several years (8). EDs are vital for the care of children and adolescent mental health problems. They are becoming more and more important due to insufficient pediatric outpatient clinic capacity (9). At the acute phase of the pandemic, when staying-home orders were first implemented, the number of presentations related to mental health issues to the ED had decreased 43% while the proportion of Diagnostic and Statistical Manual of Mental Disorders 5 (DSM-5) specified mental-health disorder related visits had increased (10). A study from Ireland also found that while hospital admissions with mental health issues fell by 2.6% during the initial lockdown but the admissions increased even above the pre-COVID levels from July 2021 to December 2021 (11). But we are lack of information about ED presentations during the pandemic and the reflection of the pandemic on child and adolescent's mental health in Turkey. Therefore, the present study first aimed to investigate how the pandemic has affected ED visits first and second year of the pandemic compared to the one year before and secondly, to assess whether COVID-19 pandemic changed the presentations of diagnoses and chief complaints of the patients across three years.

METHOD

This is a retrospective study which was conducted at one of the largest mental health hospitals in Istanbul, Turkey. Child and adolescent psychiatry unit of the hospital served as the only child psychiatry emergency unit and the inpatient unit during the pandemic.

Data was extracted from the electronic database of the hospital. The study population was described as all patients who applied to Pediatric Psychiatry Emergency Department from March to May of 2019, 2020 and 2021 as we compared these same three-month time periods for consecutive three years. Time periods were selected specifically to coincidence with the beginning and end of the strict restrictions in Turkey due to COVID-19 pandemic. March- May 2019, 2021 and 2022 was described as a pre-pandemic, pandemic, and mid-pandemic period, consecutively.

Data regarding the total number of ED visits, age, sex, means of arriving to the emergency department, treatment procedure, discharge status, and primary diagnosis at discharge were collected.

Descriptive statistical analyses, ANOVA and Chi-square tests were performed to assess data among three time periods. All P values were two-tailed and significance was set at a p value less than 0.05. Bonferroni correction was used to adjust the critical value for multiple comparisons. All analyses were performed with SPSS, version 22. The study protocol was approved by a qualified ethical board.

RESULTS

Based on descriptive statistics, a number of variables were compared among March to May 2019,

Table 1. Sociodemographic and administrative characterization of emergency psychiatric visits

	Prepandemic, March to May 2019	Pandemic, March to May 2020	Mid-pandemic, March to May 2021	*p* value
Total visits, n (%)	111 (32.8)	55 (16.3)	172 (50.9)	
Age, mean (SD)	15.46 (2.23)	15.78 (1.94)	15.70 (2.31)	P=0.59
Sex, n (%)				
Female	59 (53.2)	29 (57.7)	100 (58.1)	p=0.63
Male	52 (46.8)	26 (47.3)	72 (41.9)	
The means of arrival, n (%)				
With ambulance				
With family	19 (17.1)	14 (25.5)	31 (18.0)	p= 0.39
	92 (82.9)	41 (74.5)	141 (82.0)	
Outcome, n (%)				
Need for injection n (%)	30 (27.0)	15 (27.3)	51 (29.7)	p=0.87
Need for oral treatment	48 (43.2)	27 (49.1)	89 (51.7)	p=0.37
Blood test	23 (20.7)	10 (18.2)	30 (17.4)	p=0.78
Drug blood level	4 (3.6)	2 (3.6)	5 (2.9)	p=0.93
Discharge status, n (%)				
Referral to the inpatient clinic	30 (27.0)	17 (12.7)	14 (8.1)	p<0.001
Close monitoring	31 (27.9)	14 (25.5)	54 (31.4)	
Control at the outpantient clinic	25 (22.5)	30 (54.5)	95 (55.2)	
No need to control	25 (22.5)	4 (7.3)	9 (5.2)	

2020, 2021. The exact comparison date was determined 11th March when the first COVID-19 case was seen in Turkey and the restrictions immediately occurred after.

The study sample included 338 patients who applied to psychiatry emergency service during the same year period, March to May 2019, 2020, and 2021. Sociodemographic variables of the patients that had applied to the ED during the pandemic and the administrative characterization of the patient's visits were shown in Table 1. In total, the number of emergency department admissions decreased during the first period of pandemic months (March-May 2020), relative to the same period in 2019, from 111 patients to 55 in 2020 (a 49.5% decrease). Similarly, in the same period of 2021, the mid-pandemic months, the number increased to 177 patients (a 97.3% increase) compared to pandemic period.

The mean age of the sample was similar among the three years, which was 15.4, 15.7 and 15.7 respectively in 2019, 2020 and 2021 (p=0.5). Similarly, before and after the pandemic, the female participants ratio was 53.2, 57.7 and 58.1 respectively and remained stable (p=0.63).

The mode of arrival at the emergency department, whether with family or ambulance, was not changed among the three years (p=0.31).

With regards to comparison of outcomes of patients in the emergency department, the ratio of the need for psychopharmacological injection treatment (p=0.87) and the need for psychopharmacological oral treatment had not changed during the past three years (p=0.37). Furthermore, the ratio of consulting to blood test (p= 0.78) or drug blood level (p=0.93) remained the same between pre and mid pandemic periods compared to pandemic period.

In terms of disposition ways, the patients were separated into four categories as; referral to an inpatient unit, close monitoring at the outpatient clinic, routine control at the outpatient clinic, and no need for a control group. The ratio and the number of patients referred to the inpatient psychiatric unit was the highest in 2019 compared to the same period in 2020 and 2021 (p<0.001). When the ratio was 27.0 % in 2019, this number was 12.7% and 8.1% respectively, in 2020 and 2021. There was no statistical difference between 2020 and 2021. On the contrary, when we excluded the patients who needed to be referred to the inpatient unit and aggregated the groups as close monitoring and control group; during the pandemic and mid-pandemic periods patients in the close monitoring and control group were far higher than those during the pre-pandemic period (91.7% in 2020, 94.3% in 2021 and 69.1% in 2019; p<0.001).

The reasons for applying to the emergency department were categorized into twelve separate groups and results are presented in Table 2. We observed decreases in frequency and the percentage of the emergency service visits across most diagnostic groups between 2019 and 2020. Nevertheless, the percentage of patients in diagnostic groups of

Table 2. Diagnosis groups of emergency psychatric visits

	Prepandemic, March to May 2019	Pandemic, March to May 2020	Mid-pandemic, March to May 2021	
NSSI, n (%)	33 (29.7)	14 (25.5)	33 (19.2)	p=0.11
Suicidal behaviors, n (%)	17 (15.3)	5 (9.1)	21 (12.2)	p=0.5
Homicidal behaviors, n (%)	16 (14.4)	3 (5.5)	37 (21.5)	p=0.016*
Bipolar disorder, n (%)	23 (20.7)	6 (10.9)	23 (13.4)	p=0.14
Psychotic disorder, n (%)	10 (9.0)	3 (5.5)	27 (15.7)	p=0.65
ASD and MR, n (%)	20 (18.0)	11 (20.9)	24 (14.0)	p=0.47
Depressive disorders, n (%)	28 (25.2)	16 (29.1)	52 (30.2)	P=0.65
ADHD and CD, n (%)	34 (30.8)	16 (29.1)	34 (19.8)	P=0.087
PTSD and related disorders, n (%)	7 (6.3)	7 (12.7)	17 (9.9)	P=0.3
Anxiety disorders and OCD, n (%)	11 (9.9)	11 (20.0)	45 (26.2)	P=0.004*
SUDs, n (%)	11 (9.9)	5 (9.1)	11 (6.4)	P=0.5
Conversion disorders and dissociative disorders, n (%)	7 (6.3)	0	20 (11.6)	P=0.016*

NSSI: non-suicidal self injurious behaviors; ASB: autism spectrum disorders; MR: mental retardation; ADHD: attention deficit hyperactivity disorder; CD: conduct disorder; PTSD: post-traumatic stress disorder; OCD: obsessive compulsive disorder; SUDs: substane use disorders

autism and mental retardation, depression, trauma and related diagnosis, and anxiety and obsessive-compulsive disorder groups was higher than in 2019 but only in anxiety and obsessive-compulsive disorder group reached statistical difference. In 2021, mid-pandemic period, the ratio was higher and also statistically meaningful (in 2019 26.2%, in 2021 9.9%; p<0.001).

There were not any presentations of conversion and dissociative disorders during the pandemic period versus the pre-pandemic period when seven patients visited the emergency department. In addition, in the mid-pandemic period, visit rates in this group rose to their highest level with 20 patients.

There was a decrease in the proportion of patients represented with homicide risk during the pandemic year with 3 patients (5.5%) compared with 16 (14.4%) and 37 (21.5%) patients respectively during pre-pandemic and mid–pandemic period (p=0.016).

DISCUSSION

To our knowledge, this is the first study from Turkey evaluating the effects of the first and mid-period of the COVID 19 pandemic on child adolescent psychiatry emergency visits. We expected that COVID 19 pandemic would decrease the demand for emergency psychiatric visits and after the acute peri-pandemic period, the hospitalization rate would increase.

The overall number of child and adolescent psychiatric emergency department visits declined by 49.5% in 2020 during pandemic period with implementation of COVID-19 related measures. Previous literature found that the number of ED visits dropped by 43 % sharply between mid-March 2020 and April 2020 (10). Another report demonstrated that the weekly number of ED admissions for children aged 14 years and below was 70% lower during the of March 29 to April 25, compared to the same period of 2019 (12). The same report in which all age categories were included, the overall number of visits declined by 42% for all age group. Similarly, a report from Portugal reported that compared to the previous year, the demand for psychiatric emergency care decreased by 52.2% (13). In addition to these studies, other studies also showed a substantial reduction in applications to the emergency psychiatric care at the early period of pandemic (14,15,16).

Furthermore, we found that corresponding period of 2021, the total number of ED visits increased to higher level than the same period of 2020 and even 2019. Similarly, Leeb et. al (10) reported that after acute period of pandemic (mid-March to April) the number of visits increased again through October 2020. In addition, in a study evaluating mental-health related consultation, in early- pandemic period, patients requiring mental health consultation was lower than pre-pandemic period. However, this number exceeded pre-pandemic period by July 2020 (17). An Irish study also reported a similar initial decrease in psychiatric presentations for all age groups, especially when the restrictions and lockdown periods were implemented.

However, in following lockdowns, presentations increased for those below 18 years (18). McNicholas et. al also described after an initial decline, both routine and urgent referrals increased by %50 from September, compared with previous years (2018 and 2019) (19).

The immediate drop in visits to ED after pandemic restrictions had been declared in March-May 2019 could also show that because people were afraid of being infected in the hospital, they did not choose to apply to ED. But one year later, in the mid-pandemic period, the rise in visits to ED could have been because people were getting used to pandemic conditions and/ or they needed acute psychiatric care due to collective and cannot further be postponed negative effects of COVID 19 pandemic on mental health.

In 2020 and 2021 with the rate of 12.7 and 8.1%, compared to 2019 (26.1%), there was a statistically meaningful decrease in admission to inpatient units from emergency department. A similar result was found in a study from Canada, in which the first and second half of March were compared (20). This decrease in the rate of admission to the inpatient psychiatric unit may reflect several reasons. The first and second reasons maybe because of the drop in the overall number of ED visits and minimizing the capacity of the inpatient unit due to strict coronavirus measures. Another reason might be related to the higher threshold criteria implemented by psychiatrists while they were deciding to admit a patient to the inpatient unit aiming to minimize the risk of infection. Despite the fewer hospitalization rate, in 2020 and 2021, the ratio of patients who needed to be closely monitored and controlled frequently at the emergency service or outpatient clinic got increased compared to 2019. That is, only the patients who were in more severe clinical condition might have applied to the emergency psychiatric care. Taken together, the decreased rates of ED visits and hospitalization rates do not reflect that pandemic has no implications on mental health in children and adolescents. Indeed, the decreased rate of hospitalization might demonstrate the huge need for inpatient child and adolescent psychiatric units. But unfortunately, because of COVID-19 related measures, the total number of beds in inpatient units were lessened. Therefore, the decreased hospitalization rate might have resulted from the insufficiency of child and adolescent inpatient psychiatric units rather than the decreased number of severe psychiatric patients who had needed to be transferred to aforementioned inpatient psychiatric units. The increased need of close monitoring and control appointments support this hypothesis. Our results are in line with an Italian study in which they stated the number of ER admissions resulting in psychiatric referral also got increased. They also found that the patients who had no specific indication as result of psychiatric consultation got decreased (21). To sum up, these data show us that the severity of the clinical conditions who applied to emergency services got increased during the course of pandemic.

