

ORIGINAL ARTICLE

Assessment of Pain among Patients Recovered from COVID-19: A Cross-sectional Observational Study

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Abstract

Background: The COVID-19 pandemic has created a huge impact on the lives and health of persons worldwide, with potential for developing further effects in coming days. The long-term complications of COVID-19 are starting to emerge and a large number of patients may experience continued effects including pain. The number of patients affected by Severe Acute Respiratory Syndrome Corona Virus 2 (SARS CoV-2) is much greater than other corona viruses, so spectrum of long term post COVID-19 pain may produce huge burden. So, it is vital to assess the pain in post COVID-19 patients. This study is aimed to assess pain among the patients recovered from COVID-19.

Methods: This cross sectional observational study was carried out in pain medicine Out Patient Unit, Department of Anaesthesia, Analgesia & Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University for a period of one year following ethical approval. A total of 76 patients were included in this study according to the selection criteria. Data were collected using a pre-designed data collection sheet. Assessment of pain was carried out by Brief Pain Inventory (BPI) questionnaire. Collected data were analysed by statistical software SPSS 23.

Results: A total of 225 patients were assessed and the study period prevalence of post COVID-19 pain was 33.78 percent. The average age of the participants was 46.8±14.3 years with a male to female ratio of 43:33. After COVID-19, 49 (64.5%) patients had new onset pain, whereas 27 (35.5%) had exaggerated chronic pain. Most 21 (27.6%) patients was found in chest pain, 20 (26.3%) neck pain, 19 (25.0%) headache and 19 (25.0%) low back pain. Most of the patients (50.0%) had mild pain in intensity right now. Mean pain interference score was 3.8±2.0. The mean pain intensity was considerably higher in older patients (age>50 years), female gender, patients with two or more co-morbidities, and severe COVID-19 infection.

Conclusion: Both new onset of pain and exaggeration of chronic pain were observed among the patients recovered from covid-19 disease.

Keywords: New onset pain, Chronic pain, COVID-19, Post-COVID condition, Brief Pain Inventory (BPI)

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Introduction

The COVID-19 pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) evolved globally at an accelerated rate¹. Since the end of 2019, the whole world has been struggling with the epidemic of the new Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2), which was first detected in the Chinese province of Hubei. Not long after its outbreak, the Coronavirus Disease 2019 was declared pandemic by the World Health Organization (WHO) and has become a global health threat². The novel virus is classified as a single-stranded RNA virus of the Coronaviridae family³. In recent history, there have been recorded human infections with other viruses from this family: Severe Acute Respiratory Syndrome (SARS) caused by SARS-CoV-1 and Middle East Respiratory Syndrome (MERS) caused by MERS-CoV^{4,5}.

The main sources of infection spread are droplets and direct contact^{6,7}. The estimated spread rate ranges from 2.2 to 3.5⁸, while the average incubation time lasts about 5 days⁸. The symptoms of infection are usually nonspecific, ranging from common cold-like to severe, and sometimes lethal, respiratory infection. Studies suggest that, in many cases, the infection might be asymptomatic^{2,7,9}. Most patients experienced symptoms for 1 to 2 weeks with complete resolution, although some required hospitalization. The mortality rate of COVID-19 is on the order of 1% according to estimates published by the Centre for Evidence-Based Medicine¹⁰. Available evidence and WHO reports suggest that pain is a common symptom during infection with SARS-CoV-2. These pain-related symptoms primarily include: muscle and/or joint pain (14.8%), sore throat (13.9%) and headache (13.6%)².

In COVID-19, more than one-third of patients experience different neurological symptoms, which may involve the central nervous system (dizziness, headache, impaired consciousness, acute cerebrovascular disease, ataxia, and epilepsy), the peripheral nervous system and skeletal muscular damage¹¹. Mao et al., (2020) reported peripheral nervous system (PNS) effects in their study presenting in the form of dysgeusia (5.6%), dysosmia (5.1%), visual disturbances (1.4%), and neuralgia (2.3%)¹².

