Article

Headache in Post-COVID-19 Patients: Its Characteristics and Relationship with the Quality of Life

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Abstract: Little is known on the characteristics of headaches associated with coronavirus disease 2019 (COVID-19) in Indonesia. The objective of this study was to describe the characteristics of headache in post-COVID-19 patients, and its impact on the patients’ quality of life (QoL), as well as to determine the associated determinants of the poor QoL. A cross-sectional study was conducted in Banda Aceh, Indonesia. The demographic characteristics, clinical symptoms of COVID-19, characteristics of headache, and the QoL were collected and assessed. Headache was diagnosed and characterized using the International Classification of Headache Disorders, version 3 (ICHD-3). QoL was assessed using a Short Form 36 Health Survey (SF-36) tool. A logistic regression model was used to investigate the associated determinants of poor QoL in post-COVID-19 patients. A total of 215 post-COVID-19 patients were included in the final analysis, and 21.4% (46/215) of them had a poor QoL due to headache following COVID-19. Those who were unemployed and who contracted COVID-19 less than three months prior to the study had higher odds of having poor QoL compared to those who were employed and who contracted COVID-19 more than three months prior to the study. Low QoL was also related to headache that occurred less than one month after recovering from COVID-19 (compared to that which occurred longer than one month after); had a high frequency; had a combination sensation of pulsating, pressing, fiery, and stabbing pain; had a high severity score; and had additional symptoms accompanying the headache. In conclusion, headache related to COVID-19 is associated with low QoL among post-COVID-19 patients. A guideline on prevention measures of headache on COVID-19 patients, therefore, needs to be established to avoid long-term consequences.

Keywords: post-COVID-19 headache; prolonged COVID-19; COVID-19 sequelae; long COVID

1. Introduction

In late 2019, coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged, and confirmed cases rapidly increased worldwide, which led to a global pandemic in March 2020 [1–3]. Since then, every country has faced the consequences, not only from the infection itself, but also the economics, border restrictions, and disruptions of public services [4–6]. Although effective vaccines are available, high vaccine hesitancy is reported globally [7,8]. Most SARS-CoV-2 infections are asymptomatic; however, in symptomatic patients, complaints range from fever, cough, and dyspnea to more severe symptoms [9–17]. SARS-CoV-2 infection not only affects the respiratory system, but can also have neurological manifestations, such as dizziness,
ageusia, headache, and muscle pain [10,18–20]. Persistent COVID-19 symptoms have also been reported following COVID-19 recovery worldwide [21].

COVID-19 affects people from all backgrounds, ethnicities, and age groups [22–26]. Factors affecting the quality of life (QoL) of COVID-19 patients have previously been reported [27]. However, the QoL of patients with persistent symptoms after COVID-19 recovery is still scarce. Persistent COVID-19 not only affects the respiratory system, but also the neurological, gastrointestinal, and psychosocial systems of patients [28–30]. Distress and sleeping disorders were found to be the most common persistent psychological symptoms after COVID-19 recovery (36%; 95%CI: 22–51% and 35%; 95%CI: 29–41%, respectively) [30]. A follow-up study showed that hospitalized COVID-19 survivors showed neurocognitive impairment, psychiatric morbidity, and reduced QoL after two months [31]. Headache is the most common symptom after 6 and 9 months of COVID-19 recovery, with a prevalence of 47.1% [32–34]. However, the QoL in COVID-19 survivors with prolonged headache is not clearly understood. Patients with persistent headache often complain of bilateral headaches with a pressing sensation, with varying degrees of severity from mild to severe [35,36]. The vast majority of COVID-19 patients, 72%, reported that the post-COVID-19 headaches were different during the acute phase of COVID-19 [37]. The characteristics of headaches among COVID-19 survivors in Indonesia are unavailable. Therefore, this study was conducted: (a) to determine the characteristics of headache in post-COVID-19 patients in Indonesia; (b) to assess the impacts of headache on the QoL of post-COVID-19 patients; and (c) to determine the associated determinants of poor QoL of post-COVID-19 patients.

2. Materials and Methods

2.1. Study Design and Eligibility Criteria

A cross-sectional study was conducted to assess the characteristics of persistent headaches in post-COVID-19 patients and their relationship to QoL in a provincial referral hospital in Aceh, Indonesia. The study was conducted at the Neurology Polyclinic of Dr. Zainoel Abidin Hospital in Banda Aceh, the capital of Aceh. Patients who seek treatment at Dr. Zainoel Abidin Hospital come from all regions of Aceh, and, therefore, it could provide an overview of the characteristics of patients who represent Aceh.

