

# COMPARISON OF PATIENTS DIAGNOSED WITH FIRST EPISODE PSYCHOSIS IN THE PSYCHIATRY CLINIC IN THE 1-YEAR PERIOD BEFORE AND AFTER THE COVID-19 PANDEMIC

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## SUMMARY

**Background:** Several cases of psychosis caused directly or indirectly by the COVID-19 pandemic have been identified. Especially psychosocial stress factors are thought to trigger first-episode psychosis. The aim of this study was to compare the sociodemographic and clinical features of the cases diagnosed with psychotic disorder for the first time in the two periods 1 year before and 1 year after the date of 11.03.2020, when COVID-19 was first detected in Turkey and COVID-19 was declared as a pandemic by World Health Organization (WHO).

**Subjects and methods:** In this retrospective cohort study, we compared age, gender, marital status, and clinical characteristics of 27 pre-pandemic (PR) and 32 post-pandemic (PS) patients during their first psychotic episode.

**Results:** We compared age, gender and clinical features of PR and PS cases and no statistically significant difference was found (age  $p=0.836$ , gender  $p=0.091$ , clinical features  $p=0.579$ ).

**Conclusions:** There are a limited number of studies comparing first-episode psychosis (FEP) patients in the PR and PS periods. This is the first study conducted in Turkey on this subject. The present study may contribute to the literature by examining the impact of the pandemic process on the epidemiology of psychiatric diseases.

**Key words:** COVID-19 - first-episode psychosis – stress - psychotic disorder

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## INTRODUCTION

The new Coronavirus Disease (COVID-19) was first detected in December 2019. In March 2020, the WHO declared a pandemic due to the rapid spread of the epidemic worldwide (World Health Organization 2020). The first confirmed case of COVID-19 outbreak was reported on March 10, 2020 in Turkey. From the first case to April 11, 2022, the total number of cases reported in Turkey was 14,775,634 of which 97,666 are fatal. (Republic of Turkey Ministry of Health 2022).

Various psychiatric diseases such as depression, anxiety, panic disorder and post-traumatic stress disorder have been triggered due to the economic difficulties that emerged with the pandemic, the stress caused by quarantine and social isolation (Spoorthy et al. 2020). There are publications in the literature that psychosocial stressors will cause psychosis as well as the direct effect of viruses in pandemics. 'Influenza psychoses' have been described since the Spanish flu epidemic in the 18th century (Brown et al. 2020). At the same time, neuropsychiatric symptoms associated with severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome-related coronavirus (MERS-CoV) were detected (Rogers et al. 2020, Salehi et al. 2021). 30 months after the SARS outbreak in China, the DSM-IV showed that the cumulative incidence of psychiatric disorders was 58.9%, among which the incidence of post-SARS

psychoses was 4.4% (Tariku & Hajure 2020). Recently, several cases with psychotic episodes caused directly or indirectly by COVID-19 have been identified (Parra et al. 2020).

Coronaviruses are neurotrophic and can reach the brain by a variety of mechanisms, including the olfactory pathway, causing inflammation and ultimately peripheral and central nervous system (CNS) symptoms. It is assumed that the inflammatory response (cytokine storm) against COVID-19 causes neuropsychiatric symptoms through immunological mechanisms. It is thought that COVID-19 RNA isolation from cerebrospinal fluid sample may be proof that the virus can reach the CNS directly (Ferrando et al. 2020). There are also publications that psychosis may develop due to favipiravir and high-dose steroids used for the treatment of COVID-19 (Parra et al. 2020). In a meta-analysis study on the neuropsychiatric findings of COVID-19, it is stated that steroid-induced psychosis occurred in 0.7% of the subjects in the study during the acute phase of COVID-19 infection (Rogers et al. 2020).

The classical concept of diagnosis, which originated from Jasper's 'true reaction' and was further developed in Scandinavia by Wimmer, Faergeman and Strömngren (Fusar-Poli et al. 2016). It encompasses the group of short-term, acute psychotic episodes in response to a stressful situation, and the symptomatology is often associated with mental trauma (Zielasek & Gaebel 2015).

