



Letter to the Editor

**The role of antipsychotics against COVID-19: A topic for debate**

To the editors,

We are very grateful for the comments made to our publication “Lower risk of SARS-CoV-2 infection in individuals with severe mental disorders on antipsychotic treatment: A retrospective epidemiological study in a representative Spanish population” as well as to the Editors of Schizophrenia Research for the opportunity to respond to the observations. The relevance of the impact of COVID-19 on mental health in the general population, healthcare workers, mental health users and health care system is unquestionable and needs to be discussed (Crespo-Facorro, 2020; Vieta et al., 2020).

Firstly, we would like to emphasize that the publication derived from clinical observation in our own hospital. In particular, we noticed that severe mental health patients infected by SARS-CoV-2 who presented marked COVID-19 risk factors did not show bad prognosis. It is worth noting, that this clinical observation was also reported by other clinicians in other countries (Dratcu & Boland; Unpublished manuscript). On the other hand, the risk of COVID-19 infection and mortality in severe mental health patients in our catchment area was lower than reported in scientific literature.

The high prevalence of COVID-19 risk factors among mental health patients has been widely demonstrated. This information was not included due to the limitations of the publication format. In our study, we have only registered COVID-19 risk factors in those patients who were infected by SARS-CoV-2 ($n = 9$). In particular, we observed that the prevalence of COVID-19 risk factors was as follows: 0% diabetes, 22.2% respiratory diseases, 11.1% dementia, 11.1% cardiovascular disease, 11.1% hypertension, 33.3% smokers or 44.4% obesity.

The obesity rate among mental health patients is remarkable. On this subject, Zheng et al. found that the presence of obesity with metabolic-associated fatty liver disease (MAFLD) predicted increased risk of severe COVID-19 disease (Zheng et al., 2020). Our group showed that mental health patients under antipsychotic treatment develop a predictor of fatty liver disease in a somewhat period of time after the onset of mental health disorder (Morlán-Coarasa et al., 2016). Taken into consideration both findings, it might be interesting to explore the role of both factors in the course of COVID-19 disease among mental health users.

Antipsychotics could be used for the pharmacological management of COVID-19 complications such as anxiety, delirium, agitation or sleep disturbances. In fact, possible drug-drug interactions between antipsychotic treatments and COVID-19 treatments should be considered (Plasencia-García et al., 2021). Information about antipsychotic treatment was not provided in our publication. The main reason for the lack of this information was the word limit for letter to the Editors. In particular, we considered only those adherents (defined as proportion of the days covered of $\geq 80\%$ in the last year) patients on long-acting injectable (LAI) antipsychotic treatment such as aripiprazole (35.2%), paliperidone (51.6%), risperidone (6.9%) and zuclopenthixol (6.3%). In

this regard, and in line with the results of the letter, our group has recently reported that aripiprazole reverted the changes caused by COVID-19 in gene expression which could validate aripiprazole as treatment for COVID-19 (Crespo-Facorro et al., 2021).

From our point of view, we included in the letter some of the appreciations made by Dr. Toubasi such as the absence in the analyses of factors involved in the complex network of COVID-19 disease. Besides, in the last paragraph of the letter, we have also recognised that the findings were counterintuitive in relation to the data published so far (Canal-Rivero et al., 2021). On the other hand, most of the publications that have reported high rates of mortality or worse prognosis in mental health patients have used electronic records data which are characterized by important limitations such as not including sensitive information in the analyses (e.g., socioeconomic, lifestyle conditions, antipsychotic treatment or adherence to medication).

Lastly, we agree with the observation that multivariate analyses allows to get more realistic and nearer to the reality. However, since the main aim of the letter was to describe the prevalence and prognosis of COVID-19 in severe mental health patients under LAI treatment we considered that bivariate analyses were appropriate for the purpose of the study.

In conclusion, and as was mentioned in the original letter, the results have to be taken judiciously. On the other hand, further studies are required to elucidate possible role of antipsychotic in preventing SARS-CoV-2 infection as well as its possible protective effects against detrimental courses of COVID-19. Finally, we would like to highlight that the publication of results that differ from those previously published do not call into question their veracity. In fact, it enriches the knowledge we have about the prevalence, prognosis and transmission of SARS-CoV-2 in people diagnosed with a severe mental disorder.

Author's contributions

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

Declaration of competing interest

The authors have no conflicts of interest concerning the subject of the study.

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