Original Article

Cohort Study to Determine Safety of Psychotropic Medications in Patients with COVID-19

Muhammad Zulkernain Anjum, Ghulam Hassan and Jehanzab

ABSTRACT

Objective: This research intends to identify whether or not patients with covid-19 may safely use psychiatric drugs.
Study Design: Cohort study
Place and Duration: This study was conducted at the Sahara Medical College Narowal from September, 2021 to March, 2022.
Methods: Total 220 patients of both genders addicted to psychotropic medications were presented in this study. After obtaining informed written consent, detailed demographics of enrolled cases included age, sex, BMI, place of living and education status. PCR test was used to diagnose infectious disease. Patients were both symptomatic and asymptomatic. Patients were given antibiotics to cure from infectious disease. Outcomes were assessed in terms of safety and mortality among all cases. SPSS 24.0 was used to analyze all data.
Results: We found that 140 (63.6%) cases were males and 80 (36.4%) cases were females. Mean age of the patients was 43.6±4.19 years and had mean BMI 26.8±6.35 years. Most common psychotic drug class was second generation followed by first generation, mood stabilizers, benzodiazepines and antidepressants among all cases. Co morbidities were respiratory disease, diabetes and hypertension among all cases. We found that, patients those used mood stabilizers had severity of disease and higher ICU stay as compared to the patients those used second generation antipsychotic class. We found higher numbers of mortality among patients of using mood stabilizers.
Conclusion: In this research, we found that persons hospitalized for major mental illness who were prescribed second-generation antipsychotics had a lower chance of contracting COVID-19 than those who were prescribed valproic acid (a mood stabilizer).

Keywords: Infectious Disease, Psychotropic Drugs, Mortality, Severity

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INTRODUCTION

Conventional clinical methods in several medical fields, including psychiatry, need to be rapidly adapted in response to the new coronavirus epidemic, which is a worldwide health emergency. Infection with the coronavirus COVID-19 may spread throughout the body and affect a variety of systems.

Interstitial pneumonia is a hallmark of this illness, and in roughly one out of every twenty symptomatic cases, it causes severe respiratory distress that requires extensive life support [1, 2]. The severity and death rates are higher in the elderly and in those with preexisting medical conditions[3].

In order to prevent complications and lower death rates, contemporary clinical regimens often make use of off-label uses of chloroquine, hydroxychloroquine, antiviral medication, anticoagulant prophylaxis, and immune system immunomodulatory (e.g. interferons). [4-7].

Combining COVID-19 therapy with the essential psychotropic medicines used to treat persistent mental problems might lead to dangerous additive effects and drug-drug interactions (DDIs). The risk of QT prolongation, torsade de pointes, and other adverse events that are highly dependent on the CYP3A or CYP2D6 enzymes may be increased, for instance, when pimozide is used in conjunction with atazanavir or lopinavir/ritonavir. Both quetiapine and ziprasidone have this problem. Patients with COVID-19 may have an increase in serum levels of these psychotropic medicines if they are administered in combination with atazanavir or lopinavir/ritonavir. The current quetiapine dosage guidelines with subject matter experts should be changed to a quetiapine dose sixfold lower, based on a case reports of COVID-19 patients diagnosed with delirium. [8]

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More recent cohort studies, as well as warning Food And drug Adverse Event Reporting System, have brought attention to QTc prolongation. In order to assess the potential for QTc prolongation in individuals using psychiatric medications in addition to COVID-19, the Tisdale Scoring System is highly suggested. Factors such as age, gender, existence of infarction, sepsis, heart problems, amount of clinical signs going to prolong drugs used, low potassium density (3.5 mmol), QTc timeframe at entry (450 ms), and the number of Clinical signs going to prolong drugs used are used to categorise patients as "low," "modest," or "high" risk.[9]