Although the pathogenesis of psychoses is still unknown, stressful events or environments may cause psychiatric symptoms associated with poor susceptibility to stress in the early stages of psychosis (Horan et al. 2005). In accordance with the stress-diathesis model, the occurrence of psychotic symptoms in individuals with reactive psychosis may be associated not only with acute stress associated with the COVID-19 pandemic, but also with pre-existing psychological or biological abnormalities (Valdés-Florido et al. 2020, Taylor et al. 2019). In a report consisting of series of cases in Spain, it was reported that stress caused by the pandemic led to acute reactive psychosis (Valdés-Florido et al. 2020).

Literature shows that all recorded cases with coronavirus-induced psychosis presented with delusions. At the same time, orientation, attention deficit (60%), auditory (40%) and visual (10%) hallucinations were detected. It has been reported that the content of delusions is mostly in the form of reference and persecution delusions. In the follow-ups, it was stated that most cases benefited from low-dose antipsychotics and symptoms resolved within 2 weeks (Parra et al. 2020).

In our study, we set out from the hypothesis that there will be some quantitative and qualitative changes in newly diagnosed psychoses. This is due to the changes in psychosocial life apart from the direct effects of the COVID-19 virus during the COVID-19 pandemic process. For this reason, we planned to compare the sociodemographic and clinical features of the cases who were diagnosed with psychotic disorder for the first time in the two periods: 1 year before and 1 year after the date of 11.03.2020, when COVID-19 was declared as a pandemic by WHO and the first detection of COVID-19 was announced in Turkey. When we searched the literature, we could not find enough studies on this subject, except for the study conducted with patients diagnosed with first-episode psychosis before and after the pandemic in Italy (Esposito et al. 2021). For this reason, we think that our study will contribute to the literature and shed light on future studies.

## SUBJECTS AND METHODS

### Research design and participants

This study was designed as a retrospective cohort study. In this study, we examined patients who applied to the psychiatry clinic of a training and research hospital affiliated with the university and diagnosed with first-episode psychosis in the 1 year before (11.03.2019-11.03.2020) the start of the COVID-19 pandemic and 1 year after (11.03.2020-11.03.2021) it started.

Our study includes patients over the age of 18 who were diagnosed with FEP on the specified dates and whose clinical data we accessed from the hospital's

system. We included the cases in our study among the patients, who applied to the psychiatry outpatient clinic, emergency and psychiatry services at our hospital. On the other hand, patients under the age of 18 and patients previously diagnosed with psychotic disorder in the psychiatry clinic were excluded from the study. Patients with comorbid mental disorders and unclear diagnoses were also excluded from the study. FEP diagnosis was made according to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria (American Psychiatric Association 2013).

This study was approved by the local ethical committee (no: 2021/06-01, dated June 15, 2021). Data were scanned from the hospital's system on the dates specified retrospectively, and cases diagnosed with FEP who were not previously diagnosed with a psychotic disorder were included in the study. We reviewed the age, gender, marital status data and the clinical features during a FEP of 52 patients who were diagnosed with FEP on the specified dates and met the inclusion criteria, and compared their relationship with the pandemic. The flow chart of the study protocol is given in Figure 1.

