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ORIGINAL ARTICLE

Post-traumatic stress symptoms six months after ICU admission with COVID-19: Prospective observational study

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Abstract

Aims and Objectives: The aim of this study was to investigate the prevalence of post-traumatic stress symptoms, and to identify possible predictive factors in Norwegian intensive care unit survivors, 6 months after admission to the intensive care unit with COVID-19.

Background: The SARS CoV-2 virus causing COVID-19 has spread worldwide since it was declared a pandemic in March 2020. The most severely ill patients have been treated in the intensive care due to acute respiratory failure and also acute respiratory distress syndrome. It is well documented that these severe conditions can lead to complex and long-lasting symptoms, such as psychological distress, and was, therefore, investigated for the specific COVID-19 population.

Design: Prospective observational study.

Methods: Clinical data and patient reported outcome measures were collected by the Norwegian Intensive Care and Pandemic Registry and by the study group 6 months after admission to an intensive care unit.

Results: Among 222 COVID-19 patients admitted to Norwegian intensive care units between 10 March and 6 July 2020, 175 survived. The study sample consisted of 131 patients who responded to at least one patient reported outcome measure at 6 months following admission. The primary outcome was self-reported post-traumatic stress symptoms, using the Impact of Event Scale-6 ($n = 89$). Of those, 22.5% reported post-traumatic stress symptoms 6 months after admission. Female gender, younger age and having a high respiratory rate at admission were statistically significant predictive factors for reporting post-traumatic stress symptoms.

Conclusions: The result is in accordance with previously published research with comparable populations, suggesting that for many COVID-19 survivors psychological distress is a part of the post-acute sequelae. Results from the present study should be replicated in larger datasets.

Relevance to Clinical Practice: This project provides important insight to post-acute sequelae after COVID-19 that patients may experience after critical illness.

KEYWORDS
anxiety, COVID-19, depression, long-COVID, post COVID-19 condition, post-intensive care syndrome, post-traumatic stress, post-traumatic stress disorder, SARS-CoV-2

1 | BACKGROUND

In March 2020, the outbreak of disease caused by SARS-CoV-2 (COVID-19) was declared a pandemic (WHO, 2020). It soon became evident that many patients developed severe illness and needed intensive care, including prolonged mechanical ventilation (MV) for acute respiratory failure (ARF) (Wang et al., 2020). Many of these patients met the criteria of acute respiratory distress syndrome (ARDS), a condition associated with intensive care unit (ICU) mortality of 30%–40% (Bellani et al., 2016). At the beginning of the pandemic, mortality rates were reported up to 84.6% but have been adjusted during the pandemic, and the pooled overall ICU mortality has been reduced to 35.5% (Armstrong et al., 2021). This is comparable to critically ill patients with severe ARF and ARDS by different aetiologies and as observed during previous pandemics (Gil Cuesta et al., 2016). However, some countries have reported mortality rates of <20% during the present pandemic (Chew et al., 2022).

The burden of critical care and the consequences of critical illness have received increased attention in recent years, as decreasing mortality rates have contributed to an increased number of ICU survivors (Fan et al., 2014). The identification of the post-intensive care syndrome (PICS) has raised awareness about health issues in ICU survivors (Elliott et al., 2014). PICS conceptualises the direct effects of critical illness and patient management in the ICU on physical, psychological, and cognitive domains of health (Elliott et al., 2014). Health challenges in more than two such domains have been described in 21% of survivors 12 months after discharge from the ICU (Marra et al., 2018). Typical psychological complications in survivors include post-traumatic stress disorder (PTSD) and/or post-traumatic stress symptoms (PTSS) (Righy et al., 2019). Of note, PTSD and PTSS can have a negative impact on the quality of life (QoL) and are often underdiagnosed and under-recognised in ICU survivors (Parker et al., 2015). A recent systematic review demonstrated a high prevalence of PTSD in survivors of Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS), both a result of infection with coronaviruses (Ahmed et al., 2020). Thus, COVID-19 survivors are also at risk of developing PTSD and PTSS (Hosey & Needham, 2020; Xiao et al., 2020).

The terms "long COVID," "post COVID syndrome" and "post COVID-19 condition" have been introduced to describe health impairments that persist beyond the acute phase of infection in COVID-19 patients (Crook et al., 2021; Shah et al., 2021). The World Health Organization (WHO) has defined 'post COVID-19 condition' as a '*condition where symptoms persist for more than two months after the onset of COVID-19*' (WHO, 2021). This consensus, along with several editorials and letters, has raised awareness of the symptom burden that some COVID-19 patients may experience, in addition to the need for further research (Hosey & Needham, 2020; Sivan & Taylor, 2020). Some studies have investigated the prevalence of PTSD and PTSS and risk-associated factors in severe ill COVID-19 patients, but so far, published studies have divergent results with either small sample sizes or different lengths of follow-up (Heesakkers et al., 2022; Latronico et al., 2021; Neville et al., 2022; Schandl et al., 2021). The available evidence on long-term health impairments in COVID-19 ICU survivors is therefore still limited. Hence, the overall aim of the present study was to investigate the prevalence of PTSS and to identify possible predictive factors for developing PTSS 6 months after ICU admission, in a national cohort of COVID-19 survivors in Norway. Results for the present study are from patients admitted between 10 March and 6 July 2020, and therefore represent the first wave of ICU patients in Norway.

