

## POST-TRAUMATIC STRESS DISORDER AFTER COVID-19 INTENSIVE CARE ADMISSION: CHARACTERISTICS AND PERSPECTIVES

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### SUMMARY

An increase of psychopathology such as post-traumatic stress disorder (PTSD) is described in patients affected with COVID-19 that stayed at an intensive care unit (ICU). However, data on follow-up and on impact of contextual factors are limited. In a single-center, observational study, PTSD symptomatology was prevalent among 38% of participants ( $n=8$ ), persisting in clinical PTSD in 2 participants after one year. In patients with initial PTSD symptoms, scores on depression, anxiety and insomnia scales were significantly higher. A higher mental burden due to avoidance of contact and a reduced quality of life was also retained in patients with PTSD symptoms.

**Key words:** COVID-19 – intensive care unit - post-traumatic stress disorder

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### INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic led to more than 508 million individuals being infected and more than 6 million COVID deaths worldwide (WHO 2022). Studies investigating mental health outcomes in COVID-19 patients report an increase of psychopathology including post-traumatic stress disorder (PTSD) (Taquet et al. 2021). A recent meta-analysis revealed that PTSD symptoms may affect 1 in 5 ICU-survivors (Rigny et al. 2019). An Italian publication describes a prevalence of 23.2% of PTSD symptoms in COVID-19 ICU survivors at 1 year follow-up (Damico et al. 2021). Upon admission, COVID-19 patients were strictly isolated, with limited contact with caregivers, no visits, while COVID-19 was continuously mentioned by media (Vlake et al. 2021). COVID-19 therefore presents several features that impact mental health, leading to mental healthcare being confronted with patients with a history of COVID-19 ICU admission (Lazzari et al. 2020). For enabling adequate mental healthcare management, it is essential to gain insight on the impact of an ICU admission for COVID-19 on mental health. Our primary objective was to estimate the prevalence of psychiatric symptoms in this population. Secondary objectives were to assess factors of influence on mental health and to evaluate persistence of clinical PTSD after one year.

### SUBJECTS AND METHODS

All patients hospitalized at the ICU department of the University Hospital Brussels (UZ Brussel, Belgium) due to COVID-19 between March 2020 and May 2020 were eligible for participation in the study. Patients were asked by their treating physician to participate at hospital discharge. Patients with neurological sequelae and not able to express themselves, were not eligible for inclusion. Only patients capable of returning home have been included.

After ICU discharge, participants received self-reported questionnaires to assess symptoms of depression and anxiety (HADS), insomnia (ISS), and PTSD (PCL-5). The PTSD Checklist for DSM-5 (PCL-5) was used to assess the presence of PTSD symptoms during the last month, with a cut-off score of 33 indicating a probable diagnosis of PTSD (Blevins et al. 2015). The Hospital Anxiety and Depression Scale (HADS) was used to assess anxious and depressive symptoms with a score higher than 10 being indicative for presence of symptoms of anxiety and/or depression (Zigmond & Snaith 1983). The Insomnia Severity Index (ISI) assessed sleeping problems, with a cut off value of 15 indicating symptoms of insomnia (Bastien et al. 2001). Three visual analogue scales (VAS) evaluated pre-existent symptoms of depression, anxiety, and insomnia. Additional VAS-scales rated the influence on well-being of media, quantity of information on COVID-19,

protective measures, restriction of hospital visits, and avoidance of contact. A final VAS assessed quality of life. A cut-off value of 7 was used as a threshold for each VAS (Dutheil et al. 2017). Patients with initial PTSD symptoms (PCL-5>33) were contacted by telephone for a clinical PTSD interview (CAPS-5) one year after discharge, between March and July 2021.

Statistical analyses were performed with SPSS 26 (IBM Statistics). Data are descriptive and presented as frequencies (%) or as mean  $\pm$  standard deviation (SD). Based on a cut-off score of 33, the sample was divided in two groups (patients with and without PTSD symptoms). Univariate analyses (Fisher's-exact & Mann-Whitney-U tests) explored differences in demographic, social and psychometric variables between both groups. Significance was set at  $p < 0.05$  and all tests were two-sided.

