Is COVID-19 Associated With Posttraumatic Stress Disorder?

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ABSTRACT

Objective: To assess the prevalence of and risk factors for posttraumatic stress disorder (PTSD) in patients with COVID-19.

Methods: We conducted a cohort study between March and May 2020 at the Lille University Hospital (France), including all patients with laboratory-confirmed COVID-19. Psychological distress symptoms were measured 3 weeks after onset of COVID-19 symptoms using the Impact of Event Scale-6 items (IES-6). The evaluation of PTSD symptoms using the PTSD Checklist for *DSM-5* (PCL-5) took place 1 month later. Bivariate analyses were performed to analyze the relationship between PCL-5 scores and the demographic and health variables. The significant variables were then introduced into a multivariable linear regression analysis to establish their relative contributions to the severity of PTSD symptoms.

Results: 180 patients were included in this study, and 138 patients completed the 2 evaluations. Among the 180 patients, 70.4% patients required hospitalization, and 30.7% were admitted to the intensive care unit. The prevalence of PTSD was 6.5%, and the predictive factors of PTSD included psychological distress at the onset of the illness and a stay in an intensive care unit.

Conclusions: The prevalence of PTSD in patients with COVID-19 is not as high as that reported among patients during previous epidemics. Initial psychological responses were predictive of a PTSD diagnosis, even though most patients showing acute psychological distress (33.5% of the sample) improved in the following weeks. PTSD symptoms also increased following a stay in an intensive care unit. Future studies should assess the long-term consequences of COVID-19 on patients' mental health.

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The novel coronavirus disease 2019 (COVID-19) outbreak spread rapidly around the world.[1] COVID-19 infection is known to be associated with respiratory distress and cardiovascular, gastrointestinal, and neuropsychiatric symptoms.[2,3] Negative effects on mental health, resulting from the uncertainty and the fear of a poorly understood disease as well as the drastic physical distancing and quarantine measures, have also been reported.[4,5] These poor outcomes are supported by studies investigating the psychological impact of previous health care crises such as the 2003 severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) epidemics as well as by more recent studies conducted during the COVID-19 pandemic.[3,5] Most of these studies showed high levels of anxiety, depression, insomnia, and psychological distress in the general population[6,7] and among health care workers.[8–12]

Very few studies have investigated mental health issues in patients with confirmed COVID-19, while it is well known that surviving a critical illness can lead to psychological distress and posttraumatic stress disorder (PTSD).[13] PTSD is a psychiatric disorder caused by a terrifying event, perceived as a trauma, that directly or indirectly affects the individual.[14] Because COVID-19 is a poorly understood disease associated with a risk of premature death and no vaccines or effective medical treatments, patients suffering from this infection are considered at high risk of developing PTSD.[15,16] A PTSD diagnosis requires specific symptoms, including intrusive distressing memories and dreams, avoidance behaviors related to internal and/or external reminders of the trauma, alterations in cognition and mood, and hypervigilance, to be present for more than 1 month after the trauma. The presence of similar symptoms before 1 month supports the diagnosis of acute stress disorder. PTSD can result in long-term adverse consequences and a poor quality of life, particularly if left untreated.[17]

Until now, 3 studies have evaluated posttraumatic symptoms in patients with COVID-19 during the acute phase of the illness.[4,15,18] The first brief report, by Bo et al,[15] reported a surprisingly high prevalence of significant posttraumatic symptoms of 96.2% (*DSM-IV* criteria, total PTSD Checklist-Civilian score ≥ 50) among the 714 included patients with COVID-19. The second study, performed by Guo et al,[18] found significantly more posttraumatic symptoms in patients with COVID-19 than in healthy control subjects. Although significantly different, both patients and healthy subjects groups presented a subclinical range of symptoms (PTSD Checklist for *DSM-5* [PCL-5] scores of 8 and 4, respectively), and only 1 patient among the 103 included had severe posttraumatic symptoms (PCL-5 score ≥ 33).[18] Finally, Qi et al[4] found posttraumatic symptoms (*DSM-IV* criteria, total PTSD Checklist-Civilian score ≥ 50) in 12.2% of the 41 patients included in their study.[4] Beyond the considerable heterogeneity in their results, all 3 studies measured posttraumatic symptoms experienced by patients for a period of less than 1 month, reflecting acute stress symptoms rather