What does this paper contribute to the wider global clinical community?

- Gives important insight into post-acute sequelae COVID-19 patients experience after critical illness.
- The results are highly relevant to similar intensive care unit populations.

2 | METHODS

2.1 | Study design and setting

The present study is part of a larger longitudinal observational study (NCT04601090) conducted as a collaboration between Oslo University Hospital and the Norwegian Intensive Care and Pandemic Registry (NIPaR). The overall study aim was to describe both survival rates and long-term outcomes, and the aim of the present study was only to investigate long-term outcomes (i.e. PTSS). NIPaR is a national quality registry regulated by national legislation utilising national technological platforms (Buanes et al., 2021). To be registered in NIPaR members' units and patients need to fulfil predefined criteria. NIPaR collects data from all Norwegian hospitals with estimated case completeness of 98.8% (Buanes et al., 2021). From

the beginning of the pandemic, NIPaR has been supplemented with entries specifically addressing the ICU management of COVID-19 patients. During the pandemic, patients receiving MV in dedicated pandemic units are also included. The present study used the Strengthening the reporting of observational studies in epidemiology Checklist (STROBE) (Appendix S1) (von Elm et al., 2007).

2.2 | Study population

All ICU survivors over the age of 18 with confirmed COVID-19 determined by a polymerase chain reaction (PCR)-test and registered in NIPaR between 10 March and 6 July 2020, were eligible for inclusion in the present study. Patients, who could not read, write or understand Norwegian, were excluded from the study.

2.3 | Outcomes

The primary outcome of the present study was the prevalence of PTSS, measured with the Impact of Event Scale-6 (IES-6), and to investigate possible predictive factors for PTSS. The secondary outcomes of the present study were the prevalence of anxiety, depression, cognitive impairment, dyspnoea and the reception of rehabilitation.

2.4 | Data collection

The study utilises data from NIPaR and supplemental data collected by the study group. NIPaR reported clinical data from the ICU-stay, patient-reported outcome measures (PROM) on demographics, physical, psychological and cognitive health challenges at 6 and 12 months after ICU admission. NIPaR contacted patients electronically (Helsenorge, Digipost) or by mail. In addition, we conducted semi-structured interviews by telephone to obtain additional data regarding the Hospital Anxiety and Depression Scale (HADS), The Mini Montreal Cognitive Assessment (Mini-MoCA), and rehabilitation. Patients who could not be reached by telephone or who preferred to fill out questionnaires on paper received these by mail along with a prepaid envelope. Patients who did not respond within a month got a reminder to do so along with a new set of questionnaires. In the present study, data from the 6 months follow-up have been used.

2.4.1 | Demographic and clinical variables

Clinical data consisted of predefined risk factors for developing severe illness, a severity of illness measure (Simplified Acute Physiology Score (SAPS) II), ICU treatment (e.g. mechanical ventilation), ICU length of stay (LOS), frailty score (Clinical Frailty Scale), peripheral oxygen-saturation and respiration rate at admission. Demographic data were age, gender, education, co-habitation, work situation (e.g. sick leave), and reception of rehabilitation during and after the hospital stay.

2.4.2 | The Impact of Event Scale-6

Post-traumatic stress symptoms were measured with the Impact of Event Scale-6 (Hosey et al., 2019). The IES-6 is an abbreviation of the Impact of Event Scale-Revised (IES-R) which is widely used in ICU survivors and has good psychometric properties (Needham, 2020; Thoresen et al., 2010). The IES-6 is a self-report measure that assesses subjective distress after stressful life events and consists of six questions rated on a 5-point Likert scale ranging from 0 (not at all) to 4 (extremely). The score is calculated as the mean of the six items, and a cut-off value of ≥1.75 indicates PTSS (Hosey et al., 2019). For the present study, the outcome variable was dichotomised with the use of a cut-off value of 1.75 (Hosey et al., 2019). The IES-6 has been validated for ARDS survivors and is a recommended research instrument for ICU survivors in general (Hosey et al., 2019; Mikkelsen et al., 2020; Needham et al., 2017). The Norwegian translation of the IES-R has been validated for a Norwegian population (Eid et al., 2009). All domains had high internal consistency (Cronbach's alpha >.90) in the present study.

2.4.3 | The Hospital Anxiety and Depression Scale

The Hospital Anxiety and Depression Scale is a self-report measure initially developed to screen symptoms of anxiety and depression in hospitalised patients experiencing physical illness (Zigmond & Snaith, 1983). The questionnaire consists of 14 items: seven anxiety items and seven depression items on a scale from 0 (not at all) to 3 (very much). An overall score from 0 to 21 is calculated for each subscale. A cut-off value of eight of each scale indicates symptoms of general anxiety or depression, and higher scores can be used as a measure of severity, classified as 'mild', 'moderate' or 'severe' (Snaith, 2003). The instrument has been widely used in ICU survivors, has satisfactory psychometric properties and has been validated in a Norwegian population (Mykletun et al., 2001; Needham, 2020). All domains had high internal consistency (Cronbach's alpha >.89) in the present study.

