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Research paper

Psychological impact of COVID-19 after hospital discharge: A follow-up study on Italian recovered patients

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ABSTRACT

Background: Since COVID-19 outbreak, clinical experience on its management during the acute phase has rapidly grown, including potential effects on the psychopathological dimension. However, still few data are available regarding the impact on survivors' mental health over the long-term.

Methods: A sample of 1457 COVID-19 patients underwent a multidisciplinary follow-up protocol, approximately 3 months after hospital discharge, including a psychological evaluation. The primary outcomes were anxiety, depression, resilience, post-traumatic symptoms, and health-related quality of life. Furthermore, we examined the potential role of hospitalization and delay in the follow-up assessment on the increased burden of illness.

Results: Although a general high level of resilience emerged, suggesting most patients relied on their individual and interpersonal resources to face difficulties related to the pandemic, almost one third of the sample reported signs of psychological distress over time, especially post-traumatic symptoms, with anxiety being more represented than depression. Furthermore, hospitalization – regardless of the setting of care – and promptness in follow-up evaluation were found to play a protective role on patients' recovery and mental wellbeing.

Limitations: Selection bias of patients exclusively admitted to the hospital; absence of a control group; psychological assessment relying on self-reported instruments.

Conclusions: The current crisis demands resilience and adjustment resources, either in the acute and post-acute phase. Thus, the clinical effort should aim at relieving the traumatic impact of such condition through timely interventions. Further investigation may address potential predictors of developing a traumatic stress response, in order to identify and promptly treat at-risk subpopulations.

1. Introduction

Coronavirus disease-2019 (COVID-19) is a pandemic infection caused by the Severe Acute Respiratory Syndrome-Coronavirus-2 (SARS-CoV-2), that since its first report in China in December 2019 quickly spread all over the world.

At European level, Italy had to face a huge impact during COVID-19 first wave, especially in the northern areas, starting from the end of February 2020 (Spina et al., 2020). Within Lombardy region, the Italian epicenter of the outbreak, the province of Bergamo registered, from 20th February to 31st March 2020, over 5000 excess deaths compared with

the average of the same time length in the years 2015–2019 (Spina et al., 2020). ASST Papa Giovanni XXIII is the main public hospital of the Bergamo province, serving a population of around 1,110,000 inhabitants.

Although clinical experience on the management of the acute phase of illness has rapidly grown, still few data are available on its evolution among survivors, including its potential effects on mental health.

According to previous research focusing on pandemics (Severe acute respiratory syndrome and Middle East Respiratory Syndrome outbreaks), public health emergencies may unveil varying degrees of mental disorders (Brooks et al., 2020; Hall et al., 2008; Lee et al., 2007),

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including post-traumatic stress disorder (PTSD), mood and anxiety disorders (Rogers et al., 2020).

On this premise, it is likely that COVID-19 outbreak may be associated with the onset and/or re-exacerbation of relevant psychological and psychiatric morbidities in general population (Cerami et al., 2020; Rodriguez-Rey et al., 2020; Serafini et al., 2020; Wang et al., 2020; Xiong et al., 2020), with a potentially greater burden in subgroups of patients with confirmed and suspected infection (Wu et al., 2013). If confusion and delirium are quite common during the acute stage (Vindgaard and Benros, 2020), a scant body of evidence addressed psychopathological issues among patients in the post-acute phase. Empirical studies suggested that patients who tested positive for SARS-CoV-2 may experience adverse mental health outcomes, by means of higher PTSD, depression and anxiety levels compared with controls (Abdelghani et al., 2021; Kaseda and Levine, 2020; Mazza et al., 2020). Many researchers already addressed these disorders among affected patients, assessing in particular the perceived impact on quality of life (Madhavan and Pandurangan, 2021; Qu et al., 2021; Zhao et al., 2021). A recent review on post-COVID-19 syndrome highlighted the possible direct effects of intensive care unit stay, social isolation, and stigma in developing PTSD, anxiety, and depression symptoms, which may affect up to 26 % and 23 % of patients, respectively (Pavli et al., 2021), although no significant correlation was found between psychiatric consequences and markers of inflammation or multiorgan injury (Raman et al., 2021). Only few differences in the perceived quality of life were reported between patients admitted to ward and to ICU (Garrigues et al., 2020). The primary purpose of the present study was to investigate the psychological impact of COVID-19 infection in survivors during the post-acute phase. Furthermore, we examined the potential role of other variables, such as resilience, the occurrence of hospitalization as well as the extent of delay in the follow-up assessment, on the increased burden of illness.

2. Methods

2.1. Sample and procedure

All subjects who have been diagnosed with COVID-19 at our hospital, either discharged from the Emergency Department and/or admitted to internal wards, were identified through electronic health records. Pediatric patients (<18 years), asymptomatic pregnant women, and hospitalized subjects at the time of recruitment were excluded.

After three months from hospital discharge those subjects with a double negative nose-pharyngeal swab for SARS-CoV-2 RNA were invited to take part of a multidisciplinary follow-up protocol, including the assessment of the psychological consequences of COVID-19 beyond the physical ones (Venturelli et al., 2021). They were first evaluated by a nurse and underwent a complete blood test panel together with other instrumental diagnostic tests. Subsequently, they attended a psychological interview, including the administration of specific tests.

The Ethical Committee of our institution authorized the present study. Written informed consent was obtained from all participants for their tissues to be utilized for research.

2.2. Psychological assessment and instruments

The psychological evaluation, administered by trained psychologists, primarily addressed the patients' response to COVID-19 and hospitalization. Its main purposes were to: 1) highlight patients' personal and interpersonal resources and 2) in case of psychological distress, refer them to specialist outpatient services considered the most suitable for their needs. Four self-report questionnaires – described in the paragraphs below – were administered, then each subject received feedback on results.

