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ORIGINAL ARTICLE

ASPECTS OF QUALITY OF LIFE IMPACTED ON PATIENTS WITH PROLONGED COVID-19 SYMPTOMS (LONG COVID)

Aspek Kualitas Hidup yang terdampak pada Pasien dengan Gejala COVID-19 Berkepanjangan (Long Covid)

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ABSTRACT

Background: A subset of patients diagnosed with COVID-19 is encountering persistent post-COVID symptoms. These symptoms can significantly impede their quality of life and exert profound effects on their day-to-day functioning. **Purpose:** This study aimed to identify the dimensions of quality of life most affected in patients with long COVID symptoms. **Methods:** A cross-sectional survey was applied using the SF-36 questionnaire which was distributed on Twitter and Instagram. Furthermore, a total of 122 respondents were obtained through accidental sampling. The association between variables was analyzed using Chi-square and Mann-Whitney tests. **Results:** Respondents who completed the questionnaire (n=122) came from different regions, with West Java as the largest area of origin (37.70%). In addition, the majority were female (n=103, 84.4%) under 25 years old (n=92, 75.41%), and the three symptoms experienced were fatigue (n=108; 35.29%), brain fog (n=61;19.93%), and olfactory disturbances (n=54; 17.65%). There was an association between long COVID duration and gender (p= 0.03). However, there was no association between other demographic characteristics with long COVID duration (p > 0.05). General health (41.67 (IQR=29), p= 0.00) and vitality (40.00 (IQR=20), p= 0.02) were the two aspects of quality of life significantly altered in patients with long COVID symptoms more than 3 months. **Conclusion:** The aspects of quality of life, particularly general health and vitality, experienced a significant decline in post-COVID-19 patients with long COVID symptoms for more than 3 months.

ABSTRAK

Latar Belakang: *Pada sejumlah orang yang terinfeksi Covid-19, sebagian dapat mengalami gejala serupa Covid berkepanjangan.. Gejala-gejala*

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tersebut dapat mempengaruhi kualitas hidup dan berdampak pada aktivitas sehari-hari. ***Tujuan:*** *Penelitian ini bertujuan untuk mengeksplorasi gejala long covid, dimensi-dimensi kualitas hidup pada pasien long covid, dan mengidentifikasi dimensi yang paling terdampak.* ***Metode:*** *Penelitian menerapkan survei desain potong lintang dengan kuesioner SF-36 yang disebar secara online di media sosial Twitter dan Instagram. Dengan teknik accidental sampling diperoleh responden sebanyak 122 orang. Hubungan antar variabel penelitian dianalisis dengan uji chi-square dan Mann Whitney.* ***Hasil:*** *Responden yang mengisi kuesioner (n=122) berasal dari berbagai daerah di Indonesia, dengan provinsi Jawa Barat merupakan wilayah asal terbanyak (37.70%). Mayoritas responden berjenis kelamin perempuan (n=103; 84.43%) dan berusia di bawah 25 tahun (n=92; 75.41%). Tiga gejala long covid yang paling sering dikeluhkan adalah mudah lelah (n=108; 35.29%), brain fog (n=61;20,0%), dan gangguan penciuman (n=54; 17.65%). Terdapat hubungan bermakna antara lama gejala long covid dengan jenis kelamin responden (p=0.03), dan tidak terdapat hubungan bermakna antara karakteristik demografi yang lain dengant lama gejala long covid (p>0.05). Kesehatan umum (41.67(IQR=29); p= 0,00) dan vitalitas (40.00 (IQR=20); p= 0.02) merupakan dua aspek kualitas hidup yang skornya turun signifikan pada pasien yang menderita long covid lebih dari 3 bulan.* ***Kesimpulan:*** *Kualitas hidup khususnya kesehatan umum dan vitalitas mengalami penurunan yang bermakna pada pasien pasca Covid-19 dengan gejala long covid lebih dari 3 bulan.*

INTRODUCTION

The ongoing COVID-19 pandemic in early 2020 is emerging as a significant global health concern due to its extensive transmission and profound ramifications on individuals. The virus has rapidly proliferated, resulting in a staggering 550,218,992 confirmed cases worldwide as of July 7th, 2022. Furthermore, Indonesia has been ranked 20th, reporting a total of 6,103,552 cases (1). COVID-19 symptoms vary for each individual, ranging from mild to severe symptoms. In domestic and global cases, the symptoms vary including fever, dry cough, headache, nasal congestion, loss of smell, conjunctivitis, diarrhea, and skin rashes. However, patients can also experience severe symptoms of acute respiratory syndrome which require hospitalization (2,3).

