COVID-19 Outbreak Increases Risk of Schizophrenia in Older Adults

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Abstract

An unusual increase in first-time patients with schizophrenia (F20) was observed in January 2020 following the outbreak of COVID-19. This retrospective study aims to validate this observation and identify potential risk factors, where applicable. A total of 13,783 outpatient records from January 2020 were thoroughly investigated. Comparisons of schizophrenia incidence among outpatients between January 2020 and corresponding periods from 2017-2019 were conducted to minimize seasonal influence. The relationship between schizophrenia incidence and COVID-19 infections in China was analyzed. Limited personal information (age, gender, approximate residence) was analyzed to identify risk factors. After controlling for seasonal factors such as the Spring Festival, a positive correlation between the incidence of schizophrenia among first-time patients and the nationwide epidemic situation was identified. Statistical results further demonstrated a significant increase in median age from 39 to 50 years for first-time patients diagnosed with schizophrenia, which is unusual. Meanwhile, only slight and non-significant changes were observed in the distribution of gender and approximate residence (urban/suburban). Our data support that the COVID-19 outbreak increased the risk of schizophrenia in older adults, which is consistent with the fact that COVID-19 is more lethal to the elderly. We strongly urge that public healthcare systems in countries both with and without infected patients should prepare in advance for potential risks to public mental health.

Full Text

Preamble

COVID-19 Outbreak Increased Risk of Schizophrenia in Aged Adults

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Abstract

We observed an unusual increase in first-time patients with schizophrenia (F20) in January 2020 following the COVID-19 outbreak. This retrospective study aims to validate this observation and identify potential risk factors.

Methods: We thoroughly investigated 13,783 outpatient records from January 2020. To minimize seasonal influence, we compared schizophrenia incidence with similar periods from 2017–2019. We examined the relationship between schizophrenia incidence and COVID-19 infections in China, and analyzed limited personal information (age, gender, approximate residence) to identify risk factors.

Results: After excluding seasonal factors such as the Spring Festival, we found a positive relationship between schizophrenia incidence in first-time patients and the nationwide epidemic situation. Statistical analysis revealed a significant increase in median age from 39 to 50 among first-time patients diagnosed with schizophrenia, which is unusual. Meanwhile, only slight, non-significant changes were observed in gender distribution and approximate residence (urban/suburb).

Conclusions: Our data support that the COVID-19 outbreak increased the risk of schizophrenia in aged adults, consistent with COVID-19' s higher lethality in elders. We strongly urge public healthcare systems in countries both with and without infected patients to prepare in advance for potential risks to public mental health.

Keywords: schizophrenia, COVID-19, mental disorders, age, public health, risk factor

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Introduction

COVID-19 is spreading rapidly worldwide. In just over two months, it infected more than eighty thousand people and killed more than two thousand, according to the World Health Organization. With additional cases identified daily in over twenty countries, COVID-19 is causing far greater public concern globally than SARS (Severe Acute Respiratory Syndrome) or MERS (Middle East Respiratory

Syndrome) (Novel Coronavirus Pneumonia Emergency Response Epidemiology, 2020). Although less lethal, COVID-19' s explosive spread is causing worldwide panic and occasional chaos due to potential shortages of supplies (e.g., food) and medical resources (e.g., N95 respirators and surgical masks). Previous studies showed that severe epidemics negatively impact the mental health of healthy populations, causing anxiety, depression, and even insomnia (Chen et al., 2006). Research on the 2009 H1N1 pandemic also found that people' s tolerance for information uncertainty, self-assessment, and coping behaviors can lead to different anxiety levels (Taha et al., 2014). Yet little is known about what specific mental health risks such severe outbreaks might induce.

Unlike SARS or MERS, COVID-19' s incubation period can be as long as 27 days, according to WHO Situation Report 29. To slow COVID-19' s spread, many Chinese cities and towns implemented extremely strict regulations to control population movement, including temporary bans on public transportation and requests for citizens to stay home as much as possible. Despite the benefits of traffic control, the notable reduction in outpatient numbers we observed in recent clinics is actually a dangerous sign. Although we provided alternative support such as online counseling for people with psychological or mental problems, patients unable to see psychiatrists might face higher risks of deterioration. Once nationwide traffic control is lifted, outpatient numbers will likely surge. We hope this brief summary can provide helpful clues for psychiatrists: better understanding of what has happened enables us to prepare accordingly in advance.