2.2.1. Impact of Events Scale-Revised (IES-R)

The authors referred to the Italian validation of the Impact of Events Scale-Revised (IES-R) (Horowitz et al., 1979), a 22-item self-report measure focusing on the impact of traumatic life events on health by describing 22 emotional reactions (Craparo et al., 2013). The subject is asked to indicate, on a five-point scale, how frequently each reaction has been experienced in the previous week yielding a total score between 0 and 88, with a score ≥ 33 indicating the probable presence of PTSD.

2.2.2. Resilience Scale for Adults (RSA)

The Resilience Scale for Adults (RSA) is a 33-item self-report scale designed to assess individual, familial, and social resilience protective resources among adults (Friborg et al., 2003; Hjemdal et al., 2001). In the current study, its revised version (Friborg et al., 2006; Hjemdal et al., 2007) was used, applying a 5-point semantic differential response format in order to reduce acquiescence bias. The mean score varies from 0 (low resilience) to 5 (high resilience), with a score ≤ 2.99 - equal to three standard deviations below the mean (Bonfiglio et al., 2016) - being considered as suggestive of low protective resources against trauma and stressors. Hence, scores ≤ 2.99 were considered as pathologic.

2.2.3. Hospital Anxiety and Depression Scale (HADS)

The Hospital Anxiety and Depression Scale (HADS) consists of a self-administered questionnaire specifically developed to detect anxious and depressive states within the setting of hospital outpatient clinics (Zigmond and Snaith, 1983). Many studies confirmed its bidimensional structure, its validity and reliability (Herrmann, 1997; Moorey et al., 1991; Spinhoven et al., 1997; Zigmond and Snaith, 1983). The authors referred to the Italian validated version of the HADS (Costantini et al., 1999), including two 7-item scales, respectively for anxiety (HADS-A) and depression (HADS-D). The score for every item ranges between 0 and 3, with a maximum of 21 for each scale. Scores ≥ 11 may reveal the presence of emotional symptoms, thus being considered as pathological.

2.2.4. SF-36 Health Survey

The SF-36 Health Survey is a self-report questionnaire measuring the health-related quality of life (HR-QoL), well-known for its comprehensiveness, brevity, and high standards of reliability and validity (McHorney et al., 1993; Ware and Sherbourne, 1992). It is a generic and multidimensional instrument with 36 questions that gives a measure of the impact of illnesses on several domains of the quality of life. The answers were analyzed using an algorithm developed and provided by "Mario Negri Institute", which also published the Italian translation and validation of the questionnaire (Apolone and Mosconi, 1998). The difference between the individual score and the mean validation sample of every dimension was classified in four groups: 3 = above the mean, 2 = within 1 SD of the mean, 1 = within 2 SD of the mean, 0 = >2 SD of the mean. The latter was considered pathological for each domain of the scale.

2.3. Statistical analyses

For descriptive purposes, the RSA, IES-R, HADS-A, HADS-D, and SF-36 scores were categorized referring to the appropriate cut-offs.

All patients were grouped according to the occurrence of hospitalization, i.e., admission to Medical Units (MU) or ICU, as well as to the presence of a pathological score at IES-R and HADS-anxiety (HADS-A).

Chi-Square and unpaired Student's *t*-tests were used to compare qualitative and quantitative variables, respectively. Correlation analysis on quantitative variables was carried out by means of Pearson's correlation coefficient, reported together with the R^2 determination coefficient. Multivariable logistic regression was performed with a backward approach to obtain the set of variables independently associated with the following events: 'hospitalization', 'pathological IES-R score', and 'pathological HADS-A score'. Goodness of fitting was assessed by means

of Hosmer and Lemeshow test. Furthermore, multivariable logistic regression was used to get the most parsimonious set of SF-36 domains independently associated with the hospitalization rather than to obtain predictive models. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS), version 22. A two-tailed significance threshold of $p = .05$ was applied.

3. Results

A sample of 1457 patients were included in the statistical analyses, as they completed the psychological evaluation within the follow-up program, carried out at a mean of 97.6 ± 48.1 days from the hospital discharge (median 93, first quartile - Q_1 - of 61, and third quartile - Q_3 - of 131).

It is worth noting that the sample – almost equally divided into two groups of 778 and 779 subjects – allowed to demonstrate a difference of 0.05 from a baseline ranging from 0.05 to 0.30 at a Chi-square test carried out at a significance level of 0.05 (two tailed), with a power of 0.80 at least; then for a baseline proportion ranging from 0.35 to 0.5, the difference is approximately of 0.07. Furthermore, with such sample size, it was possible to demonstrate an effect size (difference divided by the phenomenon variability) of about 0.15 at a Student's *t*-test carried out at a significance of $\alpha = 0.05$ (two-tailed), with a power of 0.80 at least.

Demographic and clinical data of the whole sample are shown in Table 1. The mean age of the total sample was 59.4 ± 13.7 years and 37.5 % was composed of females. In relation to the psychological assessment, 4.9 % of them showed a pathological RSA score (mean: 3.9 ± 0.5), whereas 32.6 % reported a pathological IES-R score (mean: 25.9 ± 17.7). As regards anxiety and depression symptoms, 14.2 % had pathological scores at HADS-A (mean: 5.8 ± 4.1), but only 5.9 % at HADS-D (mean: 3.8 ± 3.4). Furthermore, 3.6 % of the sample showed pathological scores both at HADS-A and HADS-D, whereas 10.5 % only at HADS-A and 2.3 % exclusively at HADS-D.

Globally, 63.1 % of patients had a non-pathological score at RSA, IES-R, HADS-A, and HADS-D. Considering the SF-36 scale, the highest prevalence of pathological scores were found, in decreasing order, for physical role functioning (12.6 %), physical functioning (10.3 %), emotional role functioning alterations (6.7 %), social role functioning (6.5 %), general health perception (4.3 %), vitality (4.1 %), bodily pain (3.0 %), and mental health (1.7 %). In addition, 76.7 % of the sample showed non-pathological scores at the eight domains of the scale, 11.6 % had pathological scores at one domain, 5.4 % at two, 2.4 % at three, 1.9 % at four, 0.9 % at five, 0.5 % at six, 0.4 % at seven, and 0.2 % at all the eight domains of the SF-36.