All patients over 18 years who were confirmed to have COVID-19 by polymerase chain reaction (PCR) and who had a headache during the course of COVID-19 or who developed a headache after being discharged from the hospital were considered eligible. Patients were excluded if they were diagnosed with other secondary headaches prior to COVID-19.
cleaner), climbing one or several flights of stairs, walking short (one block) or long distances (more than a mile). Bodily pain was evaluated by the intensity of pain described by the participants during the past four weeks, and how the pain interferes with their daily activities. Four questions were used to assess how the participants’ physical health limits their work or daily activities, including whether they accomplished less than before, have difficulty performing work, or if they have cut down the time spent working with a yes or no response. The impact of the participants’ emotional state on work or daily activities was evaluated by three questions: whether they accomplished less than before, were careless, or spent less time working. SF-36 also includes two questions about how much of the time and to what extent the physical health or emotional problems affect the participants’ social function. The participants’ vitality was evaluated by four questions about whether they feel tired or worn out or the opposite, and whether they feel they have a lot of energy. Five questions were used to address their emotional well-being, which included whether they are a nervous or happy person, and whether they feel calm or down. Finally, the participants’ general health was evaluated by questions such as if they seem to get sick easily, or expect their health to get worse, or even the opposite, if they feel their health is excellent. The participants were asked to choose a response to constitute a hierarchical Guttman scale in physical function questions, in which the score for each item consistently decreases in severity or difficulty, as follows: yes, limited a lot (1); yes, limited a little (2); or no, not limited at all (3). The other questions are rated on Likert-type or frequency response scales, ranging from three response categories for the physical function items to six categories for the bodily pain items. Using the standard guideline, the scores were transformed into a linear 0 to 100 range, with a higher score representing a better QoL [38].

Explanatory variables assessed in this study included demographic characteristics, COVID-19 vaccination, the presence of specific symptoms of COVID-19, and headache characteristics. Sociodemographic data consisted of age (divided into 20–29, 30–39, 40–49, and >50-year-old), gender, occupation (grouped into employed and unemployed), monthly income (divided into <3, 3–5, 5–10, and >10 million Indonesian rupiah), and COVID-19 vaccination status (had dose 1, dose 2, or booster shot), time of COVID-19 infection (<3, 3–6, 7–12, and >12 months ago), and whether they were hospitalized during the last COVID-19 course. The presence of the specific symptoms of COVID-19, such as fever, shortness of breath, cough, cold, headache, muscle pain (myalgia), anosmia, ageusia, diarrhea, or nausea/vomiting, were also assessed, as well as the presence of comorbidities, such as hypertension, diabetes, obesity, kidney illness, heart disease, lung disease, liver disease, tumor or cancer, autoimmune disease, asthma, or others.

2.3. Statistical Analysis

The SF-36 score was used to determine the frequency (percentage) of patients’ QoL categories in eight domains, and the results were classified as good or poor QoL based on a cut-off point of 50%. A logistic regression model was used to investigate the relationships between the explanatory variables and QoL of the patients. IBM SPSS Statistics version 22 was used, and \( p < 0.05 \) was considered statistically significant.

2.4. Ethics Approval and Patient Consent

The Ethics Committee of Dr. Zainoel Abidin Hospital approved the study protocol under the number 010/EA/FK-RSUDZA/2022. Following human research regulations, all patients provided written informed consent before participating this study.

3. Results

3.1. Respondents’ Characteristics

We included 215 post-COVID-19 patients in the final analysis. The socio-demographic characteristics of the respondents are presented in Table 1. Before contracting COVID-19, more than half (62.8%) of the respondents were unvaccinated against the disease. Of those vaccinated, 37.2% received the first dose, and 39.1% were fully vaccinated. Almost half
of the respondents (45.6%) were aged between 30–39 years old, and 25.6% were between 20–29 years old. Females were more dominant than males (69.8 vs. 30.2%). About 65% of the participants were working, and 52.1% earned IDR 3–5 million. More than a third (34.4%) of the respondents contracted COVID-19 less than 3 months prior to the study. The vast majority of the respondents (90.2%) were not hospitalized during COVID-19 infection. Of those hospitalized (9.8%), only 0.9% were admitted to the ICU or RICU. Most participants complained of fever (77.2%) and headache (72.1%), whereas anosmia and ageusia only presented in 45.1% and 32.6%, respectively. A total of 20% of the participants had at least one underlying condition, such as hypertension (7.0%), obesity (5.6%), diabetes (5.1%), asthma (4.2%), cardiovascular disease (0.9%), autoimmune disease (1.4%), or kidney diseases (0.5%).