Patients hospitalized for severe mental illness are more vulnerable to infection, making it crucial to identify risk factors for infection within this population. Antipsychotic therapy is unlikely to explain for increased mortality risk, as shown in a trial of persons with severe mental illnesses contaminated with COVID-19, where death rates were similar for those taking and those not taking schizophrenia medications [10]. Nonetheless, the risks of infection and other undesirable consequences may be different for different drugs, both within and within pharmacologic groups. Based on in vitro indications of anti-SARSCoV-2 action, a number of psychiatric medicines, including several first-generation psychotropic drugs (phenelzine and hydrochloride) and antidepressant (fluvoxamine, in particular), were identified as possible therapeutic agents. There is a lack of consensus on the clinical relevance of these in vitro studies. Despite several studies establishing a link been shown between anti-depressants [11,12] and a significantly lower internal components of infection in people with COVID-19, no association has been found in small observational studies between the consumption of haloperidol16 or pioglitazone and the incidence of COVID-19 infection. These and other psychiatric medications, such as second-generation antipsychotics, may influence the host response to COVID-19 by modulating factors such the ratio of proinflammatory to anti-inflammatory cytokines. [13,14] Despite the use of these drugs in the treatment of individuals with severe mental illness, to our knowledge, no comprehensive examination of their connections with the likelihood of COVID-19 infection has been conducted in this group. [15] The major objective of this research would have been to determine the risk of COVID-19 infections caused to psychopharmacologic therapies among long-term inpatients suffering from severe mental illness. The mortality risk of patients with confirmed COVID-19 infection in the laboratory was also evaluated.

MATERIALS AND METHODS

This cohort study was conducted at Sahara Medical College Narowal and comprised of 220 patients addicted to psychotropic medications. After obtaining informed written consent, detailed demographics of enrolled cases included age, sex, BMI, place of living and education status. Patients <18 years of age and those did not provide any written consent were excluded from this study.

Patients were screened for SARS-CoV-2 using RT-PCR or a serum IgG assay and ranged in age from 18 to 70; all had a major mental disease such as schizophrenia, schizo affective, bipolar I disease, or sadness with psychotic characteristics. Adults committed to civil units are often transferred from psychiatric inpatient units at medical centers for treatment of serious and persistent mental symptoms, and they fulfill requirements for involuntary commitment underneath the Law of mental hygiene. The average duration of stay in ED is several years, in contrast to the comparatively short length of stay in acute care hospitals. All hospitals have nurses on duty around the clock, every day of the week, and they watch patients closely while they take their medications to make sure they really take them. A daily update was made to the register, and reports were filed backwards if necessary. Suspected patients are tested through reverse transcriptase-polymerase chain reaction (RT-PCR) for SARS-CoV-2. Antibodies to SARS-CoV-2 are detectable for at least 3 to 6 months after infection, and this test has been shown to have a sensitivity of 100% and specificity of 99.6%.

The main outcome was infection; individuals with just about any positive test results were deemed positive. Mortality from COVID-19 among individuals with laboratory-confirmed infection was a secondary outcome recorded in the registry and verified in the EHR. SPSS 24.0 was used to analyze all data.

RESULTS

Table No.1: Detailed characteristics of enrolled cases

Variables	Frequency	Percentage
Mean Age (years)	43.6±4.19	
Mean BMI (kg/m^2)	26.8±6.35	
Gender		
Male	140	63.6
Female	80	36.4
Education Status		
Yes	50	22.7
No	170	77.3
Place of Living		
Rural	150	68.2
Urban	70	31.8
Marital Status		
Yes	135	61.4
No	85	37.6

We found that 140 (63.6%) cases were males and 80 (36.4%) cases were females. Mean age of the patients was 43.6±4.19 years and had mean BMI 26.8±6.35

years. Majority of the cases were not educated 170 (77.3%) and 150 (68.2%) cases were from rural areas. 135 (61.4%) patients were married.(table 1).

Most common psychotic drug class was second generation 80 (36.4%) followed by first generation 65 (29.5%), mood stabilizers 50 (22.7%), benzodiazepines 15 (6.8%) and antidepressants 10 (4.5%) among all cases.(figure 1).

Among 220 cases, we found that majority of the cases 125 (56.8%) were symptomatic and frequency of asymptomatic cases were 95 (43.2%). (figure 2).