3.1. Comparison between hospitalized and non-hospitalized patients

Of the whole sample, 65.2 % of subjects were hospitalized, more frequently in MU (86.7 %), followed by ICU (13.3 %), whereas 34.8 % were admitted only to the Emergency Room (ER). A relatively small number of patients (3.1 %) needed psychological support during the hospitalization: among those showing signs of psychological suffering, 5.3 % were already undergoing psychological and/or psychiatric treatment before COVID-19 diagnosis.

Table 1 describes demographic and clinical data of patients grouped according to the occurrence of hospitalization. Hospitalized patients had a higher mean age (62.1 ± 13.1 vs 54.4 ± 13.3 ; $p < .001$) and were mostly males (68.7 % vs 50.7 %; $p < .001$). Despite the hospital setting, they less frequently reported a pathological IES-R score, although with only a trend of statistical significance (30.9 % vs 35.8 %; $p = .058$). In addition, hospitalized patients had a lower frequency of pathological HADS-A score (12.3 % vs 17.6 %; $p = .002$), with lower mean scores (5.5 ± 4.1 vs 6.4 ± 4.1 ; $p < .001$), whereas no statistically significant differences were found in terms of RSA and HADS-D scores. Furthermore, time between discharge and follow-up evaluation was significantly lower in hospitalized patients (77.5 ± 35.9 vs 135.3 ± 45.3 ; $p < .001$).

Table 1

Demographic and clinical variables of the total sample and comparison between hospitalized and non-hospitalized patients.

	Total sample	Hospitalized patients	Non-hospitalized patients	p value
N (%)	1457 (100 %)	950 (65.2 %)	507 (34.8 %)	
Age (years, mean \pm SD)	59.4 \pm 13.7	62.1 \pm 13.1	54.4 \pm 13.3	<.001
Female (N, %)	547 (37.5 %)	297 (31.3 %)	250 (49.3 %)	<.001
Time to follow-up (days, mean \pm SD)	97.6 \pm 48.1	77.5 \pm 35.9	135.3 \pm 45.3	<.001
RSA, score (mean \pm SD)	3.9 \pm 0.5	3.9 \pm 0.6	3.9 \pm 0.5	.755
RSA, pathological (N, %)	69 (4.9 %)	46 (5.1 %)	23 (4.6 %)	.095
IES-R, score (mean \pm SD)	25.9 \pm 17.7	25.3 \pm 17.4	26.9 \pm 18.3	.131
IES-R, pathological (N, %)	461 (32.6 %)	282 (30.9 %)	179 (35.8 %)	.058
HADS-A, score (mean \pm SD)	5.8 \pm 4.1	5.5 \pm 4.1	6.4 \pm 4.1	<.001
HADS-A, pathological (N, %)	201 (14.2 %)	113 (12.3 %)	88 (17.6 %)	.002
HADS-D, score (mean \pm SD)	3.8 \pm 3.4	3.8 \pm 3.4	4.0 \pm 3.6	.292
HADS-D, pathological (N, %)	84 (5.9 %)	52 (5.7 %)	32 (6.4 %)	.080
SF-36, pathological (N, %)				
General health perception (%)	60 (4.3 %)	31 (3.4 %)	29 (5.8 %)	.012
Physical functioning (%)	144 (10.3 %)	90 (9.9 %)	54 (10.8 %)	.063
Physical role functioning (%)	177 (12.6 %)	99 (10.9 %)	78 (15.7 %)	.003
Emotional role functioning (%)	94 (6.7 %)	40 (4.4 %)	54 (10.8 %)	<.001
Social role functioning (%)	92 (6.5 %)	44 (4.9 %)	48 (9.6 %)	<.001
Bodily pain (%)	42 (3.0 %)	28 (3.1 %)	14 (2.8 %)	.126
Vitality (%)	58 (4.1 %)	27 (3.0 %)	31 (6.2 %)	.002
Mental health (%)	24 (1.7 %)	18 (2.0 %)	6 (1.2 %)	.102

Legend: RSA (Resilience Scale for Adults), IES-R (Impact of Event Scale–Revised), HADS-A (Hospital Anxiety and Depression Scale–Anxiety), HADS-D (Hospital Anxiety and Depression Scale–Depression), SF-36 (SF-36 Health Survey).

Bold was used to help the reader easily detect p values that are statistically significant ($<.05$)

They also less frequently showed pathological scores at the following SF-36 domains: limitations of role due to emotional (4.4 % vs 10.8 %; $p < .001$) and physical problems (10.9 % vs 15.7 %; $p = .003$), social functioning (4.9 % vs 9.6 %; $p < .001$), vitality (3.0 % vs 6.2 %; $p = .002$), and general health perception (3.4 % vs 5.8 %; $p = .012$).

In addition, from a multivariable logistic regression model including only the statistically significant above-mentioned SF-36 domains, those found to be independently associated to the event ‘hospitalization’ or ‘non-hospitalization’ (i.e., ER) include: limitation of role due to emotional problems (OR = 2.253; 95 % CI: 1.430–3.550; $p = .0005$) and social functioning, although at a trend of significance (OR = 1.561; 95 % CI: 0.984–2.475; $p = .058$).

Results from the logistic model showed that hospitalization in MU or ICU, compared with the only ER admission, was associated only with gender (OR = 1.998; 95 % CI: 1.587–2.515; $p < .001$ for males vs females) and age (OR = 1.043; 95 % CI: 1.034–1.052; $p < .001$ for each

year increase; OR = 1.870; 95 % CI: 1.644–2.135; $p < .001$ for each five-year increase). The Hosmer-Lemeshow goodness of fit test turned out not to be statistically significant ($p = .178$).

3.2. Comparison between patients with pathological and non-pathological IES-R

Table 2 reports data of the comparison between subgroups according to the IES-R score.

