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Anxiety in patients treated in a temporary hospital in Belgrade, Serbia, during the first epidemic wave of COVID-19

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ABSTRACT

Background: It has been reported that COVID-19 patients in general often experience anxiety, depression and stress, but those problems in patients of temporary COVID-19 hospitals seem to have attracted less attention.

Methods: The study included 87 SARS-Cov-2 infected subjects accommodated and treated in a temporary hospital in Belgrade, Serbia, during the first epidemic wave of COVID-19. The patients’ level of anxiety was assessed on two occasions (at admission to the temporary hospital, and 2 weeks after discharge) using the Hamilton Anxiety Rating Scale (HAM-A). Demographic and clinical data were obtained through questionnaires or retrieved from patients’ medical records.

Results: A multiple linear regression model revealed that sex, age, the severity of COVID-19 symptoms (COVID-19_SS) and the family history of psychiatric disorder (FHPD) remain significant predictors of the level of anxiety at hospital admission (F (4, 82) = 14.916, p < 0.0001), with an R² of 0.421. Participants’ predicted level of anxiety at admission to the temporary COVID-19 hospital can be calculated as 0.931 – 0.708 × SEX + 0.029 × AGE + 0.674 × COVID-19_SS + 1.491 × FHPD, where SEX is coded as 1 for male and 0 for female, AGE is measured in years, COVID-19_SS is coded as 0 for asymptomatic, 1 for mild, 2 for moderate and 3 for severe, and FHPD as 0 for negative and 1 for positive. Comparison between individual HAM-A score at admission to the temporary hospital (median (IQR): 7.00 (2.00 – 11.75)) and 2 weeks after discharge (median (IQR): 0.00 (0.00 – 1.00)) revealed significant reduction in the level of anxiety among study participants (Z = – 7.53, p < 0.001).

Conclusion: These data indicate that psychological changes exist in those hospitalized in temporary hospitals, but that they regress soon after they leave.

1. Introduction

Since ancient times, the world has been facing an increasing number of viral diseases, of which some posed a serious threat to public health [1]. The most recent and still ongoing is the pandemic of yet unprecedented proportions, with almost 5 million confirmed...
deaths so far [2] and no end in sight. At the moment, none of the many strategies to deal with COVID-19 is perfect, but our knowledge in the field is improving every day.

To limit the transmission of Sars-CoV-2, and to provide an adequate medical treatment for patients infected with the virus, the state authorities worldwide have undertaken different measures. One of them - the idea to convert a public place into a temporary hospital - proved to be quite effective, thus has been widely used during the COVID-19 emergency. As of February 2020, in Wuhan, China, the construction of the first „cabin hospitals“ began [3]. Following China’s example, many countries, including Serbia, have modified their sports stadiums, concert halls, fair grounds and convention centers into temporary hospitals. With more hospital beds available, they were able to isolate patients with mild to moderate COVID-19 from their families and the community, while providing medical care, disease monitoring, food, and shelter [4].

Although originally related only to physical health, over time COVID-19 crisis overgrew to endanger almost all other aspects of life as well, including social relationships, personal freedom and mental wellbeing. Fear of being infected with a deadly virus, social isolation, loneliness, and frustration are all well known risk factors for the development or aggravation of mental illnesses [5-9]. Expectedly, studies have shown that large proportion of COVID-19 patients are experiencing anxiety, depression and stress [10,11].

On the other hand, those psychological problems in patients of temporary COVID-19 hospitals seem to have attracted less attention, and the studies in this field are scarce. Therefore, the main aim of this study was to determine the factors affecting the level of anxiety of COVID-19 patients hospitalized and treated in the only temporary hospital that existed in Belgrade, Serbia, during the first epidemic wave of COVID-19.

2. Materials and methods

This non-randomized single-centered prospective cohort study was conducted during the first epidemic wave of COVID-19, and included 87 SARS-CoV-2 infected subjects that were accommodated and treated between April and May 2020 in, at that time, the only temporary hospital in Serbia. This temporary hospital was set up by the Serbian Armed Forces at the Belgrade Fair, Belgrade, with 500 beds organized in 10-bedded male or female hospital rooms. The hospital consisted of an admission triage service, an internal medicine clinic, and laboratory and X-ray diagnostics. As a main criterion for the admission to hospital, all participants had to have SARS-CoV-2 infection confirmed by RT-PCR test, obtained by nasopharyngeal or oropharyngeal swab. Patients were included in the study if they were willing to participate and were at least 18 years old. Those who had history of psychoactive substance abuse, hetero- and auto-aggressive tendencies observed during hospitalization, or were pregnant or breastfeeding, were excluded from the study. Prior to entering the study, all patients signed informed consent form. The study was approved by the local Ethics committee in Belgrade (approval No 2161), and conducted in accordance with the Declaration of Helsinki and its subsequent revisions.