Table 1. Characteristics of the respondents included in this study (n = 215).

| Characteristics                  | n   | %    |
|----------------------------------|-----|------|
| **Age group (year)**             |     |      |
| 20–29                            | 55  | 25.6 |
| 30–39                            | 98  | 45.6 |
| 40–49                            | 41  | 19.1 |
| >50                              | 21  | 9.8  |
| **Gender**                       |     |      |
| Male                             | 65  | 30.2 |
| Female                           | 150 | 69.8 |
| **Employment**                   |     |      |
| Unemployed                       | 76  | 35.3 |
| Employed                         | 139 | 64.7 |
| **Monthly income (Indonesian Rupiah)** |     |      |
| <3 million                       | 46  | 21.4 |
| 3–5 million                      | 112 | 52.1 |
| 5–10 million                     | 45  | 20.9 |
| >10 million                      | 12  | 5.6  |
| **Time between COVID-19 and the study** |     |      |
| <3 months (R)                    | 74  | 34.4 |
| 3–6 months                       | 29  | 13.5 |
| 7–12 months                      | 43  | 20.0 |
| >12 months                       | 69  | 32.1 |
| **Hospitalization for COVID-19** |     |      |
| No                               | 194 | 90.2 |
| Yes                              | 21  | 9.8  |
| **Admitted to the intensive unit (ICU) or RICU due to COVID-19** |     |      |
| No                               | 213 | 99.1 |
| Yes                              | 2   | 0.9  |
| **COVID-19 symptom**            |     |      |
| Fever                            | 166 | 77.2 |
| Shortness of breath              | 31  | 14.4 |
| Cough and cold                   | 146 | 67.9 |
| Headache                         | 155 | 72.1 |
| Muscle pain/myalgia              | 111 | 51.6 |
| Anosmia                          | 97  | 45.1 |
| Ageusia                          | 70  | 32.6 |
| Diarrhea                         | 26  | 12.1 |
| Nausea/vomiting                  | 42  | 19.5 |
| Asymptomatic                     | 8   | 3.7  |
3.2. Headache Characteristics

Most participants (155/215, 72.1%) experienced headache during hospitalization or self-isolation for COVID-19, with 71.6% of them taking medication to relieve the pain (Table 2). Headache was felt all over the head by 47.4% (102/215) of the participants, whereas 21.4% of the participants could not describe the location of the pain. Among the respondents, 36 (16.7%) indicated that their headache only occurred in one area (frontoparietal, 5.6%; frontal, 5.1%; and parietal, 4.2%). Headache occurred for less than one hour in 133/215 (61.9%) of the respondents, whereas 37.7% experienced the headache for longer. Headache was complained about everyday by 33.0% of the participants, whereas for 83 of 215 (38.6%) participants, only once or twice per month. More than half of the participants (127/215, 59.1%) described the headache as a pulsating pain, 20.9% as pressing pain, 6.0% as mixed between pulsating and pressing pain, and 5.1% as stabbing pain. Based on the severity of the headache, moderate headache (46.5%), mild headache (42.3%), and severe headache (11.1%) were experienced by the participants. Some factors, including physical activities, noise, and bright light, or their combination, aggravated the headache, whereas rest, pain medication, and a combination of rest and pain medication helped ease the pain.

Table 2. Characteristics of headache reported by post-COVID-19 patients in Indonesia (n = 215).

| Characteristics                              | n  | %    |
|----------------------------------------------|----|------|
| Time between COVID-19 and the headache       |    |      |
| During treatment/during self-isolation       | 155| 72.1 |
| 1–4 weeks after recovered                    | 36 | 16.7 |
| 1–3 months after recovered                   | 9  | 4.2  |
| 4–6 months after recovered                   | 3  | 1.4  |
| >12 months after recovered                   | 5  | 2.3  |
| Unable to remember                           | 7  | 3.3  |
| Had painkillers for the headache             |    |      |
| No                                           | 61 | 28.4 |
| Yes                                          | 154| 71.6 |
| Location of the headache                     |    |      |
| Only in one point/area                       | 36 | 16.7 |
| Right side                                   | 20 | 9.3  |
| Left side                                    | 11 | 5.1  |
| Whole head                                   | 102| 47.4 |
| Cannot be described                          | 46 | 21.4 |
### Table 2. Cont.