Each individual has a different response to COVID-19 and the infection generally recovers in approximately 4 weeks. Some patients may experience similar symptoms even though they have recovered and are stated negative through a PCR test (4). According to National Institute for Health and Care Excellence (NICE), patients may experience prolonged symptoms after the acute period for up to 12 weeks or more (5). These ongoing COVID-like symptoms are known as long COVID or post-COVID conditions. A study conducted by Greenhalgh et al (6) showed that the duration of long COVID can be categorized into two distinct phases. The first phase, known as post-acute COVID-19, encompasses symptoms that persist for more than three weeks from the onset of initial symptoms. The second phase, referred to as chronic COVID-19, encompasses symptoms experienced for a duration exceeding 12 weeks.

In Switzerland, more than 25% of adult patients have not fully recovered after the infections for 6-8 months (7). Meanwhile, based on a survey of virtual communities in the Netherlands and Belgium in 2020, patients with mild or severe conditions still experience symptoms similar to COVID-19 for 3 months (8). Symptoms of long-COVID that commonly arise are fatigue, cognitive impairment, headaches, shortness of breath, muscle weakness, and anxiety disorders (8–10). The study regarding prolonged COVID symptoms is sporadic and has not been well documented.

Post-COVID-19 syndrome can affect the quality of life and the ability to carry out daily activities. A survey by Goërtz et al (8) stated that the survivors had a significantly decreased health status compared to before being infected. This was

supported by Tabacof et al (10) where patients with long COVID experience decreased physical activity, lower ability to be involved in society, and reduced ability to work. From the 156 patients studied, 85% and 69% stated that long COVID symptoms reduced their physical activity and suffered from mental health disorders.

Health-related quality of life can be used as a humanist outcome to identify the impact of a disease, the constraints experienced, and the disabilities, including physical, mental, and social aspects (11). One of the instruments utilized to evaluate the quality of life is the short form-36 questionnaire (SF-36). This questionnaire has been widely used to assess the quality of life of patients with various chronic diseases by measuring several aspects including aspects of physical functioning, physical roles, emotional health, energy/vitality, emotional well-being, social functioning, body pain, and general health (12).

Study related to the quality of life in post-COVID-19 patients is limited in developing countries, specifically in Indonesia (13,14). This study aims to identify long COVID symptoms and analyze changes in various aspects of quality of life based on the duration in the community. Therefore, the results can assist health workers in providing post-COVID-19 patients' care and making health policies related to the quality of life of the community.

METHODS

This cross-sectional study was conducted using an online survey that was circulated through Twitter and Instagram. The population size was unknown due to the limited data related to post COVID syndrome. Therefore, the target population was those that were reached through the internet.

The technique employed in this study was accidental sampling. Individuals who perused the online survey link disseminated through social media and met the eligibility requirements served as viable data sources. The inclusion criteria encompassed those who had previously contracted COVID-19 and recuperated as confirmed by a PCR test but continued to manifest symptoms similar to long COVID. To ensure valid responses in the questionnaires, respondents were asked to fill out the actual time infected by the virus through PCR tests. The parameters surveyed from May to June 2022 were demographic characteristics (age, gender, education, and working status), clinical characteristics (long COVID symptoms and comorbidity), and quality of life scores. The survey was subjected to an explanation before treatment and received informed consent from the respondents. A research ethics license was provided by Health Ethic Commission (KEPK) Poltekkes Kemenkes Jakarta II with the number of the approval document LB 02.01/I/KE/39/306/2022.

$$n = \frac{Z^2 pq}{e^2}$$

$$n = \frac{(1,96)^2 (0,5)\ (0,5)}{0,1^2}$$

$$n = 96,4$$

Where:
n = minimum sample required
Z = z-value at a 95% confidence level (1,96)
p = estimated proportion of the population attributed to the questions (50% or 0,5)
q = 1-p = 1-0,5 = 0,5
e = margin of error (10%)

A standardized short form-36 (SF-36) questionnaire instrument was used to assess the quality of life by measuring 8 aspects, namely physical function, physical role, body pain, general health, social function, vitality, emotional role, and mental health (12). This instrument consisting of 36 questions was tested for reliability and widely used to measure the quality of life in chronic diseases. The SF-36 score was determined by 3 stages, and each item was given a score in the range of 0 to 100. A value of 0 and 100 was the lowest and highest score which meant the aspect assessed showed the worst and best condition. Several questions that represented the same aspect were calculated by the average value to determine the score for each. Furthermore, the scores on each aspect were added up and the average value was seen to determine the overall quality of life. The average value ≥ 50 indicated a good quality of life, while < 50 showed a poor quality of life.