As a part of routine care at the hospital, all study participants underwent frequent around-the-clock check-ups. The therapy depended on the severity of symptoms, and included vitamins, antipyretics and/or antibiotics. Any deterioration in the clinical course lead to immediate transportation to the secondary and tertiary health care institutions for further evaluation and treatment. In patients who remained at the temporary hospital, the second RT-PCR test was performed 2 weeks after admission. Those who tested negative were discharged from the temporary hospital, and instructed to stay at home for another 2 weeks, when they were to be RT-PCR tested for COVID-19 for the third time.

Study participants also answered the questions related to their family history of psychiatric disorder, the presence of comorbidities, the level of education, simultaneous SARS-CoV-2 infection of other family members, joint hospitalization with other family members, and previous hospitalizations due to COVID-19. The data on sex, age and the severity of COVID-19 (estimated according to the recommendations by World Health Organization) were retrieved from patients’ medical records.

The patients’ level of anxiety was assessed at two occasions (at the admission to the temporary hospital, and 2 weeks after discharge) using one of the oldest, but still widely employed rating scale for severity of perceived anxiety symptoms, known as Hamilton Anxiety Rating Scale (HAM-A) [12]. While it has been criticized for its low ability to separate anxiolytic from antidepressant effects, and somatic anxiety from somatic side-effect, HAM-A is often used in clinical research trials as it is easy to administer and has a reasonable inter-rater reliability and good one-week retest reliability. It represents a questionnaire that consists of 14 items covering somatic and psychological symptoms of anxiety. Each item is scored on a 5-point rating scale, with 0 corresponding to none, 1 to mild, 2 to moderate, 3 to severe, and 4 to very severe grade. The cut off scores for mild, moderate and severe anxiety are set at 8–14, 15–23, and ≥24 points, respectively, while scores ≤7 represented minimal or no anxiety, as previously reported [12]. The original version of the test was administered in Serbian language and necessary test adjustments had to be made because of the cultural characteristics of the study population. The testing has been performed at the same time of the day and by the same psychiatrist on both occasions: first time in person, and second one over the phone. All study participants completed both questionnaires.

Statistical analysis was performed using IBM SPSS Statistics, version 20 (IBM Inc, NY, US). Continuous data were tested for normality using Kolomogorov-Smirnov test, and presented as mean ± SD when normally distributed, or as median (IQR) when the distribution was non-normal. When the independent variable was not normally distributed, square root transformation was applied before analyses assuming data normality were performed. The effect of sex, family history of psychiatric disorder, comorbidity, the level of education, severity of COVID-19, simultaneous SARS-CoV-2 infection of other family members, and joint hospitalization with other family members on the level of anxiety (expressed as HAM-A score) at the admission to the temporary COVID-19 hospital was assessed using Mann Whitney or Kruskal-Wallis test. The effect of age and the length of the previous hospitalization due to COVID-19 on the anxiety level was determined by linear regression analysis and Spearman’s rank correlation. To predict the level of anxiety at the admission to the temporary COVID-19 hospital based on the significant independent variables, multiple linear regression was calculated. The levels of anxiety at the admission to the temporary hospital and 2 weeks after discharge were compared using Wilcoxon
signed-ranks test. The differences at $p < 0.05$ were considered significant.

3. Results

There were 87 patients included in the study, and their socio-demographic and clinical characteristics are shown in Table 1. In our study population, the level of education ($H = 0.484$, $p = 0.785$), previous hospitalization due to COVID-19 (both the experience ($U = 378.50$, $p = 0.378$) and the length ($r = -0.077$, $p = 0.477$)), as well as simultaneous SARS-CoV-2 infection of other family members ($U = 871.50$, $p = 0.688$) and joint hospitalization ($H = 1.56$, $p = 0.457$) did not significantly affect the level of anxiety at admission to the temporary hospital. On the other hand, female sex ($U = 656.50$, $p = 0.014$, Fig. 1A) and older age ($r = 0.35$, $p = 0.001$, Fig. 1B) were associated with higher level of anxiety. Similar effect exhibited positive family history of psychiatric disorder ($U = 165.00$, $p = 0.026$, Fig. 2A), the presence of comorbidities ($U = 491.00$, $p = 0.001$, Fig. 2B) and more severe COVID-19 symptoms ($H = 22.49$, $p < 0.001$, Fig. 3A). A multiple linear regression model revealed that sex, age, the severity of COVID-19 symptoms and the family history of psychiatric disorder remain significant predictors of the level of anxiety at hospital admission ($F (4, 82) = 14.916$, $p < 0.0001$), with an $R^2$ of 0.421 (Table 2). Comparison between individual HAM-A score at admission to the temporary hospital (median (IQR): 7.00 (2.00–11.75)) and 2 weeks after discharge (median (IQR): 0.00 (0.00–1.00)) revealed significant reduction in the level of anxiety among study participants ($Z = -7.53$, $p < 0.001$, Fig. 3B). Fig. 3B pointing out the fact that almost all participants experienced significant drop in anxiety level after discharge.