The study protocol was reviewed and approved by the Ethical Board of the University Hospital Brussels (registration number B1432020000104). All participants gave written informed consent. Participants received no compensation for their participation. The authors affirm that this study was conducted in accordance with the World Medical Association Declaration of Helsinki.

## RESULTS

Of 52 patients eligible for participation, 46 gave consent to participate. Of those, 21 (45.65%) completed the questionnaires within 137 days (SD: 48) after hospital discharge. The median length of stay at ICU was 8 days (SD  $\pm$  14.89; IQR: 3.50-13.50). Median duration of hospitalization was 27 days (SD  $\pm$  30.29; IQR: 10.00-28.00).

After hospital discharge, 38.1% of patients (n=8) presented PTSD symptoms. Respectively 28.6% (n=6) and 38.1% (n=8) of patients met the cut-off for depression (HADS-D>10) and anxiety (HADS-A>10) (Zigmond & Snaith 1983). In patients with PTSD symptoms, scores on anxiety (13.50 $\pm$ 2.00 vs. 4.54 $\pm$ 2.60;  $p < 0.001$ ) and depression subscales (12.88 $\pm$ 2.47 vs 2.38 $\pm$ 2.32;  $p < 0.001$ ) were higher compared to patients without. Six patients (28.6%) indicated insomnia (ISI>15) (Bastien et al. 2001), with higher scores in the group with PTSD symptoms (18.25 $\pm$ 8.44 vs 6.69 $\pm$ 6.84;  $p = 0.003$ ). We noted a higher burden due to mandatory avoidance of contact in patients with compared to patients without PTSD symptoms (VAS 8.50 $\pm$ 1.19 vs 5.15 $\pm$ 3.21;  $p = 0.015$ ), as well as a higher loss of quality of life (VAS 7.13 $\pm$ 3.13 vs 3.38 $\pm$ 2.10;  $p = 0.010$ ). Impact of protective measures, information, lack of visit or media did not differ significantly between patients with and without PTSD symptoms (Table 1).

One-year post-ICU discharge, one patient within the PTSD group (n=8) was lost to follow-up. Two patients (28.6%) scored positively on CAPS-5. Psychological variables did not differ significantly between patients with and without PTSD at 1 year follow-up.

## DISCUSSION

The prevalence of PTSD symptoms in 38.1% of COVID-19 patients after ICU stay is in the higher range compared to previous findings in COVID-19 patients (6.5-31%) (Cai et al. 2020, Horn et al. 2020, Taquet et al. 2021). A reason for the higher prevalence might be the heavy impact of an ICU admission for COVID-19. A recent report identifying ICU admission as an independent risk factor for developing PTSD symptoms

**Table 1.** Comparison of psychosocial variables between patients with (PTSD+; n=8) and without (PTSD-; n=13) symptoms of PTSD according to PCL-5 score; all data are presented as means  $\pm$  SD unless specified otherwise

	PTSD+ (n=8)	PTSD- (n=13)	p-value
<b>Psychometric measures</b>			
PCL-5	45.88 ( $\pm$ 8.54)	10.85 ( $\pm$ 9.55)	
D-HADS	12.88 ( $\pm$ 2.47)	2.38 ( $\pm$ 2.32)	<0.001
A-HADS	13.50 ( $\pm$ 2.00)	4.54 ( $\pm$ 2.60)	<0.001
ISI	18.25 ( $\pm$ 8.44)	6.69 ( $\pm$ 6.84)	0.003
History of depressive symptoms (n)	1 (12.5%)	1 (8.3%)	1.000
History of anxious symptoms (n)	2 (25.0%)	3 (25.0%)	1.000
History of insomnia (n)	1 (12.5%)	3 (27.3%)	0.603
<b>Factors of impact on wellbeing during ICU-hospitalization (VAS-score)</b>			
Media	5.00 ( $\pm$ 3.46)	4.38 ( $\pm$ 3.15)	0.439
Information	6.13 ( $\pm$ 2.64)	4.00 ( $\pm$ 3.10)	0.123
Protective measures	4.88 ( $\pm$ 3.09)	2.92 ( $\pm$ 2.78)	0.076
Lack of visit	8.25 ( $\pm$ 2.55)	6.54 ( $\pm$ 3.25)	0.268
Avoiding contact	8.50 ( $\pm$ 1.19)	5.15 ( $\pm$ 3.21)	0.015
Losing quality of life	7.13 ( $\pm$ 3.13)	3.38 ( $\pm$ 2.10)	0.010