| Characteristics                              | n   | %    |
|----------------------------------------------|-----|------|
| **Duration of the headache**                 |     |      |
| Less than 1 h                                | 133 | 61.9 |
| 1–6 h                                        | 68  | 31.6 |
| 7–12 h                                       | 4   | 1.9  |
| More than 12 h                               | 10  | 4.6  |
| **Frequency of the headache**                |     |      |
| 1–2 times/month                              | 83  | 38.6 |
| 1–2 times/week                               | 32  | 14.9 |
| >2 times/week                                | 16  | 7.4  |
| Everyday                                     | 84  | 39.1 |
| **Characteristic of the headache**           |     |      |
| Pulsating                                    | 127 | 59.1 |
| Pressing                                     | 45  | 20.9 |
| Fiery                                        | 4   | 1.9  |
| Stabbing                                     | 11  | 5.1  |
| Combination pulsating and pressing           | 13  | 6.0  |
| Combination pulsating and stabbing           | 4   | 1.9  |
| Combination pressing and fiery               | 1   | 0.5  |
| Combination pressing and stabbing            | 2   | 0.9  |
| Combination pulsating, pressing, and stabbing| 2   | 0.9  |
| Combination pulsating, fiery, and stabbing   | 6   | 2.8  |
| **Severity of headache (on a pain scale of 0–10, where 0 is no pain and 10 is very painful)** | | |
| 0                                            | 3   | 1.4  |
| 1–3                                          | 88  | 40.9 |
| 4–6                                          | 100 | 46.5 |
| 7–9                                          | 22  | 10.2 |
| 10                                           | 1   | 0.9  |
| **What makes the headache worse**            |     |      |
| Activity/tired                               | 97  | 45.1 |
| Bright light                                 | 10  | 4.7  |
| Noise                                        | 15  | 7.0  |
| Activity/tired and bright light              | 4   | 1.9  |
| Activity/tired and noise                     | 20  | 9.3  |
| Bright light and noise                       | 4   | 1.9  |
| All three                                    | 9   | 4.2  |
| None                                         | 56  | 26.0 |
| **What makes the headache better**           |     |      |
| Rest                                         | 76  | 35.3 |
| Painkiller                                   | 43  | 20.0 |
| Rest and painkiller                          | 73  | 33.5 |
| None                                         | 23  | 10.7 |
| **Additional symptom during headache**       |     |      |
| No                                           | 111 | 55.8 |
| Yes                                          | 95  | 44.2 |
| **Type of symptom during headache**          |     |      |
| Fever                                        | 63  | 29.3 |
| Shortness of breath                          | 22  | 10.2 |
| Cough and cold                               | 68  | 31.6 |
| Myalgia                                      | 64  | 29.8 |
| Anosmia/ageusia                              | 27  | 12.6 |
| Diarrhea                                     | 10  | 4.7  |
| Nausea/vomiting                              | 37  | 17.2 |
| Photophobia                                  | 8   | 3.7  |
| Phonophobia                                  | 4   | 1.9  |
Ninety-five of the participants (44.2%) had additional symptom occurrence with the headache, including cough (31.6%), myalgia (29.8%), fever (29.3%), nausea/vomiting (17.2%), and anosmia/ageusia (12.6%).

3.3. QoL of the Participants with Headache in COVID-19 Infection

The QoL of the participants are presented in Table 3. The majority of the participants (80.9%) had good physical functioning; however, 36.7% had limitations due to physical problems, and 34.4% due to emotional problems (Table 3). There were 3.3% participants with poor mental health due to the headache, 17.7% with fatigue, 38.6% with pain, and 21.9% with poor social function that interferes with their daily life, meaning 56/215 (26.0%) of the participants reported poor general health. Overall, 46/215 (21.4%) of the participants had a poor QoL due to headache following COVID-19 infection.