Acute viral illnesses often present with myalgia and fatigue, as well as organ-specific symptoms, as seen with influenza, and noted in the H1N1 pandemics of 1918 and 2009, and coronavirus infection during the SARS epidemic^{13,14}. Outcomes related to these infections are almost always focused on the immediate response to the acute illness, with little attention to long-term outcomes. In a small study of 22 subjects (21 of whom were healthcare workers) infected during the SARS epidemic, a chronic post-SARS syndrome consisting of fatigue, diffuse myalgia, depression, and non-restorative sleep persisted for almost 2 years¹⁵. Similarly, some patients with chronic widespread pain report onset of symptoms after a perceived viral illness¹⁶.

Although some infections cause specific post-infectious syndromes, there is also a common stereotypical response to any type of infection that is often observed. For example, up to 12% of patients infected with 3 different pathogens, ie, Ross River virus (the cause of epidemic polyarthritides), Coxiella burnetii (cause of Q fever), and Epstein–Barr virus, experienced a post-viral syndrome of pain, fatigue, and memory difficulties for up to 12 months after infection¹⁷. Chikungunya, a tropical arboviral disease affecting millions of people around the world including Bangladesh causes debilitating pain which frequently turns into chronic pain as a long-term complication. Despite acute pain in the initial phase, a substantial group of patients suffered from post-chikungunya neuropathic pain and the prevalence in Bangladesh was 19.1%^{18,19}. Thus, the presence and severity of somatic symptoms during acute viral infection was closely correlated with the subsequent development of chronic fatigue and pain. It implies that various acute infections are capable of triggering both widespread and regional chronic pain (CP)¹⁶.

Many individuals with COVID-19 need ICU care, and individuals surviving an illness requiring ICU admission are at increased risk of long-lasting severe functional limitations, psychological distress, and chronic pain¹⁶. Pain in ICU patients can be associated with viral disease itself (myalgia, arthralgia, peripheral neuropathies), may be caused by continuous pain and discomfort associated with ICU treatment, intermittent procedural pain and chronic

pain present before admission to the ICU. Under-treatment of pain, especially when sedation and neuromuscular blocking agents are used, prone positioning during mechanical ventilation or extracorporeal membrane oxygenation (ECMO) may trigger delirium and cause peripheral neuropathies²⁰. Surveys have reported persistent chronic pain in 38% to 56% of ICU survivors when evaluated 2 to 4 years after ICU admission^{21,22}. Quality of life can also be affected for prolonged periods. Timmers et al., (2011) evaluated patients 6 to 11 years after ICU discharge and many patients experienced persistent difficulty with mobility (52%), self-care (19%), activities of daily living (52%), pain/ discomfort (57%), and cognition (43%)²³.

Mental health is also frequently affected by severe illness. Between 41% and 65% of SARS survivors have experienced persistent psychological symptoms²⁴. Between 25% and 44% of Hong Kong residents who were infected with SARS and survived were diagnosed with posttraumatic stress disorder (PTSD), and 15% experienced depression for at least 30 months after the illness. Posttraumatic stress disorder also occurred in 40.7% of SARS-infected healthcare workers²⁵.

The COVID-19 (SARS-CoV-2) pandemic has changed the social environment in which people live and work, as well as the social systems they rely on. The negative impact of social changes prompted by the COVID-19 crisis may disproportionately affect individuals. One of the most immediate effects of the pandemic is the introduction of physical distancing measures and restriction of travel²⁶. It is well known that social isolation is associated with loneliness, higher levels of depression and anxiety, poorer health behaviors, poorer sleep, higher blood pressure, poorer immune function, and pain²⁷. The COVID-19 pandemic places individuals with chronic pain at an increased risk of social isolation, smaller social network size, and reduced social role functioning, all of which have negative implications for pain interference and pain intensity over time²⁶. These numerous and persistent stressors can trigger pain and other somatic symptoms or may lead to an exacerbation of chronic pain¹⁶.

Persistent symptoms after acute COVID-19 have

been reported and a high proportion of individuals reported fatigue (53.1%), dyspnea (43.4%), joint pain (27.3%), and chest pain (21.7%). Worsened quality of life was observed among 44.1% of patients²⁸.

The potential pain-related health consequences of COVID-19 which might be nociplastic, neuropathic, or nociceptive, might have different possibilities include chronic pain as part of a post-viral syndrome or the result of viral-associated organ damage; worsening of chronic pain due to exacerbation of preexisting pain, physical or mental complaints; and chronic pain newly triggered in individuals not infected with COVID-19 by exacerbation of risk factors (poor sleep, inactivity, fear, anxiety, and depression). The COVID-19 pandemic has many characteristics that could potentially increase the prevalence of chronic pain, especially with stressors extending over many months¹⁶. Therefore, this study was designed to assess pain among the patients recovered from COVID-19.