We also found that the ratio of patients who were diagnosed with autism spectrum, mental retardation, depression, trauma and related, anxiety and obsessive-compulsive disorders got increased. But the statistical significance was only found in anxiety and obsessive-compulsive disorder groups as compared with 2019. These findings are similar to the research emphasizing that the relative risk of receiving anxiety disorder, as well as depressive disorder, were higher during the pandemic compared to the pre-pandemic period (22). Another research also reported a significant proportional increase in anxiety disorders during the COVID-19 period relative to the pre-COVID-19. In addition, anxiety rates amongst young people during COVID-19 have been reported to range from 19% to 37% in a systematic review (23). Though these results are lack of any comparison to the previous years. Another explanation for elevated rate of presentations of these disorders might be related with decreased total number of ED visits during the pandemic and mid-pandemic period. Patients with relatively more chronical psychiatric conditions such as psychosis and bipolar disorder may have been avoided applying to the ED during the pandemic unlike the patients who suffer from anxiety. It is also possible that staying at home because of the restrictions might have provided convenient conditions for many parents to strictly observe and seek medical care if their children are having any serious mental health problems. In this line, increased rate of anxiety disorders might indicate the elevated rate of acute psychiatric problems in community after COVID 19 pandemic has begun. However, we should interpret these results cau-

tiously because our data do not provide information about the clinical severity of these patients or whether these patients applying to the ED for the first time.

In our study, the increased number of presentations of anxiety related disorders with 45 patients (26.2%) are even more apparent for the mid-pandemic period, 2021, compared to the pandemic period, 2020 with 11 patients (20%). A systematic review which investigated the social isolation and loneliness on the mental health of children in the context of COVID-19 reported the duration of loneliness was more strongly associated with anxiety than intensity of loneliness. Loneliness also has longitudinal effects on later anxiety (24). This is important in the context of COVID-19 measures, as in Turkey, similar to other countries, schools were remained closed for a long period which possibly has contributed to social isolation for young people. So, it is expected that extended period of loneliness may have contributed anxiety symptoms in this age period.

Despite many stressors such as loneliness, social isolation and contamination fear, the rate of hospital presentations for self-harm or suicide ideation and attempt rates since COVID-19 pandemic, have not been accelerated. However, other studies found that there were more child and adolescents presenting with self-harm and suicide ideation after the pandemic (25, 26, 27). A study from England reported that presentations increased from 27% to 43% relative to the pre-pandemic (27). In our study, despite the rate of self-harm and suicide ideation have not been increased, the number of patients presenting with these problems were similar for the pre-pandemic and mid-pandemic period although there was an initial reduction in self-harm and suicide ideation presentations in the early period of the pandemic. Early reduction phase also was stated in several publications (28,29,30).

Moreover, when we reanalyzed our data for only females, same results have been obtained. In contrast to our findings, some studies have reported that among adolescents, school-aged girls (10-17 years) showed increased self-harm or suicidal ideation presentation rates since COVID-19. There was also a significant decline in the rate of self-harm in men aged 18-24 years (25). In line with our study, Hill et al. (28) did not find an association between suicide related behaviors and demographic characteristics including sex during COVID-19 period (27).

Our study has some limitations. First of all, our study has a retrospective design and since the child and adolescent psychiatry emergency of our hospital is mostly focused on urgent evaluation and referral, differential diagnosis sometimes is postponed to follow-up interviews in some patients, and these patients may be coded with general psychiatric examination or complaint/symptom focused ICD codes. This situation may have shown the diagnosis distribution rates to be different than they actually are.

To sum up, our study clearly stated that in line with the previous global literature, child and adolescent psychiatry admissions are also drastically reduced at the beginning of pandemic, correlated with strict preventive precautions taken in Istanbul, Turkey as well. Although, stating some controversial results and harboring some limitations, our study is especially valuable as encompassing and examining three-year time period and contributing to global child and adolescent psychiatry COVID literature on behalf of Turkey, as up to our submission date, no known publishments have yet occurred.

Disclosure statement All authors declare no conflicts of interest addressed to this study.

Data Availability Electronic hospital data utilized in this study is not accessible due to hospital's confidentiality policy and ethical considerations.

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Resilience, depression and burnout levels in caregivers of patients followed in the forensic psychiatry service

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SUMMARY

Objective: It is known that psychiatric diseases also affect the quality of life of patients' relatives. The aim of this study is to examine the level of resilience, depression and burnout of the caregivers of forensic psychiatry patients in order to recognize the mental problems that may be experienced by relatives of forensic psychiatry patients who have committed crimes in addition to psychiatric illness.

Method: 90 high-security forensic psychiatry patient relatives were included in the study. Sociodemographic data form, Beck Depression Inventory (BDI), Adult Resilience Scale (RSA) and Maslach Burnout Inventory (MBI) were administered to all participants.

Results: BDI score of caregivers was 10.8±7.7, RSA-total 99.8±12.5, emotional burnout score from MBI subscales 22.5±3.4, depersonalization score 9.4±2.2, personal success score was determined as 16.8±5.4. There was a significant difference between the duration of caregiving in terms of BDI score ($p<0.01$). The BDI score of the caregivers of the patients with criminal liability was found to be significantly higher than the score of the caregivers of the patients without criminal liability ($p< 0.01$).

Discussion: It was observed that the level of psychological resilience was good in people who took care of psychiatric patients who were subjected to forensic psychiatric examination, but they had mild depression and moderate burnout. It is seen that the relatives of the patients are affected psychologically and the necessary psychosocial support can be positive for the caregivers.

Key Words: Forensic psychiatry, caregiver, resilience, depression, burnout

INTRODUCTION

Violence is characterized as the employment of physical force with the potential to cause bodily injury or even mortality, directed at oneself or others (1). It has been documented that certain psychiatric disorders can precipitate attitudes and actions leading to violent outcomes (2). Empirical research delineates a heightened propensity for violent and criminal behaviour among individuals suffering from psychiatric disorders compared to the broader populace (3, 4). To attenuate the recurrence of criminal activities and facilitate the reintegration of forensic psychiatric patients into society, specialized forensic psychiatric services have been instituted, focusing on the appropriate treatment and rehabilitation of these individuals (5). These services supervise patients whose criminal liabilities have been influenced by afflictions such as bipolar disorder and schizophrenia, encompassing crimes from minor assaults to homicides (6).

The nomenclature "caregiver" denotes individuals, frequently close kin, aiding patients with psychiatric disorders in varied facets including personal care, transportation, and fiscal management (7). The chronic nature of mental illnesses often necessitates sustained care, leading a considerable portion of patients to reside with their families (8). Predominantly, these patients spend their entire

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day in the household setting, engendering physical, psychological, social, and economic hardships for family members involved (9,10). Several determinants, such as the progression of the psychiatric ailment, the periodicity of episodes, and the societal stigma bestowed upon these individuals, intensify the adversities encountered by caregivers, frequently culminating in diminished life quality and augmented perceived familial burden (11,12).

Psychological resilience refers to an individual's adaptive process and capacity to overcome successfully substantial stress sources such as threats, familial issues, or trauma (13,14). Individuals with high levels of psychological resilience may possess the advantage of harnessing strength in stressful situations (15). Conversely, it has been demonstrated that individuals with lower psychological resilience are prone to depression (16,17). This vulnerability is associated with a diminished resistance to stress during adolescence, increasing the lifetime risk of utilizing antidepressant and anxiolytic medications (18). It is acknowledged that caregivers of individuals with disabilities often report high scores on depression scales (19).

Depression is conjectured to be linked with burnout syndrome as defined by Maslach, a state characterized by chronic fatigue leading to adversities in individual functionality, accompanied by the progression of despondency, helplessness, and a state of emotional, physical, and intellectual exhaustion (20,21). Furthermore, there exist studies indicating a correlation between the deficiency levels in children with autism and elevated levels of despair, depression, and burnout experienced by their parents (22,23).

We observe that caregivers of individuals undergoing mental treatment encounter various challenges. We hypothesize that the psychological states of these caregivers can differ based on factors such as the characteristics of the psychiatric patients they are tending to, the diagnoses of the illnesses, and the nature of the crimes committed. Therefore, this study aims to identify the levels of psychological resilience, depression, and burnout in individuals providing care to forensic psychiatric patients. We believe that our research can serve as a guide to better understanding the mental states of caregivers and enhancing the quality of psychosocial support that can be extended to them.

METHOD

Study design and sample collection

Local ethical committee approval was obtained from Firat University Faculty of Medicine on 24.02.2022 date. This study was conducted in accordance with the ethical standards stipulated in the 1983 revision of the Helsinki Declaration. The participants included in the study were 118 caregivers (one relative per patient) of patients who were being treated at the Fethi Sekin City Hospital High Security Forensic Psychiatry Clinic for committing criminal offenses. Following the acquisition of written voluntary consent forms from all participants, structured interviews based on DSM-5 were conducted in the interview room by a psychiatric physician, and accompanying psychiatric diagnoses were determined according to the Structured Clinical Interview for DSM-5 Disorders - Clinician Version (SCID-5-CV). However, 10 individuals opted to withdraw from the study, and 8 individuals were excluded due to incomplete form submissions. All participants were administered a sociodemographic data form prepared by us, along with the Beck Depression Inventory, Psychological Resilience Scale, and Maslach Burnout Inventory. In selecting the sample group, it was required that the individuals be primary relatives of patients who had committed a criminal offense, who were visiting the patients or inquiring about them during calling hours, aged between 18 and 65, affirming that the individual they are caring for is undergoing treatment in the forensic psychiatry service, and not having any psychiatric or neurological diseases themselves, not being mentally retarded, and being literate. Furthermore, our study assessed the crimes committed by the patients who had committed a criminal offense under the scope of the Turkish penal code Article 32 (TCK 32) regarding criminal responsibility. It is required for an individual to have full criminal responsibility, to have the ability to direct their actions, and to be able to perceive the legal meanings and consequences of the crime they committed.

This law's first clause stipulates that decisions are made to apply security measures without penal liability for individuals who cannot perceive the legal meaning and consequences of the act committed due to mental illness, and whose ability to control their actions related to this act is diminished. The second clause states that, in cases where not entirely but significantly eliminating consciousness and freedom of action due to mental illness or weakness, a reduction in the penalty is applied (24).

Measurement Tools

Sociodemographic Data Form: This is a form containing clinical evaluation questions such as age, marital status, educational status, and the nature of the caregiver's relationship with the patient, designed by the researchers in line with the objectives of the study.

Beck Depression Inventory (BDI): It was developed to measure the level of depression in adults (25). Scores between 0-9 indicate minimal depression, 10-16 mild depression, 17-29 moderate depression, and 30-63 severe depression. A Turkish validity and reliability study has been conducted (26).

Psychological Resilience Scale for Adults (PRSA): Developed by Friborg et al., it encompasses subdimensions including 'self-perception' and 'future perception,' 'structural style,' 'social competence,' 'family cohesion,' and 'social resources.' Turkish validity and reliability studies were conducted by Basım and Çetin (27, 28). During the calculation, since it was desired to increase resilience as the scale scores increased, the answer boxes were evaluated from left to right as 12345, and the questions numbered 1–3–4– 8–11–12–13–14–15–16–23–24–25–27–31–33 on the scale were marked as reverse questions (28).

Maslach Burnout Inventory (MBI): It includes subscales of emotional exhaustion, personal accomplishment, and depersonalization. High scores in the desensitization and emotional exhaustion subscales and low scores in the personal achievement sub-scale are accepted as signs of burnout. Contrarily, receiving high scores in desensitization and emotional exhaustion sub-scales and low scores in personal achievement sub-scale indicates a high level of burnout, while low scores in desensitization and emotional exhaustion sub-scales and high scores in personal achievement sub-scale demonstrate a low level of burnout. The average scores taken from all three sub-scales point to a medium level of burnout. In the scoring key of the scale, the highest score that can be obtained from the emotional exhaustion dimension is 54, from the personal accomplishment dimension is 48, and from the desensitization dimension is 30. The Turkish validity and reliability study was conducted by Ergin (29, 30).