Clinical Points

- COVID-19 infection is known to be associated with negative effects on mental health, but the traumatic impact of COVID-19 infection is unknown.
- Patients with COVID-19 are at risk of developing posttraumatic stress symptoms and need long-term monitoring and care.

than PTSD. Only 1 study[19] has examined PTSD in patients with COVID-19, and it found a prevalence of 12.4%. The authors identified severe COVID-19 symptoms, living with children, and the death of a family member as risk factors for PTSD. Nevertheless, this cross-sectional study conducted in Wuhan included only patients who had been treated at the hospital, which may have led to a significant selection bias.

In the present study, we aimed to assess the prevalence of PTSD in patients with laboratory-confirmed COVID-19 at Lille University Hospital Center in France and to identify predictive or protective factors of developing PTSD.

METHODS

Study Design and Population

The recruitment took place in the Lille University Hospital Center (France) during the French government–mandated quarantine, between March 17 and May 11, 2020. Patients were eligible for inclusion if they had a laboratory-confirmed diagnosis of COVID-19 and if they volunteered to participate and were 18 years or older. Patients were excluded if they presented communication problems that prevented their ability to respond to questionnaires (eg, deafness, dementia, mental retardation).

A cohort study including 2 measuring times was conducted: (1) the first assessment occurred during the patients' consultation in the Infectious Diseases department 3 weeks after onset of COVID-19 symptoms (or during the hospitalization, for patients who were still hospitalized), and (2) the second assessment was conducted by phone, by 3 qualified investigators 1 month after the first evaluation. The 3 investigators have clinical experience in the diagnosis and care of patients with posttraumatic symptoms and practical experience with the PCL-5.

Among the 209 eligible patients, 180 patients (86%) with laboratory-confirmed COVID-19 were included. The reasons for noninclusion were the patient's inability to respond to the questionnaires because they did not speak French or because of cognitive disorders. Among the 180 patients included at baseline, 138 completed the second assessment (ie, 23.3% were lost to follow-up). The groups of respondents and nonrespondents were comparable on all except 3 variables: there were more hospitalizations and stays in the intensive care unit (ICU) in the respondent group and more health care workers in the nonrespondent group.

Participants provided their verbal informed consent to be enrolled in the study. In France, confidentiality approval is only needed from the Commission Nationale de l'Informatique et des Libertés (CNIL) for noninterventional observational studies; ethical approval is not mandatory (French law 2004–800 on bioethics, August 6, 2004). This study was approved by the CNIL and the Local Data Protection Service (DEC20-155).

Demographic Data and Clinical Assessments

At baseline, patients were asked to complete the Impact of Event Scale-6 items (IES-6), a validated self-administered 6-item brief measure of posttraumatic stress reactions that assesses subjective distress caused by traumatic events during the past 7 days; a score greater than or equal to 10 indicates a high level of distress.[20]

Medical and demographic data, retrospectively extracted from the patient medical records, included age, sex, living situation, being a health care worker, history of psychiatric disorders, psychotropic medication at the time of infection, preexisting health conditions (including obesity, cardiovascular disease, diabetes, pulmonary disease), type of care (ambulatory, conventional hospitalization, or stay in an ICU) related to the COVID-19, and impact of COVID-19 on relatives (none, relative affected by, or death of a relative).

One month later, patients completed the PCL-5, a 20-item scale exploring PTSD symptom severity over the past month; a score greater than or equal to 33 indicates a probable diagnosis of PTSD.[21–23] Moreover, to ensure the presence of the PTSD criteria as defined by the *DSM-5*, another assessment method was used: PTSD was assumed in patients reporting at least (1) 1 reexperiencing symptom, (2) 1 avoidance symptom, (3) 2 negative alterations in cognition or mood symptoms, and (4) 2 arousal symptoms. A symptom was considered as present with a score above 1.[19]

Statistical Analysis

First, we described the sample using means and standard deviations or medians with interquartile ranges (IQRs) for quantitative variables that were normally distributed or not, respectively. Numbers and percentages were used for the scores classified by level and other qualitative variables. We compared the baseline characteristics of patients who responded to the second evaluation with those who did not, using 1-way analysis of variance for quantitative variables and χ^2 tests (or Fisher tests, the nonparametric counterpart) for qualitative variables.