Univariate analysis was applied to obtain the frequency distribution of categorical variables. Age was categorized into 3 intervals, namely young adults (18-25 years old), adults (26-45 years old), and old adults (46 years old and above). Meanwhile, occupational status was grouped as active workers for respondents having permanent jobs and unemployed or retired. Bivariate analysis through Chi-Square and Mann Whitney U test

(95% confidence level) was applied to identify the difference in long COVID duration according to sociodemographic characteristics (gender, age, educational level, occupational status) and comorbidity, as well as to determine the impact of the duration on aspects of quality of life. The analytical process was carried out using the software SPSS ver.23.

RESULTS

Study related to prolonged symptoms of COVID-19 and its impact on the quality of life of people was not widely reported. Therefore, this analysis was carried out to investigate several aspects of the quality of life of people after being infected with the virus. The survey was filled in by 122 respondents with the sociodemographic characteristics described in Tables 1 and 2.

The majority of respondents were women (n=103; 84.43%) in the late adolescent group (n=92; 75.41%). Most of them came from West Java Province (n=46; 37.70%), followed by Jakarta (n=38; 31.15%) and East Java (n=10; 8.20%). More than 50% were unemployed with a diploma or bachelor's degree, and the majority had no comorbidity (n=110; 90.16%). According to Table 3, the respondents who experienced long COVID complained of fatigue (35.29%), brain fog (19.93%), and disturbances in the sense of smell (17.65%). Other post-COVID syndromes were hair loss, menstrual abnormalities, breathing problems, and gastrointestinal tract disorders. Each respondent has approximately 2-3 prolonged symptoms.

According to Table 4, the SF-36 questionnaire showed that among respondents who experienced chronic COVID-19 (> 12 weeks of symptoms), several aspects of quality of life had lower scores, namely general health, vitality/energy, emotional functioning, and well-being. All of those aspects were decreased below 50.00, which contributed to poor quality of life. The general health and vitality were significantly different in patients who experienced more than 12 weeks of symptoms, with a p-value of 0.00 and 0.02, respectively.

The bivariate analysis between demographic characteristics and long COVID showed that women had a significant difference in the duration of long COVID compared to men (p = 0.03). For other sociodemographic variables, there was no significant difference in the duration of being infected with COVID-19, as shown in Table 5. Similarly, the presence of comorbidities was not related to the length of time infected with COVID-19 (p=0.22) and long COVID duration (p=0.21).

Table 1
Provincial Distribution of Respondents from Online Survey

Province	N (122)	%
West Java	46	37.70
Special Capital Region of Jakarta	38	31.15
East Java	10	8.20
Banten	8	6.56
Central Java	6	4.92
Special Region of Yogyakarta	3	2.46
Jambi	2	1.64
East Kalimantan	2	1.64
South Kalimantan	1	0.82
West Kalimantan	1	0.82
East Nusa Tenggara	1	0.82
West Sumatera	1	0.82
Bengkulu	1	0.82
North Sulawesi	1	0.82
South Sulawesi	1	0.82

Table 2
Sociodemographic Profile of Respondents from Online Survey

Variable	N	%
Age (years)		
18-25	92	75.41
26-45	25	20.49
46-55	5	4.10
Gender		
Men	19	15.57
Women	103	84.43
Educational level		
Unknown	1	0.82
Secondary	52	42.62
Tertiary	69	56.56
Occupational status		
Active workers	60	49.18
Unemployed/retired	62	50.82
Comorbid		
Yes	12	9.84
No	110	90.16

Table 3
The prolonged COVID-19 symptoms (long COVID) reported by respondents

Type of symptoms	Frequency	%
Fatigue	108	35.29
Brain fog (poor concentration or thinking problems)	61	19.93
Smell and taste impairment (dysosmia, anosmia, parosmia)	54	17.65
Hair loss	48	15.69
Menstrual disorders	15	4.90
Respiratory disorders (shortness of breath, cough, flu-like symptoms)	11	3.59
Digestive disorders (GERD, nausea, loss or increased appetite)	6	1.96
Body pain	2	0.65
Sleeping disorders	1	0.33
Total	306	
Mean of symptoms per respondent	≈3	