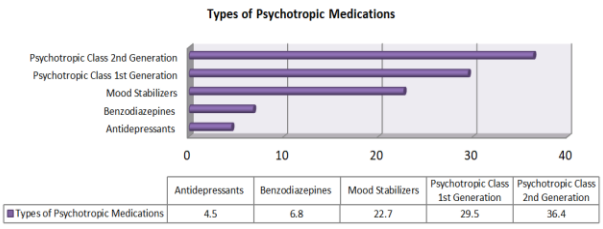

Figure No.1: Frequency of psychotropic drugs among all cases

Co morbidities were respiratory disease, diabetes, hypertension and cardiovascular disease among all cases. (table 2).

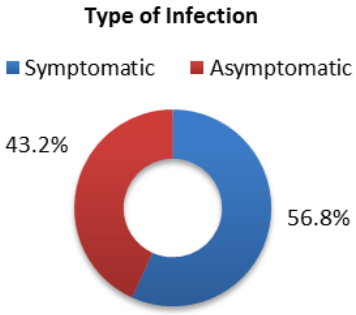

Figure No.2: Association of symptomatic and asymptomatic cases

Table No.2: Frequency of other diseases among all cases

Variables	Frequency	Percentage
Other Diseases		
respiratory disease	65	29.5
diabetes	40	18.2
hypertension	30	13.6
cardiovascular disease	17	7.7

We found that, patients those used mood stabilizers had severity of disease and higher ICU stay as compared to the patients those used second generation antipsychotic class.(table 3).

Table No.3: Severity of disease and hospital stay among cases with psychotropic drug indication

Variables	2nd Generation Of Psychotropic Drug Class (80)	1st Generation of Psychotropic Drug Class (65)	Mood stabilizers (50)	Benzodiazepines (15)	Anti-depressants (10)
Disease Severity					
Yes	30 (37.5%)	35 (53.8%)	40 (80%)	9 (60%)	5 (50%)
No	50 (62.5%)	30 (46.2%)	10 (20%)	6 (40%)	5 (50%)
Mean ICU Stay (days)	9.7±6.14	13.3±17.42	16.8±6.34	14.5±4.87	15.11±10.4

Table No.4: Comparison of mortality among all cases

Variables	2nd Generation Of Psychotropic Drug Class (80)	1st Generation Of Psychotropic Drug Class (65)	Mood stabilizers (50)	Benzodiazepines (15)	Anti-depressants (10)
Mortality					
Yes	12 (15%)	15 (23.1%)	27 (54%)	8 (53.3%)	3 (30%)
No	68 (85%)	50 (76.9%)	23 (46%)	7 (46.7%)	7 (70%)

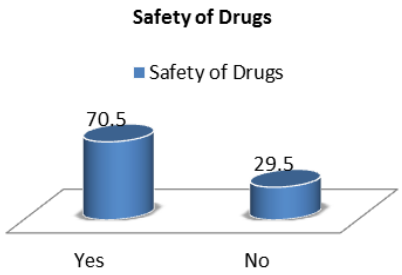

Figure No.3: Safety of psychotropic drugs-drugs interaction among all cases

We found higher numbers of mortality among patients of using mood stabilizers.(table 4). We found that 155 (70.5%) cases showed safety by using psychotropic medications with resistance to drugs used in prevention to coronavirus disease.(figure 3).

DISCUSSION

Evidence suggests that antipsychotics and COVID-19 medicines interact largely via pharmacologic and toxicokinetic drug side effects, which might result in changes in plasma drug levels that may reduce treatment effectiveness or raise the risk of harm [16]. Thus, early recognition of these interactions and rapid interventions are helpful in optimizing pharmacological therapy for the treatment of psychological diseases in COVID-19 patients.[17]

To improve pharmacotherapy and safeguard patients, pharmacological and toxicological databases are an indispensable tool for doctors to use when writing prescriptions in clinical practice. In this study, researchers analyzed six different databases to determine the prevalence of moderate-to-severe/ contraindicated/life-threatening potential drug-drug interactions. [18]