Bivariate analyses were performed to analyze the relationship between PCL-5 scores and sociodemographic characteristics (age, sex, living situation, being a health care worker or not, the impact of the COVID-19 on relatives) as well as health (history of psychiatric disorder, physical comorbidities, psychological distress at first evaluation, psychotropic medication at the time of infection, and type of care for the COVID-19) variables. The variables for which the *P* value was less than .1 were then introduced in a multivariable linear regression analysis to establish their relative contributions to PTSD symptoms severity (as assessed by the PCL-5 score).

Table 1. Bivariate Analyses: PCL-5 Score According to the Subgroup

	Respondents, n (%)	PCL-5 Score, Mean (SD)	P[a]
Age			
< 55 y	92 (51.4)	6.8 (12.0)	.982
≥ 55 y	87 (48.6)	6.9 (9.9)	
Sex			
Men	79 (43.9)	5.9 (10.7)	.224
Women	101 (56.1)	8.1 (11.1)	
Living situation			
Alone	27 (16.2)	6.6 (10.6)	.629
With someone	140 (83.8)	8.4 (11.1)	
Health care worker			
Yes	45 (29.8)	4.9 (8.1)	
No	106 (70.2)	7.4 (11.7)	
Psychotropic medication			
Yes	15 (8.3)	17.8 (15.5)	**.001**
No	165 (91.7)	5.7 (9.7)	
History of psychiatric disorder			
Yes	25 (13.9)	13.2 (14.1)	**.008**
No	155 (86.1)	5.7 (9.8)	
Physical comorbidities			
Yes	73 (40.5)	7.0 (11.8)	.864
No	107 (59.5)	6.7 (10.2)	
Type of care			
Ambulatory	53 (29.6)	4.0 (8.2)	.057
Hospitalization	71 (39.7)	6.1 (9.9)	
ICU	55 (30.7)	9.6 (12.8)	
Impact on relatives			
No	108 (60.0)	5.9 (10.0)	.150
Yes	65 (36.1)	7.3 (11.7)	
Deceased	7 (3.9)	14.1 (13.5)	
IES-6			
< 10	119 (66.5)	2.3 (3.0)	**< .001**
≥ 10	60 (33.5)	14.6 (4.7)	

[a]Boldface indicates $P < .05$.
Abbreviations: ICU = intensive care unit, IES-6 = Impact of Event Scale-6 items, PCL-5 = PTSD Checklist for *DSM-5*.

Table 2. Multivariate Analyses: Factors Associated With PCL-5 Score

	Adjusted Mean PCL-5 Score Difference [95% CI]	P[a]
Psychotropic medication	6.5 [−0.3 to 13.3]	.062
History of psychiatric disorder	1.5 [−4.1 to 7.2]	.596
Hospitalization		
No	0 (ref)	
Yes	3.1 [−0.8 to 7.0]	.119
ICU	4.6 [0.6 to 8.6]	**.024**
IES-6 ≥ 10	11.1 [7.9 to 14.3]	**< .001**

[a]Boldface indicates $P < .05$.
Abbreviations: ICU = intensive care unit, IES-6 = Impact of Event Scale-6 items, PCL-5 = PTSD Checklist for *DSM-5*.

Associations between risk factors and outcomes were presented as the difference in mean PCL-5 scores and 95% confidence intervals (95% CIs).

Data analysis was performed using R 3.6.1. The significance level was set at $\alpha = .05$, and all tests were 2-tailed.