2.4.4 | Mini Montreal Cognitive Assessment

The Mini Montreal Cognitive Assessment Version 2.1 is an abbreviation of the full version of the Montreal Cognitive Assessment (MoCA) and can be administered over the telephone (Wong et al., 2015). It consists of four items examining five cognitive domains: attention, verbal learning and memory, executive functions/language, and orientation (Wong et al., 2015). The total score ranges from 0 to 15, where a score <11 indicates cognitive impairment and was used as a cut-off in the

present study (Nasreddine, 2020). The English version of Mini-MoCA is validated for stroke patients and is a recommended screening tool for assessing cognition in survivors of ARF (Needham, 2020; Wong et al., 2015). The study group translated the Mini Montreal Cognitive Assessment (MoCA®)—Version 2.1 (English) to Norwegian using a standard forward-backward translation process. The translated version has not gone through testing of psychometrics properties but was used according to guidelines issued by MoCA Inc. ©.

2.4.5 | Modified Medical Research Council Dyspnea Scale

To evaluate self-perceived lung function, the Modified Medical Research Council Dyspnea Scale (mMRC) was used. This is a unidimensional scale related to activities of daily living and has shown high correlations with QoL in patients with chronic respiratory diseases (Cotes, 1987; Launois et al., 2012). The mMRC has not been validated for ARF patients but has been used in other studies to report dyspnoea in COVID-19 ICU patients (Aranda et al., 2021). The mMRC is an abbreviation of the Medical Research Council Questionnaire on respiratory symptoms and consists of five statements covering a wide range of dyspnoea in daily living (Cotes & Chinn, 2007; Launois et al., 2012; Mahler & Wells, 1988). Participants are asked to check one of the five statements, which are graded from 0 (not troubled with breathlessness except on strenuous exercise) to 4 (too breathless to leave the house, or breathless when dressing or undressing) (Dhont et al., 2020; Launois et al., 2012). In the present study, a cut-off value of ≥1 was used which indicates dyspnoea. The mMRC has been translated to Norwegian but has not been fully validated in the Norwegian population.

2.4.6 | Rehabilitation questionnaire

The questionnaire regarding rehabilitation was developed by the study group and consists of seven questions. Some of the questions have yes/no answers, and some have the possibility of multiple answers. The questions map if patients have received rehabilitation in the hospital and after discharge from the hospital. If patients have received rehabilitation after hospital discharge, they are asked to provide details about the rehabilitation service (e.g. full body rehabilitation institution, municipal rehabilitation or other) and for how long rehabilitation was provided. This instrument has not gone through formal psychometric testing.

2.5 | Statistical analyses

Descriptive data are presented as counts and frequencies (*n* and percentage) for categorical variables and median with range for continuous variables. To compare responder and non-responder groups, the Mann–Whitney *U*-test was used for continuous variables, as none of the data were normally distributed. Pairs of categorical data were compared using the Pearson chi-square test. Possible associations between selected predictive factors and the outcome were analysed using logistic regression models. In univariate logistic regression analyses, each possible predictive factor was investigated for an association with the outcome variable (IES-6). Variables were selected for univariate analyses based on both clinical (peripheral oxygen-saturation, respiration rate, reception of rehabilitation) and empirical (age, gender, BMI, predefined risk factor, SAPS II score, Clinical Frailty Scale, ICU LOS, duration of MV, Mini-MoCA, HADS, educational status, co-habitation, employment status) considerations. Variables associated with the dependent variable with a p-value ≤.05 in the univariate analyses were included in the multivariate logistic regression model. Standard errors and confidence intervals for the regression coefficients were estimated using bootstrap (10,000 repetitions). The strength of association between the two components in HADS (anxiety and depression) and PTSS was assessed with Spearman's rank correlation and excluded from the regression analysis due to multicollinearity between the constructs. Internal consistency in the IES-6 and HADS was analysed using Cronbach's alpha. All tests were two-sided. p-values <.05 were considered statistically significant. Data were analysed using the IBM Statistical Package for Social Science (SPSS), version 26.

2.6 | Ethics

The study followed the ethical principles for medical research described in the Declaration of Helsinki (Hurst, 2014). The study was approved by the Regional Committees for Medical and Health Research Ethics (reference number: 135310) and the institutional privacy representative. NIPaR is a national registry in which consent is not required. However, patients receive information regarding their registration and may request that their data be deleted at any time. For participants who responded to the telephone interview, we obtained oral consent prior to the interview, which was later confirmed in writing.

