

Original Article

Factors associated with the quality of life and persistent dyspnea severity in COVID-19 survivors: A cross-sectional study among healthcare workers

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Abstract

The coronavirus disease 2019 (COVID-19) pandemic had a significant impact on global health. The alterations in quality of life (QoL) and the persistent symptoms of dyspnea have been the healthcare workers' challenges during and after the pandemic. The aim of this study was to assess factors associated with the QoL and persistent dyspnea experienced by COVID-19 survivors, particularly among healthcare workers. A cross-sectional study was conducted among healthcare workers at H. Adam Malik General Hospital, Medan, Indonesia, using direct interviews to collect the data. The EuroQol 5-dimensional 5-level (EQ-5D-5L) and the self-assessment EuroQol-visual analog scale (EQ-VAS) were employed to assess the QoL of the healthcare workers; and persistent dyspnea was evaluated using the modified Medical Research Council (mMRC) scale. Several possible risk factors such as demographic characteristics (gender and age), clinical characteristics (comorbidities, history of hospitalization, oxygen usage, history of COVID-19 vaccination, the severity of previous COVID-19, existence of post-COVID syndrome) and the symptoms of the post-COVID syndrome were collected. Chi-squared test or Fisher's exact test was used to identify the risk factors associated with the QoL and persistent dyspnea. A total of 100 healthcare workers were included in the study. The EQ-5D-5L assessment found that 2% of healthcare workers experienced pain/discomfort and 4% experienced anxiety/depression. The average healthcare worker's EQ-VAS score was 87.6 ± 8.1 . There was no significant association between studied demographics and clinical characteristics with QoL dimensions. However, post-COVID symptoms of activity limitation ($p=0.004$), sore throat ($p=0.026$), headache ($p=0.012$), myalgia ($p=0.006$), and arthralgia ($p=0.001$) were associated with pain/discomfort dimension of QoL. In addition, there was a significant association between activity limitation ($p=0.012$), headache ($p=0.020$), myalgia ($p=0.015$) and arthralgia ($p=0.032$) with anxiety/depression dimension of QoL. Our data suggested that the presence of post-COVID syndrome ($p=0.006$) and the presence of post-COVID syndrome symptoms of cough ($p=0.021$) and fatigue ($p=0.015$) were associated with persistent dyspnea. In conclusion, this study suggests that the presence of post-COVID syndrome and its symptoms are associated with low quality of health-related QoL and persistent dyspnea. Therefore, cautions are needed for such patients to prevent low QoL in the future.



Keywords: Post-COVID syndrome, quality of life, dyspnea, EQ-5D-5L, mMRC

Introduction

The coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has left an ongoing impact on the world, affecting the lives of over 770 million people and altering healthcare systems globally [1-3]. Although the main focus has been put on preventing and treating the acute phase of the disease, attention is increasingly shifting to the prolonged effects experienced by the survivors, particularly healthcare workers [4]. Among the multitude of challenges the healthcare workers face, two critical aspects have emerged as paramount: the quality of life (QoL) and the persistent symptoms of dyspnea [5,6].

QoL is a multifaceted concept that encompasses various dimensions of an individual's well-being, including physical, mental, and social aspects [7]. The EuroQol 5-dimensional 5-level (EQ-5D-5L) is a widely used instrument for assessing the health-related QoL of individuals, including COVID-19 survivors [8,9]. Patients suffer from significant post-traumatic stress symptoms and depression due to the novelty of the disease and the persistence of symptoms, resulting in serious consequences for patients' QoL [10]. Understanding how COVID-19 affects QoL is not only important for healthcare workers who have contracted and survived COVID-19, but it also has consequences for the healthcare systems they serve [11,12].

Post-COVID syndrome refers to the persistence of symptoms beyond four weeks following SARS-CoV-2 infection. The most prevalent reported symptoms of post-COVID include abnormal lung functions, particularly with persistent dyspnea, neurological impairments, smell and taste disturbances, chronic fatigue, joint pain and chest pain [6]. Dyspnea, or shortness of breath, is a typical symptom that COVID-19 survivors experience and can significantly impact the daily basis [13,14]. The occurrence of dyspnea is readily apparent in patients with severe COVID-19, attributable to organ impairment affecting the lungs, heart, and blood vessels. However, it is remarkable to note that persistent dyspnea also develops in patients with only mild infections [14,15]. The aim of this study was to determine the risk factors associated with QoL and dyspnea experienced by COVID-19 survivors, with a particular emphasis on healthcare workers.

Methods

Study setting, participants and sampling

This was a cross-sectional study conducted at H. Adam Malik General Hospital, Medan, Indonesia, by analyzing healthcare workers on their physical and psychological obstacles, the effects of post-COVID syndrome, and their different interventions history in the management of dyspnea. This study included healthcare workers who had recovered from COVID-19 for more than one month, and aged 18 years or older. The data were collected using direct questionnaire-assisted interviews that were performed in Bahasa Indonesia.