Due to the large patient volume, psychiatrists from different departments first noticed the unusual incidence of schizophrenia since the COVID-2019 outbreak. In this retrospective study, we thoroughly investigated 13,783 records from January 2020 to validate this observation. Seasonal factors such as the Spring Festival were considered but could not alone explain the unexpected rise in schizophrenia. We used linear regression to identify potential relationships between schizophrenia incidence and COVID-19 infection numbers in China. Limited personal information such as age, gender, and approximate address (urban/suburb) was accessed to identify potential risk factors. Because significant changes in schizophrenia incidence were found only in first-time outpatients, these findings may also be important for the general healthy public. We again call on psychiatrists and researchers from different regions to share data and work together to counter the challenge to public mental health.

2.1 Study Overview and Participants

As a retrospective study, all records were collected from patients who visited Xuzhou Oriental People' s Hospital. We enrolled records from 4,982 first-time patients (1,168 in 2017, 1,347 in 2018, 1,257 in 2019, and 1,210 in 2020) and 44,710 returning patients (8,778 in 2017, 11,696 in 2018, 11,663 in 2019, and

12,573 in 2020) for detailed analysis. For each case included in this study, a clear clinical diagnosis was made according to the International Classification of Diseases 10th Edition (ICD-10). Diagnostic results and limited personal information (gender, age, and approximate address) were collected and analyzed to identify potential risk factors. This retrospective study was reviewed and approved by the ethical board at Xuzhou Oriental People' s Hospital.

2.2 Data Alignment

Although COVID-2019 began at the end of 2019, public awareness of the epidemic emerged in early January 2020 (Novel Coronavirus Pneumonia Emergency Response Epidemiology, 2020). We selected data from January 1st to 31st to reflect the progressive influence of the COVID-2019 outbreak. Because the 2020 Spring Festival also occurred in January and major holidays can significantly impact people' s mental states (Sansone and Sansone, 2011; Beauchamp et al., 2014), we used data from similar periods (near the Spring Festival) from 2017-2019 as a baseline to minimize seasonal influence. The Spring Festival fell on January 28th in 2017, February 18th in 2018, February 5th in 2019, and January 25th in 2020. Data from each year were aligned to the day of the Spring Festival, respectively.

It is also worth noting that before January 10th, 2020, COVID-19 pneumonia was only known as "an unknown pneumonia in Wuhan" and had not gained broad attention. On January 20th, COVID-19 was formally added to the list of Class B infectious diseases by the Chinese Center for Disease Control and Prevention (China CDC), which also requested that COVID-19, although Class B, should follow the regulations for Class A infectious diseases (e.g., smallpox and cholera). Thus, the data grouping used in this study also matched key time points during the COVID-19 outbreak.

2.3 Data Collection of COVID-19

We collected nationwide COVID-19 data from the website of the National Health Commission of the PRC (http://en.nhc.gov.cn, English version available).

2.4 Statistics

We used SPSS 20 (IBM, USA) for statistical analysis. The Mann–Whitney U test was used for age analysis, and the chi-square test was used for gender and residence analysis. The confidence level was set at $P < 0.05$ unless specified otherwise.

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1. Overview of Outpatients

As a first-class Grade 3 psychiatric hospital, Xuzhou Oriental Hospital specializes in mental disorders with over 100,000 outpatients annually. Figure 1A

[Figure 1: see original paper] shows the total number of outpatients in 2017, 2018, and 2019. Compared with similar periods in 2017–2019 (see Methods for details), there was an increase in outpatient numbers in January 2020 (Fig. 1B). However, a significant decrease in outpatients occurred in the last 11 days of January 2020 (Fig. 1C). In 2020, daily visits during the Spring Festival period (January 20–31) were 43% lower than in early and mid-January (January 1–20). From 2017–2019, daily visits were only 17% lower. This suggests that the sharp decrease in outpatients could result from both nationwide traffic restrictions and the approaching Spring Festival. To minimize seasonal influence, all subsequent analyses were calculated as the proportion of schizophrenia relative to the total number of outpatients unless specified otherwise.

2. First-Time Patients Increased in Late January 2020

Among 13,783 outpatients in January 2020, 12,015 received a final diagnosis while the rest came for counseling. There were 1,210 first-time patients (8.75%) and 12,573 returning patients (91.22%). In recent case discussions, several doctors from different departments reported a significant increase in schizophrenia (F20) among first-time patients since the COVID-19 outbreak. We analyzed both first-time and returning patients to validate this observation. Raw patient numbers are provided in Table 1 .