3 | RESULTS

3.1 | Patient characteristics

Among 222 patients admitted between 10 March and 6 July 2020, 47 (21%) patients died within 90 days after ICU admission, resulting in 175 patients eligible for 6 months follow-up (Figure 1). The final study sample consisted of 131 patients that responded to at least one of the PROM (PTSS, anxiety and depression, dyspnoea or rehabilitation questions). Clinical characteristics are presented in Table 1, and responders are compared to non-responders in Table 2 (gender, age, ICU LOS, time on MV, risk factors, Clinical Frailty Scale and SAPS II score). There were no statistically significant differences between responders and non-responders concerning any of the analysed variables. The median age of the 131 responders was 61 (25–83) years and 77.1% were male, the

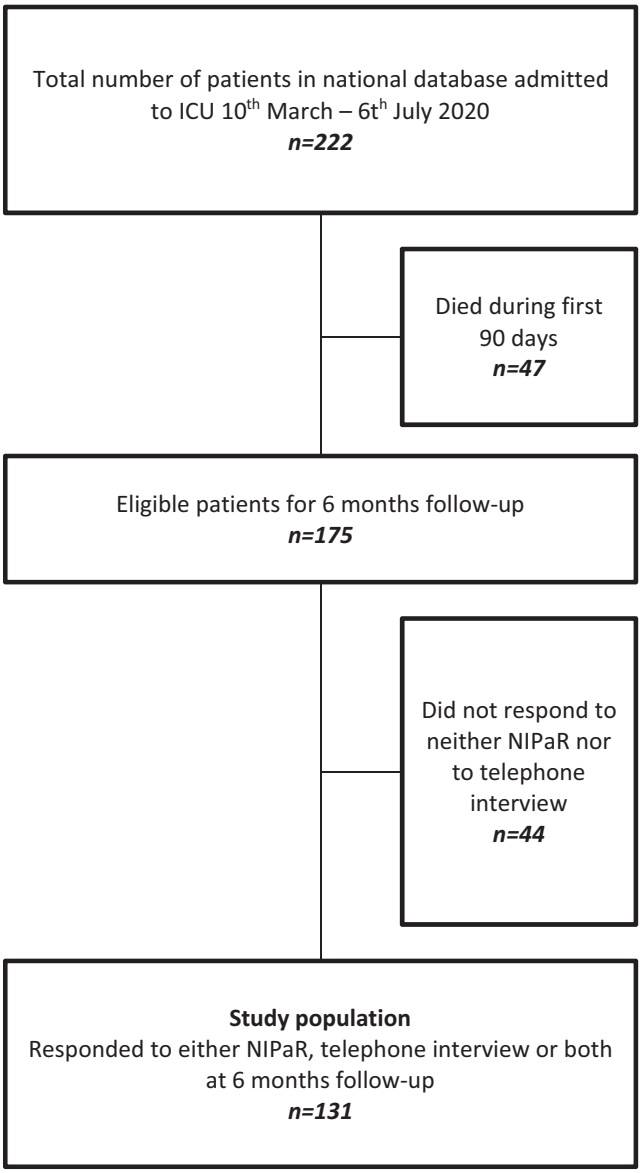

FIGURE 1 Flowchart. ICU, Intensive care unit; NIPaR, the Norwegian Intensive Care and Pandemic Registry.

median ICU length of stay was 14.6 (.8–67) days and the median time on mechanical ventilation was 11.9 (.1–56.6) days. Almost three out of five study patients (59.5%) had at least one risk factor known to be associated with severe COVID-19 development.

3.2 | Prevalence of PTSS, anxiety, depression, dyspnoea and cognitive impairment six months after ICU admission

Figure 2 presents descriptive statistics of the IES-6, HADS, Mini-MoCA, mMRC and rehabilitation. Of the 89 patients who completed the IES-6 questionnaire, 22.5% had a mean score of ≥1.75, indicating PTSS. The HADS questionnaire was completed by 119 patients, with 16.8% reporting levels above the clinical cut-off (i.e. ≥8) on the anxiety subscale and 14.3% on the depression subscale. The Mini-MoCA was completed by 102 patients, of whom 25.5% scored below the cut-off value of 11, indicating cognitive impairment. About two-thirds (60.8%) of the included patients reported having received some sort of rehabilitation after hospital discharge and 64.7% received rehabilitation during hospitalisation. The mMRC questionnaire was completed by 90 patients, and over half (56.7%) of the patients reported having episodes of breathlessness or experiencing an impact on their perceived lung function while 43.3% reported no breathlessness except on strenuous exercise.

3.3 | Factors associated with PTSS

In the univariate logistic regression analyses, age, gender and respiration rate at admission to the ICU were statistically significantly associated with the outcome and they all remained independently statistically significant in the multivariate analysis (Table 3). Younger age (OR .93, 95% CI [.85–.98]), female gender (OR 14.60, 95% CI [3.97–103.23]) and higher respiration rate at admission to ICU (OR 1.06, 95% CI [1.02–1.17]) were associated with increased odds of reporting PTSS 6 months after ICU admission.