To determine the necessary sample size, the Slovin formula was used since the population was already identified based on the COVID-19 data of H. Adam Malik General Hospital, with was 250 healthcare workers. By employing a margin of error of 5%, therefore the minimum sample size estimated was 96 healthcare workers. Based on data from the COVID-19 Team at H. Adam Malik General Hospital, we directly approached the eligible health workers and inquired about their availability to participate in interviews. There were 100 healthcare workers agreed.

Study variables and study instruments

The scale of QoL and the scale of dyspnea were considered as the dependent variables in this study. The Indonesian version of EQ-5D-5L and the self-assessment EuroQol-visual analog scale (EQ-VAS) were employed to assess the QoL of the healthcare workers objectively as developed previously [9,16]. EQ-5D-5L assesses QoL through five dimensions, namely, mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. These dimensions were scored from 1 to 5 (1, no problems; 2, slight problems; 3, moderate problems; 4, severe problems; 5, extreme problems/unable). The EQ-VAS records the patient's self-rated health on a vertical visual analog

scale. The VAS can be used as a quantitative measure of health outcome that reflect the patient's judgment, which consists of a 100-point scale ranging from 0 (worst imaginable health) to 100 (best imaginable health state) [8,17]. In this study, we classified the QoL of COVID-19 survivors as having no problems (score 1) and those having problems (score 2 to 5) in five dimensions. EQ-VAS scores were grouped into 11 groups with an interval of 10 score between groups.

Persistent dyspnea experienced during daily activities was evaluated using the modified Medical Research Council (mMRC) scale, with score ranging from 0 to 4 with 0 indicating no breathlessness except on strenuous exercise; 1, shortness of breath when hurrying on the level or walking up a slight hill; 2, walks slower than people of the same age on the level because of breathlessness or has to stop to catch a breath when walking at their own pace on the level; 3, stops for breath after walking ~100 m or after few minutes on the level; and 4, too breathless to leave the house, or breathless when dressing or undressing. The mMRC scale has been used for the assessment of dyspnea-related COVID-19 illness in previous studies [13,18]. We considered persistent dyspnea with mMRC score ≥ 1 and mMRC score 0 as no persistent dyspnea [13,19].

Some possible risk factors associated with QoL and dyspnea were assessed including demographic characteristics (gender and age), comorbidities, history of hospitalization during COVID-19, oxygen usage during acute COVID-19, history of COVID-19 vaccination, severity of COVID-19, existence of post-COVID syndrome and the type of symptoms of post-COVID syndrome, history of hospitalization was defined whether or not healthcare workers admitted and treated in hospital during the acute phase of COVID-19. History of oxygen usage was assessed including nasal cannula, rebreathing mask, non-rebreathing mask (NRM), high flow nasal cannula (HFNC), noninvasive ventilator (NIV), or machine ventilator during hospitalization or self-isolation. History of COVID-19 vaccination before confirmed COVID-19 infection was classified between vaccinated (1 to 3 times) and never vaccinated. The severity of COVID-19 was divided into asymptomatic, mild, moderate, severe and critical [20]. Post-COVID syndrome was the persistence of symptoms beyond four weeks after the acute phase of SARS-CoV-2 infection. Post-COVID syndrome was divided into acute (persistent symptoms of 4–12 weeks) and chronic (persistent symptoms in ≥ 12 weeks). The types of post-COVID syndrome symptoms vary due to impaired organs [14,21,22].

Data collection

The healthcare workers who agreed to participate in this study were interviewed directly in Bahasa Indonesia. This study was conducted at the work place of healthcare workers for three months (August to October 2022). The healthcare workers were asked related to participants' demographic data, comorbidities before COVID-19 infection, hospitalization, oxygen usage during admission in the hospital or self-isolation, duration of symptoms during and after acute phase of COVID-19 infection. The EQ-5D-5L, EQ-VAS, and mMRC questionnaires were also asked directly to healthcare workers.

Statistical analysis

Chi-squared test or Fisher's exact test was used to identify the risk factors associated with the QoL and dyspnea scale. Statistical significance was determined by a $p < 0.05$. All statistical analyses were performed by SPSS version 20 (IBM SPSS, New York, United States).

Results

Demographic and clinical characteristics of COVID-19 survivors

A total of 100 healthcare workers were included in the study and the characteristics are represented in **Table 1**. Most healthcare workers were female (86%), the largest age group was 31–45 years (45%), while less than sample workers had comorbidities (42%). Following the medical history of the healthcare workers, the majority had a history of hospitalization (75%), and only a small number required oxygen during the course of treatment (7%). The healthcare workers were mostly vaccinated (78%) before were confirmed of COVID-19. A large proportion of the healthcare workers were classified with mild COVID-19 (90%) and experienced prolonged symptoms of post-COVID syndrome (76%).