Statistical Analysis

Analyses were conducted using the SPSS (Statistical Package for Social Sciences; SPSS Inc., Chicago, IL) software package version 22. In the study, descriptive data were presented as n and % values for categorical data, and as mean ± standard deviation (Mean±SD) for continuous data. The normality of the continuous variables was tested with the Kolmogorov-Smirnov test. For the comparison of two groups, the student's t-test was applied for variables showing normal distribution, whereas the Mann-Whitney U test was utilized for variables not adhering to a normal distribution. When comparing more than two variables, One-Way ANOVA analysis was used for those meeting the normal distribution criteria, while the Kruskal-Wallis's test was performed for non-normally distributed variables. To investigate the relationships between continuous variables, Pearson correlation was utilized for normally distributed data, and Spearman correlation was employed for non-normally distributed data. A statistical significance level was accepted as $p<0.05$ in the analyses.

RESULTS

Ninety caregivers with an average age of 37.3±10.7 (min=19-max=65) were included in the study. Of the caregivers, 14.4% have been providing care for less than a year, 31.1% for 1-5 years, 12.2% for 5-10 years, and 42.2% for more than 10 years. 45.6% of the caregivers were the parents, 26.7% were the spouse, 7.8% were siblings, and 20% were other individuals of the patients (Table 1).

Table 1. Characteristics of Caregivers

		N	%
Age (Mean – SD)		37,3–10,7	
Marital Status	Single	62	68,9
	Married	28	31,1
Educational Status	Preliminary school and below	61	67,8
	High school and above	29	32,2
Residential Status	County	42	46,7
	City	48	53,3
Income	Low	54	60,0
	Average	27	30,0
	High	9	10,0
Occupational Status	Employee	44	48,9
	Unemployed	46	51,1
Comorbid Organic Disease	Yes	11	12,2
	No	79	87,8
Use of Psychiatric Medication	Yes	62	68,9
	No	28	31,1
Psychiatric Treatment History of Caregiver	Yes	76	84,4
	No	14	15,6
Duration of Caregiving	Less than 1 year	13	14,4
	1-5 years	28	31,1
	5-10 years	11	12,2
	More than 10 years	38	42,2
The Caregiver s Level of Relationship	Parents	41	45,6
	Spouse	24	26,7
	Siblings	7	7,8
	Other	18	20,0

25.6% of the patients had bipolar disorder, 23.3% had schizophrenia, 11.1% had otherwise unspecified mood disorders, 23.3% had other unspecified psychosis, and 16.7% were diagnosed with mental retardation. 34.4% of the patients were in HSFP for observation/review reasons while 65.6% were there for protective treatment; of those there for observation/review, 80.6% were found to be fully criminally responsible. 24.4% of the patients were involved due to simple assault, 14.4% due to murder, 7.8% due to sexual assault, 5.6% due to insult, 27.8% due to other reasons, and 20% due to multiple reasons (Table 2).

The caregivers had BDI scores of 10.8±7.7, PRSA total scores of 99.8±12.5, and MBI sub-scores of

Table 2. All Characteristics of Patients

		N	%
Psychiatric Diagnosis	Bipolar Disorder	23	25,6
	Schizophrenia	21	23,3
	NOS Mood Disorder	10	11,1
	NOS Psychosis	21	23,3
	MR	15	16,7
Duration of Psychiatric Disorder	<5 years	22	24,4
	5-10 years	15	16,7
	>10 years	53	58,9
The Reason of HSFP Hospitalization	Observation	31	34,4
	Preservation treatment	59	65,6
Criminal Capacity	Yes	25	80,6
	No	6	19,4
Crime	Simple Assault	22	24,4
	Murder	13	14,4
	Sexual Assault	7	7,8
	Insult	5	5,6
	Other	25	27,8
	Multiple Reasons	18	20,0
Treatment Number in HSFP	1	70	77,8
	2	12	13,3
	3	8	8,9
Non-HSFP Inpatient Treatment	Yes	61	67,8
	No	29	32,2

NOS: Non otherwise specified, HSFP: High security forensic psychiatry

Table 3. The Scale Scores of the Caregivers

	Mean – SD
BDI	10,8–7,7
PRSA-Total	99,8–12,5
MBI-Emotional Exhaustion	22,5–3,4
MBI-Desensitization	9,4–2,2
MBI-Personal Achievement	16,8–5,4

BDI: Beck Depression Inventory, PRSA: Psychological Resilience Scale for Adults, MBI: Maslach Burnout Inventory

emotional exhaustion at 22.5±3.4, depersonalization at 9.4±2.2, and personal accomplishment at 16.8±5.4 (Table 3). There was a significant difference in BDI scores based on the duration of caregiving (p=0.01), which was derived from the difference between those who have been providing care for less than a year and those for over 10 years. A significant difference was observed in BDI scores based on the psychiatric diagnosis of the patient (p<0.001), which was derived from the difference between caregivers of patients with mental retardation and caregivers of patients with other diagnoses. The BDI score of caregivers of patients who were criminally responsible was significantly higher than those of caregivers of patients who were not criminally responsible (p=0.001). Caregivers of those who were in HSFP for observation/review had significantly higher PRSA scores than those of caregivers of individuals who were there for protective treatment (p=0.034) (Table 4).

Table 4. Comparison of BDI and PRSA with Variables

		BDI*	PRSA**
		Mean – SD	Mean – SD
Psychiatric Treatment History of Caregiver	Yes	10,4–7,0	99,6–12,1
	No	12,9–10,5	101,0–14,8
p		0,627	0,708
Duration of Caregiving	Less than 1 year	6,8–6,3[a]	105,2–14,1
	1-5 years	10,4–8,4[a,b]	99,4–11,8
	5-10 years	7,7–4,4[a,b]	101,5–13,2
	More than 10 years	13,3–7,6[b]	97,8–12,1
p		**0,01**	0,316
The Caregiver s Level of Relationship	Parent	11,0–8,0	97,2–13,2
	Sibling	6,1–4,6	99,3–10,3
	Other	12,3–9,1	103,3–9,3
	Spouse	10,4–6,4	101,9–13,5
p		0,330	0,288
Psychiatric Diagnosis	Bipolar Disorder	9,3–6,0[a]	99,5–14,3
	Schizophrenia	8,3–4,4[a]	97,2–10,5
	NOS Mood Disorder	6,3–5,1[a]	107,7–11,8
	NOS Psychosis	9,0–5,9[a]	99,8–12,6
	MR	22,0–7,4[b]	99,0–11,8
p		**<0,001**	0,290
Duration of Psychiatric Disorder	<5 years	8,2–6,6	103,3–14,6
	5-10 years	8,6–4,3	99,7–10,5
	>10 years	12,4–8,4	98,5–12,0
p		0,056	0,317
The Reason of HSFP Hospitalization	Observation	10,4–7,8	103,7–14,3
	Protection Treatment	10,9–7,6	97,8–11,0
p		0,772	**0,034**
Criminal Capability	Yes	12,0–7,7	102,2–13,6
	No	3,5–3,8	109,8–16,7
p		**0,001**	0,247
Crime	Simple assault	10,1–7,7	102,2–12,8
	Insult	8,4–5,9	99,4–11,1
	Sexual assault	17,7–12,2	95,4–12,2
	Murder	11,4–7,2	93,6–8,9
	Other	10,0–7,2	102,4–12,1
	Multiple reason	10,1–6,4	99,8–14,7
p		0,607	0,315
Treatment Number of HSFP	1	10,8–8,3	100,1–12,6
	2	11,3–5,7	97,1–13,7
	3 and more	9,6–3,7	102,1–10,1
p		0,739	0,651

*Mann Whitney U or Kruskal Wallis, **Student s T or ANOVA, a,b: source group of difference

A significant difference was observed between the type of crime committed by forensic patients and the emotional exhaustion scores, a sub-scale of MBI, of their caregivers ($p<0.001$). This discrepancy stemmed from the difference between the scores of caregivers of patients who committed sexual offenses and those of caregivers of patients who committed simple assault, other, and multiple crimes. Similarly, a significant variation was found in the depersonalization scores of caregivers in terms of the patient's crime ($p=0.01$). This distinction originated from the difference in scores between the caregivers of individuals who committed only sexual offenses and those of caregivers for individuals with other offenses. A notable difference was identified between the number of treatments the patient received in HSFP and the personal accomplishment scores of the caregivers ($p=0.022$). This variation derived from the difference between caregivers of patients who stayed three or more times in HSFP and those who had 1 to 2 stays (Table 5).

Table 5. Comparison of The Subscales of MBI with Variables

		EE*	D*	PA**
		Mean – SS	Mean –SD	Mean – SD
Psychiatric Treatment History of Caregiver	Yes	22,1–3,1	9,4–2,2	16,6–5,2
	No	24,2–4,5	9,6–2,1	17,7–6,3
p			0,986	0,496
Duration of Caregiving	Less than 1 year	21,8–2,2	8,6–1,9	19,7–3,4
	1-5 years	23,1–3,7	9,8–2,1	16,2–6,0
	5-10 years	21,6–2,5	9,2–2,3	15,4–5,9
	More than 10 years	22,4–3,7	9,5–2,2	16,7–5,1
p			0,259	0,179
The Caregiver s Level of Relationship	Parent	23,0–4,0	9,3–2,4	17,0–5,8
	Sibling	21,0–1,9	8,6–,5	17,9–6,6
	Other	23,6–3,0	9,7–2,0	16,9–6,2
	Spouse	21,1–2,2	9,8–2,1	16,0–3,4
p		0,051	0,172	0,846
Psychiatric Diagnosis	Bipolar Disorder	22,9–3,0	9,4–2,6	16,7–6,4
	Schizophrenia	22,1–2,8	9,2–2,2	17,1–4,8
	NOS Mood Disorder	22,3–3,0	9,6–1,9	15,4–4,8
	NOS Psychosis	21,3–3,4	10,1–1,5	16,3–4,8
	MR	24,0–4,5	8,7–2,3	18,3–5,9
p			0,331	0,737
Duration of Psychiatric Disorder	<5 years	22,5–3,5	9,8–1,5	16,4–5,0
	5-10 years	21,9–2,9	8,9–2,9	16,3–5,6
	>10 years	22,6–3,5	9,4–2,1	17,1–5,5
p			0,709	0,818
The Reason of HSFP Hospitalization	Observation	21,9–3,8	9,5–1,5	16,6–4,7
	Protection Treatment	22,8–3,1	9,4–2,4	16,9–5,7
p			0,743	0,833
Criminal Capability	Yes	21,9–4,1	9,8–1,4	16,1–5,0
	No	21,8–2,6	8,3–1,5	18,8–2,6
p			0,067	0,247
Crime	Simple assault	21,3–2,5[a]	9,9–1,6[a,b]	15,3–4,8
	Insult	20,8–1,1[a,b]	11,0–1,7[a,b]	14,6–4,1
	Sexual assault	28,7–3,5[b]	11,0–,8[a]	14,3–7,2
	Murder	24,0–3,4[a,b]	9,8–1,6[a,b]	18,1–5,4
	Other	21,2–2,3[a]	8,2–2,5[b]	18,6–4,5
	Multiple reason	22,6–3,0[a]	9,2–2,4[a,b]	16,9–6,3
p			**0,01**	0,186
Treatment Number of HSFP	1	22,6–3,5	9,6–2,0	17,2–5,1[a]
	2	20,8–2,2	8,7–2,3	17,6–5,7[a]
	3 and more	23,4–3,3	9,2–3,3	11,9–4,9[b]
p			0,505	**0,022**

EE: Emotional Exhaustion, D: Desensitization, PA: Personal Achievement *Mann Whitney U or Kruskal Wallis, **Student s T or ANOVA, a,b: source group of difference

Table 6. Correlations Between the Scale Scores

		Age	BDI	PRSA	MBI-EE	MBI-D
BDI	r	,044				
	p	,678				
PRSA	r	-,076	-,145			
	p	,474	,174			
MBI-EE	r	**-,258**	,131	-,154		
	p	**,014**	,219	,149		
MBI-D	r	**-,211**	,034	,062	**,349**	
	p	**,046**	,749	,563	**,001**	
MBI-PA	r	,107	,030	-,008	-,152	**-,418**
	p	,314	,776	,944	,154	**,000**

BDI: Beck Depression Inventory, PRSA: Psychological Resilience Scale for Adults, MBI-EE: Maslach Burnout Inventory-Emotional Exhaustion, -D: Desensitization, -PA: Personal Achievement

A negative correlation was observed between age and the sub-scales of emotional exhaustion and dissociation. A positive significant relationship was noted between the emotional exhaustion and dissociation sub-scales. Furthermore, a negative correlation was identified between the dissociation and personal accomplishment sub-scales (Table 6).