When grouped according to the IES-R, patients showing a pathological score (32.6 %) were more frequently female (52.1 % vs 30.1 %; $p < .001$) and showed a more unfavorable psychological profile in all the administered scales. In detail, they more frequently reported a pathological score at RSA (10.1 % vs 2.4 %; $p < .001$) with a lower mean score (3.7 ± 0.6 vs 4.0 ± 0.5 ; $p < .001$), HADS-A (36.2 % vs 3.6 %; $p < .001$) and HADS-D (14.3 % vs 1.9 %; $p < .001$) with higher mean scores (respectively, 9.1 ± 4.2 vs 4.2 ± 3.0 , $p < .001$; 6.1 ± 3.9 vs 2.8 ± 2.6 ; $p < .001$). The scores of all SF-36 domains were found to be more frequently pathological in subjects with pathological IES-R scores. In particular, physical functioning (18.1 % vs 6.5 %; $p < .001$), limitation of role associated with physical (21.1 % vs 8.5 %; $p < .001$) and emotional problems (14.2 % vs 3.1 %; $p < .001$), social functioning (13.7 % vs 3.1 %; $p < .001$), vitality (8.9 % vs 1.8 %; $p < .001$), general health perception (7.8 % vs 2.5 %; $p < .001$), bodily pain (5.0 % vs 2.0

Table 2
Demographic and clinical variables of the sample grouped according to the IES-R score.

	Pathological IES-R score	Non-pathological IES-R score	p value
N (%)	461 (32.6 %)	953 (67.4 %)	
Age (years, mean \pm SD)	58.2 \pm 13.5	59.7 \pm 13.5	.053
Female (N, %)	240 (52.1 %)	287 (30.1 %)	<.001
Time to follow-up (days, mean \pm SD)	98.9 \pm 50.3	98.1 \pm 46.9	.767
RSA, score (mean \pm SD)	3.7 \pm 0.6	4.0 \pm 0.5	<.001
RSA, pathological (N, %)	46 (10.1 %)	23 (2.4 %)	<.001
HADS-A, score (mean \pm SD)	9.1 \pm 4.2	4.2 \pm 3.0	<.001
HADS-A, pathological (N, %)	167 (36.2 %)	34 (3.6 %)	<.001
HADS-D, score (mean \pm SD)	6.1 \pm 3.9	2.8 \pm 2.6	<.001
HADS-D, pathological (N, %)	66 (14.3 %)	18 (1.9 %)	<.001
SF-36, pathological (N, %)			
General health perception	36 (7.8 %)	24 (2.5 %)	<.001
Physical functioning	83 (18.1 %)	61 (6.5 %)	<.001
Physical role functioning	97 (21.1 %)	80 (8.5 %)	<.001
Emotional role functioning	65 (14.2 %)	29 (3.1 %)	<.001
Social role functioning	63 (13.7 %)	29 (3.1 %)	<.001
Bodily pain	23 (5.0 %)	19 (2.0 %)	<.001
Vitality	41 (8.9 %)	17 (1.8 %)	<.001
Mental health	18 (3.9 %)	6 (0.6 %)	<.001
Hospitalization (%)	282 (61.2 %)	632 (66.3 %)	.008
Type of admission (N, %)			.116
Emergency Room (500, 35.4 %)	179 (38.8 %)	321 (33.7 %)	
Medical Unit (791, 55.9 %)	240 (52.1 %)	551 (57.8 %)	
Intensive Care Unit (123, 8.7 %)	42 (9.1 %)	81 (8.5 %)	

Legend: RSA (Resilience Scale for Adults), IES-R (Impact of Event Scale–Revised), HADS-A (Hospital Anxiety and Depression Scale–Anxiety), HADS-D (Hospital Anxiety and Depression Scale–Depression), SF-36 (SF-36 Health Survey).

Bold was used to help the reader easily detect p values that are statistically significant ($<.05$)

%; $p < .001$), and mental health (3.9 % vs 0.6 %; $p < .001$).

In relation to hospitalization, patients with a pathological IES-R score were less frequently hospitalized (61.2 % vs 66.3 %; $p = .008$), with no differences in terms of type of admission or in time to follow-up.

Applying the logistic model, a pathological IES-R score was found to be associated with gender ($p < .001$; men vs women OR = 0.455; 95 % CI:0.358–0.579), RSA score ($p < .001$, OR = 0.335, for each unity increase; 95 % CI:0.283–0.444), and, at a borderline statistical level, with age ($p = .069$; OR = 0.992; 95 % CI:0.983–1.001 for each year increase; OR = 0.930; 95 % CI:0.918–1.006 for each five-year increase). The goodness of fit was not rejected ($p = .880$). Hospital admission (yes/no), ICU admission (yes/no), as well as admission only in ER or MU or ICU, turned out not to be significantly associated.

3.3. Comparison between patients with pathological and non-pathological HADS-A

Patients with pathological HADS-A (14.2 %) were younger (56.5 ± 14.5 vs 59.6 ± 13.3 , $p = .002$), more frequently women (67.2 % vs 32.8 %, $p < .0001$), and less frequently hospitalized (43.8 % vs 33.9 %, $p = .007$). The mean time between hospital discharge and follow-up visit was longer (105.1 ± 53.8 vs 97.3 ± 46.9 , $p = .032$).

Moreover, they more frequently showed pathological scores at the SF-36 domains (all $p < .001$), higher mean scores at IES (46.9 ± 17.2 vs 22.4 ± 15.2 , $p < .0001$) and HADS-D (8.2 ± 3.7 vs 3.1 ± 2.8 , $p < .001$), whereas lower mean scores at RSA (3.4 ± 0.6 vs 4.0 ± 0.5 , $p < .001$).

From the logistic model, pathological HADS-A score was associated with gender ($p < .001$; men vs women OR = 0.264; 95 % CI:0.186–0.376), RSA score ($p < .001$, OR = 0.136; 95 % CI:0.097–0.190, for each unity increase), and age ($p = .003$, OR = 0.982; 95 % CI:0.970–0.994, for each year increase; OR = 0.911; 95 % CI:0.857–0.969, for each five-year increase). The goodness of fit was not rejected ($p = .681$). Hospital admission (yes/no), ICU admission (yes/no), as well as admission only in ER or MU or ICU, turned out not to be significantly associated.