Table 1. Characteristics of the COVID-19 survivors included in the study (n=100)

| Characteristics | Frequency | Percentage |
|----------------------------------|-----------|------------|
| Gender | | |
| Male | 14 | 14.0 |
| Female | 86 | 86.0 |
| Age (year) | | |
| 51–60 | 19 | 19.0 |
| 41–50 | 20 | 20.0 |
| 31–40 | 32 | 32.0 |
| 19–30 | 29 | 29.0 |
| Comorbid | | |
| Yes | 42 | 42.0 |
| No | 58 | 58.0 |
| Hospitalized during COVID-19 | | |
| Yes | 25 | 25.0 |
| No | 75 | 75.0 |
| Oxygen usage during COVID-19 | | |
| Yes | 7 | 7.0 |
| No | 93 | 93.0 |
| History of COVID-19 vaccination | | |
| Yes | 78 | 78.0 |
| No | 22 | 22.0 |
| Severity of COVID-19 | | |
| Critical | 1 | 1.0 |
| Severe | 1 | 1.0 |
| Moderate | 5 | 5.0 |
| Mild | 90 | 90.0 |
| Asymptomatic | 3 | 3.0 |
| Existence of post-COVID syndrome | | |
| Chronic (>12 weeks) | 48 | 48.0 |
| Acute (4–12 weeks) | 28 | 28.0 |
| No | 24 | 24.0 |

Clinical symptoms of post-COVID syndrome

We assessed both acute and chronic post-COVID-19 syndromes in all COVID-19 survivors. Post-COVID syndrome was divided into acute (persistent symptoms of 4–12 weeks) and chronic (persistent symptoms in ≥ 12 weeks). The most frequent symptoms in post-COVID syndrome were fatigue 59 (77.6%), memory disorders 36 (47.4%), and confusion 28 (36.8%) (**Figure 1**).

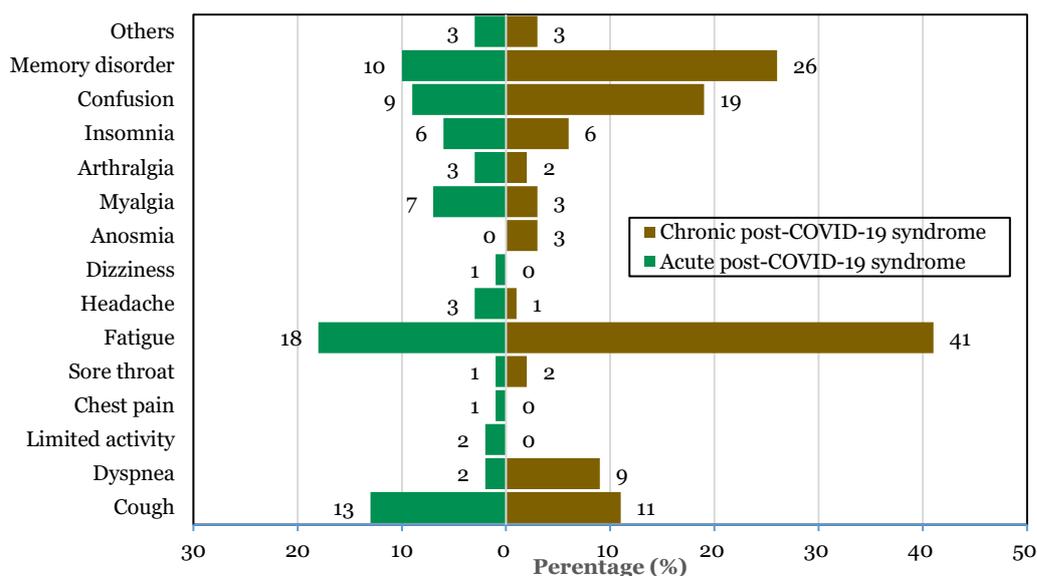


Figure 1. Clinical spectrum of acute post-COVID-19 syndrome and chronic post-COVID-19 syndrome among healthcare workers.

Quality of life of the COVID-19 survivors

Our data indicated there were no problems in the dimensions of mobility, self-care, and usual activities among the healthcare workers (**Table 2**). In the pain/discomfort dimension, two healthcare workers (2%) experienced mild and moderate problems respectively, meanwhile in the anxiety/depression dimension, four healthcare workers (4%) experienced mild problems.

Table 2. Dimensions of the EuroQol 5-dimensional 5-level (EQ-5D-5L) in healthcare workers (n=100)

| Dimensions | None (%) | Mild (%) | Moderate (%) | Severe (%) | Extreme (%) |
|--------------------|----------|----------|--------------|------------|-------------|
| Mobility | 100 | 0 | 0 | 0 | 0 |
| Self-care | 100 | 0 | 0 | 0 | 0 |
| Usual activity | 100 | 0 | 0 | 0 | 0 |
| Pain/discomfort | 96 | 2 | 2 | 0 | 0 |
| Anxiety/depression | 96 | 4 | 0 | 0 | 0 |

The average healthcare worker's score of their judgement towards their health outcome after COVID-19 infection was 87.6 ± 8.1 (**Table 3**). Out of all healthcare workers, most scored in the range of 90–99. Only seven healthcare workers believed that they were in the best imaginable health state (**Table 3**).