In current study 220 cases of psychotropic drug addicted had infectious disease COVID-19 were included. 140 (63.6%) cases were males and 80 (36.4%) cases were females. Mean age of the patients was 43.6±4.19 years and had mean BMI 26.8±6.35 years. Majority of the cases were not educated 170 (77.3%) and 150 (68.2%) cases were from rural areas. 135 (61.4%) patients were married. These results were comparable to the prior studies.[19,20] For persons with COVID-19, we observed that there are possible safety concerns with all kinds of psychotropic medicines. Considering the lack of data and the indirect nature of the populations at issue, the level of risk posed by particular agents or class of drugs was, in most instances, unknown or inaccurate. Unavoidably in clinical practice, the risk of negative outcomes has to be carefully considered on a specific instance basis, in view of a variety of confounding risk variables. As a result, it is difficult to provide suggestions that are tied to certain clinical scenarios or drugs. In addition, there is substantial overlap between the several types of safety concerns that have been studied independently. Due to the sedative impact of drugs and the increased susceptibility to respiratory infections, breathing difficulties may occur.[21]

Since the beginning of the COVID-19 pandemic,[22] several psychotropic medications and their potential risks and benefits have been the subject of preclinical and clinical studies. However, to the knowledge, this is largest study to methodically assess affiliations between the administration of individual meds and the threat of COVID-19 infectious disease between many in patients with severe mental illness. There was a reduced risk of infection with the use of 2nd antipsychotics. Paliperidone was connected with the biggest impact size. Although there was a trend toward a protective link between mortality and the use of second-generation antipsychotics, this trend was not statistically significant. Although in vitro research suggests that first-generation antipsychotics (in particular, haloperidol) interact with sigma-1-receptors to inhibit SARS-CoV-2 replication, our results go counter to what would be predicted based on this evidence. [23]

In our study, we found that majority of the cases 125 (56.8%) were symptomatic and frequency of asymptomatic cases were 95 (43.2%). Most common psychotic drug class was second generation 80 (36.4%) followed by first generation 65 (29.5%), mood stabilizers 50 (22.7%), benzodiazepines 15 (6.8%) and antidepressants 10 (4.5%) among all cases. To aid doctors in the evaluation and management of risk associated with psychotropic medicines, specific guidelines were developed. Changing the dosage of medicinal or psychiatric drugs is likely a satisfying and realistic safety precaution in many circumstances. When major side effects are possible, it may be essential to discontinue the offending drug or switch to one that poses less risk. An accurate evaluation of current psychopathy is crucial (considering, for example, that antidepressants and clonazepam are frequently prescribed inappropriately), as some patients' conditions require continuous psychotropic treatment (e.g., lengthy maintenance with psychiatric drugs or mood stabilizers), while others may benefit from reduced medication dosages or even discontinuation of treatment.[24,25]

We found that, patients those used mood stabilizers had severity of disease and higher ICU stay as compared to the patients those used second generation antipsychotic class. In current study, patients those used mood stabilizers had severity of disease and higher ICU stay as compared to the patients those used second generation antipsychotic class. Previous research showed comparable results to our study.[26]

CONCLUSION

In this research, we found that persons hospitalized for major mental illness who were prescribed second-generation antipsychotics had a lower chance of contracting COVID-19 than those who were prescribed valproic acid (a mood stabilizer).

Author's Contribution:

Concept & Design of Study:	Ghulam Hassan
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Revisiting Critically:	Ghulam Hassan, Muhammad Zulkernain Anjum
Final Approval of version:	Ghulam Hassan

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. JAMA 2020.
2. Grasselli G, Pesenti A, Cecconi M. Critical care utilization for the COVID-19 outbreak in Lombardy, Italy: early experience and forecast during an emergency response. JAMA 2020.
3. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. Int J Infect Dis 2020;94:91–95.