DISCUSSION

This study indicates that caregivers of forensic psychiatric patients have a good level of psychological resilience and mild levels of depression, albeit with moderate signs of burnout.

Some families may fragment in the face of chronic stress or crises, yet it is noteworthy that others overcome such situations with increased strength (31). It is known that individuals with high levels of psychological resilience possess greater abilities to cope with stress (32). Enhancing psychological resilience in caregivers of individuals with mental illnesses facilitates the patient's adaptation to life (33). Yağmur et al. (34) calculated the total score of the Adult Psychological Resilience Scale as 120.53 ± 19.51 in their study on caregivers of 120 patients receiving treatment in the psychiatry department of the Manisa Mental Health and Diseases Hospital. Lök et al. (35) found a PRSA score of 88.15 ± 11.62, similar to our study, when working with caregivers of patients with schizophrenia and argued that psychological resilience can be developed. In contrast, a study on the caregivers of patients diagnosed with bipolar disorder in China found that resilience was lower in the community correlated with factors such as age, occupation, and the duration of caregiving (36). Although this varies according to sociocultural changes, it suggests, as seen in many studies, that individuals caring for psychiatric patients maintain

a good level of psychological resilience. Our findings indicate that psychological resilience increases as the duration of caregiving extends. However, it has been observed that the psychological resilience of relatives of individuals with physical illnesses decreases as the treatment period prolongs (37). This situation might be related to the processes of physical and mental illnesses and their effects on relatives.

It has been determined that our sample group experiences mild symptoms of depression. It is known that caregivers generally exhibit higher levels of depression (38). Research has shown that the prevalence of depression, which affects the mental health status of patients, is higher in families with psychiatric patients compared to the general population (39, 40). In our sample group, it was observed that as the caregiving period extended, depression scores increased. It is also seen that the caregivers of individuals diagnosed with mental retardation who committed crimes have higher levels of depression. This is because mental retardation begins at a younger age and continues into adulthood. It has been found that depression scores increase as the caregiving period for parents with disabled children extends (19). In our study, the BDÖ score of caregivers of patients with criminal responsibility was found to be significantly higher than those caring for individuals without criminal responsibility, which suggests this circumstance might complicate the acceptance of the situation by the relatives of the patient.

Depressive symptoms have been noted to be an indicator of burnout (41). In Iran, burnout symptoms were identified among caregivers of patients with mental disorders (42). Khalili et al. (43), in a study with 120 schizophrenia patient caregivers, found high average scores in emotional exhaustion and depersonalization dimensions of the Maslach Burnout Inventory (MBI). Meanwhile, the personal accomplishment score was found to be low, indicating high levels of burnout syndrome in caregivers of schizophrenia patients. In another study involving 169 psychosis patients, 58% of the sample reported high levels of emotional exhaustion, 31% reported high levels of depersonalization, and 43% reported low levels of personal achievement (44). Similarly, in our study, we found that the caregivers of patients subjected to forensic psychiatric examination experienced burnout, with moderate levels in the MBI emotional exhaustion and depersonalization subscales, and high in personal accomplishment subscale, which aligns with literature findings. Additionally, in our study, a difference was observed between the type of crimes committed by the patients and the burnout subscale scores of the caregivers. Given that sexual crimes can cause more problems morally and socially, it suggests that it might have adversely affected the relatives of the patients to a greater extent.

In our study, 45.6% of the caregivers were the parents, 26.7% were the spouses, 7.8% were siblings, and 20% were other individuals. Often, the primary caregivers for mental health patients are their first-degree relatives, mainly the parents (45). We found a significant negative correlation between the age of the caregiver and the emotional exhaustion and depersonalization subscales. It is known that as the caregivers of patients with chronic diseases age, the symptoms of burnout decrease (46). This suggests that with age, accepting the illness may become easier, and this might act as a protective factor against mental distress.

To the best of our knowledge, the strong aspect of our research is that no similar topic has been studied before in psychiatric patients who have committed crimes. The limitations of our study include the restricted sample group, the fact that we did not evaluate the patients who committed crimes under separate provisions of TCK 32/1 and 32/2, not including the patients' treatment processes and disease severities in the assessment, the cross-sectional nature of the study, and it being centered in a single facility. We believe that our findings could pave the way for multi-centered studies involving a larger sample size.

In conclusion, it is observed that the caregivers of psychiatric patients who have committed crimes may have experienced individual and societal problems beyond the treatment and monitoring of mental illness. Although they have high psychological resilience, their levels of depression and burnout are also high. We believe that the content of psychosocial support to be provided to the relatives of

patients carries specific features for forensic psychiatric patients, and not overlooking this situation will be beneficial for the caregivers.

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

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Investigation of adolescents diagnosed with exogenous obesity in terms of internet, smartphone usage characteristics and psychopathologies

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SUMMARY

Objective: In this study, it was aimed to investigate comorbid psychopathologies, internet/smartphone addiction and usage characteristics in adolescents diagnosed with exogenous obesity.

Method: 48 obese patients aged 12-18 years, diagnosed with exogenous obesity, and 49 healthy adolescents without obesity were included in the study. Comorbid psychopathologies were screened with the "Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS)". Young Internet Addiction Scale (YIAS), Smartphone Addiction Scale-Short Form (SAS-SF), Addiction Profile Index-Internet Form (API-IF) were administered to the patient and control groups; Atilla Turgay DSM-IV Based Child and Adolescent Distruptive Behaviour Disorders Rating Scale (ATS) was applied to their parents.

Results: As a result of our study; In the case group, the presence of mental illness and obesity in the family, the duration of internet and smart phone use, snacking in front of the screen and spending time in virtual games were found to be significantly higher ($p<0.05$). In terms of the scales, it was determined that the YIAS, SAS-SF, API-IF and ATS scores were significantly higher in the case group ($p<0.05$). As a result of K-SADS, it was seen that adolescents with exogenous obesity had more psychiatric diagnoses when compared to the control group.

Discussion: Our study shows that besides the biological aspect of obesity, it also progresses with a high rate of mental problems. Considering the difficulty of obesity treatment and the excess of complications, biopsychosocial interventions and multidisciplinary approaches including mental health professionals are important for the prevention and treatment of pediatric obesity.

Key Words: Exogenous Obesity, Psychopathology, Internet Addiction, Smartphone Addiction

INTRODUCTION

Obesity occurs with the combination of many etiological factors. It may occur as a result of the combination of genetic/biological factors, various metabolic/hormonal factors, and psychological and cultural factors in an environment predisposing to obesity (1). Childhood obesity is mostly the result of primary, exogenous causes. Exogenic obesity is defined as a simple type of obesity that occurs due to excessive calorie intake and in which there is no underlying metabolic or endocrinological problem (2). Factors such as personal preferences, including eating behavior, physical activity preference, and income level of the country where the person lives contribute to overweight and obesity (3).

The use of technology has been increasing in recent years, especially during adolescence, and has reshaped individuals' lifestyles. During adolescence, when emotional problems, the search for identity, peer approval, and the need for socialization increase, Internet and smartphone use becomes attractive for adolescents. Intensive digital media use that starts for these reasons leads to impairments in adolescents' functioning in social-academic areas such as school, family, and peer environment (4). Individuals with intensive inter-

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net and smartphone use are likely to face obesity and its complications due to prolonged immobilization (5,6). Some studies in the literature indicate that adolescents who prefer to use the Internet in their free time have higher body mass index (BMI) values and less physical activity (7,8).

Several studies have demonstrated that risk factors associated with obesity in adolescents, including diminished self-esteem, negative body image, peer bullying, reluctance to form relationships, introversion, and social isolation, elevate the likelihood of developing mental health disorders (9,10). As a result of many studies examining the relationship between depressive disorders, anxiety disorders, and obesity, evidence has been obtained that obesity increases the risk of depression and anxiety disorders (9). In addition, in studies examining the relationship between attention deficit hyperactivity disorder (ADHD) and obesity, significant attention problems and impulsivity were found in children with obesity (11-13).

While there are studies investigating the relationship between exogenous obesity and internet addiction in the literature, studies examining the relationship between smartphone addiction (SA) and obesity are limited. It was observed that the studies were mostly conducted in community-based samples and evaluated the relationship between SA and physical activity. In general, it was found that physical activity decreased and related complications increased in people with intense smartphone use (14,15). In addition, studies examining other mental disorders (especially ADHD) and smartphone addiction in the context of obesity were not found in the literature. This study aimed to examine internet and smartphone addiction in adolescents with exogenous obesity and to investigate its relationship with ADHD and other mental disorders.

METHOD

Approval for the study was obtained from the Dicle University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee with the date 10/12/2020 and number 20.

Sample

The sample size for the study was calculated with the G*Power software package. It was found that a sample size of at least 40 participants per group was sufficient to obtain an alpha error rate of 0.05, a Cohen effect size of 0.30, and a statistical power of at least 80%. Sixty cases were planned to be included in both groups, considering there might be a 30% data loss. However, the data loss was less than calculated.

Our case group consisted of 48 individuals aged 12-18 with exogenous obesity who were admitted to the Dicle University Pediatric Endocrinology Outpatient Clinic between January and March 2021. A control group was formed with 49 age- and gender-matched healthy subjects without obesity. The control group consisted of individuals who came to the general pediatric outpatient clinic for reasons such as developmental follow-up, vaccination, and health screening. A BMI of 95th percentile and above was accepted as obesity. The presence of clinical or intellectual disability, autism spectrum disorder, history of substance abuse, and chronic medical disease were determined as exclusion criteria. Of the 62 obese subjects screened for our study, 2 had mental retardation, 7 had chronic physical disease, and 5 had previous psychiatric admission and were not included in this study. Among the 61 subjects evaluated for the control group, 3 had chronic physical illness, 2 had previous psychiatric admission, 2 had incomplete completion of the scales, 5 had BMI between 85-95 percentile and were not included in the study.

Procedure

Patients aged 12-18 years with exogenous obesity diagnosed with exogenous obesity who applied to the Dicle University Pediatric Endocrinology Outpatient Clinic between January and March 2021, the subjects constituting the control group and their families were informed about the study. Their written informed consent was obtained by explaining that participation in the study was voluntary and that they had the right to withdraw from the study whenever they wanted. “Schedule for Affective Disorders and Schizophrenia for School-

Age Children-Present and Lifetime Version (K-SADS) based on DSM-5" was conducted by a previously trained and certified researcher to determine comorbid psychopathologies. Young Internet Addiction Scale (YIAS), Smartphone Addiction Scale-Short Form (SAS-SF), Addiction Profile Index-Internet Form (API-IF) were administered to the patient and control groups, and Atilla Turgay DSM-IV Based Child and Adolescent Distruptive Behaviour Disorders Rating Scale (ATS) was administered to their parents. Internet addiction and smartphone addiction are diagnoses that have not yet been included in DSM-5 and scales with validity for these diagnoses were used.

Data Collection Tools

Sociodemographic and Clinical Data Form: It is a form prepared by the researchers that questions sociodemographic and clinical characteristics. This form was completed by the clinician after face-to-face interviews with adolescents and their families.

Young Internet Addiction Scale (YIAS): It is a 20-question scale adapted from the pathological gambling criteria of DSM-IV by Young (16). It was adapted into Turkish by Bayraktar (17). In this Likert-type scale, the options are "rarely," "sometimes," "frequently," "most of the time," and "always" and scored as 1,2,3,4 and 5, respectively. Scoring 80 and above on the scale indicates a serious impairment in functionality, and people with this score are characterized as internet addicts. Those who score between 50-79 points on the scale are defined as a "borderline symptomatic group" experiencing internet-related problems. On the other hand, those who score 49 or below on the scale are described as ordinary internet users who do not experience any problems related to internet use in their daily lives.

Addiction Profile Index-Internet Form (API-IF): This test, developed by Ögel et al., consists of 18 questions. The questions ask about the last three months. APIIF can be used in high school and university students and is valid and reliable in both populations. The items are scored between 0-4. Scoring can be made in 6 areas, including frequency of Internet use, diagnosis, effects on life, severe desire, motivation, and total score (18).