Table 3. Self-assessment of the healthcare workers based on EuroQol-visual analog scale (EQ-VAS) (n=100)

| Classification of EQ-VAS score | Frequency (%) | Mean \pm SD of EQ-VAS score |
|--------------------------------|---------------|-------------------------------|
| 70–79 | 10 | 71.8 \pm 3.0 |
| 80–89 | 29 | 81.8 \pm 2.9 |
| 90–99 | 54 | 92.1 \pm 3.1 |
| 100 | 7 | 100 \pm 0.0 |

Persistent dyspnea among COVID-19 survivors

A total of 39 healthcare workers were identified as having dyspnea in this study (**Table 4**). Healthcare workers with persistent dyspnea ($mMRC \geq 1$) were male 35.7%, group age 41–50 years, 26.2% healthcare workers with comorbid 29.3%. According to this result, the sub group with oxygen usage during COVID-19 was 42.9% compared to those without oxygen usage at 29%. A sub group of 40.9% without COVID-19 vaccination history suffered persistent dyspnea. All healthcare workers with severe-critical COVID-19 had persistent dyspnea, while only 27.8% of healthcare workers with previous mild COVID-19 had persistent dyspnea. There were 29% of healthcare workers with post-COVID syndrome experienced dyspnea ($mMRC 1-3$).

Table 4. Persistent dyspnea assessed by mMRC scale among COVID-19 survivors (n=100)

| Characteristic | Total | Frequency (%) | | | | |
|---------------------------------|-------|--------------------------|----------------|----------|---------|---------|
| | | Without dyspnea (mMRC 0) | Dyspnea mMRC 1 | mMRC 2 | mMRC 3 | mMRC 4 |
| Gender | | | | | | |
| Male | 14 | 9 (64.3) | 3 (21.4) | 2 (14.3) | 0 (0.0) | 0 (0.0) |
| Female | 86 | 60 (69.7) | 20 (23.3) | 4 (4.7) | 2 (2.3) | 0 (0.0) |
| Age (years) | | | | | | |
| 51–60 | 19 | 13 (68.4) | 5 (26.3) | 1 (5.3) | 0 (0.0) | 0 (0.0) |
| 41–50 | 20 | 11 (55.0) | 5 (25.0) | 3 (15.0) | 1 (5.0) | 0 (0.0) |
| 31–40 | 32 | 23 (71.9) | 7 (21.9) | 1 (3.1) | 1 (3.1) | 0 (0.0) |
| 19–30 | 29 | 22 (75.9) | 6 (20.7) | 1 (3.4) | 0 (0.0) | 0 (0.0) |
| Comorbid | | | | | | |
| Yes | 42 | 31 (73.8) | 7 (16.7) | 2 (4.8) | 2 (4.8) | 0 (0.0) |
| No | 58 | 38 (65.5) | 16 (27.6) | 4 (6.9) | 0 (0.0) | 0 (0.0) |
| Hospitalized during COVID-19 | | | | | | |
| Yes | 25 | 16 (70.7) | 6 (24.0) | 2 (8.0) | 1 (4.0) | 0 (0.0) |
| No | 75 | 53 (64.0) | 17 (22.7) | 4 (5.3) | 1 (1.3) | 0 (0.0) |
| Oxygen usage during COVID-19 | | | | | | |
| Yes | 7 | 4 (57.1) | 2 (28.6) | 1 (14.3) | 0 (0.0) | 0 (0.0) |
| No | 93 | 66 (71.0) | 21 (22.6) | 5 (5.4) | 1 (1.1) | 0 (0.0) |
| History of COVID-19 vaccination | | | | | | |

| Characteristic | Total | Frequency (%) | | | | |
|----------------------------------|-------|--------------------------|----------------|----------|-----------|---------|
| | | Without dyspnea (mMRC 0) | Dyspnea mMRC 1 | mMRC 2 | mMRC 3 | mMRC 4 |
| Yes | 78 | 56 (71.8) | 16 (20.5) | 6 (7.7) | 0 (0.0) | 0 (0.0) |
| No | 22 | 13 (59.1) | 7 (31.8) | 0 (0.0) | 2 (9.1) | 0 (0.0) |
| Severity of previous COVID-19 | | | | | | |
| Asymptomatic | 3 | 2 (66.7) | 1 (33.3) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Mild | 90 | 65 (72.2) | 20 (22.2) | 5 (5.6) | 0 (0.0) | 0 (0.0) |
| Moderate | 5 | 2 (40.0) | 2 (40.0) | 1 (20.0) | 0 (0.0) | 0 (0.0) |
| Severe | 1 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (100.0) | 0 (0.0) |
| Critical | 1 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (100.0) | 0 (0.0) |
| Existence of post-COVID syndrome | | | | | | |
| Yes | 76 | 47 (61.8) | 21 (27.6) | 6 (7.9) | 2 (2.6) | 0 (0.0) |
| No | 24 | 22 (91.7) | 2 (8.3) | 0 (0.0) | 0 (0.0) | 0 (0.0) |