*Legend:* PTSD: post-traumatic stress disorder; SD: standard deviation; PCL-5: PTSD Checklist for DSM-5; HADS: Hospital Anxiety and Depression Scale; D-HADS: depression subscale; A-HADS: anxiety subscale; ISI: insomnia severity index, VAS-score between 0-10

strengthens this hypothesis (Horn et al. 2020). Other work also confirms our findings of more severe depressive symptoms and a lowered quality of life among COVID-19 patients with PTSD symptoms (Yuan et al. 2021). Re-assessment at one year follow-up identified clinical PTSD in 2 out of 7 patients who screened positively. Upon today, data on evolution of clinical PTSD after ICU admission for COVID-19 are not available. Although, a recent meta-analysis estimates the prevalence of PTSD in general ICU survivors to augment from 15.93% at 3 months to 18.96% at 12 months (Righy et al. 2019). Among COVID-19 patients, a 20% increase of PTSD symptoms 6 months after discharge has been described (Tu et al. 2021). Use of two different PTSD measures and lack of reassessment of the asymptomatic group in our study impedes clear comparison with these findings.

Patients with PTSD symptoms experienced a higher burden due to mandatory avoidance of contact. Other work confirms that mental burden during a pandemic can be exacerbated by loneliness and lack of social support and that social support influences post-traumatic growth (Saltzman et al. 2020). Our colleague described that anxiety to get re-infected made the patients of this study create a socially avoidant lifestyle. A weak social network led to feelings of hopelessness (Berends et al. 2021). Social support may be important to promote positive adaptation (Saltzman et al. 2020, Berends et al. 2021).

Limitations of this study include the small sample size. The low response rate (45.65%) might suggest response bias, while a non-response bias can neither be excluded. By only reassessing patients with initial symptoms, our results might underestimate the prevalence of clinical PTSD after one year. Strengths of this study are the attention for contextual factors and the unicity of longitudinal clinical data on this specific population. Further research with attention to evolution of mental health symptoms and importance of contextual factors in COVID-19 ICU survivors is needed.

## CONCLUSION

PTSD symptoms occurred in 38% of COVID-19 ICU survivors, persisting into clinical PTSD in 2 out of 7 cases after one year. We report a significant impact of PTSD symptoms on quality of life and psychiatric comorbidity. Avoidance of contact and lack of social support are associated with increased occurrence of PTSD symptomatology. Further research focusing on mental health of COVID-19 ICU survivors is warranted.

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**Conflict of interest:** None to declare.

## Contribution of individual authors:

Lukas Claus served as lead for conceptualization, methodology, formal analysis and writing (initial draft & review) and contributed for investigation.

Kinge Berends served as lead for investigation and contributed for conceptualization, methodology and writing (review).

Elisabeth De Waele served as lead for resources (recruitment participants), contributed for methodology and writing (review).

Seline Van den Aemele contributed for conceptualization, methodology, supervision, and writing (review).

Cleo L. Crunelle served as lead for validation, and contributed for conceptualization, formal analysis, methodology and writing (initial draft & review).

Nathalie Vanderbruggen served as lead for supervision, and contributed for conceptualization, methodology and writing (review).

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