Methods

This observational study was carried out at Pain Medicine Outpatient Unit, Department of Anaesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka from January 2021 to December 2021. All adult patients aging ≥ 18 years, suffering from pain after resolution of COVID-19, who were RT-PCR for COVID-19 positive, recovered from COVID-19 at least 14 days prior to the study were included. Patients with cognitive dysfunction, psychological disease and neuromuscular disease were excluded from this study. Following approval from Institutional Review Board (IRB) of Bangabandhu Sheikh Mujib Medical University and obtaining informed written consent from each individual, patients were enrolled in this study who fulfill the selection criteria.

Patients were offered a comprehensive medical assessment with detailed history and physical examination. Data on all clinical characteristics, including comorbidities (e.g. Diabetes Mellitus, Hypertension, Chronic Low Back Pain, Bronchial Asthma, COPD, CKD, Headache, Hypothyroidism, and Connective tissue disease), clinical and pharmacological history and body measurements

were collected in a structured data collection sheet. In particular, data on specific symptoms (pain) potentially correlated with COVID-19 was obtained using standardized tools, e.g. Brief Pain Inventory (BPI) questionnaire. Patients were asked to retrospectively recount the presence or absence of pain before, during, and after COVID-19 and whether each symptom persists at the time of the visit.

Brief Pain Inventory (BPI): The Brief Pain Inventory is a medical questionnaire used to measure pain, developed by the Pain Research Group of the WHO Collaborating Centre for Symptom Evaluation in Cancer Care. The Brief Pain Inventory (BPI) is widely used around the world today to help with measuring a patient’s pain intensity and the amount of interference on their ability to function in everyday life. BPI was originally intended to help measure cancer patient’s pain, but today it is used in cancer related cases as well as non-cancer related cases. In this largely used questionnaire, three numerical rating scales each ranging from 0 (no pain) to 10 (maximal pain) is used to assess minimal, maximal and average pain intensity over the last 24 hour. Patients are asked to report all sites of pain on a diagram of the body and to specify the location of the most intense pain. The BPI also includes a series of numerical rating scales (equally ranging from 0 to 10) to assess the extent that pain interferes with general activity, mood, walking, sleep, work, relationship with others and life enjoyment (from 0: does not interfere, to 10: complete interference)²⁷. Ferreira et al. (2011) determine the optimal cutpoints for mild, moderate, and severe pain based on patients’ rating of worst pain in patient group (1–4= mild pain, 5–7=moderate, and 8–10=severe) for pain intensity and interference^{29,30}.

Statistical analysis:

Statistical analysis were carried out by using the Statistical Package for Social Sciences version 23.0 for Windows (SPSS Inc., Chicago, Illinois, USA). A descriptive analysis was performed for all data. The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. Unpaired t-test was used for continuous variables. ANOVA test was used to analyze the continuous variables, shown with mean and standard deviation. P values <0.05 was considered as statistically significant.

Results

During the study period, total 225 patients were assessed. Among them, 76 patients were included according to selection criteria. Study period prevalence was 33.78 percent.

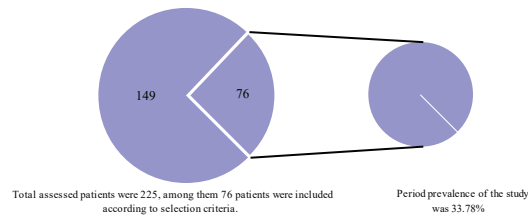


Fig 1: Pie chart showing Period prevalence of the study population.