Associations between demographic and clinical characteristics with quality of life

Since only two dimensions of the EQ-5D-5L (pain/discomfort dimension and anxiety/depression dimension) were reported by the COVID-19 survivors, we analyzed the risk factors for these two dimensions only (**Table 5**). The mobility, self-care, and usual activity dimensions were not analyzed. The statistical analysis indicated no significant associations between all studied risk factors (demographic data, comorbidities before COVID-19 infection, history of hospitalization, history oxygen usage, history of COVID-19 vaccination, severity of previous COVID-19 and existence of post-COVID syndrome) and both pain/discomfort and anxiety/depression dimensions (**Table 5**).

Table 5. Associations between risk factors and the quality-of-life dimensions among COVID-19 survivors

| Characteristics | Quality of life (EQ-5D-5L) | | | | | |
|----------------------------------|----------------------------|-----|----------------------|--------------------|----|----------------------|
| | Pain/discomfort | | | Anxiety/depression | | |
| | n (%) | | p-value ^a | n (%) | | p-value ^a |
| Yes | No | Yes | | No | | |
| Gender | | | 0.410 | | | 0.355 |
| Male | 0 | 14 | | 0 | 14 | |
| Female | 4 | 82 | | 4 | 84 | |
| Age (year) | | | 0.677 | | | 1.000 |
| >50 | 1 | 18 | | 2 | 17 | |
| ≤50 | 3 | 78 | | 2 | 79 | |
| Comorbid | | | 0.482 | | | 0.926 |
| Yes | 1 | 41 | | 2 | 40 | |
| No | 3 | 55 | | 2 | 56 | |
| Hospitalized during COVID-19 | | | 0.239 | | | 0.427 |
| Yes | 2 | 23 | | 2 | 23 | |
| No | 2 | 73 | | 2 | 73 | |
| Oxygen usage during COVID-19 | | | 0.575 | | | 0.529 |
| Yes | 0 | 7 | | 0 | 7 | |
| No | 4 | 89 | | 4 | 89 | |
| History of COVID-19 vaccination | | | 0.168 | | | 0.319 |
| Yes | 2 | 76 | | 3 | 75 | |
| No | 2 | 20 | | 2 | 20 | |
| Severity of previous COVID-19 | | | 0.575 | | | 0.529 |
| Asymptomatic-mild | 4 | 89 | | 4 | 89 | |
| Moderate-critical | 0 | 7 | | 0 | 7 | |
| Existence of post-COVID syndrome | | | 0.251 | | | 0.197 |
| Yes | 4 | 72 | | 5 | 71 | |
| No | 0 | 24 | | 0 | 24 | |

^a Analyzed using Chi-squared test or Fisher' exact test as appropriate

Associations between clinical symptoms of post-COVID syndrome and quality of life

Our data indicated that some of the clinical symptoms of post-COVID syndrome such as limited activity ($p=0.004$), sore throat ($p=0.026$), headache ($p=0.012$), myalgia ($p=0.006$) and

arthralgia ($p=0.001$) were associated with pain/discomfort dimension of QoL (**Table 6**). A significant association was also found between activity limitation ($p=0.012$), headache ($p=0.020$), myalgia ($p=0.015$) and arthralgia ($p=0.032$) with anxiety/depression of QoL (**Table 6**). Data analysis was not performed for the dimension of mobility, self-care, and usual activity of QoL because there were no problems reported by the COVID-19 survivors included in this study.

Table 6. Association between post-COVID syndrome symptoms and quality of life dimensions (pain/discomfort and anxiety/depression) among COVID-19 survivors (n=76)