RESULTS

Baseline Characteristics

Among the 180 patients, 56.1% were men, the mean (± SD) age was 53 (± 16) years, 29.8% were health care workers, and 16.2% declared they lived alone. Regarding history and treatment, 13.9% of patients had a history of a psychiatric disorder, 8.3% were under treatment with psychotropic medication (antidepressants or anxiolytic), and 40.6% had physical comorbidities (9.4%, 6.7%, 25.6%, and 12.8% suffered from obesity, diabetes, cardiovascular disease, and pulmonary disease, respectively). The medical management of COVID-19 required hospitalization for 70.4% of the patients (with a median length of stay of 11 days) and a stay in an ICU for 30.7% of patients (with a median length of stay of 8 days). Among the 180 patients, 40.0% reported having a relative also affected by COVID-19, and 3.9% had lost a relative due to the disease. Finally, the mean (± SD) IES-6 score was 7.4 (± 6.0) out of 24, and 33.5% of patient scores were greater than or equal to 10.

PTSD and Associated Factors at 1 Month

At 1 month, the median (IQR) PCL-5 score was 6.8 (10.9) out of 80, 9 patients (6.5%) had a score greater than or equal to 33, and 10 (7.2%) reported all PTSD criteria as defined by the *DSM-5*. All of the patients with a probable diagnosis of PTSD at 1 month (regardless of the rating method) had an IES-6 score greater than or equal to 10 at baseline.

As described in Table 1, bivariate analyses revealed that psychotropic medication, preexisting psychiatric disorder, hospitalization, and a high IES-6 score (≥ 10) were associated with a higher PCL-5 score.

Having been hospitalized in ICU and having an IES-6 score greater than or equal to 10 were still associated with a higher PCL-5 score in the multivariate linear regression analysis presented in Table 2. Patients with a high level of distress (IES-6 ≥ 10) at baseline had 11.1 points more than those with a low level ($P < .001$). In the case of a stay in the ICU, the PCL-5 score was 4.6 points higher than in cases where hospitalization was not necessary ($P = .024$).

DISCUSSION

The aim of this study was to assess the prevalence of PTSD as well as its associated factors in patients with confirmed COVID-19. The results showed that 6.5% of the 138 followed patients presented with probable PTSD (PCL-5 score ≥ 33)[21] and that psychotropic medication, hospitalization, and distress during the acute phase of COVID-19 were significantly associated with the severity of the PTSD symptoms.

The presumed prevalence of PTSD found in our study is close to the rate of PTSD following natural disasters (typically 5%–10%)[24] and is slightly less than the prevalence measured in a recent study conducted among Wuhan hospital–discharged patients.[19] In contrast, it is much smaller than the PTSD prevalence of 25%–50% reported in previous studies conducted during the 2003 SARS or MERS epidemics.[5,25,26] This may be a result of higher levels of trauma for SARS or MERS related to the overall higher mortality rates of these infections compared with COVID-19 (10%–20%, 30%–40%, and 2%–5%, for 2003 SARS, MERS, and COVID-19, respectively).[2]

The risk factors identified in the present study are in line with those documented in the recent literature.[24,27] The main risk factor was the presence of distress during the acute phase of illness, suggesting that the stronger the participants' psychological initial responses, the more severe were their later PTSD symptoms. A stay in an ICU was also found to be associated with increased PTSD symptoms, which is consistent with a recent review and meta-analyses showing rates of PTSD between 20% and 25% among ICU survivors.[27,28] Importantly, as shown in the Liu et al study,[19] the severity of the infection was associated with a greater psychological impact. In agreement with data showing that the PTSD prevalence is related to the severity of the traumatic events,[24,29] one could assume that COVID-19 infection was more likely to be traumatic for patients who developed severe symptoms, justifying their stay in an ICU. Of note, although not statically significant, psychotropic medication use at the time of illness was also associated with the severity of PTSD symptoms, further suggesting that having a psychiatric disorder at the time of contracting the illness was a risk factor for developing PTSD symptoms. These results suggest that, as classically described in the PTSD literature, COVID-19–related PTSD arises from the association between patients' psychological vulnerability and the traumatic impact of the disease.

