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LONGITUDINAL EVALUATION OF THE HEALTH-RELATED QUALITY OF LIFE IN COVID-19 PATIENTS: A COMPARISON BETWEEN PRE-INFECTION AND THREE MONTHS POST-DISCHARGE

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The infectious disease COVID-19, caused by the SARS-CoV-2 virus, continues to be a significant global public health emergency. Alongside the undeniable effects on physical health, there is evidence of a serious impact on mental health as well.

Our study aimed to assess changes in health-related quality of life in COVID-19 patients before hospitalization for SARS-CoV-2 infection and three months after discharge.

Data were collected from 70 participants hospitalized for COVID-19. Participants were examined twice, after admission to the hospital and three months after discharge. Quality of life was measured with the 36-item Short Form Survey (SF-36), Pittsburgh Sleep Quality Index (PSQI), Patient Health Questionnaire-9 (PHQ9), and Generalized Anxiety Disorder 7-item (GAD-7). The statistical significance of two variables in the same sample at two distinct points in time was compared using a paired-sample T-test.

There was a significant difference in PHQ9 scores before and after hospitalization ($t = 4.738$, $p < 0.01$). We found no significant change in PSQI score before hospitalisation or three months after discharge ($t = -.622$, $p = 536$). Our results showed a significant increase in GAD7 and a significant decrease in physical functioning (PF) ($t = 5.929$, $p < 0.01$) and role limitations due to physical health problems (RP) ($t = 4.385$, $p < 0.01$) scores. The findings indicate that there was no statistically significant difference between pre-infection and three months after discharge in the SF-36 questionnaire's role limitations due to emotional problems (RE) and social functioning (SF) components.

In summary, the results of our study suggest that COVID-19 patients have physical and mental health problems that may persist even after recovery and negatively affect their quality of life.

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Key words: *Health-Related Guality of Life, Coronavirus Disease, 36-Item Short Form Survey, Pittsburgh Sleep Guality Index, Patient Health Guestionnaire-9, Generalized Anxiety Disorder 7-Item*

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Introduction

The infectious disease COVID-19, caused by the SARS-CoV-2 virus, continues to represent a significant global public health danger. The majority of patients who were released passed through various phases of recovery, while consequences on long-term health are presently being evaluated (1). Alongside the clear impacts on physical health, there is evidence of a substantial influence on mental health as well (2). Besides the symptoms of illness themselves, experiences during hospitalisation, physical and social isolation, and death of family members or other patients are factors that could worsen mental health status (3). Additionally, coronavirus can induce immunological reactions that have serious effects on an infected person's mental health and brain function (4). The specific process by which coronavirus affects the brain is unclear. However, it can enter the brain via the olfactory bulb, pass the blood-brain barrier, and interact with ACE2 receptors (5). Furthermore, physiologic abnormalities in the brain, like microglia stimulation and cytokine activation may be connected to mental disorders (6). Experienced stress and compensating mechanisms are two well-known and plainly observable elements that

effect one's actions and symptom presentations (7). A previous investigation on COVID-19 infection suggested that coronavirus infection was associated with long-term mental issues and neuropsychiatric effects (8). COVID-19 patients, in particular, exhibited symptoms of psychological distress symptoms that can result in persistent dysfunction and a reduction in their quality of life; recent data also show an increased chance of having post-traumatic stress disorder during hospitalization (9, 10). Here we provide research in which health-related quality of life parameters were investigated in COVID-19 patients before and three months post-hospital release.

Aim

Our study aimed to assess changes in health-related quality of life in COVID-19 patients before hospitalization for SARS-CoV-2 infection and three months after discharge.

Methods

Research Methodology and Participant Profile

This observational, longitudinal study was carried out in the Infectious Diseases Clinic, University Clinical Centre of Niš, Serbia, from January 2022 to May 2022. Participants were examined twice, during admission to the hospital and three months after discharge. Inclusion criteria were SARS-CoV-2 infection and a minimum age of 18. A positive PCR test done at the time of admission to our hospital proved the patient's infection with SARS-CoV-2. Participants were removed if they had poor questionnaire completion, exhibited evidence of prior mental illness or dementia, had spent more than 12 hours in the Intensive Care Unit, or experienced a fatal outcome. The participants' ages varied from 23 to 79. Demographic data and prior illnesses were gathered from hospital records and self-reported upon admission. Written informed permission was gained by each subject. The study followed the principles specified in the Helsinki Declaration. The Niš University Clinical Centre Ethics Committee accorded their consent to the study proposal.