4. Cao B, Wang Y, Wen D, et al. A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. N Engl J Med 2020;382(19):1787-99.
5. Jin Y-H, Cai L, Cheng Z-S, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Military Med Research 2020;7(1):4.
6. World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: interim guidance. 2020. https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected. Accessed 14 May 2020.
7. World Health Organization. Landscape analysis of therapeutics as 21st March 2020. 2020. https://www.who.int/blueprint/priority-diseases/key-action/Table_of_therapeutics_Appendix_17022020.pdf. Accessed 14 May 2020.
8. Sampson MR, Cao KY, Gish PL, et al. Dosing recommendations for quetiapine when co-administered with HIV protease inhibitors. J Clin Pharmacol 2019;59:500–9.
9. Tisdale JE, Jaynes HA, Kingery JR, et al. Development and validation of a risk score to predict QT interval prolongation in hospitalized patients. Circ Cardiovasc Qual Outcomes 2013; 6:479–87.
10. Nemani K, Conderino S, Marx J, Thorpe LE, Goff DC. Association between antipsychotic use and COVID-19 mortality among people with serious mental illness. JAMA Psychiatr 2021;78(12): 1391-1393.
11. Plaze M, Attali D, Petit AC, et al. Repurposing chlorpromazine to treat COVID-19: the recovery study. Encephale 2020;46(3):169-172.
12. Reis G, Dos Santos Moreira-Silva EA, Silva DCM, et al. Together investigators. Effect of early treatment with fluvoxamine on risk of emergency care and hospitalisation among patients with COVID-19: the together randomised, platform clinical trial. Lancet Glob Health 2022;10(1): e42-e51.
13. Hoertel N, Sánchez-Rico M, Vernet R, et al. AP-HP/Universities/INSERM COVID-19 Research Collaboration and AP-HP COVID CDR Initiative. Association between antidepressant use and reduced risk of intubation or death in hospitalized patients with COVID-19: results from an observational study. Mol Psychiatr 2021; 26(9):5199-5212.
14. Hoertel N, Sánchez-Rico M, Vernet R, et al; AP-HP/Universities/INSERM COVID-19 research collaboration and AP-HP COVID CDR Initiative. Observational study of haloperidol in hospitalized patients with COVID-19. PLoS One 2021;16(2): e0247122.
15. Hoertel N, Sánchez-Rico M, Vernet R, et al; AP-HP/Universities/INSERM COVID-19 Research Collaboration and AP-HP COVID CDR Initiative. Observational study of chlorpromazine in hospitalized patients with COVID-19. Clin Drug Investig 2021;41(3):221-233.
16. Izci F, Kulacaoglu F: Drug interactions between COVID-19 and psychiatric medications: a mini review. J Neurobehav Sci 2020;7:103-8.
17. Zhang K, Zhou X, Liu H, Hashimoto K: Treatment concerns for psychiatric symptoms in patients with COVID-19 with or without psychiatric disorders. Br J Psychiatr 2020;217:351.
18. Shareef J, Belagodu Sridhar S, Thomas S, et al. Potential Psychotropic and COVID-19 Drug Interactions: A Comparison of Integrated Evidence from six database programs. Cureus 2021;13(12): e20319.
19. Ostuzzi, G., Papola, D., Gastaldon, C. et al. Safety of psychotropic medications in people with COVID-19: evidence review and practical recommendations. BMC Med 2020;18:215.
20. Jönsson AK, Schill J, Olsson H, Spigset O, Hägg S. Venous thromboembolism during treatment with antipsychotics: a review of current evidence. CNS Drugs. 2018;32(1):47–64.
21. Morgan ET. Impact of infectious and inflammatory disease on cytochrome P450-mediated drug metabolism and pharmacokinetics. Clin Pharmacol Ther 2009;85(4):434–8.
22. Stip E, Arnone D, Abdel Aziz K, Javaid SF. Diversity of mechanism of action of psychotropic drugs in their antiCOVID-19 properties. Mol Psychiatr 2021;26(12):7093-7097.
23. Gordon DE, Hiatt J, Bouhaddou M, et al. Comparative host–coronavirus protein interaction networks reveal pan-viral disease mechanisms. Science 2020;370(6521):eabe9403.
24. Beckett RD, Stump CD, Dyer MA: Evaluation of drug information resources for drug-ethanol and drug-tobacco interactions. J Med Libr Assoc 2019; 107:62-71.
25. Izci F, Kulacaoglu F: Drug interactions between COVID-19 and psychiatric medications: a mini review. J Neurobehav Sci 2020;7:103-8.
26. Murphy S, O'Reilly D, Owen R, Akbari A, Lowthian E, Bedston S, et al. Variations in COVID-19 vaccination uptake among people in receipt of psychotropic drugs: cross-sectional analysis of a national population-based prospective cohort. Br J Psychiatr 2022.