The mean age of patients was 46.8±14.3 years, Median (IQR) age was 46.5 ranging from 37 to 55 years. 43 (56.6%) patients were male, 33 (43.4%) patients were female. Most of the patients 27 (35.5%) were service holder then 21 (27.6%) were housewife,

Table I: Demographic characteristics of the study population

Variables	Number	(%)
Age (years)		
21-40	30	(39.5%)
41-60	34	(44.7%)
>60	12	(15.8%)
Mean±SD	46.8±14.3	
Median (IQR)	46.5	(37-55)
Gender		
Male	43	(56.6%)
Female	33	(43.4%)
Occupational status		
Student	2	(2.6%)
Farmer	2	(2.6%)
Housewife	21	(27.6%)
Businessman	8	(10.5%)
Service holder	27	(35.5%)
Retired	11	(14.5%)
Others	5	(6.6%)
BMI (kg/m²)		
<18.5	3	(3.9%)
18.5-24.9	43	(56.6%)
25.0-29.9	28	(36.8%)
≥30.0	2	(2.6%)
Mean±SD	24.2±3.3	
Median (IQR)	23.8	(22.3-26.6)
Current smoker	20	(26.3%)
Non-smoker	44	(57.9%)
Past-smoker	12	(15.8%)

Values are expressed as mean±SD or in frequency. Within parenthesis are percentages per column total.

11 (14.5%) were Retired, 8 (10.5%) were Businessman. 43 (56.6%) patients had BMI within normal range (18.5-24.9). 28 (36.8%) patents were overweight (25-29.9) and Mean BMI was 24.2±3.3 kg/m² . 44 (57.9%) patients were non-smoker, 20 (26.3%) were current smoker and 12 (15.8%) patients were past smoker (**Table I**).

Table II shows, 63 (82.9%) patients had COVID-19 duration from 11 to 20 days with a mean duration of COVID-19 was 16.0±5.3 days. 31(40.8%) patients had mild severe COVID-19, 31 (40.8%) patients had moderate COVID-19, 11 (14.9%) had severe COVID-19 and only 3 (3.9%) had critical COVID-19. 45 (59.2%) patients had two or more co-morbidities. 20 (26.3%) patients had atleast one co-morbidity and 11 (14.5%) patients had no co-morbidity. 38 (50.0%) patients received treatment at home, 30 (39.5%) patients received treatment in hospital and 8(10.5%)

Table II: Clinical characteristics of the study population

Variables	Number	(%)
Duration of COVID-19 (days)		
<10	3	(3.9%)
11-20	63	(82.9%)
21-30	8	(10.5%)
>30	2	(2.6%)
Mean±SD	16.0±5.3	
Severity of COVID-19		
Mild	31	(40.8%)
Moderate	31	(40.8%)
Severe	11	(14.5%)
Critical	3	(3.9%)
Co-morbidities		
One	20	(26.3%)
Two or more	45	(59.2%)
No co-morbidities	11	(14.5%)
Treatment received		
Home	38	(50.0%)
Hospital	30	(39.5%)
ICU	8	(10.5%)
Medication received		
Steroid	41	(53.7%)
Antibiotics	62	(82.9%)
Antiviral	30	(40.8%)
LMWH	36	(59.2%)
Others	5	(6.6%)
Post COVID-19 pain		
New onset pain	49	(64.5%)
Exaggerated chronic pain	27	(35.5%)

Values are expressed as mean±SD or in frequency. Within parenthesis are percentages per column total. Comorbidities: Diabetes mellitus, Hypertension, Chronic low back pain, Bronchial asthma, COPD, CKD, Headache, Neck Pain, Headache, Connective tissue disease.

patients got treatment at ICU. 62(53.9%) patients received antibiotics, 41(35.7%) patients received steroid, 30(26.1%) patients received antiviral and 36(31.1%) patients received Low Molecular Weight Heparin.

In post COVID-19 period, 49(64.5%) patients had new onset of pain and 27(35.5%) patient had exaggerated chronic pain.

Most 21 (27.6%) patients had chest pain followed by 20 (26.3%) neck pain, 19 (25.0%) headache, 19 (25.0%) Low back pain, 13 (17.1%) Upper back pain, 14 (18.4%) Lower limb pain, 19 (25.0%) Shoulder joint pain, 18 (23.7%) Hip joint pain, 10 (13.2%) Knee joint pain and 10(13.2%) had Wrist joint pain (**Figure II**).