3.4. Results of correlation analyses

Correlation analyses highlighted a significant direct correlation between the IES-R score and levels of HADS-A ($r = 0.639$, $p < .001$, $R^2 = 0.408$) and HADS-D scores ($r = 0.514$, $p < .001$, $R^2 = 0.264$). Significant inverse correlations emerged between IES-R and RSA scores ($r = -0.319$, $p < .001$, $R^2 = 0.102$) as well as perceived general and mental health (respectively, $r = -0.317$, $p < .001$, $R^2 = 0.101$; $r = -0.462$, $p < .001$, $R^2 = 0.213$). The number of days between the hospital discharge and the follow-up evaluation showed no significant correlation with the IES-R scores.

HADS-A scores showed also a significant direct correlation with HADS-D scores ($r = 0.663$, $p < .001$, $R^2 = 0.440$), whereas an inverse correlation was found with RSA scores ($r = -0.468$, $p < .001$, $R^2 = 0.219$). The time between the hospital discharge and the subsequent assessment had a significant positive relationship with increased HADS-A scores ($r = 0.112$, $p < .001$, $R^2 = 0.013$), and a negative relationship with the levels of mental and general health perception at SF-36 (respectively, $r = -0.059$, $p = .026$, $R^2 = 0.004$; $r = -0.056$, $p = .034$, $R^2 = 0.003$).

4. Discussion

To the best of authors' knowledge, the present article is the first available study primarily assessing the psychological impact of COVID-19 during the post-acute phase through a comprehensive follow-up assessment in such a great sample of recovered patients.

For instance, most of the existing evidence investigated the psychological and social consequences of the pandemic on the general population, health care professionals, and patients with psychiatric disorders

(Cénat et al., 2021). Only a few previous works published in the last year focused on psychiatric symptoms among patients recovered from COVID-19, although on smaller samples (Bo et al., 2021; Zhang et al., 2020). In the only cohort study conducted in a larger group of patients (Huang et al., 2021), the assessment of quality of life, anxiety, and depression over a 6-month follow-up exclusively relied on EQ-5D-5L, a generic questionnaire that may lack accuracy as it focuses on a limited number of health dimensions.

Our findings, coming from a psychological evaluation conducted approximately three months after discharge, revealed a general high level of resilience among patients. In fact, a great proportion of them were likely to successfully rely on their personal and interpersonal resources to face challenges triggered and/or directly caused by the pandemic and did not show signs of psychological distress.

Nevertheless, almost a third of the sample reported symptoms that could be inscribed within the frame of PTSD, such as avoidance symptoms (i.e. “I tried not to talk about it”), intrusiveness symptoms (i.e. “Pictures about it popped into my mind”), and hyper-arousal symptoms (i.e. “I was jumpy and easily startled”). Anxiety was more frequently represented than depression, in line with other recent studies (Méndez et al., 2021; Poyraz et al., 2021). Consistently with available evidence (Di Crosta et al., 2020; Pavli et al., 2021), these symptoms were more represented among females. The comparison with pre-pandemic data on the prevalence of mental disorders in the Italian population highlights the critical burden of COVID-19: for instance, in a study published in 2006 by de Girolamo and colleagues, only 2.3 % of the general population suffered from PTSD and 11.1 % from any anxiety disorder. Even though in the present study a structured diagnosis was not achievable and a more detailed evaluation would have been associated with a lower prevalence of PTSD syndromes, our findings are in line with most recent data on the Italian general population developing PTSD symptoms during the peak of COVID-19 pandemic (De Girolamo et al., 2006).

As expected, the impact on patients' quality of life after the acute phase was huge: among the most frequently reported feelings, a great sense of limitation of their life, due to either physical and emotional problems, as well as complaints about the reduction of their functioning, both at a somatic and a social level. The perceived reduction of the quality of life could be associated with the so-called post-COVID-19 syndrome, but since such condition was not officially recognized at the time of follow-up evaluation, further investigations on such regard were not performed due to the lack of specific data.

Taken as a whole, these results underline that COVID-19 represents a potential traumatic experience for everyone, regardless of the specific patient's circumstances (Saraswathi et al., 2020). Hence, the risk of developing a post-traumatic stress response should be considered since the early phase of illness. Acknowledging that the patient may be living or face a traumatic experience can help to guide a proper intervention at different stages, addressing the psychological suffering in the most accurate and appropriate way.

Indeed, during the acute phase, this may lead to the prompt activation of specific protocols aimed at reducing the traumatic impact of the experience. Accordingly, previous research on short term consequences of COVID-19 emphasizes the need to focus on the acute psychological distress and the perceived emotional impact of events associated with COVID-19 on mental health (Bridgland et al., 2021). The above-mentioned aspects are tightly linked with the accessibility to health services. During the emergency, a great percentage of patients infected by SARS-CoV-2 received first assistance and treatment at the ER, then being discharged with the indication of self-isolation at home. Apparently in contrast with literature results, the occurrence and the type of hospitalization (ICU or MU) were not discriminatory for the development of PTSD symptoms, whose prevalence was found to be quite similar. Therefore, although the hospitalization setting does not seem to represent a statistical predictive factor for the onset of psychological distress, non-hospitalized subjects experienced and reported higher levels of anxiety, regardless of the place of admission. They also

perceived a greater limitation of their identity role especially due to emotional distress, a decreased social functioning and vitality, enhanced physical problems, as well as a general worsening of their health. In contrast, hospitalized patients seemed to less frequently show PTSD symptoms. The percentage of inpatients reporting such symptomatology is double compared with the one reported in a recent meta-analysis, according to which the pooled prevalence of PTSD in ICU survivors at 3-month follow-up was 15.9 % (Righy et al., 2019). It is worth noting that subjects with this kind of distress showed significantly lower levels of resilience, higher levels of anxiety and depression, as well as a lower perceived quality of life.