Smartphone Addiction Scale-Short form (SAS-SF): The SAS-SF was developed by Kwon et al. to measure the risk of smartphone addiction in adolescents. It consists of 10 items and is a six-point Likert scale. The validity and reliability study of the Turkish version was conducted by Noyan et al. Scale scores vary between 10-60. According to the study by Kwon et al., the cut-off score on the scale was 33 and above for women and 31 and above for men. As the score obtained from the test increases, the risk for addiction is considered to increase (19,20).

Atilla Turgay DSM-IV Based Child and Adolescent Distruptive Behaviour Disorders Rating Scale (ATS): It is a scale prepared by Turgay for evaluating behavioral disorders in children and adolescents, considering DSM-IV diagnostic criteria (21). With this scale, attention deficit hyperactivity disorder, oppositional defiant disorder, and conduct disorder are screened and evaluated. The scale consists of 41 questions: nine questions investigate attention deficit, nine questions investigate hyperactivity and impulsivity, eight questions investigate oppositional defiant disorder, and 15 questions investigate conduct disorder (22).

Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS): It was developed by Kaufman et al. in 1997 from DSM-III-R and DSM-IV diagnostic criteria and is a semi-structured form including interviews with parents and children/adolescents designed to detect both past and present mental disorders. The K-SADS was revised in November 2016 by Kaufman et al. following DSM-V diagnoses (23). The Turkish validity and reliability study of the revised interview version was conducted by Ünal et al. in 2019 (24).

Statistical analysis

The data obtained from the study were recorded in IBM SPSS 22.0 for Windows program. The Shapiro-Wilk normality test was performed to evaluate the normal distribution. Mean and standard deviation values were given for numerical vari-

ables. Number (n) and percentage (%) values were written for categorical variables. The chi-square test was used to compare categorical data, and the independent sample t-test was used for numerical data. $p<0.05$ was considered significant.

RESULTS

Among the case group, 47.9% (n=23) were female and 52.1% (n=25) were male adolescents diagnosed with primary obesity. In the control group, 49% (n=24) were female and 51% (n=25) were male. The case and control groups were similar in terms of gender (p=0.917). The mean age of the case group was 14.20 ± 1.85 years, and the mean age of the control group was 14.51 ± 1.87 years. The mean age of the whole sample was 14.36 ± 1.86 (n=98). The case and control groups were similar in terms of age (p=0.427). A comparison of the groups in terms of sociodemographic data is given in Table 1.

The physical characteristics of the groups (height, body weight, body mass index, and percentile ratio of body mass index) are presented in Table 2.

When the digital media use of the cases was analyzed, it was learned that all adolescents in the case and control groups had smartphone use and internet access (n=97). The mean age of the adolescents in the case group was 9.65 ± 2.54 years (min:4-max:15 years), while the mean age of the control group was 9.41 ± 2.76 years (min:4-max:15 years), and the groups were similar in this respect (p=0.660). The comparison of the groups in terms of internet usage characteristics is given in Table 3.

When the internet usage purposes of the groups other than games were examined (more than one option was allowed), 77.1% (n=37) of the case group stated that they used the Internet for watching movies, videos, and listening to music, 50% for communication (n=24), 68.8% (n=33) for education, 54.2% (n=26) for social media, and 12.5% (n=6) for shopping. In the control group, 65.3% (n=32) watched movies videos and listened to music, 55.1% (n=27) used the Internet for communication, 75.5% (n=37) used it for education, 46.9% (n=23) used it for social media, and 26.5% (n=13) used it for shopping. The groups are similar in these respects (p>0.05)

The comparison of the case and control groups in terms of scale scores and cut-off scores of the scales is given in Table 4.

After the K-SADS, 87.5% (n=42) and 77% (n=37) of adolescents diagnosed with obesity had at least one lifetime psychiatric diagnosis. In the control group, this rate was 44.9% (n=22) for lifetime psychiatric diagnoses and 48.9% (n=24) for current psychiatric diagnoses. The lifetime and current psychiatric diagnoses rate was significantly higher in obese adolescents (p<0.001 and p=0.004).

The comparison of the groups in terms of comorbid mental diagnoses is given in Table 5.

Adolescents diagnosed with obesity showed higher rates of all psychopathologies compared to normal-weight adolescents, and the difference between the groups was statistically significantly higher in terms of depressive disorder, anxiety disorders, and ADHD. When anxiety disorders were evaluated

Table 1. Comparison of sociodemographic data of case and control groups

		Case		Control		
		n (%)	Mean (SD)	n (%)	Mean (SD)	p
Age		48	14,2 (–1.85)	49	14.5 (–1.87)	0.422*
Gender	Female	23 (47.9)		24 (49)		0.917**
	Male	25 (52.1)		25 (51)		
SES	Under 3,000	20 (41.7)		13 (26.5)		
	between 3,000-6,000	14(29.2)		12 (24.5)		0.119**
	6,000 and above	14 (29.2)		24 (49)		
Parental mental illness	Yes	10 (20.8)		1(2)		**0.004****
	No	38 (79.2)		48 (98)		
Parental obesity	Yes	20 (41.7)		7 (14.3)		**0.003****
Age	No	28 (58.3)		42 (85.7)		

(SES: Socioeconomic Status, Mean: Mean, SD: Standard deviation, *Independent sample T-test, p<0.05
**Chi Square test, p<0.05)

Table 2. Comparison of physical characteristics of the case group and control group

	Case group (n=48)		Control group (n=49)		P
	Mean	SD	Mean	SD	
Height (cm)	163.04	9.82	163.32	10.83	0.892
Weight (kg)	81.37	15.4	54.3	11.04	**0.001**
BMI	30.40	3.70	20.23	1.91	**0.001**
BMI/persentile	98.1	1.67	40.86	24.11	**0.001**

(BMI: Body mass index, cm: Centimeter, kg: Kilogram, mean: Average, SD: Standard deviation, *Independent sample T-test, p<0.05)

individually, it was found that separation anxiety disorder was significantly higher than healthy controls.

DISCUSSION

This study aimed to investigate adolescents with exogenous obesity and normal weight regarding sociodemographic characteristics, Internet and smartphone addiction, ADHD, and other psychopathologies. As a result of our study, the presence of parental mental illness and obesity, duration of internet and smartphone use, snacking in front of the screen, and spending time in virtual games were significantly higher in the case group compared to the control group. YIAS, SAS-SF, API-IF, and ATS scores were significantly higher in the case group. In addition, according to the K-SADS interview, it was observed that adolescents with exogenous obesity had more psychiatric diagnoses throughout life and now had depressive disorder, anxiety disorder, and ADHD diagnoses more than the control group.

There are studies showing that obesity is observed more in children and adolescents whose parents have chronic diseases such as DM, obesity, and depression (25,26). It is thought that familial psychopathology may combine with other factors (such as low socioeconomic level, maternal obesity, and broken family) and lead to childhood obesity. It is suggested that a child growing up in a non-ideal environment may not be guided correctly in healthy life choices, such as appropriate food selection and regular physical activity, which may result in obesity (27).

Some authors have reported that genetic predisposition is 25-80% effective in developing obesity and that obesity in the family is the strongest risk source for childhood obesity (28). In addition to increasing the frequency of obesity with genetic predisposition, it is thought that the presence of obesity in the family may increase the frequency of obesity due to parents' dietary habits such as food preference and meal frequency, sedentary lifestyles including lack of physical activity, spending too much time in front of the screen and children modeling parents with obesity (29,30). Our study results seem to be compatible with the literature in this respect.

Studies investigating the effects of eating in front of television and screens suggest that more snacking occurs with the screen and that it affects the

Table 3. Comparison of case group and control group in terms of Internet usage characteristics

		Case n (%)	Mean (SD)	Control n (%)	Mean (SD)	p
Snacking in front of the screen	Yes	28 (58.3)		12 (24.5)		**0.001****
	No	20 (41.7)		37 (75.5)		
Internet usage time	By family		4.19 (–2.23)		2.59 (–1.44)	**0.001***
	According to the child		3.05 (–1.76)		1.93 (–1.42)	**0.001***
	By family		3.66 (–2.43)		2.13 (–1.48)	**0.001***
Smartphone usage time	According to the child		2.61(–1.89)		1.46 (–1.27)	**0.001***
	Yes	1 (2.3)		8 (18.2)		**0.030***
Internet quota	No	42 (97.7)		36 (81.8)		
	Game	31 (64.6)		20 (40.8)		**0.036****
Internet usage pattern	Out of game	17 (35.4)		29 (59.2)		
	Film, video, music	37 (77.1)		32 (65.3)		**0.048****
	Communication	24 (50)		27 (55.1)		
	Education	26 (54.2)		37 (75.5)		
	Social media	26 (54.2)		23 (46.9)		
	Shopping	6 (12.5)		13 (26.5)		

(*Independent sample T test, p<0.05 **Chi Square test, p<0.05)

Table 4. Comparison of case and control groups in terms of scale scores

		Case		Control		
		Mean (SD)	N (%)	Mean (SD)	N(%)	p
YIAS		36.6 (–14.2)	48	28.7 (–6.54)	49	**0.001***
YIAS-CS	?50 points		8 (16.7)		0	**0.001****
	<50 points		40 (83.3)		49	
API-IF		1.97 (–0.60)		1.41 (–0.49)		**0.001***
API-IF-SS	IUF	3.52 (–0.85)		2.38 (–0.81)		**0.001***
	Diagnosis	10.43 (–4.04)		7.04 (–4.20)		**0.001***
	IOL	8.95 (–5.54)		5.48 (–3.39)		**0.001***
	SC	3.72(–2.29)		2.20 (–1.81)		**0.001***
	Motivation	2.89(–2.03)		3.24 (–2.37)		0.439*
APIIF-CS	? 2 points		23 (49.9)		5 (10.2)	**0.001****
	< 2 points		25 (52.1)		44 (89.8)	
SAS-SF		26.6 (–11.7)		18.6 (–6.93)		**0.001***
ATS		17.9 (–11.6)		11.4 (–10.3)		**0.005***

(YIAS: Young Internet Addiction Scale, CS: Cut-off Score, API-IF: Addiction Profile Index Internet Form, SS: Subscale, IUF: Internet Use Frequency, IOL: Impact on Life, SC: Severe Craving, SAS-SF: Smartphone Addiction Scale Short Form, ATS: Atilla Turgay DSM-IV Based Child and Adolescent Distruptive Behaviour Disorders Rating Scale, *Independent sample T-test, p<0.05 **Chi-Square test, p<0.05)

amount and content of the diet in an unhealthy way. There are comments that one of the reasons for this may be advertisements (31,32). Data suggest that eating with family reduces the risk of obesity (33). From this point of view, it can be said that obese adolescents who participated in our study have unhealthy eating habits following the literature. A study examining snacking habits and screen time found that adolescents with unhealthy snack consumption had more screen time (34). Many studies in the literature report a positive relationship between internet addiction and obesity risk. It has been reported that individuals with IA are likely to encounter obesity and related complications because they remain in a sedentary position in front of the computer for a long time (5,6). In a study conducted with 584 high school students in our country, internet addiction, and disordered eating attitudes were examined, and it was reported that the BMI values of the group with IB (10.1% of all cases) were statistically significantly higher than the non-IB group (35). A school-based cross-sectional study conducted with 10287 adolescents aged 14-17 years in seven European countries showed a relationship between internet use scores and overweight/obesity (36).

It has been reported that easy access to technology and the increasingly widespread use of smartphones and computers reduce physical activity in children (37). Many studies have shown that increased time spent with devices such as TV, computers, tablets, and phones is associated with obesity and overweight in children. A study involving 811 children found that obese children had more screen time than children with normal weight (38). In a study conducted with 230 female and 220 male Portuguese adolescents, computer use for 4 hours or more on weekdays was found to be associated with overweight/obesity (7). In another study conducted with 2467 students, obesity and internet usage time were investigated, and it was concluded that the majority of children with BMI values above normal spent more than 3 hours on the Internet (39). Similarly, the average daily internet and smartphone usage time of obese adolescents who participated in our study was 3 hours or more.