4 | DISCUSSION

The main finding of the present study was that almost one in four (22.5%) of the responders reported symptoms of PTS 6 months after admission to a Norwegian ICU during the first wave of the pandemic. This corresponds well with results from pre-pandemic studies with both ARF and mixed ICU populations, and with a meta-analysis that reported an overall pooled prevalence of PTSD symptoms in 19.8% of ICU survivors (Bienvenu et al., 2018; Dijkstra-Kersten et al., 2020; Righy et al., 2019). A more recent meta-analysis including severe ill COVID-19 patients found an even lower pooled prevalence of PTSD at 16% but emphasises the substantial heterogeneity between the included studies (Nagarajan et al., 2022).

There are still few large studies with long-term follow-up data within the COVID-19 ICU population, and the prevalence of PICS is even more divergent in this group than in mixed ICU populations (Heesakkers et al., 2022; Latronico et al., 2021; Neville et al., 2022; Schandl et al., 2021). A study from Sweden found that 35% of ICU survivors after COVID-19 reported symptoms of PTS, 5 months after ICU discharge (Schandl et al., 2021), while a study from the United States had a prevalence of 20.3%, 6 months after ICU treatment (Neville et al., 2022). In contrast, two other studies reported exceptionally low prevalence (9.8% and 6%) at 12 months after ICU treatment and this exemplifies the great divergence in COVID studies so far (Heesakkers et al., 2022; Latronico et al., 2021). The wide range in results rates may be explained by different methodologies, different measurement time-points and small sizes in some studies. It is also important to keep in mind that the selection criteria for receiving ICU treatment varied broadly

TABLE 1 Characteristics of the study sample at time of ICU admission (*n* = *131*).

	n	%	Median (range)
Clinical characteristics			
Age	131		61 (25–83)
Gender			
Female	30	22.9	
Male	101	77.1	
BMI (kg/m^2)	81		27.2 (19.5–42.4)
Peripheral oxygen-saturation (%)	119		89 (47–100)
Respiration rate (per minute)	125		28 (12–78)
SAPS II score	131		32 (6–59)
ICU length of stay (days)	131		14.6 (0.8–67)
Received mechanical ventilation	111	84.7	
Type of mechanical ventilation			
Invasive mechanical ventilation	95	85.6	
Non-invasive ventilation only	16	14.4	
Time on mechanical ventilation (days)	111		11.9 (0.1–56.6)
Any risk factor			
Yes	78	59.5	
No	53	40.5	
Risk factors[a]			
Cardiovascular disease	41	32.1	
Obesity	20	15.3	
Asthma	20	15.3	
Diabetes mellitus I or II	16	12.2	
Immune deficit	8	6.1	
Chronic lung disease (asthma not included)	7	5.3	
Kidney disease	7	5.3	
Cancer	6	4.6	
Neurological disease	4	3.1	
Smoker	1	0.8	
Liver disease	1	0.8	
Pregnancy	0	0	
Sociodemographic characteristics (*n* = 93)	*n*	%	
Co-habitation			
Living with someone	79	84.9	
Living alone	14	15.1	
Educational status			
Primary/secondary school	53	57.0	
Higher education—College/university	40	43.0	
Employment status before COVID-19 illness (*n* = 92)			
Working	46	50	
Retired	31	33.7	
Sick leave/disabled	12	13	
Other (student/unemployed/unpaid work)	3	3.3	

[a]Some have more than one risk factor.

during the pandemic due to both strain on the healthcare systems in different countries, as well as already established differences. Therefore, comparison between countries should also be done with caution, especially with pandemic data. In addition, countries used a variety of strategies to manage the pandemic during the first wave and some healthcare systems were overwhelmed

TABLE 2 Characteristics of responders and non-responders.

	Responders (*n* = 131)			Non-responders (*n* = 44)			*p*-value
	n	%	Median (range)	*n*	%	Median (range)	
Age			61 (25–83)			57 (25–82)	0.08
Gender							0.56
Male	101	77		32	73		
Female	30	23		12	27		
Risk factor							0.96
Yes	78	60		26	60		
No	53	40		18	40		
SAPS II score	131		32 (6–59)	44		32.5 (11.0–47)	0.98
Clinical Frailty Scale	97		2 (1–7)	19		2 (1–4)	0.87
ICU LOS	131		14.6 (0.8–67)	44		14 (1.1–60.4)	0.44
Duration of MV	111		11.9 (0.1–56.6)	36		11.7 (0.1–48.1)	0.63

Abbreviations: ICU LOS, intensive care unit length of stay; MV, mechanical ventilation; SAPS, Simplified Acute Physiology Score II.

