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Running title: Psychopathological burden of COVID-19 at three months follow up

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Abstract

BACKGROUND: The well-known COVID-19 pandemic totally transformed people's lives, paving the way to various psychopathological symptoms. In particular, patients may experience a short- and long-term decreasing in their wellbeing. In this vein, the aim of this paper is to assess the COVID-19 patients' psychopathological profile (Post Traumatic Stress Disorder, distress, anxiety and depression symptoms), detecting possible differences linked to the ventilatory treatments.

METHODS: Outpatients who recovered from COVID-19 were asked to provide socio-demographic and clinical information, and to complete a brief psychological screening evaluation (Impact of Event Scale-Revised - IES-R, Depression Anxiety Stress Scale - DASS-21).

RESULTS: Overall, after informed consent, 163 Italian patients took part in this research. Of them, 31,9% did not undergo any ventilatory therapy, 27,6% undertook oxygen therapy; 28,2% underwent noninvasive mechanical ventilation and 12.3% received invasive mechanical ventilation. Although no statistically significant differences were revealed among patients stratified by spontaneous breathing or ventilatory therapies, they reported statistically significant more depression (4.5+5.2 vs 3.5+3.2; p=.017) and anxiety (4.3+4.5 vs 2.4+2.6; p<.00001) symptoms than normative groups. Moreover, patients experiencing COVID-19 disease as a trauma, complained statistically significant higher levels of depression, anxiety and stress symptoms than who did not describe a clinically relevant traumatic experience (p<0.001).

CONCLUSIONS: Thus, this study suggests to healthcare professionals to consider COVID-19 experience as a potential real trauma for patients and underlines the necessity to define patients' psychopathological profile in order to propose tailored and effective preventive and supportive psychological interventions.

Keywords: Post Traumatic Stress Disorder, distress, anxiety, depression, COVID-19

Introduction

The well-known pathogen called severe acute respiratory syndrome coronavirus-type 2 (SARS-CoV-2) resulting in Coronavirus-19 disease (COVID-19), first spread in the Chinese city of Wuhan in December 2019. Then, it reached the worldwide population. In Italy, the first case was diagnosed on 21st February 2020. Since 8th March 2020, the increasing rising of cases has obliged Italy to apply various limitation measurements that have totally transformed people's lives. A few days after, on 11th March 2020, the World Health Organization proclaimed the state of worldwide pandemic.[1]

The present SARS-CoV-2 has caused a higher death toll, compared to earlier coronavirus forms (SARS-CoV e MERS-CoV).[2] Such viruses occur at first as respiratory diseases, sometimes together with gastrointestinal symptoms. Besides, they may impact both on the cardiovascular system and on the central nervous system[3-6] with also well-known long-term effects.[7]

In addition, such pandemic has a relevant psychopathological side which deserves considerable attention. Focusing on Italy, previous studies and daily clinical practice pointed out depressive and anxiety post-traumatic symptoms, especially among women [8] between eighteen and forty-nine years.[9] Besides gender and age, these symptoms seem to be also influenced by the geographical area where people live, such that higher levels of anxiety and depression were reported in Northern Italy, where the number of patients affected by COVID-19 disease was higher.[9] Furthermore, during the lock-down period, the Italian population experienced a worsening in their sleep quality,[10] especially people living in Northern Italy than those living in the South.[11] An Italian investigation pointed out a connection between a low quality in sleeping and a high risk of infections, due to the resulting reduction of the subject's immune response and, possibly, due to a higher vulnerability to the virus.[11]

The virus spreading caused the collapse of hospital emergency departments as a great number of people affected by COVID-19 disease had to be hospitalized due to their complex clinical condition. They underwent various kinds of ventilator therapies characterized by an increasing use of oxygen and level of invasiveness. Specifically, the mainly used ones were the following: low flow oxygen support, high flow or non-invasive continuous positive airway pressure oxygen therapies, and invasive mechanical ventilation.