Although more studies examine IA, SA, and internet/smartphone use patterns, studies investigating

Table 5. Comparison of case group and control group in terms of current psychiatric diagnoses

K-SADS		Case		Control		
		N	%	N	%	P
Depressive Disorder	Yes	8	16.7	0	0	0.003*
	No	40	83.3	49	100	
SeAD	Yes	5	10.4	0	0	0.027*
	No	43	89.6	49	100	
SoAD	Yes	12	25.0	5	10.2	0.055*
	No	36	75.0	44	89.8	
SP	Yes	21	43.8	17	34.7	0.361*
	No	27	56.3	32	65.3	
GAD	Yes	9	18.8	3	6.1	0.059*
	No	39	81.3	46	93.9	
Anxiety Disorders (total)	Yes	30	62.5	20	40.8	0.033*
	No	18	37.5	29	59.1	
OCD	Yes	3	6.3	0	0	0.117*
	No	45	93.8	49	100	
ED	Yes	1	2.1	0	0	0.495**
	No	47	97.9	49	100	
ADHD	Yes	18	37.5	7	14.3	0.009*
	No	30	62.5	42	85.7	
ODD	Yes	7	14.6	2	4.1	0.091*
	No	41	85.4	47	95.9	
CD	Yes	0	0	0	0	
	No	48	100	49	100	
Tic Disorder	Yes	3	6.3	0	0	0.117*
	No	45	93.8	49	100	
PTSD	Yes	4	8.3	0	0	0.056*
	No	44	91.7	49	100	
ExD	Yes	3	6.3	0	0	0.117*
	No	45	93.8	49	100	
Psychiatric Diagnosis	Yes	37	77	24	48.9	0.004
	No	11	23	25	51.1	

(SeAD: Separation Anxiety Disorder, SoAD: Social Anxiety Disorder, SP: Specific Phobia, GAD: Generalized Anxiety Disorder, OCD: Obsessive Compulsive Disorder, ED: Eating Disorder, ADHD: Attention Deficit Hyperactivity Disorder, ODD: Oppositional Defiant Disorder, CD: Conduct Disorder, PTSD: Post Traumatic Stress Disorder, ExD: Externalizing Disorder *Chi Square test p<0.05)

the purposes of internet use in obese children and adolescents are limited. In a study conducted in our country, it was found that while the use of smartphones for functions such as social media, gaming, online messaging, and video watching was positively associated with SA, the use of smartphones for phone calls, e-mail, and news reading was negatively associated with SA (40). According to a study conducted with high school students in Mersin province, participants who did not use the Internet to obtain information had 2.06 times more IA than those who did (41). In a study conducted with obese children and adolescents, children and adolescents diagnosed with obesity were divided into two groups, IA and non-IA, and it was found that obese people with IA spent more time on social networking sites and playing online games. In contrast, obese people without IA used the Internet mostly for information searches and homework (42). The use of the Internet and smartphones for playing games may increase the potential for addiction by increasing the pleasure felt during this action and leading to longer periods of use, whereas in use for purposes such as obtaining information and reading news, both the duration of use is less and the pleasure similar to playing games may not be felt (43). Our study observed that adolescents diagnosed with obesity had a higher duration of Internet and smartphone use and mostly used the Internet/smartphone to play games, which is consistent with the literature. The fact that internet and smartphone addiction scale scores were higher than in the control group and internet/smartphone use for news reading and general information search was lower supports these findings.

When the literature is examined, it is seen that the number of studies examining the relationship between SA and obesity is less than the number of studies examining the relationship between IA and obesity. Studies examining the relationship between SA and physical activity are predominant among these studies. In a study conducted with 325 university students, the relationship between SA and overweight was examined, and the SA scale scores of the participants were found to be significantly different between overweight and normal weight groups. In a study investigating the relationship between eating disorders and SA and IA in university students, a positive relationship was found between SA and IA test scores and BMI values of individuals (14). In a study published in 2021 investigating the relationship between problematic smartphone use and obesity in school-age children and adolescents, similar to our study, problematic smartphone use was associated with obesity (15). In addition, in our research, no study involving a clinical sample in which smartphone addiction was evaluated in obese adolescents was found.

When the literature is examined, the recent increase in publications on the relationship between ADHD and obesity draws attention. In studies conducted on children and adolescents, more attention deficit and impulsivity have been reported in obese individuals (44,45). A diagnosis of ADHD was found in a large proportion (58%) of children treated for obesity, and the BMI of children with ADHD was higher than the control group (13). In another study conducted with adolescents in our country, the ADHD level of the obese group was found to be significantly higher than the non-obese group (46). In parallel with the literature, our study shows that adolescents with obesity were diagnosed with more ADHD.

It was observed that adolescents diagnosed with obesity showed more psychopathologies than normal-weight adolescents, and the difference between the groups was statistically significantly higher regarding depressive disorders and anxiety disorders. When anxiety disorders were analyzed individually, it was found that separation anxiety disorder was higher in the case group than the control group. Obesity itself may lead to psychiatric problems, and some psychiatric disorders may lead to obesity. Despite many studies conducted in recent years, the question of whether psychiatric disorders and mental problems are the cause or consequence of pediatric obesity has still not been clearly answered (47). In the literature, there are studies examining the relationship between obesity and self-esteem, emotion regulation, peer bullying, avoidance of establishing relationships, introversion and social isolation, stigmatization, depression, anxiety, night snacking, and food addiction. In a study conducted by Erermiş et al. with obese adolescents, a significantly higher rate of DSM-IV diagnosis (most commonly major depressive disor-

der) was found in more than half of the participants compared to non-obese adolescents (9). In a study conducted by Vila et al. using K-SADS with 155 obese subjects aged 5-17, 88 children received at least one DSM-IV diagnosis. The most commonly diagnosed mental disorder in this study was anxiety disorder (48). It has been reported that overweight and obese adolescents have higher levels of depressive symptoms; the risk of depression increases in individuals with BMI>40, the duration of depression is longer, and the prognosis is worse (49,50). In a study conducted with obese individuals, it was reported that the frequency of anxiety disorders and phobias increased, social phobia was observed more frequently in women, and being overweight increased the risk of social phobia and specific phobia in women (49). In the study conducted by Vila et al. using K-SADS in 2004, at least one anxiety disorder was found in 63 of 155 children. Of these 63 children, 34 were diagnosed with social phobia, 14 with generalized anxiety disorder, 11 with separation anxiety disorder, 2 with agoraphobia, and 2 with posttraumatic stress disorder. A study by the same authors reported that separation anxiety disorder and social phobia were the most frequently observed psychopathology in obese children and adolescents (48).

Since our cross-sectional study showed a positive association between obesity and IA, SA, and mental disorders, but it cannot explain the causal relationship between these pathologies. Longitudinal studies are needed to evaluate the causal relationship. Since the sample size is limited, community-based studies with large samples are needed. Self-report scales were used because there are no universal criteria for internet and smartphone addiction diagnoses. Determining universal criteria for these diagnoses will enable the use of more standardized criteria for studies.

Our study shows that obesity is associated with a high rate of mental problems in addition to its biological aspects. Considering the difficulty of obesity treatment and the high rate of complications, biopsychosocial interventions and multidisciplinary approaches involving mental health professionals are important for preventing and treating pediatric obesity. Considering the increasing prevalence of obesity in children and adolescents, young people diagnosed with obesity should be evaluated in terms of comorbid IA, SA, ADHD, and other psychopathologies, and clinicians should be careful in this respect.

In this regard, there is a need for community-based and longitudinal studies with larger samples to understand the causality between obesity and psychopathologies.

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A current overview of palliative care: Palliative psychiatry

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SUMMARY

Palliative psychiatry is an approach that aims to improve the quality of life of patients and their families by trying to prevent or alleviate suffering through timely evaluation and treatment when faced with physical, mental, social, and spiritual problems associated with serious life-threatening mental illnesses. The fact that individuals with serious mental illness are a disadvantaged group in accessing health services, the rate of physical diseases that are difficult to treat compared to the general population is quite high in this population, their physical diseases are diagnosed later and their compliance with treatment is more difficult, this special group continues to live with a low quality of life and it results in death at an earlier age of 15-20 years. Therefore, considering the burden of serious mental illness on both the family and society, it is clear that palliative care is needed. However, the need for palliative care for individuals with psychiatric illnesses remained in the background, and discussion of the need for palliative care became possible at the beginning of the 21. century. This study was written to raise awareness about where we are in benefiting from palliative care services in our country and in the world and to draw attention to the role of psychiatric nurses, whose role in patient advocacy is at the forefront, in psychiatric palliative care. Psychiatric nurses should realize that there is a serious gap in the field of psychiatric palliative care in our country and should focus on studies in this field.

Key Words: Nursing, palliative care, mental illness

INTRODUCTION

Palliative care emerged in the 1950s as an extension of the hospice concept, which has been in existence since the Middle Ages. By the mid-19th century, hospices primarily operated by religious orders served as care facilities for "incurably" terminally ill patients and shelters for the impoverished (1). They played a pivotal role in facilitating access to modern health services for their beneficiaries. Initially, religious officials and later healthcare professionals worked within hospice settings, interacting with dying patients and amassing considerable knowledge about the process of dying. Over time, awareness increased regarding unmet needs of patients and their families. Pain and symptom management became focal points, with the primary aim of alleviating the individual's suffering and addressing not only the emotional, psychosocial, and spiritual needs of the patient but also of their family. Traditionally, while palliative care mainly catered to individuals diagnosed with cancer, its scope has progressively encompassed those with neurological disorders, primarily AIDS and multiple sclerosis, as well as those with progressive chronic diseases (2). A holistic and humanistic approach has become foundational to palliative care practices (3).

While palliative care providers were initially focused on end-of-life care, over time, they began to prioritize the early detection, accurate assessment, and treatment of physical, psychosocial, or spiritual pain and other issues. Their objective shifted to preventing suffering, ensuring comfort, and enhancing the quality of life for patients and

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their families confronting life-threatening illnesses (2). Today, palliative care has become a standard of care for individuals with advanced and severe conditions, such as cancer or heart failure, and is recognized as a complement to curative treatment. Deviating from traditional perspectives, contemporary palliative care models have emerged, encompassing care from the diagnosis stage through to death, post-mortem, and the family's grieving process. These models include personalized, advanced interventions and run concurrently with curative treatments (4).

The outcomes of comprehensive palliative care services on patients, healthcare professionals, institutions, and the healthcare system are profound. Palliative care facilitates both the family's and the patient's acceptance of the process, enhances the quality of life, well-being, and life expectancy, prepares the patient and family for the grieving process, manages grief, and offers counseling (2,4,5). It increases care satisfaction for the individual, family, and healthcare professional, reduces the need for institutional care, decreases repeated admissions and visits to healthcare facilities, and reduces care costs (4, 6-9).

This review is written with the intention of highlighting the importance and necessity of palliative care services for individuals with serious mental illness, and to initiate discussion on the concept of palliative psychiatry, a relatively new term in the international literature, at a national level as well. It is essential for nurses, who are in a profession fundamentally rooted in caregiving, to show interest in and take responsibility for psychiatric emergency care. It is believed that palliative psychiatric care can help overcome challenges faced by individuals with serious mental illness and their families, who are often considered a disadvantaged population from various perspectives, in accessing holistic and individualized care.

Palliative Care in Psychiatric Services

Palliative care practices, which are so significant and beneficial for all stakeholders in healthcare services, are observed to target individuals and their families with chronic diseases such as cardiovascular diseases (38.5%), cancer (34%), chronic respiratory diseases (10.3%), AIDS (5.7%), and diabetes (4.6%) (10). However, from a contemporary perspective, it is noticed that discussions have begun regarding the concept of palliative care for individuals with severe mental illnesses, introducing the term "palliative psychiatry" into the discourse (5, 11, 12). In essence, psychiatric care and treatment have accompanied palliative care practices since the very inception of the palliative care concept. Yet, the debate surrounding the need for palliative care for individuals with psychiatric illnesses became feasible only in the early twenty-first century (13).

When considering the burden of serious chronic mental illnesses on the patient, family, and society at large, the need for individualized palliative care becomes evident. Drawing from a philosophy of holistic, humanistic, and personalized care that has become a part of the standard of care in many chronic illnesses, it is clear that individuals and families with chronic mental disorders will also benefit from palliative care practices (5,12). However, it is notable that palliative care applications directed towards individuals with serious chronic mental illnesses are relatively new and limited in scope.