### Statistical Analysis

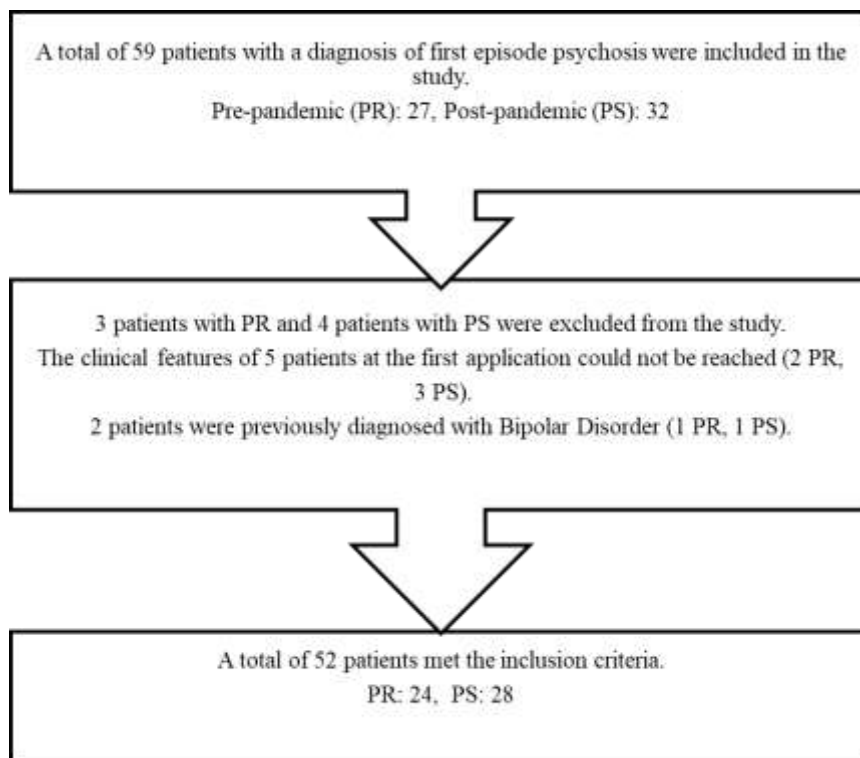
IBM SPSS Statistics for Windows, Version 22.0. (IBM Corp. Armonk, NY: USA.) was used for all statistical analysis. Descriptive parameters are expressed as mean  $\pm$  standard deviation or number (percentage). Chi-square or Fisher's test was used in the comparison of categorical data, depending on suitability. The normality of the distribution was tested by Kolmogorov Smirnov tests. Student's T test was used to compare parametric data, and Mann Whitney U test and Kruskal-Wallis test were used to compare non-parametric data. A p value of  $<0.05$  was accepted statistically significant.

## RESULTS

A total of 52 people, 24 PR and 28 PS, were included in the study. The mean age of the PR cases was  $35.63 \pm 10.06$  years, and the mean age of the PS cases was  $36.43 \pm 16.40$  years. No significant difference was detected in terms of age of PR and PS ( $p=0.836$ ).

The relationship between gender and pandemic groups is shown in Table 1. When we evaluated the relationship between the PR and PS group and gender, we detected borderline statistical significance in the number of females ( $\chi^2=2.849$ ,  $SD=1$ ,  $p=0.091$ ).

In addition, it was noted that 10 (41.7%) of the PR cases were married, 14 (58.3%) were single, and 11 (39.3%) of the PS cases were married and 17 (60.7%) were single. When we examined the relationship between marital status and pandemic, no statistically significant difference was detected ( $p=0.862$ ).



**Figure 1.** Flow-chart of the study enrollment protocol

**Table 1.** Gender distribution before and after the pandemic

Relationship with the pandemic	Gender		Total n (%)
	Woman n (%)	Man n (%)	
Pre-Pandemic	5 20.8%	19 79.2%	24 (46.2%)
Post-Pandemic	12 42.9%	16 57.1%	28 (53.8%)
Total n (%)	17 (32.7%)	35 (67.3%)	52 (100.0%)

**Table 2.** Clinical features of the cases before and after the pandemic

Relationship with the pandemic	Psychosis Clinical Features			Total n (%)
	Delusion n (%)	2 or more symptoms n (%)	Negative symptoms n (%)	
Pre-Pandemic	7 46.7%	11 40.7%	6 60.0%	24 (46.2%)
Post-Pandemic	8 53.3%	16 59.3%	4 40.0%	28 (53.8%)
Total n (%)	15 (28.8%)	27 (51.9%)	10 (19.2%)	52 (100.0%)

The clinical features of the cases were reviewed retrospectively and are shown in Table 2 according to their relationship with the pandemic. When we look at the relationship between the clinical features of psychosis and the pandemic, no statistically significant difference was detected ( $p=0.579$ ). Patients with and without 2 or more symptoms in the PR and PS periods were compared, and no statistically significant difference was found ( $p=0.416$ ). Of the 5 female patients who applied in the pre-pandemic period, 2 (40%) had delusions, 2 (40%) had 2 or more symptoms (delusions, hallucinations, agitation, aggression, somatic complaints etc.), and 1 (20%) had negative symptoms.