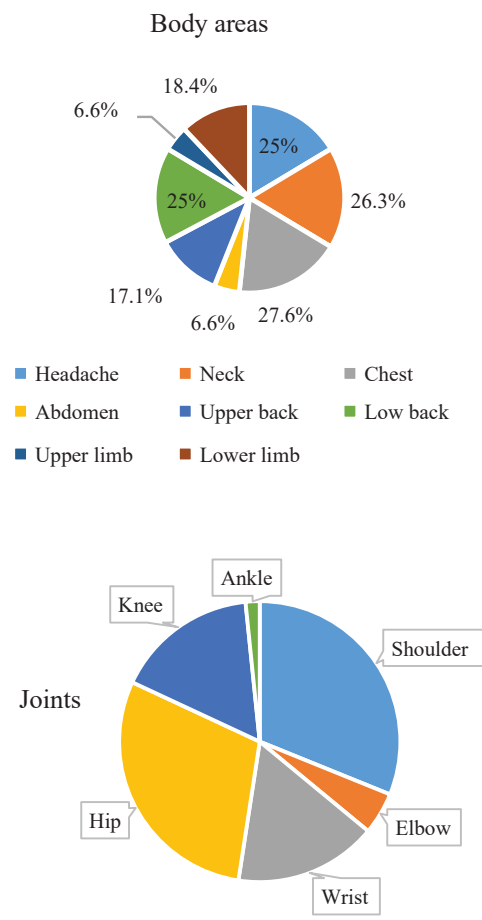


Figure II: Distribution of the study patients according to location of pain

Table III shows that 44 (57.9%) patients had moderate worst pain in past 24 hours, 26 (34.4%) had severe worst pain in last 24 hours, only 6 (7.9%) patients had mild worst pain in last 24 hour. 58 (76.3%) patients had mild least pain in past 24 hours, 17 (22.4%) patients had moderate least pain in past 24 hours and 1 (1.3%) patients had severe least pain in past 24 hours. Thirty six (47.4%) patients had moderate pain on average, 35 (46.1%) patients had mild pain on average and 5 (6.6%) patients had severe pain on average. Thirty eight (50.0%) patients had mildly intense pain right now, 36 (47.4%) patients had moderate pain right now and 2 (2.6%) patients had severe pain right now.

Table III: Severity of post COVID-19 pain by brief pain inventory score

Brief pain inventory score	Values	(%)	Mean±SD
Worst pain in last 24 hours			
Mild (0-3)	3	(7.9%)	2.7±0.5
Moderate (4-6)	44	(57.9%)	4.9±0.8
Severe (≥7)	26	(34.2%)	8.0±1.0
Total	76	(100.0%)	5.8±1.9
Least pain in last 24 hours			
Mild (0-3)	58	(76.3%)	1.7±1.1
Moderate (4-6)	17	(22.4%)	4.6±0.8
Severe (≥7)	1	(1.3%)	7.0±0.0
Total	76	(100.0%)	2.5±1.7
Average pain in last 24 hours			
Mild (0-3)	35	(46.1%)	2.5±0.7
Moderate (4-6)	36	(47.4%)	4.9±0.9
Severe (≥7)	5	(6.6%)	7.0±0.0
Total	76	(100.0%)	3.9±1.6
Pain intensity at present			
Mild (0-3)	38	(50.0%)	2.2±0.9
Moderate (4-6)	36	(47.4%)	4.9±0.8
Severe (≥7)	2	(2.6%)	7.0±0.0
Total	76	(100.0%)	3.6±1.7

Values are expressed as mean±SD or in frequency. Within parenthesis are percentages per column total.

Figure III shows that mean pain interference with standard deviation in general activity was 4.2±2.4, mood was 4.6±2.4, walking activity was 3.4±3.0, normal work was 2.8±2.5, relation with other people 2.2±2.3, sleep was 4.9±2.5 and enjoyment of life was 4.4±2.2.

Mean pain interference score was found 3.8 ±2.0. Out of the 7 domain of pain interference, sleep and mood are mostly affected.

Table IV shows that mean post COVID-19 pain

intensity was significantly higher in age group >50 years, female patients, who have two or more co-morbidities, got treated in hospital or ICU and severe or critical COVID-19.