Fig. 2 [Figure 2: see original paper] shows the relative change in incidence for first-time outpatients (Fig. 2A) and returning outpatients (Fig. 2B) near the Spring Festival. Compared with averaged data from 2017–2019, we found a slight decrease in incidence among returning outpatients. For first-time outpatients, schizophrenia incidence increased 25% compared with early January and 10% compared with the averaged 2017–2019 data. These results confirm previous observations and suggest that the unusual rise in schizophrenia among first-time patients cannot be attributed to the holiday season alone.

3. A Positive Relationship Between Schizophrenia and COVID-19 Outbreak

To further examine the relationship between the rise in schizophrenia and the COVID-19 outbreak, we collected COVID-19 data from the website of the National Health Commission of the PRC (see Methods for details). Figure 3A [Figure 3: see original paper] shows the proportion of schizophrenia among first-time outpatients in January 2020 alongside nationwide COVID-19 case numbers. Both datasets showed highly consistent trends of change in January 2020, particularly in late January. To obtain reliable linear regression, we further clustered the data into six groups with five-day intervals, similar to Fig. 2. Linear regression showed good fit with an R^2 value of 0.753, suggesting a positive relationship between the unusual rise in schizophrenia among first-time patients and the COVID-19 outbreak.

4. Age is a Critical Risk Factor in New Schizophrenia Caused by COVID-19

To identify potential risk factors in COVID-19-induced schizophrenia, we analyzed limited personal information (age, gender, approximate address). One known feature of COVID-19 is its much higher lethality in elders, especially those with underlying diseases (Guan et al., 2020; Novel Coronavirus Pneumonia Emergency Response Epidemiology, 2020). Risk gradually increases in patients over 50 years of age, and 27% of patients over 65 have severe cases (Guan et al., 2020). Fig. 4A [Figure 4: see original paper] shows the age distribution of first-time patients diagnosed with schizophrenia, revealing an obvious right shift toward older ages. The median age significantly increased from 39 (2017–2019, n = 261) to 50 (2020, n = 45) (P = 0.011, Mann–Whitney U test), indicating that age is a risk factor in COVID-19-induced schizophrenia.

Gender is known to be a risk factor in multiple mental disorders (Riecher-Rossler et al., 2018; Keane et al., 2006). Figure 4B shows gender differences in schizophrenia between 2017–2019 and 2020. We found a slight but non-significant difference (^{2} = 0.884, P = 0.347, chi-square test), suggesting gender is not a risk factor here. This is also consistent with COVID-19 case reports showing no gender difference (Guan et al., 2020).

According to official reports from China CDC, by the end of January 2020, most COVID-19 infections occurred in urban regions, especially large cities such as Wuhan, with far fewer cases in suburban areas where population density is low. To examine whether residence is also a risk factor in COVID-19-induced schizophrenia, we investigated approximate addresses of first-time outpatients. We found a slight decrease in urban visits from 40.8% (2017–2019) to 35.29% (2020) (^{2} = 0.367, P = 0.545, chi-square test), which could be due to strict traffic control in urban areas.

Discussion

Previous research has shown that major crises and disasters can cause people to experience negative emotions such as anxiety, depression, and anger in the short term (Kane et al., 2018). Long-term effects include post-traumatic stress disorder, depression, phobia, obsessive-compulsive disorder, and substance abuse (Inoue et al., 2019; Reifels et al., 2019). Although these effects are widespread, such mental disorders have relatively limited impact on patients' social functioning (Razzouk, 2017). This retrospective study unexpectedly found that COVID-19 was associated with an abnormal short-term increase in first-onset schizophrenia cases. This may be a dangerous signal because schizophrenia belongs to severe mental disorders (Organization, 2017) that seriously affect patients' social functioning. Although the pathogenesis of schizophrenia remains unknown, stressful events or environments may lead to deterioration of psychiatric symptoms, possibly related to poor stress susceptibility in early stages of

schizophrenia (Horan et al., 2005). Recent news reports of abnormal or even anti-social behaviors have set off alarm bells, making it urgent to pay sufficient attention to the incidence of severe mental disorders.