Individuals with severe chronic mental illnesses experience significant functional impairments due to cognitive decline, persistent symptoms, and symptoms arising from the illness and its treatment. This often leads to long-term disruptions in various areas of life, including impairments in social functionality and challenges in education and employment (14, 15). Approximately 10% of this population requires long-term care, which is often provided by family members (16). Reflecting today's community-based mental health services, greater responsibility is thrust upon families and caregivers in the care process, even when they may not be fully prepared (17). Thus, severe mental disorders pose a substantial burden on the patient, family, and society at large (16).

Additionally, due to genetic predispositions,

unhealthy lifestyle behaviors, and the side effects of psychotropic medications, these individuals carry higher risks for serious health issues like cardiovascular diseases, neoplasms, respiratory illnesses, hepatitis, liver cirrhosis, metabolic syndrome, and AIDS (18). When compared to the general population, this patient group, with increased death risks from neoplasms, cardiovascular, respiratory, and gastrointestinal diseases (15, 19, 20), has a mortality rate at least double that of the general population due to comorbid conditions (15). Furthermore, unexplained injuries, suicides, and incidents of homicide also represent health and safety risks this population faces (21). In summary, individuals with severe mental illnesses have a 3.7-fold higher mortality rate for various reasons (22, 23) and tend to live shorter lives due to numerous comorbidities, dying 15-25 years earlier than the general population.

While the specialized health needs of individuals with serious mental illnesses are evident, they remain a disadvantaged group within the intricate health system of the modern age due to cognitive challenges, impaired social skills, loss of capacity, and inadequate support systems. This inequality they face in attending health screenings, seeking help, and accessing treatment and care is also pertinent to accessing palliative care (11, 14).

There are studies that focus on the planning and assessment of palliative care services for individuals with chronic physical diseases (24). However, there is limited research concerning the access to palliative care for individuals with serious mental illnesses. Literature in this domain reveals that individuals with mental disorders; have lesser access to palliative care services in the final months of their lives, have higher needs for emergency service, are more frequently hospitalized in psychiatric wards, and very few receive palliative care consultation (24-29). Stigmatization, negative experiences in service processes, attribution of physical symptoms to psychiatric disorders, and the lack of knowledge and experience among mental health professionals about when and how to refer individuals to other appropriate services pose barriers to the highly vulnerable psychiatric patients' access to palliative care (11).

The aim of palliative psychiatry is to improve the quality of life of individuals with serious mental illnesses, known to be a vulnerable population (5, 24). Individuals with serious mental illnesses are at risk of therapeutic neglect (5,9,24) which overlooks the autonomy of the patient and their families and situations marked by inadequate communication, and/or they face potential challenges like multiple emergency interventions, emergency hospitalizations, clinical admissions, intensive care treatments, and extended hospital stays, denoting overly aggressive care. Consequently, the approach of palliative psychiatry holds the potential to enhance the care quality, autonomy, and self-determination of these patients (5). There are two concepts of recovery in psychiatry: clinical and personal. Clinical recovery targets the reduction in disease symptoms and loss of function, long-term mental stability with little or no relapses, and enhancement of psychosocial functionality (30,31). Personal recovery, on the other hand, focuses on promoting individual processes of personal growth, regaining independence, and deriving meaning from life through peer support, supported employment, housing, and shared decision-making (31,32). Palliative psychiatry inherently embodies both types of recovery, supporting individuals in determining their own fate, autonomy, dignity, and achieving individual life goals through acceptance. Moreover, palliative psychiatry aims to function in connection with other approaches targeted at prevention, improvement, rehabilitation, or recovery throughout the illness process (30,32).

Trachsel (2019) delineates the scope of palliative psychiatry as follows (13):

• Provide support to individuals in coping with and accepting distressing psychological symptoms,

• Acknowledge the lifelong persistence of serious mental illnesses and focus on enhancing the quality of life,

• Neither hasten nor delay an individual's death,

• Integrate the physical, psychological, social, and spiritual aspects of patient care,

• Offer a team support system to assist patients and family members in co-ping,

• Utilize a team approach to cater to the needs of patients and their families,

• Positively influence the course of a serious mental illness by augmenting the individual's quality of life,

• Make it applicable by supporting prevention, improvement, rehabilitation, or recovery with other therapies.

Most serious mental illnesses follow a chronic course accompanied by relapses. The comorbidities and high mortality rates in individuals with serious mental illnesses are well-acknowledged (19,33). These outcomes suggest that the priority for individuals with serious mental illnesses should not be combating the illness, but optimally managing its symptoms and decreased functionality. Viewed in this light, psychiatric treatments and palliative care appear to share common ground (5). Interventions aiming to enhance the quality of life rather than achieve remission, as seen in instances like long-term psychiatric inpatient care for clozapine-resistant schizophrenia patients (34); decisions to abstain from rehospitalizations involving continual involuntary refeeding cycles for severe enduring anorexia nervosa (35); and the choice of sedation to alleviate anxiety in terminally ill patients (36), can be regarded as practices of palliative care.

Recommendations for psychiatric palliative care practices found in the literature can be enumerated as follows (21,28,33,37-39):

Patient-Centered

• Ensure that patients continue their psychiatric medications as needed in the presence of psychotic symptoms (monitor drug-drug interactions, observe drug effects and side effects) (28,40).

• In the case of cognitive symptoms, individual assessments should be conducted since patients' decision-making capacities may vary (33,37).

• In the presence of negative symptoms, caregivers should be informed to prevent potential misconceptions regarding perceived disinterest (28,33, 38).

Community Services

• Conduct initiatives aimed at overcoming challenges such as housing issues and social isolation that might hinder access to palliative care (21).

• Develop interventions to enhance access of individuals with mental illnesses to centers like community mental health (21).

Health System-Oriented

• Facilitate communication across specialties (39).

• Encourage the tailoring of services based on both psychiatric and medical care needs of the patient (21).

• Address concerns of both psychiatric and medical teams when providing care and treatment to individuals with serious mental illnesses and their families (39).

• Provide cross-training between mental health professionals and medical teams (for example, initiatives to prevent attributing symptoms of physical illness to mental illness) (21).

• Launch initiatives to integrate screening services with units interacting with this population, to detect progressive diseases that might be overlooked due to coexisting diagnoses (24,40).

• Enhance the awareness of the mental health and medical teams about palliative care, establishing a common ground for discussions in this domain (21, 41,42,43).

In psychiatric care and treatment settings, palliative care can be beneficial for a significant portion of individuals with severe mental illness. Given that psychiatric palliative care can be considered a relatively new field, there is limited literature on the subject. Studies in the literature examine palliative psychiatric care in relation to chronic mental disorders such as schizophrenia, eating and feeding disorders, neurocognitive disorders, bipolar disorder, and depression. However, outside of these conditions, there is a lack of evidence-based literature. Therefore, this study focuses exclusively on pallia-

tive psychiatric care in the context of schizophrenia, feeding and eating disorders, and neurocognitive disorders.

Palliative Psychiatric Care in Turkey

Palliative care in Turkey is a relatively novel field of interest. Historically, efforts to develop palliative care began in the late 2000s, and in 2008, the Turkish Ministry of Health's Cancer Control Department implemented the National Palliative Care Program. As the name of the program suggests, palliative care has primarily focused on cancer patients and their families. In terms of legal regulation for palliative care, the "Directive on the Procedures and Principles of Palliative Care Services" was enacted on October 9, 2014, with directive number 640 (44). Palliative care has garnered considerable attention among scientists and nurses, leading to significant national-level research (4,6,9). However, the emphasis in these studies has predominantly been on cancer patients and symptom management (30-35). When we look at the concept of palliative care from a broader perspective, it can be argued that, within a national framework, both academically and clinically, palliative care services should be evaluated in a wider context. This includes considering non-cancer chronic diseases and severe mental illnesses. From the onset of illness, individuals and their families should be addressed not only physically but also mentally and psychosocially.

Schizophrenia and Other Disorders Accompanied by Psychosis: Globally, the number of individuals with treatment-resistant schizophrenia is estimated to be around 24 million (13). These figures highlight the significant percentage of individuals with schizophrenia in populations worldwide. Due to the inherent positive, negative, and cognitive symptoms of schizophrenia, coupled with its chronic trajectory, it stands among the mental disorders associated with the most significant functional losses (29). However, the likelihood of receiving palliative care for those with schizophrenia is known to be less compared to individuals with other physical illnesses (28). Barriers to palliative care for patients with schizophrenia include communication difficulties, cognitive deterioration, lack of insight, delusions, health professionals' unfamiliarity with how to administer palliative care to schizophrenic patients, absence of palliative consultation procedures in psychiatric services, amplification of these challenges in advanced stages of the disease, and insufficient social resources (21,36).

Suggestions for the palliative care of patients with schizophrenia include:

• Planning interventions to enhance individual functionality,

• Interventions to prevent the emergence of comorbid diseases in individuals, • Including this population in early screening systems,

• Performing comprehensive assessments specific to the individual to prevent the confusion of physical symptoms with mental ones,

• Encouraging health-seeking behaviors of individuals and combating challenges like stigmatization and internalized stigma,

• Conducting initiatives aimed at enhancing social resources,

• Early detection, assessment, and treatment of pain and other symptoms to improve quality of life, • Psychosocial assessment of the family and necessary interventions (e.g., burnout, stress, emotional challenges, physical illnesses),

• Understanding an individual's end-of-life care preferences during remission,

• End-of-life care,

• Grief counseling (35).

Eating and Feeding Disorders: Globally, it is known that eating disorders (anorexia nervosa, bulimia nervosa, binge eating disorder) affect one in every six women and one in every forty men (35). If not detected and treated in the early stages, eating disorders can lead to fatal physical deteriorations, characterized by a decline in quality of life and social functionality (38). The most common types of eating disorders, Anorexia Nervosa (AN) and Bulimia Nervosa (BN), are chronic conditions where recovery is typically expected within the first 12 years after diagnosis. As the duration of the illness increases, the likelihood of recovery diminishes. A comprehensive, patient-centered palliative

care approach that respects the patient's right to request care not only in the hospital but anywhere, has been adopted for Anorexia Nervosa to reduce potential damage (35).

Suggestions for the palliative care of patients with eating disorders include:

• Management of symptoms,

• Implementation of interventions aimed at enhancing the quality of life,

• Strengthening of family relationships,

• Preservation of dignity and privacy,

• Supporting activities that the individual can participate in within the community, taking into account their level of disability,

• Providing an environment where the individual can make their own decisions,

• Providing emotional or spiritual support when needed,

• Understanding and respecting the individual's end-of-life care preferences (35).

Neurocognitive Disorders: In the literature of palliative care, much like the broader spectrum of neurocognitive diseases, there is a predominant focus on Alzheimer's disease (43). Alzheimer's disease, and the irreversible cognitive decline associated with it, deprives individuals of their ability to live independently, hence exerting a multitude of negative physical, psychological, and social impacts on the individual, family, and society (42, 43). The care and treatment needs of individuals vary greatly between the early and late stages of the disease (43). For individuals with dementia, palliative care aims to prolong life by treating in the early stages of the disease, enhance the quality of life by providing comfort in the later stages, and offer support for a dignified death. The objectives of palliative care in dementia involve maintaining the individual's existing functions, enhancing comfort, and ensuring the continuation of life (42,43).

Suggestions for the palliative care of patients with neurocognitive disorders include:

• Early detection of the disease,

• Endeavors to increase the comfort of the individual,

• Maintaining or striving to improve functionality,

• Enhancement of social resources,

• Inclusion of family and caregivers in the patient's care (42),

• Addressing the psychosocial issues faced by caregivers,

• Reviewing and respecting end-of-life care decisions made by the individual in the early stages of the disease (43).

Conclusion and Recommendations

The high prevalence of treatable comorbidities, which cause pain and reduce life expectancy in individuals with severe mental disorders, highlights the need to incorporate these individuals into comprehensive palliative care services. All mental health professionals must unanimously recognize the palliative care needs of individuals with severe mental disorders. Due to factors such as the holistic and trans-cultural nature of care, its relevance and acceptability in the health system and society, there is a need for national studies in this field.

Psychiatric nurses, who act as advocates for individuals with severe mental disorders, should recognize the significant gap in psychiatric palliative care in our country and prioritize work in this area. Leading the effort to produce methodologically sound studies that help define the current challenges for this disadvantaged population is the responsibility of psychiatric nurses.