Table 3. Quality of life of respondents based on the domains (n = 215).

| QoL Domain                        | Mean ± SD          | Good n (%) | Poor n (%) |
|-----------------------------------|--------------------|------------|------------|
| Physical functioning              | 674.66 ± 224.85    | 174 (80.9) | 41 (19.1)  |
| Role limitations due to physical health | 206.06 ± 139.79   | 136 (63.3) | 79 (36.7)  |
| Role limitations due to emotional problems | 186.51 ± 103.35 | 141 (65.6) | 74 (34.4)  |
| Pain                              | 112.16 ± 41.12     | 132 (61.4) | 83 (38.6)  |
| Energy/fatigue                    | 245.26 ± 63.62     | 177 (82.3) | 38 (17.7)  |
| Emotional well-being              | 365.07 ± 70.08     | 208 (96.7) | 7 (3.3)    |
| Social functioning                | 121.26 ± 38.65     | 168 (78.1) | 47 (21.9)  |
| General health                    | 290.44 ± 79.88     | 159 (74.0) | 56 (26.0)  |
| Total QoL                         | 2201.41 ± 517.85   | 169 (78.6) | 46 (21.4)  |

3.4. Factors Associated with the QoL Based on the Participants’ Characteristics

Our study showed that unemployment status and contracting COVID-19 less than 3 months prior to the study were associated with poor QoL ($p < 0.05$). Individuals with headache who had received the first and second dose of the COVID-19 vaccine were approximately 2.5 times more likely to have poor QoL compared to those who were unvaccinated (OR: 0.39; 95%CI: 0.18–0.84 and OR: 0.41; 95%CI: 0.20–0.87, respectively). Participants who had been COVID-19-positive less than 3 months prior to the study had almost five times greater odds of poor QoL compared to those who were infected between 7–12 months prior to the study (OR: 0.19, 95%CI: 0.06–0.59, with $p = 0.004$) and those who were positive more than 12 months prior to the study (OR:0.21, 95%CI: 0.08–0.52, with $p = 0.001$). Age group, sex, the history of hospitalization, monthly income, symptoms during COVID-19 infection, and comorbidity were not associated with the QoL of the participants (Table 4).

3.5. Factors Associated with the QoL Based on the Headache Characteristics

The headache characteristics that are associated with the QoL of the participants are presented in Table 5. The participants who started to have headache 1–4 weeks after recovering from COVID-19 had approximately nine times greater odds of poor QoL compared to those who had headache after one month from COVID-19 recovery, with OR: 8.85; 95%CI: 1.05–74.50, and $p = 0.027$. It is understandable that poor QoL was associated with those who took the medication (OR: 7.49, 95%CI: 2.23–25.18). Having a headache between 1–6 h or more than 6 h were associated with increased odds of poor QoL compared to participants who experienced the headache for less than 1 h (OR: 2.35, 95%CI: 1.16–4.77, and OR: 4.24, 95%CI: 1.33–13.52, respectively). Experiencing headache everyday was associated with nine times greater odds of poor QoL compared to those who only had headache once-to-twice per month (OR: 9.13, 95%CI:3.33–24.98, $p = 0.001$).
### Table 4. Sociodemographic and COVID-19 factors associated with the QoL of patients.