Table 4
Differences in SF-36 Scores based on the Duration of prolonged COVID-19 symptoms (long COVID)

Aspect of Quality of Life	***Long COVID* durations**		***p-value****
	4-12 weeks (n=75) Median (IQR)	**>12 weeks (n=47) Median (IQR)**	
Physical functioning	85.00 (20)	85.00 (25)	0.48
Physical roles	50.00 (50)	50.00 (50)	0.48
Body pain	67.50 (33)	67.50 (23)	0.54
General Health	58.33 (29)	41.67 (29)	0.00**
Social Functioning	62.50 (25)	62.50 (25)	0.13
Vitality/Energy	50.00 (30)	40.00 (20)	0.02**
Emotional functioning	66.67 (33)	33.33 (33)	0.82
Emotional well-being	56.00 (28)	52.00 (32)	0.13

**Mann Whitney U test*

***Significant difference at 95% confidence level*

DISCUSSION

This observational study showed that the quality of life in respondents with long COVID symptoms was significantly altered. According to the results, female respondents were overrepresented as young adults and there was a significant difference in the duration of long COVID compared to men (p=0.03). This was in line with a cohort study of post-COVID-19 patients in the UK, where women aged under 50 years experienced more symptoms including fatigue (OR 2.06, 95% CI 0.81-3.31) and shortness of breath (OR 7.15, 95% CI 2.24- 22.83) than men (15). In addition, psychological impacts such as anxiety due to the COVID-19 pandemic were also experienced by women than men (16,17).

Other sociodemographic characteristics, namely age, education level, and working status, had no significant relationship with the duration of the infection and long-term symptoms. All age levels with different work activities can be infected through the air and experience post-COVID-19 syndrome. However, in some studies, longer duration of symptoms was evident in adult patients aged 30-69 (7,15,18)). In this study, 90.16% of respondents did not have comorbidities but experienced long COVID with different durations. This was in line with the study from Dennis et al (19) which observed 201 subjects (average age 44 years) with a low prevalence of comorbidities and only 18% who received hospital care while infected. The results showed that 4 months after being recovered from COVID-19, 98% experienced symptoms of fatigue, muscle pain (88%), and shortness of breath (87%). Meanwhile, 25% of subjects showed mild multiorgan disorders on MRI examination. The findings were evidence of the prevalence of long COVID in the low-risk group among the majority of studies focused on those with severe symptoms and hospitalized patients (19).

Table 5
The Differences of Acute and Post-COVID Durations Based on Sociodemographic Profile

Variables	Acute COVID-19 duration		*p-values**	Long COVID duration		*p-values**
	≤ 2 weeks	> 2 weeks		4-12 weeks	>12 weeks	
Gender						
Men	13	6	0.78	16	3	0.03**
Women	67	36		59	44	
Age (years)						
18-25	62	30	0.45	57	35	0.59
26-45	14	11		14	11	
46-55	4	1		4	1	
Educational Level						
Unknown	0	1	0.33	1	0	0.73
Secondary level	33	19		32	20	
Tertiary level	47	22		42	27	
Occupational status						
Active worker	37	23	0.37	39	21	0.43
Unemployed/ retired	43	19		36	26	
Comorbid						
Yes	10	2	0.22	5	7	0.21
No	70	40		70	40	

**Chi-square test*
***Significant difference at 95% confidence level*

The most frequent prolonged symptom reported by respondents (35.29%) was fatigue. This was consistent with several studies, where fatigue was a condition experienced by those infected with mild and severe symptoms (7–9,15,20). The higher intensity of fatigue symptoms than before the infection was suspected to involve complex body processes. Furthermore, the infection caused multi-organ damage since the SARS-CoV-2 virus entered the body through the ACE2 angiotensin-converting enzyme-2 receptor which was spread in different body tissues. These receptors were present in the nasal and oral mucosa, lung tissue, liver, heart, brain, spleen, and kidney (21). Changes also occurred in the bodies of patients in the central and peripheral nervous systems, including chronic inflammation in brain cells and neuromuscular connections and atrophy in skeletal muscles thought to cause chronic fatigue (22). Psychological factors such as anxiety during quarantine also contributed to chronic fatigue (16).