Several studies explored the psychological consequences suffered by COVID-19 patients in association with the severity and the kind of ventilatory therapy carried out. However, the findings are not yet consistent concerning the impact that the hospitalisation and the kind of ventilatory therapy may have. For instance, a previous study focusing on COVID-19 patients showed that having been in intensive care unit (ICU) was not a significant factor predicting psychopathological symptoms.[12] Conversely, another research highlighted more traumatic experiences linked to this kind of hospitalization:[13] being hospitalised in ICU was a predictor for developing Post Traumatic Stress Disorder - PTSD[14,15] as well as depression, insomnia and anxiety.[16] Again, severe symptoms of PTSD have been generally detected in groups of inpatients despite the specific unit.[17] Other researchers shown that patients who underwent ventilatory therapies reported higher level of PTSD than who did not receive such kind of therapy and who spent the course of the disease at home.[15, 18,19]

In addition, another research demonstrated that, regardless of the illness severity, all inpatients experienced sleeping, anxiety and depression problems, but patients developing a more severe clinical condition reported also more panic, distress, anxiety and depression problems.[4] However, other studies did not find any statistically significant correlations between the illness severity and the PTSD, depressive and anxiety symptoms.[20-25] Moreover, an Italian research shown that higher risk of developing Long Covid - defined as the persistence of physical or psychological symptoms for more than four weeks after recovery from the acute phase of the disease - does not depend on the severity of the virus.[8] Therefore, further studies are needed to assess possible differences concerning psychopathological symptoms in COVID-19 patients with different disease severity and undergoing various kind of ventilatory treatments.

This issue is particularly crucial as psychopathological syndromes might become chronic if not properly detected and taken in care. In this regard, several researches about past coronavirus epidemic unveiled that who survived COVID-19 showed higher level of distress, depression, anxiety and PTSD than normative group, not only during the acute phase of disease, but also one year after their illness and discharge from hospital.[26-28] Therefore, a quick and effective evaluation of the psychological distress of people affected by COVID-19 and the effective taking care of them by the healthcare system could play a crucial role for preventing this form of psychological malaise become chronic and disabling.

In this vein, the present study aims to provide a picture on the psychopathological profile of COVID-19 patients (PTSD, distress, anxiety, and depression symptoms) linked to the disease severity and the type of ventilatory treatment provided.

Methods

Participants

The sample is composed of outpatients who recovered from COVID-19 or still suffering from it, who have been treated in care hospitals located in the North of Italy (ASL 3 Genovese) from 1st March 2020 to 30th July 2020. They underwent a three-month follow-up. As the taking care of these participants was part of the clinical practice, no exclusion criteria have been set concerning sex, nationality and previous clinical conditions. The only requested criteria were a sufficient understanding of Italian language, and adequate clinical and cognitive conditions necessary to consciously take part to the present research.

Procedure

According to the normal clinical practice offered to COVID-19 patients, participants were first reached by phone for proposing the clinical and research pathways. Secondly, they were visited by the Fiumara Cardiology Rehabilitation service for a multidisciplinary assessment comprising cardiology, respiratory, physiatrist, diabetes, endocrine and rheumatology evaluations. Then, after providing a written consent form, participants were interviewed by a clinical psychologist (MF) who collected the necessary socio-demographic and clinical information, and conducted the psychological screening evaluation. The IES-R e DASS-21 scales were also administered. If necessary, participants were suggested to be taken in charge by the Mental Health Centres operating where the individual lives.

Measures

Schedule for socio-demographic and clinical data: The form includes questions to collect socio-demographic (i.e., age, gender, nationality, profession) and clinical data (i.e., COVID-19 patient's stay, COVID-19 clinical management, length of hospital stay).

Impact of Event Scale-Revised - IES-R:[29,30] it is composed of 22 items for evaluating the presence of the Post Traumatic Stress Disorder (PTSD) in accordance with DSM – 5 (Diagnostic and Statistical Manual of Mental Disorders).[31] The occurrence of the PTSD symptoms is detected during the last 7 days through a 5-points Likert scale (ranging from 0-never to 4-very often). IES-R is composed by the following three sub-scales: intrusion (strong thoughts and desabling emotions deriving from the trauma experience), avoidance (tendency to avoid thoughts and stimulations linked to the stressful situation) and iper-arousal (state of overvigilance and tension characterised by somatic manifestation). The 33-points cut off highlights people at high risk of PTSD symptoms.