| Factor                          | n   | %   | Poor QoL n (%) | OR (95%CI) | p-Value |
|---------------------------------|-----|-----|----------------|------------|---------|
| **Age group (year)**            |     |     |                |            |         |
| 20–29 (reference group (R))     | 55  | 25.6| 14 (25.5)      | 1          |         |
| 30–39                           | 98  | 45.6| 14 (14.3)      | 0.49 (0.21–1.12) | 0.090  |
| 40–49                           | 41  | 19.1| 9 (22.0)       | 0.82 (0.32–2.14) | 0.691  |
| >50                             | 21  | 9.8 | 9 (42.9)       | 2.20 (0.76–6.31) | 0.144  |
| **Sex**                         |     |     |                |            |         |
| Male (R)                        | 65  | 30.2| 10 (15.4)      | 1          |         |
| Female                          | 150 | 69.8| 36 (24.0)      | 1.74 (0.80–3.76) | 0.160  |
| **Employment**                  |     |     |                |            |         |
| Unemployed (R)                  | 47  | 21.9| 17 (36.2)      | 1          |         |
| Employed                        | 168 | 78.1| 29 (17.3)      | 0.37 (0.18–0.75) | 0.006  |
| **Monthly income (Indonesian Rupiah)** |     |     |                |            |         |
| <3 million (R)                  | 46  | 21.4| 9 (19.6)       | 1          |         |
| 3–5 million                     | 112 | 52.1| 25 (22.3)      | 1.18 (0.50–2.77) | 0.702  |
| 5–10 million                    | 45  | 20.9| 11 (24.4)      | 1.33 (0.49–3.60) | 0.375  |
| >10 million                     | 12  | 5.6 | 1 (8.3)        | 0.37 (0.04–3.28) | 0.375  |
| **Time between COVID-19 and the study** |     |     |                |            |         |
| <3 months (R)                   | 74  | 34.4| 26 (35.1)      | 1          |         |
| 3–6 months                      | 29  | 13.5| 9 (31.0)       | 0.83 (0.33–2.09) | 0.693  |
| 7–12 months                     | 43  | 20.0| 4 (9.3)        | 0.19 (0.06–0.59) | 0.004  |
| >12 months                      | 69  | 32.1| 7 (10.1)       | 0.21 (0.08–0.52) | 0.001  |
| **Hospitalization for COVID-19**|     |     |                |            |         |
| No (R)                          | 194 | 90.2| 39 (20.1)      | 1          |         |
| Yes                             | 21  | 9.8 | 7 (33.3)       | 1.99 (0.75–5.26) | 0.167  |
| **Admitted to the intensive unit (ICU) or RICU due to COVID-19** |     |     |                |            |         |
| No (R)                          | 213 | 99.1| 46 (21.6)      | 1          |         |
| Yes                             | 2   | 0.9 | 0 (0.0)        | 0.00 (0.00–NA) | 0.999  |
| **Additional symptoms when positive for COVID-19** |     |     |                |            |         |
| Headache                        | 163 | 75.8| 39 (23.9)      | 2.02 (0.84–4.85) | 0.114  |
| Others (R)                      | 52  | 24.2| 7 (13.5)       | 1          |         |
| Loss of smell (anosmia)         | 97  | 45.1| 20 (20.6)      | 0.92 (0.48–1.77) | 0.801  |
| Others (R)                      | 118 | 54.9| 26 (22.0)      | 1          |         |
| Loss of taste (ageusia)         | 70  | 32.6| 14 (20.0)      | 0.88 (0.44–1.79) | 0.729  |
| Others (R)                      | 145 | 67.4| 32 (22.1)      | 1          |         |
| **Comorbidity**                 |     |     |                |            |         |
| No comorbidity (R)              | 172 | 80.0| 36 (20.9)      | 1          |         |
| Had comorbidity                 | 43  | 20.0| 10 (23.3)      | 1.15 (0.52–2.54) | 0.740  |

### Table 5. Headache characteristics factors associated with the QoL.

| Factor                          | n   | %   | Poor QoL n (%) | OR (95%CI) | p-Value |
|---------------------------------|-----|-----|----------------|------------|---------|
| **Time between COVID-19 and the headache** |     |     |                |            |         |
| During treatment/during self-isolation | 155 | 72.1| 35 (22.6)      | 6.71 (0.88–51.45) | 0.067  |
| 1–4 weeks after recovered       | 36  | 16.7| 10 (27.8)      | 8.85 (1.05–74.30) | 0.027  |
| More than 1 month (reference group (R)) | 24  | 11.2| 1 (4.2)        | 1          |         |
| **Had painkillers for the headache** |     |     |                |            |         |
| No (R)                          | 61  | 28.4| 3 (4.9)        | 1          |         |
| Yes                             | 154 | 71.6| 43 (27.9)      | 7.49 (2.23–25.18) | 0.001  |
| **Location of the headache**    |     |     |                |            |         |
| Only in one point/area (R)      | 36  | 16.7| 4 (1.1)        | 1          |         |
Table 5. Cont.