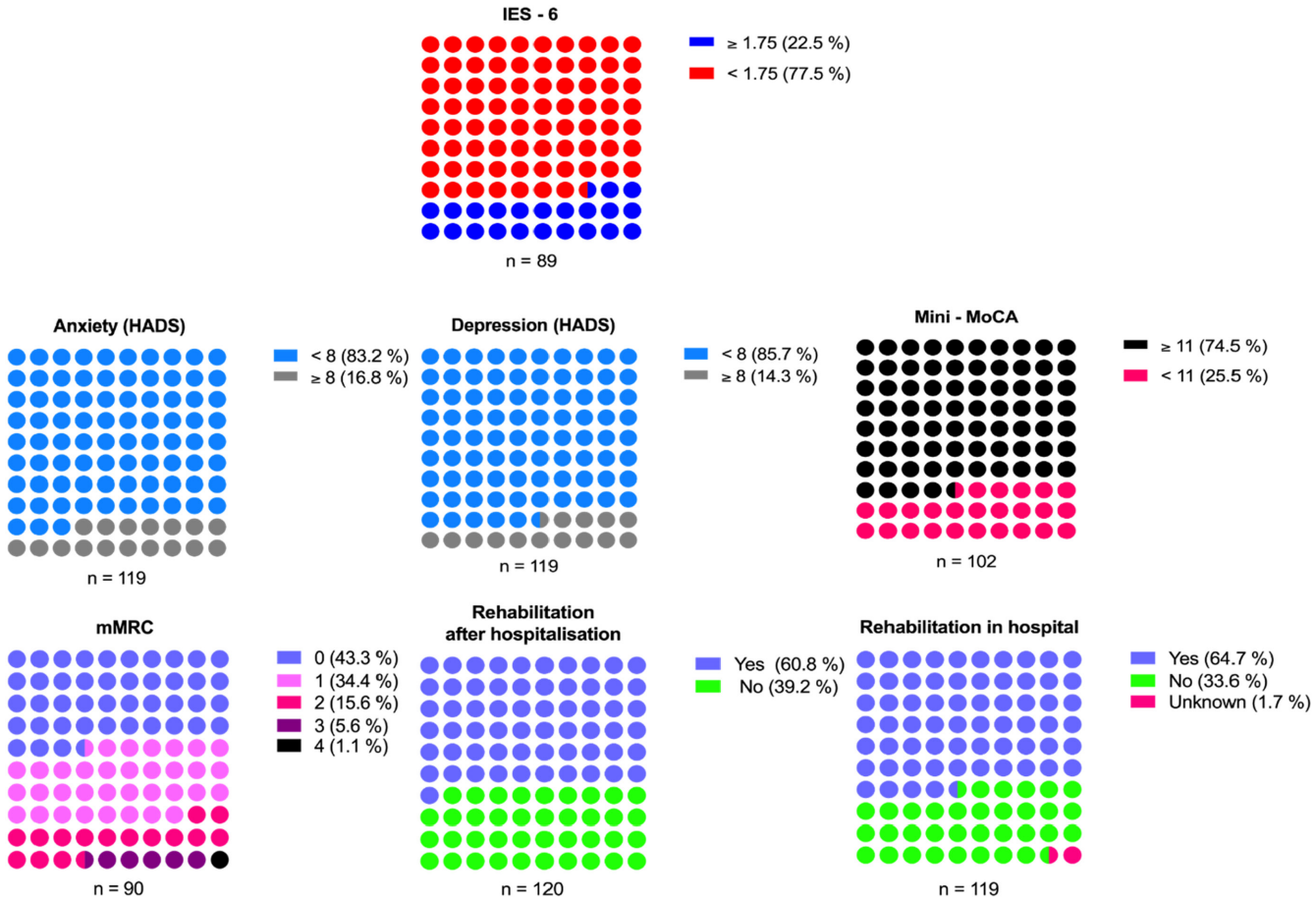

FIGURE 2 Prevalence of PTSS, anxiety, depression, dyspnoea, cognitive impairments and rehabilitation—reported 6 months after ICU admission. HADS, Hospital Anxiety and Depression Scale; *IES-6* Impact of Event Scale-6, cut-off ≥1.75 indicating post-traumatic stress symptoms; Mini-MoCA: Mini Montreal Cognitive Assessment; mMRC: Modified Research Council Dyspnea Scale. 0—Not troubled with breathlessness except on strenuous exercise, 1—Troubled by shortness of breath when hurrying on the level or walking up a slight hill, 2—Walks slower than people of same age on the level because of breathlessness or has to stop to catch breath when walking at their own pace on the level, 3— Stops for breath after walking about 100 yards or after a few minutes on the level, 4—Too breathless to leave the house, or breathless when dressing or undressing

TABLE 3 Logistic regression analyses. Predictive factors associated with IES-6 score ≥ 1.75.

	Univariate analyses			Multivariate analyses		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value
During admission						
Age	.95	.90–.96	.03	.93	.85–.98	<.01
Gender (ref. male)	7.62	2.43–23.97	<.01	14.60	3.97–103.23	<.01
BMI (kg/m^2)	.96	.84–1.10	.56			
Risk factor (ref. no)	.89	.32–2.41	.81			
SAPS II Score	.99	.95–1.05	.97			
Clinical Frailty Scale	.66	.33–1.32	.24			
ICU LOS (days)	1.03	.97–1.06	.09			
Duration of MV (days)	1.03	.99–1.06	.15			
Peripheral oxygen-saturation	1.01	.95–1.06	.86			
Respiration rate (per minute)	1.05	1.00–1.11	.04	1.06	1.02–1.17	.02
At six months						
mMRC	1.66	.97–2.85	.06			
Mini-MoCA (sum score)	.93	.71–1.22	.61			
Educational status (ref. Primary/Secondary school)	1.04	.38–2.82	.94			
Co-habitation (ref. living with someone)	1.04	.26–4.21	.95			
Employment status						
Received rehabilitation after hospital discharge (ref. no)	1.03	.35–3.07	.95			

Note: Level of significance <0.05. IES-6 score as a dichotomous dependent variable.