Instruments

Quality of life was examined with the 36-item Short Form Survey (SF-36), Pittsburgh Sleep Quality Index (PSQI), Patient Health Questionnaire-9 (PHQ9), and Generalized Anxiety Disorder 7-item (GAD-7). A widely adopted measure for assessing health-related quality of life is the SF-36. Eight scales are measured by SF-36 (11-13): Physical functioning (PF) measures the ability to carry out physical tasks, including walking, using stairs, and house maintenance.

Role limitations due to physical health problems (RP) measure the influence of physical health issues on everyday obligations, such as employment or other regular activities. Bodily pain (BP) measures the degree and effect of pain on everyday activities. The questionnaire covers items for general health (GH), vitality, role limitations due to emotional problems (RE), social functioning (SF), and mental health (MH). GH examines self-reported overall health status, including perceived changes in health throughout time. Vitality examines the levels of energy and fatigue. RE analyzes the impact of emotional health problems on everyday activities, including employment or other regular activities. MH assesses psychological discomfort and well-being, whereas SF measures the effect of physical or emotional challenges on relationships. Scores vary from 0 to 100; lower scores imply greater dysfunction, while higher scores represent reduced dysfunction (13). The SF-36 analyzes two distinct dimensions: a physical dimension and a mental dimension (11-13). The assessment of the physical and mental factors is influenced by each scale in a different way (12). Instead of using an SF-36 overall score, for this study, we used the scores separately for PF, RP, SF, and RE in statistical processing. The Pittsburgh Sleep Quality Index, or PSQI, is a questionnaire developed to quantify a person's sleep quality over one month. Nineteen separate items make up the test, which examines seven major aspects of sleep quality: subjective sleep quality, sleep latency, sleep length, habitual sleep efficiency, disturbance in sleep, usage of medications for sleep, and disruption of daily routines. One overall score is derived by adding the outcomes of these seven component scores (14). The Patient Health Questionnaire-9, known as PHQ-9, is a self-administered depression screening instrument. The Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) provides nine diagnostic criteria for major depressive disorder, which are reflected in the PHQ-9. With a total score that can vary from 0 to 27, each item is rated on a scale of 0 to 3. Higher scores suggest greater depression severity (15). The Generalized Anxiety Disorder-7-item Scale is referred to as the GAD-7. The existence and severity of generalized anxiety disorder (GAD) symptoms are assessed using this seven-item screening questionnaire (16).

Statistical Analysis

Demographic data were presented as mean ± SD. Descriptive statistical analysis was applied for the demographic information, and a paired-sample T-test was applied to evaluate the statistical significance of two variables in the same sample at two different points in time. IBM SPSS Statistics 26 was used for data processing, and $p < 0.05$ was regarded as significant.

Results

Data were gathered from 70 individuals hospitalized for COVID-19. Most of them were male (60%) and had a secondary level of education (45.71%). The mean age of the subjects was 52.03 ± 15.76 years, and the median period since the positive PCR test was 4 days. Specific demographic information is presented in Table 1. The PHQ9 mean score calculated for the duration of hospitalization was 6.600 ± 4.284, and 3 months later it was 4.314 ±

3.0. In contrast, the PSQI and GAD-7 mean scores were higher three months following discharge. In addition, the mean values of RE and SF were similarly greater, although PF and RP were decreased three months after infection (Table 2). To compare the scores of these questionnaires, we performed a paired-sample test for statistical significance between the scores obtained one month before COVID-19 infection and three months after hospital discharge (Table 3). PHQ9 scores before and after hospitalization differed significantly, according to our statistical findings (t = 4.738, p < 0.01). We found no significant change in PSQI score before hospitalisation and three months after discharge (t = -.622, p = 536). According to our findings, the GAD7 score significantly increased 3 months after hospital discharge (t = -3.978, p < 0.01), and there was a significant decline in physical functioning (PF) (t = 5.929, p < 0.01) and RP (t = 4.385, p < 0.01) scores from pre-COVID-19 infection to 3 months post-hospital discharge. The results demonstrate that there was no difference in statistical significance in RE and SF components of the SF-36 questionnaire between pre-infection and 3 months after discharge. Paired samples t-test indicated a RE mean difference of -.043 (SD = .428), with a t-value of -.840 and a p-value of .404 and an SF mean difference of -.053 (SD = .231), with a t-value of -1.903 and a p-value of .051.