| Factor                                      | n     | %     | Poor QoL n (%) | OR (95%CI)      | p-Value |
|----------------------------------------------|-------|-------|----------------|-----------------|---------|
| Right side                                  | 20    | 9.3   | 1 (5.0)        | 0.42 (0.04–4.05) | 0.454   |
| Left side                                   | 11    | 5.1   | 1 (9.1)        | 0.80 (0.08–8.01) | 0.849   |
| Whole head and indescribable                | 148   | 68.8  | 40 (27.0)      | 2.96 (0.99–8.91) | 0.053   |
| Duration of the headache                    |       |       |                |                 |         |
| <1 h (R)                                    | 133   | 61.9  | 20 (15.0)      | 1                |         |
| 1–6 h                                       | 68    | 31.6  | 20 (29.4)      | 2.35 (1.16–4.77) | 0.017   |
| >6 h                                        | 14    | 6.5   | 6 (42.9)       | 4.24 (1.33–13.52) | 0.015   |
| Frequency of the headache                   |       |       |                |                 |         |
| 1–2 times/month                             | 83    | 38.6  | 5 (6.0)        | 1                |         |
| 1–2 times/week                              | 32    | 14.9  | 7 (21.9)       | 4.37 (1.27–14.99) | 0.019   |
| >2 times/week                               | 16    | 7.4   | 3 (18.8)       | 3.60 (0.77–16.91) | 0.105   |
| Every day and NA                            | 84    | 39.1  | 31 (36.9)      | 9.13 (3.33–24.98) | <0.001  |
| Characteristic of the headache              |       |       |                |                 |         |
| Pulsating (R)                               | 127   | 59.1  | 22 (17.3)      | 1                |         |
| Pressing                                    | 45    | 20.9  | 7 (15.6)       | 0.88 (0.35–2.22) | 0.786   |
| Fiery                                       | 4     | 1.9   | 0 (0.0)        | 0.00 (0.00–NA)   | 0.999   |
| Stabbing                                    | 11    | 5.1   | 3 (27.3)       | 1.79 (0.44–7.29) | 0.417   |
| Any combination of those                    | 28    | 13.0  | 14 (50.0)      | 4.77 (2.00–11.41) | <0.001  |
| Severity score of headache                 |       |       |                |                 |         |
| 0–3 (R)                                     | 91    | 42.3  | 9 (9.9)        | 1                |         |
| 4–6                                         | 100   | 46.5  | 26 (26.0)      | 3.20 (1.41–7.27) | 0.005   |
| >6                                          | 24    | 11.2  | 11 (45.8)      | 7.71 (2.68–22.20) | <0.001  |
| What makes the headache worse               |       |       |                |                 |         |
| None (R)                                    | 56    | 26.0  | 11 (19.6)      | 1                |         |
| Activity/tired                              | 97    | 45.1  | 20 (20.6)      | 1.06 (0.47–2.42) | 0.885   |
| Bright light                                | 10    | 4.7   | 1 (10.0)       | 0.46 (0.05–3.98) | 0.476   |
| Noise                                       | 15    | 7.0   | 2 (13.3)       | 0.63 (0.12–3.21) | 0.577   |
| Combination                                 | 37    | 17.2  | 12 (32.4)      | 1.96 (0.76–5.09) | 0.165   |
| What makes the headache better              |       |       |                |                 |         |
| None (R)                                    | 23    | 10.7  | 3 (13.0)       | 1                |         |
| Rest                                        | 76    | 35.3  | 10 (13.2)      | 1.01 (0.25–4.03) | 0.989   |
| Painkiller                                  | 43    | 20.0  | 14 (32.6)      | 3.22 (0.82–12.68) | 0.095   |
| Rest and painkiller                         | 73    | 34.0  | 19 (26.0)      | 2.35 (0.63–8.79) | 0.206   |
| Having additional symptoms during headache  |       |       |                |                 |         |
| No (R)                                      | 120   | 55.8  | 13 (10.8)      | 1                |         |
| Yes                                         | 95    | 44.2  | 33 (34.7)      | 4.38 (2.15–8.95) | <0.001  |

Having a combination of a pulsating, pressing, and stabbing headache increased the odds of poor QoL by almost five times compared to a headache with a pulsating sensation only (OR: 4.77, 95%CI: 2.00–11.41, p < 0.001). Having a severe headache also increased the odds of poor QoL by almost eight times compared to participants who only had a mild headache, with OR: 7.71, 95%CI: 2.68–22.20, and p < 0.001. Participants with additional symptoms accompanying headaches were more than four times as likely to have poor QoL (OR: 4.38, 95%CI: 2.15–8.95). The location of the headache and the factors that aggravate and ease the headache were not associated with the QoL of the participants (Table 5).

4. Discussion

Headache is one of the main neurological symptoms of SARS-CoV-2 infection, and is almost two times more prevalent in COVID-19 patients than other respiratory viral infections [38]. A previous study showed that the global prevalence of headache in COVID-19 was 25.2% (26,464 out of 104,751 cases) [39]. Headache was the first reported symptom of COVID-19 in 42.2% (84/199), with prolonged headache persisting in 13.6% (27/199), and of those, more than 10.2% (20/199) lasted for more than 3 months [38]. The proposed
The pathomechanism of headache in COVID-19 patients is probably the result of direct neuronal damage of the trigeminal nerve by SARS-CoV-2, or the indirect effects of hypoxia, coagulopathy, and cytokine storm (such as IL-1β, IL-6, and TNF-α) that are involved in various pathological pain mechanisms [40,41].