Depression Anxiety Stress Scale - DASS-21:[32,33] It evaluates depression (low mood, apathy, anhedonia, self-devaluation), anxiety (activation state of the autonomic nervous system) and stress (arousal levels). The evaluation refers to the previous week according to the 4-points Likert scale (ranging from 0-never to 3-very often). Three sub-scales can be detected. As far as depression, there are the following cut-offs according to a continuum of severity: normal (0 to 4), slight (5 to 6), medium (7 to 10), severe (11 to 13), and highly severe ($\geq$14).

As far as anxiety, the continuum of severity is assessed through the following cut-offs: normal (0-3), slight (4-5), medium (6-7), severe (8-9), and highly severe ($\geq$10).

As far as stress, cut-offs are the following: normal (0-7), slight (8-9), moderate (10-12), severe (13-16), highly severe ($\geq$17).

In this research, scores starting from a medium level and going upward were considered the clinical cut-off for relevant psychopathological symptoms for all sub-scales.

Data analysis

Categorical variables are presented as frequencies and percentages and were compared by chi-square test or Fisher's exact test. Continuous variables are reported as mean and standard deviation (SD) or median and interquartile range (IQR) according to their distribution. Normally distributed variables were compared by

means of unpaired Student's t test. Non-normally distributed variables were compared with the U Mann-Whitney non-parametric test.

Specifically, patients' psychological profiles were compared with regard to normative sample, different kinds of ventilatory treatments, and stratification of DASS-21 for IESR.

The statistically significant p value was set <0.05 and all analysis were two-tailed.

All analyses were performed with R environment 3.6.3 (R. Foundation for Statistical Computing, Vienna, Austria).

Ethical statement

The study protocol conformed to the Declaration of Helsinki and it was approved by the Ethics Committee of Liguria Region (n° 430/2020CER).

Each participant has been orally and written informed about the aims and nature of the current research. Prior to collect data, participants provided a signed informed consent on a voluntary bases and without any reimbursement. The personal data protection and the possibility to withdraw any consequences were guarantee along the research.

Results

Sample characteristics

The whole total sample was composed of 207 people, but 44 people were excluded because of some language difficulties or tendency to derailment. As a whole, 163 people (response rate 78.74%) have taken part in this research. Mean age of this sample was 57 ± 10.98 years old.

The majority of participants were men (53.4%), Italian (82.1%), were hospitalised (84.0%) and did use some kinds of ventilatory therapy (68.1%). Concerning work and private life, 34 people (21.4%) experienced to be at high risk of contagion as they were currently working in the social-health sector and 20 people (12.5%) recently lost at least one family member due to COVID-19. More than half of the sample (51.2%) complained some sleep disorders, as well. From a psychological perspective, 46.0% were not in charge for any kind of psychological treatment at the moment of the psychological assessment; 34.4% reported traumatic experiences related to COVID-19 and the most referred symptom was depression (41.5%). For details, see table 1.

INSERT HERE TABLE 1

Comparisons regarding DASS-21 scores with normative sample

As for DASS-21 subscales, the research sample reported statistically significant more depression (4.5±5.2 vs 3.5±3.2; p=0.017) and anxiety (4.3±4.5 vs 2.4±2.6; p<0.00001) symptoms than normative samples (Table 2).

INSERT HERE TABLE 2

Comparisons between the absence or presence of different types of ventilatory therapy

No statistically significant differences were revealed regarding sleep disorders among patients stratified by spontaneous breathing (at home or in hospital), oxygen therapy, non-invasive or invasive mechanical ventilation (p=0.305).

Moreover, considering patients above the clinical cut-off, no differences were unveiled on the levels of traumatic experience, depression, anxiety and stress symptoms between patients with spontaneous breathing or with different kinds of ventilator therapies. Focusing only on spontaneous breathing, no differences are emerged between COVID-19 outpatients (n=26) and inpatients (n=26). Finally, there are no differences between patients with (n=52) or without (n=111) ventilation (Table 3).