| Post-COVID syndrome symptom | Quality of life dimensions | | | | | | | | | | |
|-----------------------------|----------------------------|---|-----|----|-------------------------|------------------------------|---|-----|----|-------------------------|--------|
| | Pain/discomfort dimension | | | | | Anxiety/depression dimension | | | | | |
| | Yes | | No | | p -value ^a | Yes | | No | | p -value ^a | |
| n | % | n | % | n | | % | n | % | | | |
| Cough | Yes | 2 | 2.6 | 21 | 27.6 | 0.580 | 1 | 1.3 | 22 | 28.9 | 1.000 |
| | No | 2 | 2.6 | 51 | 67.1 | | 4 | 5.3 | 49 | 64.5 | |
| Dyspnea | Yes | 1 | 1.3 | 10 | 13.2 | 0.472 | 1 | 1.3 | 10 | 13.2 | 0.553 |
| | No | 3 | 3.9 | 62 | 81.6 | | 4 | 5.3 | 61 | 80.3 | |
| Limited activity | Yes | 1 | 1.3 | 1 | 1.3 | 0.004* | 1 | 1.3 | 1 | 1.3 | 0.012* |
| | No | 3 | 3.9 | 71 | 93.4 | | 4 | 5.3 | 70 | 92.1 | |
| Chest pain | Yes | 0 | 0.0 | 1 | 1.3 | 1.000 | 0 | 0.0 | 1 | 1.3 | 1.000 |
| | No | 4 | 5.3 | 71 | 93.4 | | 5 | 6.6 | 70 | 92.1 | |
| Sore throat | Yes | 1 | 1.3 | 2 | 2.6 | 0.026* | 1 | 1.3 | 2 | 2.6 | 0.187 |
| | No | 3 | 3.9 | 70 | 92.1 | | 4 | 5.3 | 69 | 90.8 | |
| Fatigue | Yes | 3 | 3.9 | 56 | 73.7 | 1.000 | 3 | 3.9 | 56 | 73.7 | 0.310 |
| | No | 1 | 1.3 | 16 | 21.1 | | 2 | 2.6 | 15 | 19.7 | |
| Headache | Yes | 2 | 2.6 | 2 | 2.6 | 0.012* | 2 | 2.6 | 2 | 2.6 | 0.020* |
| | No | 2 | 2.6 | 70 | 92.1 | | 3 | 3.9 | 69 | 90.8 | |
| Dizziness | Yes | 0 | 0.0 | 1 | 1.3 | 1.000 | 0 | 0.0 | 1 | 1.3 | 1.000 |
| | No | 4 | 5.3 | 71 | 93.4 | | 5 | 6.6 | 70 | 92.1 | |
| Anosmia | Yes | 0 | 0.0 | 0 | 0.0 | 1.000 | 0 | 0.0 | 0 | 0.0 | 1.000 |
| | No | 4 | 5.3 | 72 | 94.7 | | 5 | 6.6 | 71 | 93.4 | |
| Ageusia | Yes | 0 | 0.0 | 3 | 3.9 | 1.000 | 0 | 0.0 | 3 | 3.9 | 1.000 |
| | No | 4 | 5.3 | 69 | 90.8 | | 5 | 6.6 | 68 | 89.5 | |
| Myalgia | Yes | 0 | 0.0 | 0 | 0.0 | 0.006* | 0 | 0.0 | 0 | 0.0 | 0.015* |
| | No | 4 | 5.3 | 72 | 94.7 | | 5 | 6.6 | 71 | 93.4 | |
| Arthralgia | Yes | 3 | 3.9 | 7 | 9.2 | 0.001* | 3 | 3.9 | 7 | 9.2 | 0.032* |
| | No | 1 | 1.3 | 65 | 85.5 | | 2 | 2.6 | 64 | 84.2 | |
| Diarrhea | Yes | 3 | 3.9 | 2 | 2.6 | 1.000 | 2 | 2.6 | 3 | 3.9 | 1.000 |
| | No | 1 | 1.3 | 70 | 92.1 | | 3 | 3.9 | 68 | 89.5 | |
| Insomnia | Yes | 0 | 0.0 | 0 | 0.0 | 0.505 | 0 | 0.0 | 0 | 0.0 | 1.000 |
| | No | 4 | 5.3 | 72 | 94.7 | | 5 | 6.6 | 71 | 93.4 | |
| Confusion | Yes | 1 | 1.3 | 11 | 14.5 | 1.000 | 1 | 1.3 | 11 | 14.5 | 1.000 |
| | No | 3 | 3.9 | 61 | 80.3 | | 4 | 5.3 | 60 | 78.9 | |
| Memory disorder | Yes | 1 | 1.3 | 27 | 35.5 | 0.340 | 2 | 2.6 | 26 | 34.2 | 0.663 |
| | No | 3 | 3.9 | 45 | 59.2 | | 3 | 3.9 | 45 | 59.2 | |
| Others | Yes | 3 | 3.9 | 33 | 43.4 | 0.285 | 3 | 3.9 | 33 | 43.4 | 0.345 |
| | No | 1 | 1.3 | 39 | 51.3 | | 2 | 2.6 | 38 | 50.0 | |

^a Analyzed using Chi-squared test or Fisher' exact test as appropriated

* Statistically significant at $p<0.05$

Associations between demographic and clinical characteristics with persistent dyspnea

Our data indicated that demographic data, comorbidities before COVID-19 infection, history of hospitalization, history of oxygen usage, history of COVID-19 vaccination, and severity of previous COVID-19 were not associated with the presence of dyspnea (**Table 7**). However, there was a significant association between the presence of post-COVID syndrome and the persistence of dyspnea ($p=0.006$).