4. Discussion

In the present study, we assessed the level of anxiety of COVID-19 patients at admission to the temporary hospital, and evaluated its association with different socio-demographic and clinical characteristics. In addition, we compared patients’ anxiety levels at admission and 2 weeks after discharge from the temporary hospital. Our results revealed that sex, age, family history of psychiatric disorder, the presence of comorbidities, and the severity of COVID-19 significantly affect the level of anxiety at temporary hospital admission, and that the level of anxiety significantly reduces after discharge.

Anxiety represents a psychological state characterized by the constant worry that, even in the absence of imminent danger, something bad may happen [13]. It is one of the most common conditions encountered in psychiatry [14], and the leading symptom of psychological stress during the pandemic [15]. Ever since it became obvious that COVID-19 will have a massive impact on society in general, studies in several countries were performed to measure anxiety in different groups of affected individuals: patients infected with the Sars-CoV-2 virus [16], students perplexed with inconsistent education delivery methods [17], healthcare workers overwhelmed with extensive workload and severity of COVID-19 cases [18], as well as in general population [19].

Previous investigations have shown that the lack of social support significantly affects both short- and long-term anxiety [20], stressing the perils of isolation and quarantine in terms of mental health. While the impact of regular hospitalization due to COVID-19 has been evaluated [21], the studies on anxiety of patients treated in temporary COVID-19 hospitals are mostly lacking. As to our best knowledge, the only currently available report is from China, and describes those patients as worried and feeling marginalized due to the lack of medical staff, poorer medical equipment, and poorer comfort compared to standard hospitals [22]. In the present study, according to the previously set up cut-off scores for HAM-A scale [23], the individual levels of anxiety of COVID-19 patients at admission to the temporary hospital ranged from minimal to severe. The levels observed 2 weeks after discharge from the hospital still varied widely, but intra-individual comparison revealed significant decrease. While it has been noticed that the discharge from the

| Table 1 | Socio-demographic and clinical characteristics of COVID-19 patients admitted to the temporary hospital ($n = 87$). |
|---------|---------------------------------------------------------------------------------------------------------------|
| Sex | Male: 42 (48.3%)  
Female: 45 (51.7%) |
| Age (years) | Mean ± SD: 41.8 ± 13.0  
Range: 20 - 78 |
| Presence of comorbidities | Yes: 32 (36.8%)  
No: 55 (63.2%) |
| Level of education | Primary: 3 (3.4%)  
Secondary: 66 (75.9%)  
Tertiary: 18 (20.7%) |
| Family history of psychiatric disorder | Yes: 8 (9.2%)  
No: 79 (90.8%) |
| COVID-19 diagnosis among family members | Yes: 51 (58.6%)  
No: 36 (41.4%) |
| Joint hospitalization with family members | Yes: 21 (24.1%)  
No: 66 (75.8%) |
| Previous hospitalizations due to COVID-19 | Yes: 12 (13.8%)  
No: 75 (86.2%) |
| Length (days): | Median (IQR): 0.0 (0.0–0.0)  
Range: 0 - 13 |
| Severity of COVID-19 | Asymptomatic: 25 (28.7%)  
Mild: 47 (54.0%)  
Moderate: 4 (4.6%)  
Severe: 11 (12.6%) |
Fig. 1. A. The effects of sex on the level of anxiety of SARS-CoV-2 infected patients at admission to the temporary COVID-19 hospital. Fig. 1B. The effects of age on the level of anxiety of SARS-CoV-2 infected patients at admission to the temporary COVID-19 hospital.

Fig. 2. A. The effects of family history of psychiatric disorder on the level of anxiety of SARS-CoV-2 infected patients at admission to the temporary COVID-19 hospital. Fig. 2B. The effects of comorbidities on the level of anxiety of SARS-CoV-2 infected patients at admission to the temporary COVID-19 hospital.