Another neurological manifestation suffered with prolonged symptoms of COVID-19 was poor concentration, which was known as brain fog. Acute COVID-19 infection caused septic encephalopathy, non-immunological responses, such as hypoxia and hypotension, as well as adaptive autoimmunity in the brain (22). Long-term cognitive problems were also suspected in patients with critical illness who had ventilator support while hospitalized (15,20). A neurological study of 100 infected individuals showed that 81% experienced brain fog and when evaluating cognitive function with standardized instruments, there was a significant decrease in focus and ability to remember ($p < 0.01$) (23). The presence of impaired cognitive function following COVID-19 presented significant health concerns due to the ongoing uncertainty surrounding its duration and impact on individuals' quality of life.

Furthermore, 17.65% of respondents suffered from smell and taste disorders. In cohort studies, the prevalence of this symptom varied from 11% to 45.1% after acute infection. The emergence of smell and taste disorders after acute infection was due to the entry of the SARS-CoV-2 virus into the olfactory epithelial tissue. The non-neuronal expression of ACE2 receptors in these tissues allowed the virus to enter, trigger an inflammatory response, and interfere with the function of olfactory support cells. This caused a decrease in sensory nerve function, ionic balance disturbance, and reduced signaling to the brain, resulting in a

loss of smell. Expression of ACE2 receptors on the mucous membranes of the oral cavity, specifically the tongue, also permitted the entry of the SARS-CoV-2 virus, causing degradation of taste cells and increasing the threshold to experience taste (24).

Assessment of quality of life as a post-COVID-19 patients' health outcome was the most widely conducted study. From the evaluation of the quality of life, based on the SF-36 score, it was found that aspects of general health and vitality had significant differences in the group of respondents with a duration of long COVID >12 weeks ($p<0.05$). This was in line with Mc Fann et al (25), where almost all aspects of quality of life except mental health in patients who experience long COVID were lower than those without symptoms of long COVID ($p<0.05$). Meanwhile, Chen et al (26) showed that 7 out of 8 (except for aspects of physical functioning) from post-COVID-19 patients had significant differences compared to the general Chinese population. This multicenter observation was conducted on patients from 12 hospitals in the Wenzhou region, China who were randomly selected and followed up one month after discharge from the hospital. Gender factors (specifically women), age, and length of stay in hospital were significantly related to the quality of life scores (26).

Emotional functioning and well-being were lower in long COVID >12 weeks. Even though the differences were not statistically significant, mental health issues posed considerable concerns. During the pandemic, there were dramatic changes in social life that contributed to psychiatric symptoms such as depression and anxiety. About six to eight months after diagnosis, 111 out of 431 adults in Switzerland had symptoms of depression as long-term consequences (7). Hawes et. al mentioned that the transition to e-learning and remote working were significant stressors for young people (17). However, conflicting findings were also reported, and staying at home for young adults was associated with reduced social anxiety symptoms due to loose social pressures experienced in daily life.

This study described the changes in quality of life after the pandemic and the need for health facilities to prepare services for the long-term impact. Decreasing the quality of life in patients with prolonged symptoms requires monitoring from health workers because the patients' long-term health was affected.

Research Limitation

Considering the limitations of this study, there are two notable factors to consider. Firstly, the sample size for the coverage area of Indonesia is relatively small, which may affect the generalizability of the findings. Secondly, the survey questions are in a recall format and lack direct guidance, potentially introducing biases. However, the results can add to the facts regarding long-term COVID-19 cases, which are still a new health phenomenon. The prevalence in the health care system needs attention to improve people's quality of life.

CONCLUSION

In conclusion, the quality of life of respondents with a duration of long COVID for 4-12 weeks was significantly different from those above 12 weeks. Respondents with longer duration of symptoms had lower scores on general health and vitality/energy. Long COVID was a new health phenomenon that requires attention in healthcare systems. Long-term management efforts needed to be planned by policymakers to improve the quality of life of the Indonesian people.

CONFLICT OF INTEREST

The authors confirm the accuracy of the results and no conflict of interest in this study.

AUTHOR CONTRIBUTION

HQ collected the data, drafted the initial manuscript, and completed the statistical analysis. NP designed the study, compiled the literatures and editing the manuscript. All authors have contributed intellectually to the manuscript.

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