INSERT HERE TABLE 3

Comparisons between DASS-21 scores stratified by IESR score

Considering data above the clinical cut-offs for DASS-21 subscales, patients reporting traumatic experience related to COVID-19 disease complained statistically significant higher levels of depression, anxiety and stress symptoms than who did not described a clinically relevant traumatic experience (p<0.001; Table 4).

INSERT HERE TABLE 4

Discussion

As COVID-19 pandemic triggered different psychopathological symptoms of various severity, the aim of this study was to catch a picture of the psychopathological profile of 163 COVID-19 patients living in North of Italy, one of the regions mainly affected by the virus during the first wave according to the presence or the absence of ventilatory therapy.

Overall, the majority of participants were Italian men and hospitalised. Almost three quarters underwent oxygen/ventilatory therapy. Concerning work and private life, a quarter of the sample experienced high risk of contagion as they were currently working in the social-health sector. This data was attended and also already described in literature as working in front-line position can be perceived as highly dangerous in case of such contagious pathogen.[34-39]

More than twenty people recently lost at least one family member due to Covid-19 disease, as well. This result requests further investigation because it may be associated with the possibility to develop prolonged grief or major depression disorder or PTSD.[40] In addition, more than half of the current sample complained some sleep disorders coherently with previous literature, detecting insomnia disorders among discharged post-COVID-19 patients,[16,41] independently of the kind of ventilatory therapy.[4]

Moreover, the psychological screening evaluation enabled to collect intrusive dreams occurring during the hospitalization or after discharge characterized by contents already present in literature:[13] relatives' bereavement, imprisonment, blood, tormented travel and feeling of suffocation. Thus, detecting people experiencing a recent bereavement and sleep disorder linked to COVID-19 may be crucial for offering preventive and supportive intervention for the wellbeing of the individual. This clinical issue deserves further investigation to understand the possible correlation with the severity of clinical condition or with the type of ventilatory therapy.

In general, 35.5 % were provided with one section of clinical counselling, 18.5% were taken in charge by the territorial service or by interdisciplinary rehabilitative Cardiac Unit with a focused traumatic treatment and 46.0% were not in charge for any kind of psychological treatment.

From a psychological perspective, the current sample reported statistically significant more depression and anxiety symptoms than normative sample.[33] This finding confirms one time again the negative psychopathological impact of COVID-19 pandemic. Indeed, several researches have shown important levels of depression and anxiety symptoms in post-COVID-19 patients. [4,16,21,22, 42-44]

From a clinical perspective, no differences were unveiled in patients with spontaneous breathing or various ventilator therapies regarding the levels of traumatic experience, stress, anxiety and depression symptoms. These data are in line with part of the previous literature reporting higher levels of psychopathological symptoms in hospitalized patients regardless the disease severity and the kind of clinical treatments received.[20-25] Coherently, these findings seem to be an interesting confirmation that psychological effects are not related to the level of pulmonary involvement, rather to the illness experience itself. Although further research is needed, it is reasonable to assume that no differences were unveiled as each disease pathway has involved peculiar stressful risk factors for the individual mental health. Thus, for instance, who stayed at home perceived to be more isolated and under-monitored than who was hospitalized, and were afraid of transmitting the virus to other family members. These condition and personal beliefs were already reported as relevant stressors for the individual.[42] Again, who underwent oxygen therapy (OT) usually maintained full disease awareness along the care path, possibly developing fear her/his clinical parameters can worsen. People underwent non-invasive mechanical ventilation (NIV) had a long hospital stay which was frequently characterized by fears of being intubated or dying. They also complained the impossibility to communicate with loved ones and healthcare professionals as usual. These elements can be considered as sound risk factors for mental health as highlighted by recent research.[13] In addition, those who were intubated for being treated with invasive mechanical ventilation (IMV) were unconscious for most of the time. On one hand, sedation may be a protective factor as hypothesized by some research; on the other hand, can trigger traumatic feelings after discharge in a "long-COVID syndrome".[45] Finally, it has also to be said that, besides the disease course, the persistence of post-infection physical problems is a significant contributor for developing PTSD, depression, and anxiety, as evidenced in the literature.[8,46]