Table 7. Factors associated with the presence of dyspnea among COVID-19 survivors

| Characteristics | Dyspnea (mMRC score ≥ 1) | | |
|-----------------|--------------------------------|----|-------------------------|
| | Yes | No | p -value ^a |
| Gender | | | 0.681 |
| Male | 5 | 9 | |
| Female | 26 | 60 | |
| Age (year) | | | 0.112 |

| Characteristics | Dyspnea (mMRC score ≥ 1) | | |
|----------------------------------|--------------------------------|----|----------------------|
| | Yes | No | p-value ^a |
| >50 | 6 | 13 | |
| ≤ 50 | 24 | 57 | |
| Comorbid | | | 0.376 |
| Yes | 11 | 31 | |
| No | 20 | 38 | |
| Hospitalized during COVID-19 | | | 0.533 |
| Yes | 9 | 16 | |
| No | 22 | 53 | |
| Oxygen usage during COVID-19 | | | 0.121 |
| Yes | 4 | 3 | |
| No | 27 | 66 | |
| History of COVID-19 vaccination | | | 0.255 |
| Yes | 22 | 56 | |
| No | 9 | 13 | |
| Severity of previous COVID-19 | | | 0.121 |
| Asymptomatic-mild | 27 | 66 | |
| Moderate-critical | 5 | 2 | |
| Existence of post-COVID syndrome | | | 0.006* |
| Yes | 29 | 47 | |
| No | 2 | 22 | |

^a Analyzed using the Chi-squared test or Fisher's exact test as appropriated

* Statistically significant at $p < 0.05$

Association between clinical symptoms of post-COVID syndrome and persistent dyspnea

Our analyses suggested that post-COVID syndrome symptoms of cough ($p=0.021$) and fatigue ($p=0.015$) were both associated with persistent dyspnea among COVID-19 survivors (**Table 8**). Other post-COVID syndrome symptoms such as limited activity, chest pain, sore throat, headache, dizziness, anosmia, ageusia, myalgia, arthralgia, diarrhea, insomnia, confusion, memory disorder and other were not associated with persistent dyspnea among COVID-19 survivors (**Table 8**).

Table 8. Association between post-COVID syndrome symptoms and persistent dyspnea among COVID-19 survivors (n=76)

| Post-COVID syndrome symptom | | Dyspnea (mMRC score ≥ 1) | | | | p-value ^a |
|-----------------------------|-----|--------------------------------|------|----|------|----------------------|
| | | Yes | | No | | |
| | | n | % | n | % | |
| Cough | Yes | 4 | 5.3 | 19 | 25.0 | 0.021* |
| | No | 24 | 31.6 | 29 | 38.2 | |
| Dyspnea | Yes | 5 | 6.6 | 6 | 7.9 | 0.521 |
| | No | 23 | 30.3 | 42 | 55.3 | |
| Limited activity | Yes | 1 | 1.3 | 1 | 1.3 | 1.000 |
| | No | 27 | 35.5 | 47 | 61.8 | |
| Chest pain | Yes | 0 | 0.0 | 1 | 1.3 | 1.000 |
| | No | 28 | 36.8 | 47 | 61.8 | |
| Sore throat | Yes | 1 | 1.3 | 2 | 2.6 | 1.000 |
| | No | 27 | 35.5 | 46 | 60.5 | |
| Fatigue | Yes | 26 | 34.2 | 33 | 43.4 | 0.015* |
| | No | 2 | 2.6 | 15 | 19.7 | |
| Headache | Yes | 0 | 0.0 | 4 | 5.3 | 0.290 |
| | No | 28 | 36.8 | 44 | 57.9 | |
| Dizziness | Yes | 0 | 0.0 | 1 | 1.3 | 1.000 |
| | No | 28 | 36.8 | 47 | 61.8 | |
| Anosmia | Yes | 0 | 0.0 | 0 | 0.0 | 0.551 |
| | No | 28 | 36.8 | 48 | 63.2 | |
| Ageusia | Yes | 2 | 2.6 | 1 | 1.3 | 0.310 |
| | No | 26 | 34.2 | 47 | 61.8 | |
| Myalgia | Yes | 0 | 0.0 | 0 | 0.0 | 0.30 |
| | No | 28 | 36.8 | 48 | 63.2 | |
| Arthralgia | Yes | 4 | 5.3 | 6 | 7.9 | 0.646 |
| | No | 24 | 31.6 | 42 | 55.3 | |
| Diarrhea | Yes | 1 | 1.3 | 4 | 5.3 | 1.000 |
| | No | 27 | 35.5 | 44 | 57.9 | |
| Insomnia | Yes | 0 | 0.0 | 0 | 0.0 | 0.751 |
| | No | 28 | 36.8 | 48 | 63.2 | |

| Post-COVID syndrome symptom | | Dyspnea (mMRC score ≥ 1) | | | | p-value ^a |
|-----------------------------|-----|--------------------------------|------|----|------|----------------------|
| | | Yes | | No | | |
| | | n | % | n | % | |
| Confusion | Yes | 5 | 6.6 | 7 | 9.2 | 0.464 |
| | No | 23 | 30.3 | 41 | 53.9 | |
| Memory disorder | Yes | 12 | 15.8 | 16 | 21.1 | 0.192 |
| | No | 16 | 21.1 | 32 | 42.1 | |
| Others | Yes | 16 | 21.1 | 20 | 26.3 | 0.185 |
| | No | 12 | 15.8 | 28 | 36.8 | |