Considering that inpatients could present more critical conditions than those discharged after the access to ER only, such findings strengthened the crucial role of the hospital care also for mental and emotional outcome. Some relevant considerations may arise: first, the importance of feeling taken in charge by the healthcare system as a protective factor for mental health, even in emergency situations like COVID-19 pandemic, when physical illness represents the major health threat. The limited accessibility to medical healthcare support may burden the patients' perception of loneliness and isolation, thus stressing the importance of healthcare system efficiency (Leigh-Hunt et al., 2017; Ozbay et al., 2007). Secondly, the need to promptly activate psychological and psychiatric outpatient services, in order to identify and appropriately address critical situations that may lead to chronic symptomatology, if not adequately treated (Cooke et al., 2020). In such regard, the time interval between hospital discharge and follow-up assessment plays a relevant role in patients' mental wellbeing. People who had the chance to be shortly evaluated after the acute phase reported lower levels of anxiety, while increasing signs of anxiety and decreasing levels of perceived general and mental health affecting the quality of life were documented in patients who waited longer. On this basis, the opportunity to meet and assess people early after hospital discharge gave the professionals the possibility to identify subjects at greater risk of developing psychological distress and promptly apply precautionary interventions to minimize the probability of symptoms' worsening. Furthermore, being aware that a follow-up evaluation was already planned represented a protective factor for patients discharged in the later phase of the crisis, as they could feel they were not left alone to face potential challenges related to the post-acute phase.

Certain methodological limitations may have hindered the robustness of the above-mentioned results. Firstly, the selection bias of patients exclusively admitted to the hospital may have limited the generalizability of results, as well as the absence of a control group from the general population. Moreover, a possible limitation is due to the psychological assessment relied on self-reported instruments. The dichotomization of scales' scores in two categories (pathological vs non pathological) could not allow their distinction in terms of severity.

The current crisis demands resilience and adjustment resources, either in the acute and post-acute phase. Thus, the clinical effort should aim at relieving the traumatic impact of such condition, through timely interventions on patients' psychological suffering and coping strategies.

Further long-term studies may address potential predictors of developing a traumatic stress response. Comparisons with other waves of infection may be helpful in better understanding the psychological impact of COVID-19.

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CRediT authorship contribution statement

AMB and LB were involved in data acquisition and together with LC and CL contributed to study conception and design. BMC performed the data analyses. All authors contributed to data interpretation and critical

revision of the manuscript, with MSS and EB as clinical experts. LB, CL, and LC wrote the original draft, CP contributed to reviewing and editing the manuscript. All authors had access to and verified all the data and had final responsibility for the decision to submit for publication.

Conflict of interest

Authors have no conflicts of interests to declare.