Table 1. Demographic data of participants

Variables	**Total N (%), N□70**
Age in years (mean + SD)	52.03 ± 15.76
Gender	
Male	42 (60)
Female	28 (40)
Education level	
Primary school	6 (8.57)
Secondary school	32 (45.71)
Faculty	24 (34.29)
Master degree	7 (10)
Doctoral degree	1 (1.43)
Marital status	
Single	9 (12.86)
Married	50 (71.43)
Divorced	6 (8.57)
Widowed	5 (7.14)
Employment status	
Student	3 (4.29)
Employed	40 (57.14)
Unemployed	27 (38.57)
Chronic illness	
Yes	41 (58.57)
No	29 (41.43)

Table 2. Descriptive statistics

Paired Samples Statistics					
		Mean	**N**	**Std. Deviation**	**Std. Error Mean**
Pair 1	PHQ9	6.6000	70	4.28479	.51213
	PHQ9_3	4.3143	70	2.99537	.35802
Pair 2	PSQI	4.6000	70	3.16869	.37873
	PSQI_3	4.8000	70	2.59095	.30968
Pair 3	GAD7	5.3000	70	2.80966	.33582
	GAD7_3	7.1571	70	3.60610	.43101
Pair 4	PF	.8343	70	.15430	.01844
	PF_3	.6686	70	.28363	.03390
Pair 5	RP	.6500	70	.32804	.03921
	RP_3	.4464	70	.32385	.03871
Pair 6	RE	.7190	70	.31929	.03816
	RE_3	.7620	70	.28454	.03401
Pair 7	SF	.6632	70	.24923	.02979
	SF_3	.7157	70	.18945	.02264

Table 3. Paired Samples Correlations

Paired Samples Test									
		Paired Differences					**t**	**df**	**Sig. (2tailed)**
		Mean	**Std. Deviation**	**Std. Error Mean**	**95% Confidence Interval of the Difference**				
					Lower	**Upper**			
Pair 1	PHQ9 - PHQ9_3	2.28571	4.03658	.48246	1.32323	3.24820	4.738	69	**.000**
Pair 2	PSQI - PSQI_3	-.20000	2.68976	.32149	-.84135	.44135	-.622	69	.536
Pair 3	GAD7 - GAD7_3	-1.8571	3.90572	.46682	-2.7884	-.92586	-3.978	69	**.000**
Pair 4	PF - PF_3	.16571	.23383	.02795	.10996	.22147	5.929	69	**.000**
Pair 5	RP - RP_3	.20357	.38845	.04643	.11095	.29619	4.385	69	**.000**
Pair 6	RE - RE_3	-.04300	.42820	.05118	-.14510	.05910	-.840	69	.404
Pair 7	SF - SF_3	-.05250	.23087	.02759	-.10755	.00255	-1.903	69	**.051**

$P < 0.01$

Discussion

As we are in the fourth year since the whole world was confronted with COVID-19, one of the most crucial problems facing global health systems today is to identify and comprehend the unavoidable effects of the SARS-CoV-2 viral infection.

Based on one of the first cross-sectional studies of individuals recovering from COVID-19 in Wuhan, SARS-CoV-2 virus infection is typically associated with several psychiatric disorders, including depression, anxiety, and even suicide. According to this study, 10% of COVID-19 survivors report anxiety or depression, and 29.5% of survivors experience sleep disturbances one month and six months after discharge, respectively (17). Our study's findings suggest that after hospital discharge, the features and standard of sleep in the COVID-19 recovered patients do not dramatically alter. It is essential to keep in mind that the study's sample size was quite small, which could have reduced its ability to identify significant changes. Only a few factors have been linked to improved sleep quality. Poor sleep quality has been connected to female sex, younger age, and persons with a history of mental issues (18). Lack of sleep severely influences cognitive function and quality of life (19, 20). In addition, sleep interruptions could increase depression and anxiety while reducing pain thresholds (21).

A recently published meta-analysis analysed the cumulative prevalence of mental diseases among COVID-19 survivors (22). Despite significant variance across the 27 studies, it was clear that mental and psychological health outcomes are essential for COVID-19 survivors. Prevalence rates for posttraumatic stress disorder (PTSD), anxiety, psychological distress, depression, and sleep disorders were as follows: 22% for anxiety, 36% for psychological distress, 21% for depression, and 35% for sleep disorders. The following risk variables have been connected to an enhanced risk of anxiety, depression, or other unfavourable mental health outcomes: indicators of inflammation, especially IL-6 (23), severity of illness, duration of symptoms, severity of illness at 6-month follow-up, and female sex (24, 25). Based on our results, there seems to be a statistically significant difference in the incidence of generalized anxiety disorder before and after COVID-19 infection, as shown by the GAD7 questionnaire. It is noteworthy to underline that the elevation in GAD7 scores identified in our study could be connected to a range of factors, such as the physical and emotional stress associated with hospitalisation and treatment for COVID-19, as well as the social and economic disruption generated by the pandemic (26, 27). One Chinese study applied the SF-36 questionnaire to investigate the health-related quality of life of COVID-19 patients (28). This showed a worse score at one-month follow-up, with psychological impairment described mainly in women, suggesting that the female gender may be a risk factor for psychological quality of life in these patients (28). In our study, the physical functioning (PF) component of the SF-36 was compared 3 months after discharge to the period before infection. The results showed a significant decrease in the ability to perform physical activities after the patients had recovered from COVID-19. These findings support other studies that have shown COVID-19 to have long-term health impacts, including reduced physical functioning (1). Our findings also indicate a significant decline in RP—as a measure of the impact of physical health problems on daily activities among those who had COVID-19 and recovered. The reduction in physical role functioning may have several effects on the overall well-being of COVID-19 survivors. For instance, it would make it more difficult for them to carry out routine tasks like work or household, which would increase stress and reduce life pleasure (28). Another Chinese study that evaluated health-related quality of life using the SF-36 found that COVID-19 hospitalization had a detrimental impact on patients' quality of life for up to three months following release (12). In this research, poor quality of life appeared to be related to age, gender, and physical symptoms after discharge, suggesting that older adults, particularly women and those with recurrent physical symptoms, are most at risk for poor quality of life.