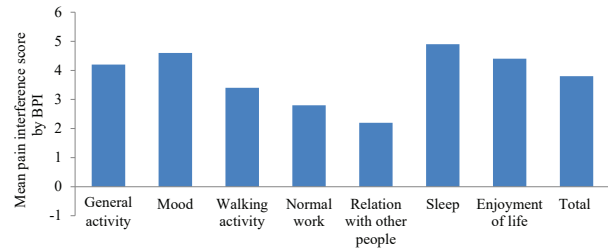


Figure III: Bar diagram showing pain interference score by BPI

Table IV: Difference of post COVID-19 pain intensity among the study population

Variables	Number of patients	Pain intensity Mean±SD	P value
Age (years)			
≤50	47	3.3±1.7	^a 0.026 ^s
>50	29	4.2±1.6	
Gender			
Male	43	3.2±1.6	^a 0.007 ^s
Female	33	4.2±1.6	
BMI (kg/m²)			
<25.0	46	3.5±1.7	^a 0.328 ^{ns}
≥25.0	30	3.9±1.6	
Co-morbidities			
One	20	3.0±1.4	
Two or more	45	4.3±1.5	^b 0.001 ^s
None	11	2.1±1.6	
Hospitalization			
Hospitalized	38	4.1±1.6	^a 0.028 ^s
Nonhospitalized	38	3.2±1.7	
Treatment received			
Home	38	3.2±1.7	
Hospital	30	3.9±1.6	^b 0.062 ^{ns}
ICU	8	4.5±1.6	
Severity of COVID-19			
Mild	31	2.8±1.6	
Moderate	31	4.1±1.6	^b 0.002 ^s
Severe	11	4.0±1.4	
Critical	3	5.7±1.7	

Values are expressed as mean±SD. ^s= significant; ^{ns}= not significant, ^aP value reached from unpaired t-test. ^bP value reached from ANOVA test. P value <0.05 is considered as statistically significant

Discussion

Coronavirus disease 2019 (COVID-19) is a contagious disease of the respiratory system. Initially detected in Wuhan, China in December 2019, a severe

acute respiratory syndrome caused by novel beta-coronavirus known as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) has spread all over the world, leading to an ongoing pandemic. Common symptoms of COVID 19 include fever, cough, headache, bodyache, fatigue, breathing difficulties, loss of smell and loss of taste etc^{2,8}.

At least a third of people who are infected do not develop noticeable symptoms. Of those people who develop symptoms, large majorities are mild (81%), with 14% progressing to severe pneumonia and 5% developing acute respiratory distress syndrome (ARDS), respiratory failure, shock, sepsis, and/or multisystem organ failure (MOF)³¹. Although the respiratory symptoms are the main presentation of COVID-19, signs and symptoms of an extra-pulmonary involvement are also seen among the clinical picture of the disease.

Pain is one of the extrapulmonary expression of COVID-19. It can occur during the acute phase of the disease as well as short- or long-term complications. Pathophysiology of COVID-Pain includes, Renin-angiotensin system disequilibrium which can play a key role in the modulation of the inflammatory response that characterizes COVID-pain, The SARS-CoV-2 infection could directly impact the balance between the neuromodulation systems of the nociception, Macrophages and other immune cells activation can stimulate the production of inflammatory mediators (eg, IL-1 β , TNF, and bradykinins). These processes can facilitate the sensory cells injury and can lead to chronic pain through sensitization/activation processes³².

As the pandemic condition comes down from its devastating curve, the world is relieved from threatening condition but various post COVID syndrome is emerging. The World Health Organization (WHO) estimates that approximately 10% of all infected people may develop post-COVID syndrome (WHO, 2021) and among them 56–90% patient had pain problems³³. And secondary to the COVID-19 pandemic, chronic pain is expected to rise in both the immediate and long-term³⁴. Seemingly, this is one of the first study done in Bangladesh to assess the post COVID pain and disabilities.

According to the study, the mean age of the study population was found 46.8 ± 14.3 , which is lower than the other western studies. This is probably due to the sociocultural background of Bangladesh, where the proportion of the elderly population (5%) is lower than that in Western world (North America, 16%; Europe, 21%)^{28,35,36}.

In this study, number of male respondents were more than female (56.6% male and female 43.4%). Which is similar to the other studies done in Bangladesh in Post COVID syndrome^{37,38}. MERS-CoV and SARS-CoV are more likely to infect the males than females^{39,40}. Women have more robust innate and adaptive immunity compare to male. So they are less likely to be affected by many bacteria and viruses than men⁴¹.