As expected, patients reporting traumatic experiences related to COVID-19 disease complained statistically significant higher levels of depression, anxiety and stress symptoms than patients who did not describe a clinically relevant traumatic experience. This finding suggests to healthcare professionals the necessity to consider COVID-19 experience as a possible traumatic event requesting a holistic patients' taking care. To this regard, the psychological intervention can play the difference. Indeed, literature and clinical experience constantly show that each kind of traumatic event may potentially pave the way to detrimental psychopathological consequences, in particular PTSD and anxious and depression symptoms.[31,47] In this case,

secondary prevention through early interventions against chronic PTSD and its consequences may result in better positive outcomes for mental health.[48] Similarly, a recent study reported that, in a population of COVID-19 survivors, the recovery from PTSD shortened from 64 to 36 months for people asking for some kind of psychological intervention.[49] Thus, tailored preventive and supportive interventions for COVID-19 patients and survivors are a sound urgency.

Limits and strengths

The present research is not without limits. Firstly, the characteristics and the size of the current sample prevented to carry on further statistical analysis. Secondly, detailed clinical and neuropsychological data were not present. Thus, further research should enrich the characterization of the sample providing more clinical data, and a neuropsychological profile. As a note, several people have reported attention, concentration and memory problems. For this reason, during the last months, patients have had the chance to go to neurological and neuropsychological services for further information.

In addition, this study involved patients living in North Italy, strictly affected by COVID-19 pandemic so the sample can be considered high representative. However, all patients came from a single area of the city of *edited out for blind review*, therefore the generalization of results could be misleading.

However, this study provides a vivid picture of COVID-19 patients focusing on their psychological profile. Moreover, different types of psychological interventions are displayed such, suggesting tips for future research and clinical practice. Overall, this study enriched and strengthened previous literature, suggesting to healthcare professionals to consider COVID-19 experience as a potential real trauma for the patients: independently of the specific kind of ventilatory therapy adopted, who experienced post-traumatic stress complained also higher level of anxiety and depression. However, further research is necessary.

Conclusion

This study suggests the importance of a holistic taking care of the COVID-19 patient and survivors, regardless of the disease severity and the type of treatment received. Indeed, those who have experienced this disease

reported higher levels of anxiety and depression symptoms than the normative population. Moreover, COVID-19 disease can be experienced as a real trauma and, in this case, this can exacerbate psychopathological symptoms, in particular anxiety, depression and distress. The psychological intervention should therefore accompany the patient in the medium and long term, aiming to reach the optimal recovery of subjective psycho-physical wellbeing. To this regard, as practical tip, it would be recommended a screening assessment during scheduled medical check-up for detecting possible psychological symptoms in patients recovered from COVID-19. Afterwards, psychological or psychotherapeutic interventions should be offered according to specific needs reported by the patients or caregivers. [50] The early intervention is pivotal for avoiding both the recrudescence of the current malaise and secondary symptoms of Long Covid syndrome.[51] Regarding this, the Italian government provided some suggestions to cope with the psychological impact of the sanitary emergency.[52] Moreover, it would be suggested to provide phone-based psychological intervention and/or support intervention trough digital platforms.[53] Overall, it would be beneficial for everyone - patients, caregivers and healthcare professionals - to have dedicated occasions to think about their experiences, exchanging feedbacks and perceptions in order to validate reciprocal feelings and to find novel resources fostering wellbeing.

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Authors' Contribution:

Ferraris Marta: has given substantial contributions to study concept, data collecting and to write the manuscript

Maffoni Marina: has given substantial contributions to data analysis and to write the manuscript

De Marzo Vincenzo: has given substantial contributions to data analysis and to write the manuscript

Pierobon Antonia: has given substantial contributions to data analysis and to write the manuscript

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All authors read and approved the final version of the manuscript.

