

### Covid-19, hypercoagulability and risk of mortality in schizophrenia

Carles Garcia-Ribera<sup>1,3</sup>  
Marina Carrasco<sup>2</sup>  
Ada Ruiz-Ripoll<sup>3</sup>

<sup>1</sup> Servicio de Psiquiatría. UAB Hospital de Sant Pau. Barcelona

<sup>2</sup> Servicio de Hematología. Unidad de Hemostasia.  
UAB Hospital de Sant Pau. Barcelona

<sup>3</sup> Societat Catalana de Psiquiatria i Salut Mental. Barcelona

#### Dear Editor,

Covid-19 disease has been linked to a high risk of hypercoagulability that can severely condition the evolution of this respiratory syndrome in the acute phase; and also due to the possible sequelae of a chronic thrombosis, as is the case of chronic pulmonary thromboembolism; or due to complications associated with anticoagulant treatment such as bleeding<sup>1</sup>. The pathophysiology of this hypercoagulable state that is largely unknown, is characterized by an increase in D-dimer. This has led to the suggestion of systematic prophylaxis with heparin in hospitalized patients, being assessed individually in outpatients. Although due to the atypicality of this hypercoagulable state, more specific interventions are also recommended depending on the altered parameters<sup>2</sup>.

It has been observed that patients diagnosed with schizophrenia have a higher mortality from Covid-19. It does not appear that these patients present a higher rate of virus infection, but the morbidity and mortality rate is clearly higher, regardless of sociodemographic factors and clinical comorbidity. This has led to consider the diagnosis of schizophrenia a risk factor for mortality from Covid-19 at the level of the older factor<sup>3,4</sup>.

It has been suggested that the medical comorbidities and the social isolation of the schizophrenic patient would facilitate the presentation of a more complex and serious medical situation, conditioning a more torpid evolution once hospitalized. However, as has been commented, mortality remains high even after adjusting the models for comorbid clinical factors, including those related to the metabolic syndrome. Thus, it has been postulated that this increased risk of mortality could be related more specifically to the nature of the schizophrenic disorder itself or

to its psychopharmacological treatment. In this sense, alterations in the immune response observed in schizophrenia are pointed out, such as: dysfunctions in the major histocompatibility complex, in the response of T cells or in the signaling of pro-inflammatory cytokines; as well as an increased risk of presenting pneumonia related to side effects of antipsychotic drugs such as dysphagia and increased salivation<sup>3,4</sup>.

A factor that has not been specifically mentioned and that we want to highlight is the increased risk of thromboembolic phenomena related to antipsychotic treatment<sup>5</sup>. This increased risk has been related to collateral effects such as sedation and immobilization; with weight gain; or with the presence of hyperprolactinemia that would facilitate the aggregation of platelets. Due to this, extreme precautions must be taken when other thromboembolic risk factors such as: clinophilia, immobilization, nutritional deficiencies in B12, B6 and Folic Acid, that facilitate a state of hyperhomocysteinemia, tobacco or coffee consumption, or concomitant treatment with anovulatory agents, for referring some of them.

In addition, this increased risk of patients undergoing antipsychotics of presenting thromboembolic phenomena may be increased by prostration and immobilization in the context of a viral condition and it is possible that pathophysiological mechanisms specifically linked to the inflammatory response caused by the Covid-19 virus that further increase the risk are added.

Therefore, in the current context of pandemic, we call attention to extreme precautions in the care of the patient with schizophrenia in case of presenting a viral syndrome; consider establishing hygienic measures that reduce thromboembolic risk and assess the need for thromboembolic prophylaxis, regardless of other criteria applied in the general population such as an increase in D-dimer. It must be remembered that schizophrenic patients frequently suffer distortions in the perception of their corporality or in the ability to express their discomfort or their symptoms that can facilitate inattention.

Finally, in our opinion, patients with severe mental health problems under treatment with antipsychotics represent a priority risk group for vaccination.

---

## LETTER TO THE EDITOR

---

### REFERENCES

1. Asakura, H., & Ogawa, H. (2021). COVID-19-associated coagulopathy and disseminated intravascular coagulation. *International Journal of Hematology*. <https://doi.org/10.1007/s12185-020-03029-y>
2. Tomo, S., Kumar, K. P., Roy, D., Sankanagoudar, S., Purohit, P., Yadav, D., ... Misra, S. (2021). Complement activation and coagulopathy - an ominous duo in COVID19. *Expert Review of Hematology*. <https://doi.org/10.1080/17474086.2021.1875813>
3. Nemani, K., Li, C., Olfson, M., Blessing, E. M., Razavian, N., Chen, J., ... Goff, D. C. (2021). Association of Psychiatric Disorders with Mortality among Patients with COVID-19. *JAMA Psychiatry*. <https://doi.org/10.1001/jamapsychiatry.2020.4442>
4. Tzur Bitan, D., Krieger, I., Kridin, K., Komantscher, D., Scheinman, Y., Weinstein, O., ... Feingold, D. (2021). COVID-19 Prevalence and Mortality Among Schizophrenia Patients: A Large-Scale Retrospective Cohort Study. *Schizophrenia Bulletin*. <https://doi.org/10.1093/schbul/sbab012>
5. Liu, Y., Xu, J., Fang, K., Xu, Y., Gao, J., Zhou, C., ... Wang, C. (2021). Current antipsychotic agent use and risk of venous thromboembolism and pulmonary embolism: a systematic review and meta-analysis of observational studies. *Therapeutic Advances in Psychopharmacology*. <https://doi.org/10.1177/2045125320982720>