Conclusion

In summary, the results of our study demonstrate that COVID-19 patients have physical and mental health issues that may persist even after recovery and negatively affect their quality of life. The fact that our study was done at one site and the sample size was quite limited should be emphasized, as this may hamper the generalizability of our findings. However, our study underlines the importance of continuing surveillance and care for COVID-19 survivors to make sure they receive the necessary treatment to address any long-term health concerns. The long-term health implications of COVID-19 may be better understood in the future through research utilizing broader samples and more diverse populations.

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PROCENA KVALITETA ŽIVOTA POVEZANOG SA ZDRAVLJEM KOD PACIJENATA ZARAŽENIH VIRUSOM COVID-19 PRE INFEKCIJE I TRI MESECA NAKON OTPUSTA SA BOLNIČKOG LEČENJA

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Infektivno oboljenje COVID-19, izazvano SARS-CoV-2 virusom, i dalje predstavlja značajnu globalnu pretnju po zdravlje ljudi. Pored toga što ovo oboljenje nesumnjivo utiče na fizičko zdravlje, postoje i dokazi o njegovom ozbiljnom uticaju na mentalno zdravlje.

Naše istraživanje imalo je za cilj da proceni promene u kvalitetu života kod obolelih od COVID-19 pre hospitalizacije i tri meseca nakon otpusta iz bolnice.

Podaci su dobijeni od 70 ispitanika sa postavljenom dijagnozom COVID-19 koji su bili hospitalizovani na Klinici za infektivne bolesti Univerzitetskog kliničkog centra u Nišu. Bili su ispitani dva puta: nakon prijema na bolničko lečenje i tri meseca nakon otpusta. Kvalitet života meren je na osnovu sledećih upitnika: 36-*Item Short Form Survey* (SF-36), *Pittsburgh Sleep Quality Index (PSQI), Patient Health Questionnaire-9 (PHQ9) i Generalized Anxiety Disorder 7-Item* (GAD-7). Statistička značajnost dveju promenljivih merena u istom uzorku u dva različita trenutka poređena je uz pomoć uparenog T-testa.

Postojala je statistički značajna razlika u PHQ9 skorovima pre hospitalizacije i posle nje ($t = 4,738$; $p < 0,01$). Nije bilo značajne promene PSQI skora pre hospitalizacije i tri meseca nakon otpusta ($t = -0,622$; $p = 536$). Naši rezultati pokazali su statistički značajan porast GAD7 i značajan pad skora komponente fizičkog funkcionisanja (engl. *phisical functioning* – PF) ($t = 5,929$; $p < 0,01$), kao i skora komponente ograničenja zbog fizičkih zdravstvenih problema (engl. *emotional regulation* – RP) ($t = 4,385$; $p < 0,01$). Prema dobijenim rezultatima, nije bilo statistički značajne razlike između perioda pre infekcije i perioda nakon otpusta iz bolnice u komponentama SF-36 upitnika koje se odnose na ograničenja usled emocionalnih problema i na domen socijalnog funkcionisanja (engl. *social functioning – SF)*.

Na osnovu rezultata našeg istraživanja može se zaključiti da oboleli od COVID-19 imaju fizičke i mentalne zdravstvene probleme koji mogu trajati i nakon oporavka od infekcije i negativno uticati na kvalitet života.

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***Ključne reči**: kvalitet života, oboljenja izazvana koronavirusom, 36-Item Short Form Survey, Pittsburgh Sleep Quality Index, Patient Health Questionnaire-9, Generalized Anxiety Disorder 7-item*