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References

- Abdelghani, M., Hassan, M.S., Alsadik, M.E., Abdelmoaty, A.A., Said, A., Atwa, S.A., 2021. Post-traumatic stress symptoms among an Egyptian sample of post-remission Covid-19 survivors: prevalence and sociodemographic and clinical correlates. *Middle East Curr. Psychiatry* 28, 20. <https://doi.org/10.1186/s43045-021-00102-y>.
- Apolone, G., Mosconi, P., 1998. The Italian SF-36 health survey: translation, validation and norming. *J. Clin. Epidemiol.* 51, 1025–1036.
- Bo, H.X., Li, W., Yang, Y., et al., 2021. Posttraumatic stress symptoms and attitude toward crisis mental health services among clinically stable patients with COVID-19 in China. *Psychol. Med.* 51, 1052–1053. <https://doi.org/10.1017/S0033291720000999>.
- Bonfiglio, N.S., Renati, R., Hjemdal, O., Friborg, O., 2016. The resilience scale for adults in Italy: a validation study comparing clinical substance abusers with a nonclinical sample. *Psychol. Addict. Behav.* 30, 509–515. <https://doi.org/10.1037/adb0000176>.
- Bridgland, V.M.E., Moeck, E.K., Green, D.M., et al., 2021. Why the COVID-19 pandemic is a traumatic stressor. *PLoS ONE* 16, e0240146. <https://doi.org/10.1371/journal.pone.0240146>.
- Brooks, S.K., Webster, R.K., Smith, L.E., et al., 2020. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *Lancet* 395, 912–920. [https://doi.org/10.1016/S0140-6736\(20\)30460-8](https://doi.org/10.1016/S0140-6736(20)30460-8).
- Cénat, J.M., Blais-Rochette, C., Kokou-Kpolou, C.K., et al., 2021. Prevalence of symptoms of depression, anxiety, insomnia, posttraumatic stress disorder, and psychological distress among populations affected by the COVID-19 pandemic: a systematic review and meta-analysis. *Psychiatry Res.* 295, 113599. <https://doi.org/10.1016/j.psychres.2020.113599>.
- Cerami, C., Santi, G.C., Galandra, C., et al., 2020. Covid-19 outbreak in Italy: are we ready for the psychosocial and the economic Crisis? Baseline findings from the PsyCovid study. *Front. Psychiatry* 11, 556. <https://doi.org/10.3389/fpsy.2020.00556>.
- Cooke, J.E., Eirich, R., Racine, N., Madigan, S., 2020. Prevalence of posttraumatic and general psychological stress during COVID-19: a rapid review and meta-analysis. *Psychiatry Res.* 292, 113347. <https://doi.org/10.1016/j.psychres.2020.113347>.
- Costantini, M., Musso, M., Viterbori, P., et al., 1999. Detecting psychological distress in cancer patients: validity of the Italian version of the hospital anxiety and depression scale. *Support Care Cancer* 7, 121–127. <https://doi.org/10.1007/s005200050241>.
- Craparo, G., Faraci, P., Rotondo, G., Gori, A., 2013. The impact of event scale - revised: psychometric properties of the Italian version in a sample of flood victims. *Neuropsychiatr. Dis. Treat.* 9, 1427–1432. <https://doi.org/10.2147/NDT.S51793>.
- De Girolamo, G., Polidori, G., Morosini, P., et al., 2006. Prevalence of common mental disorders in Italy. *Soc. Psychiatry Psychiatr. Epidemiol.* 41, 853–861. <https://doi.org/10.1007/s00127-006-0097-4>.
- Di Crosta, A., Palumbo, R., Marchetti, D., et al., 2020. Individual differences, economic stability, and fear of contagion as risk factors for PTSD symptoms in the COVID-19 emergency. *Front. Psychol.* 11, 567367. <https://doi.org/10.3389/fpsyg.2020.567367>.
- Friborg, O., Hjemdal, O., Rosenvinge, J.H., Martinussen, M., Aslaksen, P.M., Flaten, M.A., 2006. Resilience as a moderator of pain and stress. *J. Psychosom. Res.* 61, 213–219. <https://doi.org/10.1016/j.jpsychores.2005.12.007>.
- Friborg, O., Hjemdal, O., Rosenvinge, J.H., Martinussen, M., 2003. A new rating scale for adult resilience: what are the central protective resources behind healthy adjustment? *Int. J. Methods Psychiatr. Res.* 12, 65–76. <https://doi.org/10.1002/mpr.143>.
- Garrigues, E., Janvier, P., Kherabi, Y., et al., 2020. Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. *J. Infect.* 81. <https://doi.org/10.1016/j.jinf.2020.08.029>.
- Hall, R.C.W.H., Hall, R.C.W.H., Chapman, M.J., 2008. The 1995 Kikwit ebola outbreak: lessons hospitals and physicians can apply to future viral epidemics. *Gen. Hosp. Psychiatry* 30, 446–452. <https://doi.org/10.1016/j.genhosppsych.2008.05.003>.
- Herrmann, C., 1997. International experiences with the hospital anxiety and depression scale. A review of validation data and clinical results. *J. Psychosom. Res.* 42, 17–41. [https://doi.org/10.1016/S0022-3999\(96\)00216-4](https://doi.org/10.1016/S0022-3999(96)00216-4).
- Hjemdal, O., Friborg, O., Martinussen, M., Rosenvinge, J.H., 2001. Preliminary results from the development and validation of a Norwegian scale for measuring adult resilience. *Psychol. Assess.* 38, 310–317.
- Hjemdal, O., Friborg, O., Stiles, T.C., Rosenvinge, J.H., Martinussen, M., 2007. Resilience predicting psychiatric symptoms: a prospective study of protective factors and their role in adjustment to stressful life events. *Clin. Child. Psychol. Psychiatry* 12, 91–104. <https://doi.org/10.1177/1359104507071062>.
- Horowitz, M., Wilner, N., Alvarez, W., 1979. Impact of event scale: a measure of subjective stress. *Psychosom. Med.* 41, 209–218. <https://doi.org/10.1097/00006842-197905000-00004>.
- Huang, C., Huang, L., Wang, Y., et al., 2021. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet* 397, 220–232. [https://doi.org/10.1016/S0140-6736\(20\)32656-8](https://doi.org/10.1016/S0140-6736(20)32656-8).
- Kasada, E.T., Levine, A.J., 2020. Post-traumatic stress disorder: a differential diagnostic consideration for Covid-19 survivors. *Clin. Neuropsychol.* 34, 1498–1514. <https://doi.org/10.1080/13854046.2020.1811894>.
- Lee, A.M., Wong, J.G., McAlonan, G.M., et al., 2007. Stress and psychological distress among SARS survivors 1 year after the outbreak. *Can. J. Psychiatr.* 52, 233–240. <https://doi.org/10.1177/070674370705200405>.
- Leigh-Hunt, N., Bagguley, D., Bash, K., 2017. An overview of systematic reviews on the public health consequences of social isolation and loneliness. *Public Health* 152, 157–171. <https://doi.org/10.1016/j.puhe.2017.07.035>.
- S, P., Madhavan, S., Pandurangan, V., 2021. Prevalence, pattern and functional outcome of post COVID-19 syndrome in older adults. *Cureus* 13 (8), e17189. <https://doi.org/10.7759/cureus.17189>.
- Mazza, M.G., De Lorenzo, R., Conte, C., et al., 2020. Anxiety and depression in COVID-19 survivors: role of inflammatory and clinical predictors. *Brain Behav. Immun.* 89, 594–600. <https://doi.org/10.1016/j.bbi.2020.07.037>.
- McHorney, C.A., Ware, J.E., Raczek, A.E., 1993. The MOS 36-item short-form health survey (SF-36): II. Psychometric and clinical tests of validity in measuring physical and mental health constructs. *Med. Care* 31, 247–263. <https://doi.org/10.1097/00005650-199303000-00006>.
- Méndez, R., Balanzá-Martínez, V., Luperdi, S.C., Estrada, I., Latorre, A., González-Jiménez, P., Feced, L., Bouzas, L., Yépez, K., Ferrando, A., Hervás, D., Zaldívar, E., Reyes, S., Berk, M., Menéndez, R., 2021. Short-term neuropsychiatric outcomes and quality of life in COVID-19 survivors. *J. Intern. Med.* 290 (3), 621–631. <https://doi.org/10.1111/joim.13262>.
- Moorey, S., Greer, S., Watson, M., et al., 1991. The factor structure and factor stability of the hospital anxiety and depression scale in patients with cancer. *Br. J. Psychiatry* 158, 255–259. <https://doi.org/10.1192/bjp.158.2.255>.
- Ozbay, F., Johnson, D.C., Dimoulas, E., 2007. Social support and resilience to stress: from neurobiology to clinical practice. *Psychiatry (Edgmont)* 4, 35–40.
- Pavli, A., Theodoridou, M., Maltezou, H.C., 2021. Post-COVID syndrome: incidence, clinical spectrum, and challenges for primary healthcare professionals. *Arch. Med. Res.* 52 (6), 575–581. <https://doi.org/10.1016/j.arcmed.2021.03.010>.
- Poyraz, B.Ç., Poyraz, C.A., Olgun, Y., Gürel, Ö., Alkan, S., Özdemir, Y.E., Balkan, I.İ., Karaali, R., 2021. Psychiatric morbidity and protracted symptoms after COVID-19. *Psychiatry Res.* 295, 113604. <https://doi.org/10.1016/j.psychres.2020.113604>.
- Qu, G., Zhen, Q., Wang, W., Fan, S., Wu, Q., Zhang, C., Li, B., Liu, G., Yu, Y., Li, Y., Yong, L., Lu, B., Ding, Z., Ge, H., Mao, Y., Chen, W., Xu, Q., Zhang, R., Cao, L., Chen, S., Li, H., Zhang, H., Hu, X., Zhang, J., Wang, Y., Zhang, H., Liang, C., Sun, L., Sun, Y., 2021. Health-related quality of life of COVID-19 patients after discharge: a multicenter follow-up study. *J. Clin. Nurs.* 30, 1742–1750. <https://doi.org/10.1111/jocn.15733>.
- Raman, B., Cassar, M.P., Tunnicliffe, E.M., et al., 2021. Medium-term effects of SARS-CoV-2 infection on multiple vital organs, exercise capacity, cognition, quality of life and mental health, post-hospital discharge. *EclinicalMedicine* 31, 100683. <https://doi.org/10.1016/j.eclinm.2020.100683>.
- Righy, C., Rosa, R.G., Da Silva, R.T.A., et al., 2019. Prevalence of post-traumatic stress disorder symptoms in adult critical care survivors: a systematic review and meta-analysis. *Crit. Care* 23, 213. <https://doi.org/10.1186/s13054-019-2489-3>.
- Rodríguez-Rey, R., Garrido-Hernansaiz, H., Collado, S., 2020. Psychological impact and associated factors during the initial stage of the coronavirus (COVID-19) pandemic among the general population in Spain. *Front. Psychol.* 11, 1540. <https://doi.org/10.3389/fpsyg.2020.01540>.
- Rogers, J.P., Chesney, E., Oliver, D., et al., 2020. Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic. *Lancet Psychiatry* 7, 611–627. <https://doi.org/10.3389/fpsyg.2020.01540>.
- Saraswathi, I., Saikarthik, J., Senthil Kumar, K., Madhan Srinivasan, K., Ardhanaari, M., Gunapriya, R., 2020. Impact of COVID-19 outbreak on the mental health status of undergraduate medical students in a COVID-19 treating medical college: a prospective longitudinal study. *PeerJ* 8, e10164. <https://doi.org/10.7717/peerj.10164>.
- Serafini, G., Parmigiani, B., Amerio, A., Aguglia, A., Sher, L., Amore, M., 2020. The psychological impact of COVID-19 on the mental health in the general population. *QJM* 113, 531–537. <https://doi.org/10.1093/qjmed/hcaa201>.
- Spina, S., Marrazzo, F., Migliari, M., Stucchi, R., Sforza, A., Fumagalli, R., 2020. The response of Milan's emergency medical system to the COVID-19 outbreak in Italy. *Lancet* 395, e49–e50. [https://doi.org/10.1016/S0140-6736\(20\)30493-1](https://doi.org/10.1016/S0140-6736(20)30493-1).
- Spinhoven, P.H., Ormel, J., Sloekers, P.P.A., Kempen, G.I.J.M., Speckens, A.E., Van Hemert, A.M., 1997. A validation study of the hospital anxiety and depression scale (HAD) in different groups of dutch subjects. *Psychol. Med.* 27, 363–370. <https://doi.org/10.1017/S0033291796004382>.
- Venturelli, S., Benatti, S.V., Casati, M., et al., 2021. Surviving COVID-19 in Bergamo Province: a post-acute outpatient re-evaluation. *Epidemiol. Infect.* 149, e32. <https://doi.org/10.1017/S0950268821000145>.
- Vindegaard, N., Benros, M.E., 2020. COVID-19 pandemic and mental health consequences: systematic review of the current evidence. *Brain Behav. Immun.* 89, 531–542. <https://doi.org/10.1016/j.bbi.2020.05.048>.