Abbreviations: BMI, body mass index; CI, Confidence interval; HADS, Hospital Anxiety and Depression Scale; ICU LOS, intensive care unit length of stay; Mini-MoCA, Mini Montreal Cognitive Assessment; mMRC, Modified Research Council Dyspnea Scale; MV, mechanical ventilation; OR, Odds ratio; SAPS, Simplified Acute Physiology Score II.

and may not have been able to provide optimal care, including rehabilitation, while healthcare systems in other countries were less congested and therefore may have been able to provide rehabilitation after ICU discharge. The degree of rehabilitation has not been described in any of the referred papers (Heesakkers et al., 2022; Latronico et al., 2021; Neville et al., 2022; Schandl et al., 2021) and is potentially an important variable when investigating long-term outcomes after critical illness. The variations between countries have been confirmed in a recent meta-analysis that shows significant differences in prevalence estimates from different parts of the world (Nagarajan et al., 2022). Latter may explain why the prevalence of anxiety and depression in the present study are in the lower range than what previously has been reported in ICU survivors and in COVID-19 ICU patients (Bienvenu et al., 2018; Davydow, Desai, et al., 2008; Dijkstra-Kersten et al., 2020; Martins et al., 2022; Schandl et al., 2021). Finally, a recent meta-analysis showed that neuropsychiatric symptoms can increase over time; therefore, results from the present study might change with a larger study population and longer follow-up (Premraj et al., 2022).

Our analyses suggest that females and younger patients have increased odds of developing and reporting PTSS. These findings are in line with a previous systematic review, and the observed variables are recognised risk factors for developing post-ICU PTSD (Davydow, Gifford, et al., 2008). Due to the limited sample size, the confidence intervals in our analysis are very broad, thus limiting the precision of our estimates. In the present study, the mMRC score was close to significant in the univariate logistic regression analysis and could as such indicate that there is some association between dyspnoea and having PTSS. However, we did not have enough statistical power to analyse this variable in a multivariate model. We choose to define dyspnoea as a score of ≥1 in the mMRC, resulting in 56.7% of the participants reporting this symptom at 6 months follow-up. (Aranda et al., 2021) reported similar results using the same cut-off, with 55% reporting this symptom in a cohort of 113 COVID-19 patients with ARDS, about 8 months after their first positive PCR-test results. Dyspnoea is an important and complex long-term symptom within the ICU population and can often not be explained by findings in chest imaging or pulmonary function tests (Parker et al., 2021). Both mMRC score and ICU LOS were borderline statistically significant

($p = .06$ and $p = .09$, respectively) in the univariate analyses and could have been investigated in a multivariate logistic regression model if the sample size had made it possible.

Another finding in our study is the relatively high number of patients with indications of cognitive impairment with 25.5% of the patients scoring below the recommended cut-off value in Mini-MoCA (Nasreddine, 2020). Cognitive deficits are acknowledged as common in ICU survivors and are described to occur in one-third of ARF patients as long as 12 months after discharge (Pandharipande et al., 2013). Some have argued that the prevalence of cognitive impairments will be higher in COVID-19 ICU patients due to prolonged time on MV, use of sedatives and high prevalence of ICU delirium, and little to no access to family members (Hosey & Needham, 2020). These are all known risk factors for developing cognitive deficits after ICU (Lee et al., 2020; Pun et al., 2021). This may explain why so many COVID-19 patients experience cognitive deficits after ICU stay (Pun et al., 2021) and that 25% of the patients in the present study show symptoms of cognitive impairment such as memory difficulties, 6 months after ICU admission. Data on levels of sedation and ICU delirium have not been available for the present study. Although it is unclear whether the effects of COVID-19 on the brain are indirect or direct, or both, COVID-19 can have a long-term negative impact on cognitive and emotional health (Hampshire et al., 2021).

It has been argued that the COVID-19 population would suffer even greater from the extraordinary circumstances of the pandemic and therefore may present a higher degree of psychological distress and cognitive impairments post-ICU (Hosey & Needham, 2020). In contrast, the present study found that the prevalence of PTSS, anxiety and depression are comparable and even lower than in ICU populations without COVID-19 (Bienvenu et al., 2018; Davydow, Desai, et al., 2008; Righy et al., 2019). This is also found in a recent meta-analysis comparing ARDS caused by other agents with SARS-CoV-2 ARDS, finding a lower incidence of anxiety and depression in COVID-19 patients (Fazzini et al., 2022). There could be many reasons for the results in the present study. The healthcare system in Norway has operated within its capacity and has been able to provide a normal standard of intensive care as well as post-ICU rehabilitation to COVID-19 patients throughout the pandemic. About 60% of the patients in the present study received some kind of rehabilitation after their hospital stay and almost 65% received rehabilitation while in hospital. In recent years, the importance of both early rehabilitation in the ICU and post-ICU rehabilitation has received more attention as a possible preventive measure for developing PICS (Brown et al., 2019). This might have contributed to the relatively low prevalence of symptoms of psychological distress in the present study. Alternatively, our questionnaire regarding rehabilitation may not be sufficiently sensitive to explore the complexity of this subject. In addition, we did not have data on Norwegian ICU patients without COVID-19 or from pre-pandemic ICU patients for comparison, to substantiate this assumption.

