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Letter to the Editor



Letter on: "Lower risk of SARS-CoV2 infection in individuals with severe mental disorders on antipsychotic treatment: A retrospective epidemiological study in a representative Spanish population"

We read with interest the article by Canal-Rivero et al. (2021) that investigated the association between the use of antipsychotics and SARS-CoV-2 infection. The authors found that patients with severe mental disorders on antipsychotics have significant lower risk of SARS-CoV-2 infection compared to the general population. Also, they found that patients on antipsychotics have lower risk for COVID-19 related hospitalization, Intensive Care Unit (ICU) admission and deaths. Because their findings are important to current practice and may guide future studies, several concerns deserve attention.

First of all, the absence of data about the comparison group is worrisome. Since the comparison group may have several factors that may predispose them to SARS-CoV-2 infection for example several studies showed that obesity increased the risk of SARS-CoV-2 infection which may explain why the comparison group had higher rates of infection (Roca-Fernández et al., 2021). Similarly, the comparison population may have several comorbidities like diabetes, cardiovascular diseases and chronic kidney diseases that can render them susceptible to severe and fatal COVID-19 as these comorbidities have been linked to adverse outcomes among COVID-19 patients (Fresán et al., 2021). Also, the use of concomitant medications is another concern as several medications have been associated with better COVID-19 outcomes like metformin and statins and the use of these drugs maybe was higher among the mental disorders group. Without the aforementioned data about the comparison group and the use of regression models, the confounding bias can be of a major concern.

Second, the literature supports the evidence that patients with mental disorders had higher risk of COVID-19 infection by around 10 folds for schizophrenia patients and 7 folds for bipolar disorders patients (Wang et al., 2021) as patients with mental disorders tend to neglect protecting themselves and delaying the seek for medical attention. In regards the COVID-19 outcomes among patients with mental disorders, the literature is more consistent as a recently published meta-analysis showed that patients with mental disorders had higher odds for ICU admission, mechanical ventilation and death compared to normal population even after adjusting for the most important comorbidities and medications (Toubasi et al., 2021). Likewise, a new preprint article showed that the risk of dying from COVID-19 among patients with mental disorders was higher compared to dying due to other causes (Kirov and Baker, 2021). Furthermore, studies showed that patients with severe mental disorders like schizophrenia had higher risk of COVID-19 mortality compared to milder mental disorders like mood disorders (Nemani et al., 2021; Toubasi et al., 2021). Moreover, some studies showed that patients with severe mental disorders may have lower rates of admission not due to the milder course of COVID-19 but due to the characteristics of those patients for example they may have more social

isolation, less autonomy and tend more to ask for do not resuscitate order (Ruijs et al., 2011) as these are very important factors in the literature that is associated with the decision to admit or refuse patients to the ICU.

Lastly, the article did not provide any information about the types of antipsychotics that were used as different drugs cause different effects for example some mental disorders medications showed to adversely interact with and decrease the efficacy of COVID-19 treatment medications (Mohebbi et al., 2020). In comparison fluvoxamine showed promising preliminary results in the treatment of COVID-19 patients in randomized clinical trials (Lenze et al., 2020).

In conclusion, the results of this article must be interpreted cautiously as several adjusted retrospective cohort studies contradict its results. In the future, well controlled prospective studies are needed to explore the association between antipsychotics use and the development of COVID-19 and its related outcomes.

Declaration of competing interest

The authors declare that there is no conflict of interest.

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Author contributions

All the authors have participated and have made substantial contributor for this paper.

References

Canal-Rivero, M., Catalán-Barragán, R., Rubio-García, A., Garrido-Torres, N., Crespo-Facorro, B., Ruiz-Veguilla, M., 2021. Lower risk of SARS-CoV2 infection in individuals with severe mental disorders on antipsychotic treatment: a retrospective epidemiological study in a representative Spanish population. Schizophr. Res. 229, 53-54

Fresán, U., Guevara, M., Trobajo-Sanmartín, C., Burgui, C., Ezpeleta, C., Castilla, J., 2021. Hypertension and related comorbidities as potential risk factors for COVID-19 hospitalization and severity: a prospective population-based cohort study. J. Clin. Med. 10 (6).

Kirov, G., Baker, E., 2021. COVID-19 and Mortality Risk in Patients With Psychiatric Disorders, 2021.2004.2008.21255046.

Lenze, E.J., Mattar, C., Zorumski, C.F., Stevens, A., Schweiger, J., Nicol, G.E., Miller, J.P., Yang, L., Yingling, M., Avidan, M.S., Reiersen, A.M., 2020. Fluvoxamine vs placebo and clinical deterioration in outpatients with symptomatic COVID-19: a randomized clinical trial. JAMA 324 (22), 2292–2300.

Mohebbi, N., Talebi, A., Moghadamnia, M., Nazari Taloki, Z., Shakiba, A., 2020. Drug interactions of psychiatric and COVID-19 medications. Basic Clin. Neurosci. 11 (2), 185–200

- Nemani, K., Li, C., Olfson, M., Blessing, E.M., Razavian, N., Chen, J., Petkova, E., Goff, D. C., 2021. Association of psychiatric disorders with Mortality among patients with COVID-19. JAMA Psychiatry 78 (4), 380–386.
- Roca-Fernández, A., Dennis, A., Nicholls, R., McGonigle, J., Kelly, M., Banerjee, R., Banerjee, A., Sanyal, A.J., 2021. Hepatic steatosis, rather than underlying obesity, increases the risk of infection and hospitalization for COVID-19, 8 (336).
- Ruijs, C.D., Kerkhof, A.J., van der Wal, G., Onwuteaka-Philipsen, B.D., 2011. Depression and explicit requests for euthanasia in end-of-life cancer patients in primary care in the Netherlands: a longitudinal, prospective study. Fam. Pract. 28 (4), 393–399.
- Toubasi, A.A., AbuAnzeh, R.B., Tawileh, H.B.A., Aldebei, R.H., Alryalat, S.A.S., 2021.

 A meta-analysis: the mortality and severity of COVID-19 among patients with mental disorders. Psychiatry Res. 299, 113856.
- Wang, Q., Xu, R., Volkow, N.D., 2021. Increased risk of COVID-19 infection and mortality in people with mental disorders: analysis from electronic health records in the United States, 20 (1), 124–130.

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