Research has found that severe epidemics like SARS in 2003 can result in sharp rises in suicide rates, especially among elders (Chan et al., 2006), possibly due to collapse of social networks and difficulty obtaining medical services. As mentioned earlier, COVID-19 is also more lethal to elders, especially those over 65 (Guan et al., 2020). These findings all suggest that aged people may be mentally sensitive to the COVID-19 outbreak. Our results show that the COVID-19 outbreak increased schizophrenia risk in aged adults. Even more concerning, since the outbreak began, the daily lives of many Chinese people have been completely changed. To slow COVID-19' s rapid spread, many large cities have shut down public or even private transportation (e.g., Wuhan). When previous urgent crises occurred (e.g., SARS, Fukushima Daiichi, Chernobyl nuclear disaster), only limited numbers of people were affected or socially isolated, yet this still caused mental abnormalities such as alcohol abuse, depression, and PTSD (Morita et al., 2015; Pearson et al., 2013; Bromet et al., 2011). We have never encountered or foreseen a situation like today, where millions of people are restricted from going outside to minimize infection risk. Please note that our study only investigated unusual changes in schizophrenia during the first month since the COVID-19 outbreak. We might face more serious conditions in the near future because nobody knows how long the epidemic or strict regulations will last.

Another issue that differs greatly from previous situations like SARS in 2003 is that the world has become an information society over the past 20 years. Even if you live in a city with few or no infections, COVID-19' s rapid spread can still mentally affect you through various social media platforms. Uncountable news and information are generated on the Internet daily, and almost everyone has a smartphone to obtain the latest COVID-19 updates through social media (e.g., Twitter, Facebook, TikTok). While timely, transparent information is critically helpful for stopping severe infectious diseases like COVID-19, too much information might also burden everyone's nerves, especially after weeks of traffic control. This could also increase the risk of severe mental disorders such as schizophrenia.

Finally, please note that Xuzhou, where our hospital is located, has about 8 million population, with only 23 confirmed COVID-19 infections by the end of January 2020. If mental disorder numbers are already rising here in Xuzhou, what would the situation be like in Wuhan—a city with over 15 million population, where nearly twenty thousand have been infected by COVID-19? While nobody can answer this question now, everyone, especially psychiatrists, should prepare emergency plans to avoid mental hazards caused by the COVID-19 outbreak.

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Data Availability Statement

The data used in this study are available on request from the corresponding author.

Conflict of Interests

The authors declare that they have no conflict of interest.

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Figure 1. Overview of outpatients. (A) Yearly outpatients from 2017 to 2019. (B) Daily visits in January 2020 and similar periods from 2017–2019. (C) Daily visits in early (20 days before Spring Festival), middle (10 days before Spring Festival), and late January 2020 (Spring Festival). Similar periods: 20 days before Spring Festival (January 4–13 in 2017, January 23–February 1 in 2018, January 12–21 in 2019, January 1–10 in 2020, 10 days total), 10 days before Spring Festival (January 14–23 in 2017, February 2–11 in 2018, January 22–31 in 2019, January 11–20 in 2020, 10 days total), and Spring Festival (January

24–February 3 in 2017, February 12–22 in 2018, February 1–11 in 2019, January 21–31 in 2020, 11 days total). Data from 2017, 2018, and 2019 were averaged.

Figure 2. Relative change of incidence of first-time patients (A) and returned patients (B) near Spring Festival of 2017–2019 and 2020. Incidence is the proportion of schizophrenia in the total number of first-time outpatients. The relative change was calculated as the ratio to the first data point (in percentage). Data were aligned in the same way as Fig. 1C.

Figure 3. Coincidence of unusual increase of schizophrenia and outbreak of COVID-19. (A) Change of incidence in first-time outpatients (left Y-axis) and the number of infections with COVID-19 (right Y-axis). Data were aligned similarly to Fig. 1C except with an interval of 5 days. Please note that the right Y-axis is logscale due to the explosive growth of COVID-19. (B) Linear regression of schizophrenia and outbreak of COVID-19.

Figure 4. Risk factors in schizophrenia induced by COVID-19. (A) Distribution of age. (B) Distribution of gender. (C) Distribution of approximate residence. Data from the entire month of January 2020 were used. Data from similar periods in 2017–2019 were averaged.

Table 1. Diagnosis classification of outpatients in January 2020

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Note: Figure translations are in progress. See original paper for figures.