Finally, we did observe a significant difference in questionnaire completion, with a higher response rate to the telephone interviews (HADS, Mini-MoCA, rehabilitation questionnaire). This could indicate that for this type of study, telephone interviews and direct contact with the patients are beneficial. However, a smaller response rate was observed for the cognitive test, Mini-MoCA, which can be explained by the number of patients that could not speak Norwegian at a high enough level and were as such excluded from this test.

4.1 | Strengths and limitations

A strength of the present study is the collaboration with a national registry and the potential to investigate almost every single COVID-19 ICU survivor treated in Norway. In addition, we did have the opportunity to compare responders and non-responders and were thus able to investigate for a possible selection bias and concluded that the responders are representative of the whole population of COVID-19 survivors cared for in Norwegian ICUs. Since this study is a collaboration with a registry, we were not in full control of the selection of research instruments and this was a compromise since there are multiple research groups receiving data from the registry. We did, however, compensate for this in some way by including HADS and Mini-MoCA in our own data collection, which both are recommended research instruments for assessing anxiety, depression and cognition in ARF patients (Needham, 2020).

Limitations include a lack of data on patients' mental health history, delirium in the hospital and ethnicity. These are all variables described as possible risk factors for developing PTSD or PTSS, as well as anxiety and depression, after ICU treatment (Lee et al., 2020). A low number ($n = 89$) of respondents for the primary outcome (IES-6) limited the number of variables we were able to include in our multivariate regression model to avoid overfitting. Due to a limited sample, there is a low degree of precision in our estimates, which is reflected in broad CI. Thus, all our statistical results should be interpreted with caution. Our findings need replication in larger datasets.

5 | CONCLUSIONS

In the present study, 22.5% of the responders to IES-6 had PTSS 6 months after ICU admission, with female gender, younger age, and having a higher respiratory rate at admission to the ICU, being statistically significant predictive factors.

6 | RELEVANCE TO CLINICAL PRACTICE

This project is conducted as a collaboration between multiple professions (nurses, physicians and physiotherapist) reflecting the real world of ICU treatment. This also ensures that the results will be conveyed in a multidisciplinary setting. The results from the study give an important insight into which post-acute sequelae COVID-19 ICU patients experience 6 months after their stay. This information is also highly relevant to other ICU populations. Increasing the

knowledge of which predictive factors that can lead to long-lasting symptoms after ICU treatment can also contribute to identifying patients at high risk at an earlier stage and prevent the development or severity of the symptoms. This is important knowledge for both nurses and other clinical personnel working in the ICU, hospital wards and rehabilitation facilities.

7 | IMPACT STATEMENT

The results from this study are comparable with earlier research on ARF and ARDS patients, and some of the prevalence numbers are even lower than what is reported earlier. Female gender and younger age are known predictive factors for psychological distress after ICU treatment and are confirmed in this study while having a higher respiration rate at admission to ICU is to our knowledge not described in earlier research and provides new insight into the field. In addition, one in four of the patients in the present study show signs of cognitive impairment confirming that this is a common symptom after ICU treatment.

AUTHOR CONTRIBUTIONS

Kristina Struksnes Fjone: Conceptualisation; data curation; formal analysis; investigation; writing—original draft; writing—review & editing. **Eirik Alnes Buanes**: Conceptualisation; funding acquisition; methodology; project administration; resources; supervision; writing—review & editing. **Milada Cvancarova Småstuen**: Data curation; formal analysis; supervision; validation; visualisation; writing—review & editing. **Jon Henrik Laake**: Funding acquisition; validation; visualisation; writing—review & editing. **Jan Stubberud**: Conceptualisation; validation; visualisation; writing—review & editing. **Kristin Hofsø:** Conceptualisation; data curation; formal analysis; funding acquisition; methodology; project administration; resources; supervision; validation; visualisation; writing—original draft; writing—review & editing.

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The authors have checked to make sure that our submission conforms as applicable to the Journal's statistical guidelines *described here*. There is a statistician on the author team, Milada Cvancarova Småstuen. The authors affirm that the methods used in the data analyses are suitably applied to their data within their study design and context, and the statistical findings have been implemented and interpreted correctly. The authors agree to take responsibility for ensuring that the choice of statistical approach is appropriate and is conducted and interpreted correctly as a condition to submit to the Journal. Frequently used statistical methods (descriptive, graphical methods, parametric & nonparametric tests, linear & logistic regression) were used as the main statistical approach.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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