



Psychiatric outcomes in patients hospitalized during the first wave of COVID-19 in Milan: A cohort study

As for previous pandemics, COVID-19 had a significant impact on the mental health of the affected population. From the inflammatory action of the virus to the psychological distress related to isolation and the uncertainty of prognosis, there are many factors that weigh on the mental status of people with COVID-19 disease (Stearo et al., 2020). Such multifactorial risk for a deterioration of mental health suggests the need to identify groups of patients with psychiatric vulnerability and to establish strategies of intervention based on scientific evidence (Holmes et al., 2020). However, at the peak of the pandemic several studies did not explain how and when diagnoses were made, nor if a broadly accepted diagnostic instrument was used (Taquet et al., 2021). In this short letter we report the findings of a rigorous follow-up that was conducted on a cohort of patients hospitalized for COVID-19 at the ASST Santi Paolo e Carlo University Hospital in Milan, Italy. The aim of the study was to identify psychiatric outcomes one year after recovery from a COVID-19 hospitalization and possible associations between these and the clinical, anamnestic, and sociodemographic variables of the sample.

We conducted a retrospective cohort study of the first 100 patients who accepted to participate among those discharged between March and April 2020. All patients who accessed the hospital's multidisciplinary follow-up outpatient service were asked to participate between 9 and 12 months after discharge. The only exclusion criteria employed were an age < 18 and insufficient understanding of the Italian language. Patients were 72% male, with an average age of 58.7 years old ($SD = 11.8$), a minimum of 28 and a maximum of 83 years. A medical investigator employed the Mini International Neuropsychiatric Interview (MINI-Plus), for the assessment of current and lifetime psychiatric diagnoses. The clinical interview was conducted in person or by remote contact, whenever necessary. Furthermore, a team of medical and psychological investigators retrospectively collected several participants' socio-demographic and clinical variables from hospital inpatient and outpatient charts.

The Kendall rank correlation coefficient was employed to measure the ordinal association between available clinical-demographic variables and the psychiatric diagnoses of patients. Bivariate correlation was used to explore the association between psychiatric outcomes and the sample characteristics, which were divided into demographic (gender, age, socioeconomic status), pre-hospitalization vulnerability (BMI, therapy for COVID-19 infection at home, smoking history), and hospitalization measures (presence of delirium, days of hospitalization, oxygenation intensity, bereavement during the pandemic). Almost one third (29%) of subjects screened positive for a diagnosis of a new psychiatric disorder, and a novel onset of psychiatric morbidity did not dif-

fer significantly in patients with and without a positive history of mental illness (respectively 42% and 58% of the sample). New psychiatric disorders were grouped into stress reactions (19%), anxiety, somatoform and obsessive-compulsive disorders (12%), and mood disorders (5%).

Concerning demographic characteristics, advanced age clearly represented a protective factor against the onset of new psychiatric disorders ($r_t = -0,203$, $p = 0,008$). Although this has been previously shown (Parlapani et al., 2021), reducing the surveillance over the mental health of more advanced age groups cannot be advised. Indeed, despite a lower frequency of psychiatric outcomes, these patients show worse adaptation to their onset compared to younger individuals (Hamm et al., 2020). Despite a lower risk of contracting SARS-Cov2 infection, women in our cohort were more vulnerable to psychiatric post-COVID symptoms ($r_t = 0,190$, $p = 0,029$). Such considerable differences confirm the need for differentiated pathways of care that were commonly proposed before the pandemic (The Lancet Psychiatry, 2016).

The correlation between the onset of new psychiatric disorders and some pre-admission vulnerability factors, such as an overweight and/or obesity condition ($r_t = 0,185$, $p = 0,026$) and a positive medical history for cigarette smoking ($r_t = 0,203$, $p = 0,026$), were statistically significant. Moreover, subjects who reported taking a therapy to control the infection prior to hospitalization were more likely to receive a new psychiatric diagnosis ($r_t = 0,269$, $p = 0,005$). Although these findings should be interpreted with caution, taken together they might suggest a higher risk of novel psychiatric diagnoses in patients with a higher baseline inflammatory condition (obesity and smoking) or a longer period of symptomatic illness managed at home.

Of note, variables related to the severity of hospitalization such as oxygenation intensity, days of hospitalization, or requirement of intensive care, as well as bereavement during convalescence, were not associated with new psychiatric diagnoses, unlike some studies which endorsed the neuroinflammatory hypothesis (Stearo et al., 2020) of psychiatric pathology in COVID patients. The impact of delirium, a putative risk factor for neuropsychiatric outcomes (Stearo et al., 2020), could not be reliably investigated by our study given the very low incidence observed in our cohort, perhaps due to a selection bias of COVID survivors.

The strengths of this study are the rigorous follow-up conducted through a broadly accepted diagnostic instrument for all patients and the real-world nature of the cohort. However, the following limitations must be considered: first, the reduced sample size did not allow more sophisticated statistical modelling that would enrich our findings. Second, given the choice of recruiting a consecutive, chronological cohort

of discharged patients, our sample had considerable heterogeneity with a broad age range and substantial gender imbalance. Further research on larger cohorts is necessary to confirm the generalizability of our findings. Finally, the cross-sectional nature of diagnostic formulation in our study limits the possibility of drawing firm conclusions on participants' previous psychiatric history due to the inaccuracy of retrospective reporting; however, the MINI-Plus is extensively employed in research to minimize recall inaccuracy on previous experienced symptoms.

In conclusion, hospitalization linked to COVID-19 appears to be associated with the onset of psychiatric disorders, in a historical moment in which the evidence of long-term mental health outcomes of the infection itself are mounting (Taquet et al., 2021). Consistently, our findings coupled stress reactions, anxiety and mood disorders with individual variables that are perhaps predictive of the so-called "long COVID" psychiatric manifestations. Further investigation on the onset and course of physical symptoms such as fatigue, pain or dyspnea in these patients will help to clarify the relationship between mental and physical aspects of this emerging clinical syndrome.

Conflict of interest

The authors declare no conflict of interest.

Funding source

The study was part of the RECOVER clinical database funded by DG Welfare Regione Lombardia

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