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Table 1. Socio-anagraphic, clinical and psychological data (n=163)

	n (%)
Gender	
Male	87 (53.4)
Nationality	
Italian	133 (82.1)
Traumatic risk factors	
profession at risk of contagion (healthcare professions)	34 (21.4)
death of a family member due to COVID-19	20 (12.5)
sleep disorders	83 (51.2)
COVID-19 clinical management	
Spontaneous breathing	52 (31.9)
OT	45 (27.6)
NIV	46 (28.2)
IMV	20 (12.3)
Psychological support	
proposal to be taken in charge	58 (35.5)
already in charge by sanitary assistance services	14 (8.6)
taken in charge during the recovery	12 (7.4)
EMDR	4 (2.5)
none	75 (46.0)
	Median [IQR]

Length of hospital stay (days)		
OT	/	13 [6.0, 24.0]
NIV	/	24 [18.0, 33.0]
IMV	/	45 [33.0, 60.0]
Instruments administred		
IESR (>33)	56 (34.4)	22 [9.5, 42.0]
DASS-21- Depression (>10)	66 (41.5)	2 [0, 7.0]
DASS-21- Anxiety (>8)	46 (28.9)	3 [1.0, 6.0]
DASS-21- Stress (>15)	41 (26.1)	4 [1.0, 10.0]

Note. OT, oxygen therapy; NIV, noninvasive mechanical ventilation; IMV, invasive mechanical ventilation; IQR, interquartile range; EMDR= Eye Movement Desensitization and Reprocessing

Table 2. DASS-21 comparisons with normative data

DASS-21	Normative sample M (DS)	Research sample M (DS)	t	p
DASS-Depression	3.5 (3.2)	4.5 (5.2)	2.42	0.017
DASS-Anxiety	2.4 (2.6)	4.3 (4.5)	5.16	<0.00001
DASS-Stress	6.4 (3.8)	5.9 (5.8)	-1.05	0.29

Table 3. Patients' psychological data stratified according to the absence or presence of different types of ventilatory therapy: n (%) and median [IQR]

	Patient's at home	Patient's in hospital			
	Spontaneous breathing (n=26)	Spontaneous breathing (n=26)	OT (n=45)	NIV (n=46)	IMV (n=20)
IESR (≥33)	12 (21.4) 28.5 [9.5, 43.8]	8 (14.3) 19.5 [13.5, 41.3]	14 (25.0) 21.0 [9.0, 41.0]	17 (30.4) 22.0 [7.3, 42.0]	5 (8.9) 24.0 [11.5, 31.5]
DASS-21					
Depression (≥10)	10 (15.2) 1.5 [0, 7.8]	13 (19.7) 3.0 [1.3, 7.0]	16 (24.2) 2.0 [0.5, 6.0]	22 (33.3) 3.0 [0, 11.0]	5 (7.6) 2.0 [0, 5.0]

Anxiety (≥8)	9 (19.6)	5 (10.9)	11 (23.9)	15 (32.6)	6 (13.0)
	3 [1.0, 6.8]	3.0 [1.0, 5.0]	3.0 [1.0, 5.5]	3.0 [1.0, 7.0]	3.0 [0.5, 6.0]
Stress (≥15)	9 (22.0)	8 (19.5)	11 (26.8)	11 (26.8)	2 (4.9)
	6.0 [3.0, 11.5]	4 [1.0, 10.0]	4.0 [1.3, 10.5]	3 [2.0, 8.0]	4.0 [1.0, 6.0]

Note: comparisons not significant (p>.05)

Table 4. DASS-21 scores stratified by IESR scores, according to their clinical cut-off in brackets

DASS-21	IESR (≥33)		p
	No	Yes	
	n (%)	n (%)	
	107 (65.6)	56 (34.4)	
Depression (≥10)	29 (27.9)	37 (67.3)	<0.001
Anxiety (≥8)	10 (9.6)	36 (65.5)	<0.001
Stress (≥15)	5 (4.9)	36 (66.7)	<0.001