Importantly, compared to the 6.5% of patients presenting with probable PTSD at 1 month, 33.5% presented with psychological distress at baseline, which appears consistent with recent studies reporting high rates of patients with posttraumatic symptoms in the acute phase of COVID-19.[4,15] This result emphasizes that, even though stress symptoms at the onset of COVID-19 symptoms are associated with severity of PTSD symptoms, initial psychological distress is only a modest predictor of PTSD.[29] This also brings up a question about which factors may have promoted resilience (ie, the resources that contribute to successful adaptation to adversity).[30] Among these factors, it appears that the regular medical follow-up of patients diagnosed with COVID-19 and their psychological support, which has been proposed in our hospital during the epidemic, were probably determinants.[30]

Our study presents significant methodological strengths. First, most of the previous studies conducted during epidemics limited their inclusion to patients treated in a hospital,[19,31] whereas we included consecutive patients with laboratory-confirmed COVID-19 at University Hospital Center of Lille in France, including those who did not require hospitalization. Because our data suggest that the traumatic impact of the infection is probably more important for patients with severe symptoms who require hospitalization, we can assume that previous studies selected patients who were the most psychologically impacted by the infection. Second, the scientific literature regarding the impact of epidemics predominantly consists of self-reported data with potential selection bias, as patients with more severe symptoms are more likely to respond to psychological questionnaires than patients with mild symptoms.[5] To limit this bias in our study, the diagnosis of probable PTSD was established by investigators who systematically contacted all patients with a diagnosis of COVID-19.

The main limitation of this work is that approximately 23% of the included patients did not respond to the second assessment. However, we found significant differences between the groups of respondents and nonrespondents for only 3 variables. First, there were both more hospitalizations and more stays in the ICU in the respondent group. Since a stay in the ICU is associated with more severe PTSD symptoms, the proportion of patients with probable PTSD might be lower than our estimate. Second, there were more health care workers in the nonrespondent group, which is in line with previous work showing that health care workers are particularly reluctant to address their psychological problems.[32] The second limitation is that this is a monocentric study. Nevertheless, the Lille University Medical Center is a Regional Hospital that admits patients from the whole of northern France, including cities that were differentially impacted by the epidemic. Finally, it should be noted that we were not able to consider the COVID-19 severity score in our analysis, but hospitalization appeared as a relevant proxy to identify the role of the severity of the disease in the development of PTSD.

Finally, while this study, along with that of Liu et al,[19] assessed PTSD by considering symptoms lasting at least 1 month after the traumatic event, PTSD symptoms can also appear months later.[2] Although rates of PTSD generally decrease months after trauma,[24] several authors showed that the prevalence of PTSD among SARS survivors was 9.8% in the early recovery phase and increased up to 25.6% after 30 months.[33]

Likewise, in previous studies that measured the impact of a traumatic event, the authors reported long-term consequences of the trauma and, for a subset of patients, a delayed onset or increase of posttraumatic symptoms over several years (eg, police officers exposed to a life-threatening event,[34] patients with traumatic injury,[35] and Vietnam veterans[36]). It is, therefore, too early to consider that the present results reflect the definitive impact of the epidemic, and future studies should investigate the PTSD prevalence among COVID-19 patients more than 1 month after this traumatic experience.

To the best of our knowledge, this is the first longitudinal study to assess PTSD in patients diagnosed with COVID-19, showing a prevalence of 6.5%. The identification of the 2 main risk factors for PTSD (ie, psychological distress and a stay in the ICU) should allow for improvements in the detection of at-risk patients to propose preventive interventions. This study paves the way for future investigations of the long-term consequences of the COVID-19 epidemic on patients' mental health. More precisely, this suggests that patients affected by COVID-19 should be considered as at-risk patients for developing PTSD and should benefit from regular monitoring to detect as early as possible the occurrence of posttraumatic symptoms.

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Author contributions: Drs Horn, Vaiva, and D'Hondt and Mr Duhem designed the study. Dr Vuotto collected the data. Mr Astier and Mss Noel and Henry conducted the phone interviews with patients. Dr Wathelet analyzed the data. Drs Horn, Wathelet, and D'Hondt wrote the first draft. Drs Fovet and Amad critically reviewed the manuscript. All authors contributed to and approved the final version.

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