Of the 12 female patients who applied after the pandemic, 3 (25%) had delusions, 9 (75%) had 2 or more symptoms, and there was no patient with only negative symptoms.

## DISCUSSION

In this study, we compared the cases diagnosed with PR and PS in the 1-year period in terms of age, gender, and clinical features of psychosis.

In a large population-based cohort study that retrospectively reviewed more than 200,000 patients, it was emphasized that the risk of psychotic disorder increased

significantly in the 6-month follow-up period after COVID-19 (Taquet et al. 2021). Anxiety disorder was observed in 17.4% of the patients, psychotic disorders were observed in 1.4%, and the first psychotic attack was observed in 0.4%. It is stated that the psychiatric clinical course is caused by psychosocial factors other than the direct effect of the coronavirus. For a similar purpose, PR and PS cases were compared in our study and it was aimed to reveal the differences.

In the study conducted with FEP patients in Italy; on the other hand, the mean age of PS patients was  $43.5 \pm 15.8$  years, and it was detected to be statistically significantly higher than the period of PR (Esposito et al. 2021). Similarly, in another study, new cases of psychosis associated with exposure to the psychosocial stress of COVID-19 were observed in older group of people (Vindegaard & Benros 2020). On the other hand, Varatharaj et al. (2020) in another study of 153 cases with COVID-19 conducted in the UK, reported that 23 (15.0%) of the cases met the psychiatric diagnostic criteria and 10 (43%) of these cases had FEP. With this study, it was noted that FEP cases were younger than the remaining cases. However, in our study, it was observed that the mean age of "FEP" cases seen in both periods was similar. When all the aforementioned studies are evaluated, we think that age is a variable risk factor in patients presenting with FEP after the pandemic.

In a study conducted with university students in the USA, the effect of socioeconomic status on psychosis during the COVID-19 period was examined (Oh et al. 2021). It has been determined that economic troubles and the stress it creates increase the risk of psychosis. At the same time, this study found an association between the cases' parents' higher educational status and a lower probability of experiencing a first psychotic attack. Since our study was retrospective, data on socioeconomic status and education level of the cases could not be reached, and it was concluded that more studies should be done on this subject. However, it is known that the income level of the population in the settlement where the study was conducted is below the average of the socioeconomic level of the individuals in Turkey.

Gender is known as a risk factor for multiple mental disorders. In a study on the psychological impact of the COVID-19 pandemic, it was concluded that depression and anxiety are more common in women during the pandemic period (Vindegaard & Benros 2020). A study included 258 university students examining the effect of the coronavirus pandemic on mental health. The study results showed that the mental health level of women is lower than that of men (Abuhmaidan & Al-Majali 2020). Similarly, another study found that middle-aged women were more prone to short reactive psychotic episodes accelerated by psychosocial factors such as loss and isolation caused by the coronavirus pandemic (Opjordsmoen 2001, Hu et al. 2020). However, accor-

ding to another study, a slight but non-significant difference was found in patients diagnosed with psychosis after the COVID-19 pandemic, suggesting that gender is not a risk factor (Hu et al. 2020). Our study shows women present with the diagnosis of FEP more than men in the PS period. This is an expected result since it is known that stress and anxiety disorders are more common in women.