Fig. 3. A. The effect of disease severity on the level of anxiety of SARS-CoV-2 infected patients at admission to the temporary COVID-19 hospital. Fig. 3B. The individual levels of anxiety at admission to the hospital and 2 weeks after discharge.
hospital can itself be a trigger for short-term anxiety [24], our finding corresponds well with the opposite reports describing the beneficial effect of leaving the hospital [25]. This can certainly be attributed to the improvement in the clinical course of COVID-19 (which was the requirement for discharge from the hospital), but also to the existence of the discharge plan (if the symptoms did not grow worse, patients were planned to leave the hospital 2 weeks after admission), which is expected to ease the stress for hospitalized patients [25].

Sex differences in anxiety disorder are well known, with women displaying higher prevalence rates of lifetime diagnosis and greater illness burden [26,27]. This has been explained by temperamental differences between sexes, higher sensitivity of women to lifetime adversity [26,28], but also by differential neurotransmission that can modulate emotional behavior [29]. In the present study, in line with the previous observations, higher level of anxiety at admission to the COVID-19 temporary hospital has been observed in women. If we assume the observed anxiety to be triggered by a specific disease-related trauma, especially in the midst of the pandemic, hormonal axis can be at least partly responsible for this finding [30].

Previous studies of age and anxiety usually reported their inverse association. Namely, it seems that older adults worry less and display similar somatic and affective symptoms of anxiety as compared to their younger counterparts [31], unless the trigger for the anxious responding concerns physical health [32]. In our study, older patients exhibited higher level of anxiety at the admission to the hospital. Supposing the COVID-19 diagnosis was the main reason for the elevated anxiety in our study subjects, our finding corresponds well to the previous reports.

In addition, both older age and anxiety are usually associated with higher prevalence of different psychiatric or somatic comorbidities [33]. It has been observed that, besides acute disease triggering anxious reaction, chronic illness or medications used for their treatment can cause anxiety as well [34]. Among our study subjects, the presence of comorbidities was associated with significantly higher level of anxiety, most probably due to the already present health anxiety that is expected to be worsen by additional (in this case COVID-19) diagnosis. Moreover, we have observed that asymptomatic COVID-19 patients mainly displayed minimal or no anxiety, while severe cases exhibited moderate to severe symptoms. This fits well to the expectations that the severity of the anxiety-causing disease would affect the severity of the anxiety itself.

Finally, in our study positive family history of psychiatric disorder lead to increased anxiety of COVID-19 patients admitted to the temporary hospital. Several genetic twin studies investigating anxiety demonstrated that this disorder displays low heritability [35, 36], suggesting that the positive family history should not play an important role in its development. However, in spite of the modest genetic influence, it seems that anxiety aggregates in families, proposing the role of familial environmental factors in its etiology [37]. Having a parent or a close relative with anxiety or depression seem to predispose an individual to develop similar behavior. Therefore, in the presence of a potential trigger of an anxious reaction, such as diagnosis of COVID-19 and admission to the hospital, more attention should be paid to those who have a positive family history of psychiatric disorder.

5. Study limitations

It should be noted that our study has several limitations, including modest number of participants, short follow-up, single-centered design, as well as the lack of data on other factors that could affect the level of anxiety in COVID-19 patients in a temporary hospital, such as financial stressors, the availability of social and emotional support, the level of physical activity, alcohol drinking status, or intake of drugs. While we do believe our findings to be genuine, larger and more thorough studies would be needed to confirm their accuracy and to assess their importance.

6. Conclusions

The level of anxiety of COVID-19 patients at admission to the temporary hospital is affected by sex, age, family history of psychiatric disorder, the presence of comorbidities, and the severity of COVID-19 symptoms. In addition, the level of anxiety significantly reduces after hospital discharge.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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| Summary of parameter estimates using multiple linear regression for the level of anxiety at admission to the temporary COVID-19 hospital as a dependent variable. |
|---|
| B | SE of B | β | t | p |
|---|---|---|---|---|
| Constant | 0.931 | | | |
| Sex | −0.708 | 0.250 | −0.239 | −2.826 | 0.0059 |
| Age | 0.029 | 0.011 | 0.250 | 2.707 | 0.0083 |
| Severity of COVID-19 | 0.674 | 0.147 | 0.417 | 4.582 | <0.0001 |
| Family history of psychiatric disorder | 1.491 | 0.440 | 0.291 | 3.385 | 0.0011 |
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