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Sertraline and cognitive behavioral therapy in the treatment of psychogenic dysphonia: A case report

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SUMMARY

Psychogenic dysphonia (PD) is the inability of the structurally normal vocal cords to perform their proper vocalization function. In other words, it can be defined as the inappropriate or incorrect use of the normal vocal organ. The role of emotional stress is important in the formation of psychogenic dysphonias. It is a transformative clinical condition that is difficult to diagnose and treat. There are various studies in the literature regarding the diagnosis, evaluation and treatment approaches of patients with psychogenic dysphonia. The combination of sound therapy and psychotherapy is often used together, as psychogenic dysphonia symptoms and psychological factors mutually influence each other. Pharmacotherapy can also be among the treatment approaches, but this method is only applied in certain situations. The success of treatment may vary depending on the patient's symptoms, response to treatment, and other factors. Therefore, it is important to develop an individualized treatment plan for each patient. There are limited studies on pharmacotherapy in treatment. In this case report, it is aimed to discuss a male psychogenic dysphonia case who responded dramatically to sertraline treatment in the light of the literature.

Keywords: Psychogenic dysphonia, conversion disorder, sertraline, voice disorders.

INTRODUCTION

Psychogenic dysphonia refers to loss of voice in the absence of obvious structural or neurological pathology. It can also be named as functional, converse and hysterical dysphonia (1). It is a disorder that is more common in women with a ratio of 8:1. The prevalence rates reported in a study conducted on patients admitted to voice disorder clinics are between 4-5% (2). Although the etiology is still not clear, it has been stated that a psychologically stressful event in the patient's life plays a role in triggering the condition. The diagnosis of psychogenic dysphonia can usually be made after a thorough physical examination and evaluation by an otolaryngologist (ENT) and neurologist. A person with dysphonia may have a laryngoscopy or fiberoptic endoscopy test performed to determine if there are any organic problems with their vocal cords or airways. If these tests return normal results, the person may be dysphonic for a psychological reason (3, 4). Psychogenic dysphonia can be treated with different approaches, such as speech therapy, psychotherapy, and medication. In this case report, we will present a case of psychogenic dysphonia in male gender, which did not improve as a result of cognitive behavioral therapy and sound therapy, but improved with sertraline treatment.

CASE HISTORY

Mr. Ü.A is a 32-year-old, single, high school graduate, working male patient. The patient, who had no previous psychiatric treatment history, was referred to the psychiatry outpatient clinic from the otolaryngology outpatient clinic with the complaint of sudden onset of hoarseness and intermittent inability to speak. The patient stated that as a result of an argument with his boss and his colleagues at work

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about 3 weeks ago, he could not answer his boss, could not speak, and then experienced hoarseness. He stated that this situation he experienced in front of his colleagues made him very embarrassed and that he could not go to work for a certain period of time. The patient was examined in the otorhinolaryngology and neurology department. When no organic cause could be found for his hoarseness, he was referred to the psychiatry outpatient clinic. The patient stated that he felt tired, unhappy and unhappy, and experienced an intense sense of shyness. In the mental state examination of the person, he was consciously oriented and cooperative. Himself care was good, he looked him age. Speech volume and speed decreased. Voice volume was low. He had hypophonia. Mood was depressive and anxious. The affect was anxious. There was no psychotic finding in perception. His thought process and associations were normal. There were concerns and concerns that he could not improve in his thought content. His psychomotor activity was decreased. In psychometric scales, Hamilton Depression Rating Scale (HDRS) was evaluated as 27 points and Hamilton Anxiety Rating Scale (HARS) was evaluated as 21 points. It was determined in the Minnesota Multiphasic Personality Inventory (MMPI) that the patient had dependent personality traits and expressed his feelings with bodily complaints. In the neurological examination of the patient, who had no special history or family history, the voice was quite hypophonic, and involuntary movements were observed due to excessive strain on speech, and strain on the chin and lips. All other neurological examinations were normal. Routine hematological examinations (blood count, detailed blood biochemistry, routine urinalysis, thyroid function tests, and thyroid antibodies, B12-folic acid levels) were found to be normal, and no abnormality was found in further laboratory examinations. Cranial magnetic resonance was evaluated as normal. Ear, nose, and throat consultation was requested in terms of hoarseness, and no anomaly was detected in the laryngoscope examination. The patient was re-evaluated in terms of speech disorder, and a diagnosis of major depressive disorder and psychogenic dysphonia was made according to DSM-5 as a result of the acute onset of the present disorder after psychogenic stress, the individual's psychiatric examination and psychometric test evaluations. The patient was started on sertraline 50 mg/day. The dose was gradually increased to 100 mg/day. In addition, psychotherapy and sound therapy were initiated. Voice therapy was carried out in the form of supporting the voices that can be extracted in psychogenic voice disorders and applying special techniques in order to make the voices that cannot be produced. The person was followed from the outpatient clinic for about 3 months. At the control examination after three months of treatment, the patient's HDRS decreased to 7 points and the HARS to 6 points. The tone of voice was high, the articulation and prosody of the speech were normal, and the patient's speech was evaluated as close to normal by him and his relatives. The patient's hoarseness improved dramatically. Informed consent was received from him and him family regarding this case report.

DISCUSSION

PD is defined as the loss of sound structure and intensity that cannot be explained by structural or neurological problems, and this loss in phonation is associated with psychogenic processes such as anxiety disorder, depression, personality disorder and conversion disorders. The prevalence of conversion dysphonia among all conversion disorders is 4-5% (3). Conversion dysphonia's usually occur after conditions that develop close to psychogenic trauma and can cause hoarseness, such as pharyngitis due to viral infections. More rarely, however, very severe and persistent converse dysphonia's may occur under unclear or unrelated conditions and may have preceded the onset of stress factor dysphonia for months or years. In psychogenic dysphonia, the voluntary use of the voice is affected and there is no articulation. However, vegetative vocal functions such as coughing, laughing, sighing or crying are usually not affected (5). As in our patient, while the patient had difficulty in making sounds and saying words, other vocal functions such as coughing and laughing were intact.

The etiology of psychogenic hoarseness is multifactorial. In our case, voice disorder started acutely immediately after the stress factor. It is important to take a detailed medical history when evaluating a patient with hoarseness. The information

obtained in the anamnesis may be useful in determining the cause of hoarseness or detecting another underlying condition. Psychogenic dysphonia is a type of conversion disorder in which the ability to vocalize is impaired. In psychogenic mutism, the patient does not make an effort to talk. About 5% of psychogenic dysphonia's are cases of psychogenic mutism (3). While PD was included under the motor symptom or deficit type of conversion disorder in the DSM-IV (as aphonia), it was included under the speech symptom type as dysphonia in the DSM-5 (6). Today, there is a consensus that it is not sufficient to exclude organic diseases for the diagnosis of PD, and psychiatric evaluation with a multidisciplinary approach is essential (7,8). Its treatment should be approached multidisciplinary. In the literature, some clinical features that distinguish patients with functional voice disorders from organic diseases have been described by other disciplines (9). For example; These features include acute onset, variable symptom severity on examination of different speech activities, susceptibility to suggestion, symptom relief with distraction, rapid regression and improvement potential of symptoms, increased muscle contraction with paradoxical vocal fatigue, denial and indifference for abnormal speech/voice. It is frequently emphasized that there is a sudden onset especially in psychogenic voice disorders (9). Usually, PD starts acutely and there are problems related to stress in the past (10). In our patient, hoarseness started suddenly after an event that was stressful for him. The diagnosis should be made after the otolaryngologist and psychiatrist both evaluate the patient. Ultimately, the diagnosis should be made with an integrated, multidisciplinary approach (10, 11). An empathetic, supportive approach is essential in patients with PD. The patient should be discussed carefully and openly. It is wrong to give the message that there is no underlying cause. Because this message may cause the patient to abandon the treatment. Role-playing and malingering discourses are dangerous. It should be emphasized that the symptoms are unconscious. Evaluation of the patient's personality traits also helps to determine the treatment framework. In a recent study on patients with dysphonia, including patients with functional dysphonia, differences in the tendency to activate the introversion, neuroticism and behavioral inhibition system were reported in these patients (12). Our patient was found to have dependent and alexithymic personality patterns in the MMPI test. Avoidance tendencies of the patient, alexithymia and somatoform tendencies can be detected in PD patients (13,14).

Research on the neurobiology of psychogenic dysphonia suggests that neurotransmitters in the brain such as serotonin and dopamine may also play a role in this speech disorder. Serotonin plays an important role as a chemical messenger that enables communication between nerve cells in the brain. Decreased serotonin levels can cause increased stress responses in the brain and increased muscle tension of the vocal cords, which can lead to symptoms of psychogenic dysphonia. Brain imaging techniques, particularly functional magnetic resonance imaging (fMRI), are important tools used to investigate the pathophysiology of psychogenic dysphonia (15). These techniques can reveal changes in communication between different regions of the brain and changes in brain activity. SSRIs are drugs used to treat conditions such as depression, anxiety, and obsessive-compulsive disorder by increasing serotonin levels in the brain. Research on the effects of SSRIs on psychogenic dysphonia is limited. However, some studies have shown that SSRIs can improve symptoms of psychogenic dysphonia. However, more research is needed on the specific effects of SSRIs on the neurobiology of psychogenic dysphonia. In conclusion, the pathophysiology of psychogenic dysphonia is not yet fully understood and more research is needed on this subject.

The treatment of PD actually begins with the explanation of the diagnosis to the patient and the acceptance of the treatment plan by the patient (16). The relationship between psychosocial stress factor and dysphonia symptom should be explained to the patient. If the link between his symptom and his psychological state is not explained to the patient, he may not understand the importance of treatment. The relationship between the brain, nerve and vocal cord triad in psychogenic dysphonia should be explained. As in all PD's, comorbid anxiety disorder, depressive disorders, post-traumatic stress disorder and hypochondriasis are high in PD (17, 18). There are no studies other than a few uncontrolled studies showing the antidepressant or anxiolytic efficacy in patients with PD. Only

randomized non-placebo-controlled studies have shown some antidepressant efficacy for PD (19). Therefore, if there is a comorbid diagnosis, antidepressants can be started. In our patient, sertraline treatment was started because dysphonia was accompanied by anxiety and depressive symptoms. The patient received simultaneous cognitive behavioral therapy and sound therapy. The content of CBT includes information about PD and the stress response cycle, attempts for the patient to manage stress and develop new behavioral patterns, and helps patients to recognize and change their useless thoughts. It is important to identify and change the thought patterns that reinforce the patients' symptoms and that do not work (16). The patient can be given daily vocal exercises such as blowing, whistling, spelling. The way the patient with psychogenic aphonia/dysphonia forces himself to speak further increases the hoarseness functionally. Thus, it pulls the patient into a vicious circle (16). In fact, the aim of sound therapy is to break this vicious circle. In the past, some researchers suggested voice therapy as an alternative treatment for patients who did not respond to psychotherapy interventions (20). In a more recent study, it was shown that there was a 93.1% response to voice therapy in patients with PD. In addition, in the same study, the rate of relapse was found to be high in those who received only voice therapy (11). In fact, sound therapy has similar purposes to psychotherapy. Voice therapy is similar to the behavioral component of cognitive behavioral therapy. The goal in voice therapy is to create a more adaptive voice. In sound therapy, a natural sound is created by using non-communicative sounds such as throat clearing, coughing, gargling and laughing. After switching to natural voice, there is a gradual transition to speech production. Voice therapy is usually planned as 2-4 sessions and each session lasts 40 minutes (11).

Despite the importance of psychological factors in the etiology of PD, the fact that it responds to a functional intervention and at the same time decreases regeneration with psychotherapy supports the importance of a holistic approach in these patients. This also makes this PD an interesting model to demonstrate the link between chronic stress, emotional dysregulation, and functional neurological loss. As with all FNBs, a multidisciplinary holistic approach is essential in the treatment of PD. Mental health professionals should cooperate with an otolaryngologist both in the differential diagnosis and in the treatment process. In order to prevent unwanted diagnosis and treatment attempts, the diagnosis should be shared with the otolaryngologist as soon as it is clear. Approaching the problem only psychologically or only functionally makes diagnosis and treatment difficult. As a result, dysphonia symptom and psychological factors mutually affect each other. Integrated therapy, in which psychotherapy and voice therapy are used together, is the gold standard approach in the treatment of PD.

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