In a psychosis-related study, the relationship between psychosocial factors, including stressful life events, was extensively investigated and psychosocial factors were found to be an important risk factor for both the onset and exacerbation of psychosis symptoms (Fusar-Poli et al. 2017). Although there are a limited number of original studies related to COVID-19-related FEP, there are many case reports in the literature. In a study, three female cases presented with acute psychotic attack induced by social isolation due to the fear of Covid-19 infection. The COVID-19 PCR tests of all these three patients came back negative (Elliot & Martin 2021). In the case report containing 4 cases in United Kingdom, it is stated that all cases met the diagnostic criteria for acute stress response and brief psychotic episode, psychosocial stress factors were present in all cases, and clinical findings improved after a two-week treatment period (Lazzari et al. 2020). A case series consisting of 6 cases have been published in Italy. These cases were reported to have emerged in the month following the national quarantine announcement in Italy and the global outbreak of the pandemic. The study suggested that irregular daily routines and fear of infection might have triggered FEP during quarantine (D' Agostino et al. 2021). In a study conducted on patients who had a history of hospitalization due to COVID-19 followed by recovery after treatment, it was found that 1 out of every 10 patients developed temporary post-traumatic stress disorder. In addition, this study claims that female gender and the presence of psychiatric illness in the past are risk factors for post-traumatic stress disorder that develops after COVID-19 infection (Tarsitani et al. 2021). In a study conducted in China, while the prevalence of post-traumatic stress disorder in the mainland was 4.6%, the prevalence was found to be 18.4% among high-risk people living in the provinces of China where the number of COVID-19 positive cases was highest (Sun et al. 2020). Although our study cannot definitively explain that the psychosocial stressors caused by the pandemic are the predisposing factors for the emergence of FEP. Since it was determined that the majority of FEP cases in the PS period were women and it was known that women were more prone to stress, it was thought that the stress factor was related to FEP.

In a review examining the relationship between psychiatric diseases and COVID-19, it is stated that COVID-19 infection causes neuroinflammation which gets triggered by the duration and frequency of exposure to stress factors. Common mental symptoms of cases

infected with COVID-19 at the time of admission were observed to be insomnia, aggressive behaviors, delusions, and severe anxiety (He et al. 2021). Series of cases published in Madrid have determined that cases with COVID-19-related psychosis presented with structured reference and somatic delusions (Rentero et al. 2020). Similarly, in other studies in the literature, it has been determined that cases present with somatic delusions and that psychosocial stress causes neurobiological changes. (Brown et al. 2020, Heinz et al. 2019). In Spain, 33 cases diagnosed with reactive psychosis triggered by COVID-19 in the first two months of the pandemic were examined. In the study suicide attempts observed in 8 (24.2%) cases, delusions in 28 (84.8%) cases, hallucinations in 14 (42.4%) cases, and disorganized speech in 13 (39.4%) cases (Valdés-Florido et al. 2022). In our study, delusions in 8 (53.3%) cases, 2 or more symptoms (delusions, hallucinations, agitation, aggression, somatic complaints, etc.) in 16 (59.3%) cases, and negative symptoms in 4 (40.0%) cases were found. In another study, psychotic attack characteristics of FEP cases admitted in Italy between 2019 and 2020 were compared. No significant qualitative difference was found in terms of duration or psychometric scores compared to the previous year (Esposito et al. 2021). In our study, the clinical features of FEP patients in the PR and PS periods were compared and no statistically significant difference was detected. This is an expected result considering the small number of cases since we investigated a short period of 1 year PR and PS. It was thought that etiological factors such as stress in the emergence of first-episode psychosis before and after the pandemic would not change the clinical features of the cases at the time of application.

Our study had some limitations. This study was carried out retrospectively, since COVID-19 PCR test could not be performed at the time of an episode in patients diagnosed with FEP, the direct relationship between this and COVID-19 could not be investigated, and no scale for measuring the severity of psychosis could be reached. Since there are not many studies similar to ours in the literature, our results provide early findings after the pandemic, a further evaluation of these results with follow-up studies will yield more valuable results. Nevertheless, we believe that it is a valuable study in terms of comparing the socio-demographic and clinical characteristics of patients diagnosed with FEP before and after the pandemic.

## CONCLUSIONS

We believe that the population with stress-related psychosis should be followed closely in terms of relapse risk and transition to long-term psychotic disorders. We think further studies with more data at a later date can provide a more comprehensive analysis, and details on neurotrophic effects of coronaviruses.

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### Contribution of individual authors:

Şeyma Sehliskoğlu: study design, data collection, first draft, statistical analysis.

Behice Han Almiş: study design, first draft, statistical analysis.

All authors approval of the final version.

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