^a Analyzed using Chi-squared test or Fisher' exact test as appropriated

* Statistically significant at $p < 0.05$

Discussion

The risk of exposure was increased during the COVID-19 pandemic phase, particularly healthcare workers having direct contact with COVID-19 patients. Our study revealed that the majority of healthcare workers were women (86%). Some studies have reported that patients after COVID-19 infection develop a poorer QoL, women tend to experience frequent anxiety, and develop severe anxiety symptoms early after discharge [23-25]. Some studies have proposed mechanisms to explain the association between certain risk factors, one of which, the female gender has been postulated that hormones may have been involved in persisting the hyperinflammatory status of the COVID-19 acute phase even after recovery [26-28]. Also, higher immunoglobulin G (IgG) antibody responses have been reported in women during the COVID-19 acute phase, and have been linked to sustaining the disease's manifestations [29-31]. Aged individuals find it more difficult to overcome the acute phase of COVID-19 due to the increased risk of the disease severity, possibly with multiple underlying pre-existing comorbidities [32].

The pandemic altered not only social contacts of the general population, but also induced fear, stress, financial concerns, and worries about health, which could lead to a lower health-related QoL and their self-rated health. The EQ-VAS assessment purposed to capture the healthcare worker's self-rated health after COVID-19 infection. A previous study reported the average EQ-VAS score for patients after COVID-19 infection was 56.6 [33], while this study found a higher average score of 87.6.

Our study found there was no association between the characteristics of healthcare workers and their QoL, but existing post-COVID syndrome showed an association with persistent dyspnea ($p=0.006$). A study reported a significant number of COVID-19 patients with comorbidities experienced persistent dyspnea and persistent symptoms after discharge, suggesting that existing comorbidities are associated between condition after COVID-19 [34].

Dyspnea is one of the main causes of hospital admissions for COVID-19 cases. As a result of internal pathological changes, dyspnea may persist even after recovery. Exploring the underlying mechanisms behind this condition, there are two suggested hypotheses. First, a prolonged pro-inflammatory response (hyper-inflammatory cytokine storm), caused by SARS-CoV-2 infection, can trigger an atypical reaction from the immune system and mast cells, leading to a sequence of events that affect the respiratory, immune, and central nervous systems. Second, social and emotional factors related to the COVID-19 pandemic, such as post-traumatic stress, hospitalization, treatments, social alarm, lockdowns, work and family conditions, and psychological issues like anxiety or depression, could potentially contribute to post-COVID-19 symptoms [22]. Previous studies found that mental health problems such as depression, post-traumatic stress disorder, depression, anxiety and fear can persist up to eight weeks after the acute phase of COVID-19, and can last more than 6 months after being cured of the infection [35-37].

This study reported that symptoms of post-COVID syndrome, such as limited activity, headache, myalgia and arthralgia were significantly associated with both health-related QoL dimensions of pain/discomfort and anxiety/depression. The previous research, correlation analysis between symptoms and QoL described moderate for pain and fatigue and low for breathlessness. The correlation of the three symptoms with QoL suggests that the amelioration in EQ-5D could be influenced by symptom improvement after rehabilitation [38]. The COVID-19 infection impacts many organ systems, including pulmonary, hematologic, cardiovascular, neuropsychiatric, renal, endocrine, and gastrointestinal. Prolonged symptoms (more than 4

weeks) after the acute phase of COVID-19 was defined as post-COVID syndrome, and the symptoms could be grouped into symptom clusters that should be explored by clinical phenotypes, expressing different impacts on QoL and persistent dyspnea. Further study is needed to explore the underlying pathogenic mechanisms of each symptom and how it relates to the alteration of QoL and persistent dyspnea [10,13].

Addressing persistent dyspnea due to post-COVID syndrome while simultaneously improving the QoL involves a holistic approach that considers both physical and mental well-being. The identification of symptoms is required for early intervention and provide post-acute medical, psychological, and physical rehabilitation to enhance the recovery after a COVID-19 infection, including the ability to return to work [21,24].

There were some limitations of this study that need to be discussed. The sample size was relatively small due to a single-center study design, the majority of healthcare workers had a history of mild COVID-19. These limitations might lead to bias when generalizing the results. Our study did not provide assessment of QoL and persistent dyspnea before the COVID-19 infection and during the acute phase of COVID-19 as a comparison with the current assessment.

Conclusion

Post-COVID syndrome was found significantly associated with persistent dyspnea among healthcare workers. Certain symptoms of post-COVID syndrome, such as activity limitation, sore throat, headache, myalgia, and arthralgia was related to QoL. Additionally, cough and fatigue showed an association with persistent dyspnea. A comprehensive strategy in detection and management are necessary for resolving persistent dyspnea and enhancing QoL at the same time.

Ethics approval

This study was approved by Ethical committee of Universitas Sumatera Utara on 18th October 2021 (Approval No: 127/KEP/USU/2021).

Competing interests

The authors declare that there is no conflict of interest.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

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