- Wang, C., Pan, R., Wan, X., et al., 2020. A longitudinal study on the mental health of general population during the COVID-19 epidemic in China. *Brain Behav. Immun.* 87, 40–48. <https://doi.org/10.1016/j.bbi.2020.04.028>.
- Ware, J., Sherbourne, C.D., 1992. The MOS 36-item short form health survey (SF-36): I conceptual framework and item selection. *Med. Care* 30, 473–483. <https://doi.org/10.1097/00005650-199206000-00002>.
- Wu, P., Cowling, B.J., Wu, J.T., Lau, E.H.Y., Ip, D.K.M., Nishiura, H., 2013. The epidemiological and public health research response to 2009 pandemic influenza A (H1N1): experiences from Hong Kong. *Influenza Other Respir. Viruses* 7, 367–382. <https://doi.org/10.1111/j.1750-2659.2012.00420.x>.
- Xiong, J., Lipsitz, O., Nasri, F., et al., 2020. Impact of COVID-19 pandemic on mental health in the general population: a systematic review. *J. Affect. Disord.* 277, 55–64. <https://doi.org/10.1016/j.jad.2020.08.001>.
- Zhang, J., Lu, H., Zeng, H., et al., 2020. The differential psychological distress of populations affected by the COVID-19 pandemic. *Brain Behav. Immun.* 87, 49–50. <https://doi.org/10.1016/j.bbi.2020.04.031>.
- Zhao, Y., Yang, C., An, X., Xiong, Y., Huang, L., Jia, J., Xu, Q., Zhang, L., Zhao, J., Xu, A., et al., 2021. Follow-up study on COVID-19 survivors one year after discharge from hospital. *Int. J. Infect. Dis.* 112, 173–182. <https://doi.org/10.1016/j.ijid.2021.09.017>.
- Zigmond, A.S., Snaith, R.P., 1983. The hospital anxiety and depression scale. *Acta Psychiatr. Scand.* 67, 361–370. <https://doi.org/10.1111/j.1600-0447.1983.tb09716.x>.