The phenotype of headache in this study was bilateral (47.4%) with a pulsating sensation (59.1%), which required 71.6% of the participants to take medication which relieved the pain. Similar results were found in a previous study showing that pulsating headache (50.9%) was predominant in COVID-19 patients with prior headache, and the majority of the patients also needed to take analgesics (84.3%); of those, analgesics improved the pain in only 32% cases, and 12.4% completely recovered from headache [42]. The phenotype of headache in COVID-19 infection shows similarity with migraine or tension-type headache, and should be cautiously analyzed [43]. Headache in other viral infections, such as dengue, also occurred bilaterally; however, these were mostly reported in a throbbing (59.2%) or pressing pattern (40.7%), and were usually associated with nausea, photophobia, and phonophobia [44,45].

The majority of the participants (80.9%) in this study had good physical functioning, with only 36.7% having limitations due to physical problems, and 34.4% due to emotional problems. Overall, more than a fifth of the participants had a poor QoL due to headache following COVID-19 infection related to pain, social function, fatigue, and mental health. A recent study found that post-COVID-19 sequelae affected the ability to perform self-care, increased anxiety/depression disorder, and reduced usual activities such as full-time employment [46]. Cognitive dysfunction and reduced usual activities and self-care highlight that patients with post-COVID-19 sequelae may have a reduced ability to participate in social functions [46]. The poor QoL in COVID-19 survivors with headache was associated with unemployment, as well as contracting COVID-19 less than 3 months prior the study. Economic downturns, such as difficulty in obtaining food and medicine, temporary or permanent layoffs, and a decrease in monthly income, might increase the financial burden, which results in an impaired QoL in patients with post-COVID-19 syndrome. A significant improvement in work productivity, self-reported good health, functional status, and health-related QoL were also reported between 3-6 months after COVID-19 recovery [47].

Our study also found that participants with a combination of pulsating, pressing, and stabbing headache were 4.7 more likely to have a poor QoL, and when they had to take painkillers, this increased to 7.5 greater odds of an impaired QoL. A previous study found that participants with migraine-like symptoms, such as pulsating headache, aggravation by physical activity, photophobia, and phonophobia, have a higher headache intensity and self-rated disability [48]. The pooled prevalence of poor QoL in COVID-19 survivors with persistent headache was 21% (95%CI: 3–47%) based on the EQ-5D-5L questionnaire [49]. Another study found that a prior history of migraines worsens the QoL in COVID-19 survivors with headache as a sequelae, with a Headache Impact Test-6 (HIT-6) score of 58.6 ± 13.2 when compared to no prior migraine (47 ± 12.2, p = 0.005) [50]. These results suggest that migraine-like symptoms in long COVID-19 headache are concerning due to their association with the course of the disease and their effect in the patients’ quality of life [48]. Being partially or non-responsive to analgesic treatment is the characteristic of headache in COVID-19 patients, which is why previously, indomethacin has been proposed as an alternative choice of drug [51]. To shed light in differentiating prolonged headache in COVID-19 patients from other headaches, several criteria were set for the ICHD-3 as a guideline for physicians and researchers to validate future investigations [52].

There are some limitations of this study that should be discussed. The number of the sample size is relatively low. Therefore, further studies that include a bigger sample size from multiple centers from the Indonesian archipelago would provide more comprehensive results. In our present study, the QoL of the individuals was assessed using the SF-36 questionnaire. Although this tool is valid and commonly used in population studies, it is less commonly used to assess the QoL in headache patients. Therefore, further studies might also need to include a more specific questionnaire for headache, such as the Headache...
Attributed Lost Time (HALT). In addition, the QoL tool from WHO [53] could also be considered to enhance the comparability between studies around the globe.

5. Conclusions

Investigating the phenotypic criteria of COVID-19-related headache is important, as the impact of this symptom is debilitating in patients’ quality of life. Physicians and researchers should not only differentiate the characteristics of headache in COVID-19 to other diseases, but also unravel the mysteries of the triggering mechanism of headache in COVID-19; thus, a better understanding of the management of COVID-19-related headache might be achieved.

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