We have found that study period prevalence of the post COVID pain was 33.78% (95% CI: 27.60-39.96%). This result is similar to a study done by Fernández-de-Las-Peñas et al. (2021)³⁵. Among the patient, 64.5% population had new onset of post COVID-19 pain. Soares et al. (2021) found the similar result in patient suffering from new onset of post COVID pain⁴². And 35.5% patients had exaggerated chronic pain. This result is also similar to other studies^{16,26}.

This study reveals that most prevalent site of post COVID pain is chest, head, neck, followed by low back pain, shoulder joint pain and hip joint pain. Soares et al. (2020) and Bileviciute-Ljungar et al. (2022) found the most prevalent site of post COVID pain is head and neck^{42,43}. Another study done in Bangladesh by Mahmud et al. (2021) they also found the most prevalent site of post COVID pain is Head, body and chest³⁸.

According to Initiative on Methods, Measurements, and Pain Assessment in Clinical Trials (IMMPACT) recommendations, clinically meaningful pain was defined by a numerical rating score (NRS) ≥ 3 for average pain intensity⁴⁴. In our study, we have found that majority of the patients (47.4%) have average pain intensity more than 3. Only 6.6% patients have severe pain.

In our study, mean pain interference score was found 3.8 ± 2.0 . Out of the 7 domain of pain interference,

sleep and mood are mostly affected. Ghetti (2022) and Ojeda et al. (2021) almost found the similar results^{45,46}. In this study, we observed that pain intensity were significantly higher in elderly population aging more than 50 years. The results is very much similar to other studies^{47,48}. In different studies, it was evident that increasing age is related to increase severity of the disease course. So perception of pain is increased in elderly population^{49,50}.

This study also observed that pain intensity is significantly higher in female respondents. Mahmud et al. (2021) also found, Post COVID-19 features were significantly higher among women³⁸. Ganesh et al. (2022) found women have more Central Sensitization syndrome (CS) due to they have persistent elevations of proinflammatory cytokine and chemokines (eg. IL- 6, IL-8 and tumor necrosis factor alpha) at least 3 months after COVID-19 infection. This CS syndromes and elevated IL-6 are thought to play an important role in higher pain intensity in women. Because CS syndromes share a common pathophysiologic mechanism with central neuroinflammation and remodeling of brain and spinal cord pathways leading to enhanced sensitivity to multiple stimuli, sympathetic hyperactivity, and decreased efficacy of inhibitory pathways⁵¹.

We have found that, patients who have comorbidities two or more have suffered more intensified pain. Kemp et al. (2020) also found co-morbidities plays an important role for development of chronic pain after COVID-19. In our study, we found that Hospital admitted patient have significantly higher pain intensity than patient who have got treatment in home. More intense pain was observed in patients who got treated in ICU. Clauw et al. (2020) found that patients who have admitted in hospital had more pain. Among them, who had admitted in ICU had persistent chronic pain¹⁶. Everyday procedures in ICU, such as tracheal tube suctioning, turning, positioning, and line insertion contributed to this pain⁵³.

In our study, we also have found that patient who got treatment in hospital and ICU, they have more functional limitation. This result is also similar to the study done by Norrefalk et al., (2021)³³. According to Gustafson et al. (2018), Post-ICU population have significant weakness and pain and they have growing

evidence of motor and sensory disruption. Prolonged period of immobilization, sedation, and ventilation, in ICU increased risk of ICU-acquired weakness (ICUAW) among COVID-19 survivors^{48,54}.

Conclusion

The present study observed a substantial proportion of patients have been suffering from post-COVID pain. It necessitates the timely recognition of pain in post-COVID period which will help to make treatment plan and strategies to mitigate the potential impact on health, and also reduce the magnitude of burden in societies.

Limitations

There were certain limitations of the current study. It was conducted in a single center. The study results will be more reflective if it could be done in multiple center with larger sample size. The characteristics of pain (nociceptive/neuropathic) was not done in this study.

Declaration

Author contributions

Conception and development of the idea *AKMA, MMK, MMH*

Data collection *MMH, SS, SA*

Data analysis *MMH, EA, MMK*

Writing - Original Draft Preparation *MMH, EA*

Review & Editing *AKMA, DKB, MMK*

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Conflict of interests None

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References

- 1 Dashraath P, Wong JLJ, Lim MXK, Lim LM, Li S, Biswas A, Choolani M, Mattar C, Su LL. Coronavirus disease 2019 (COVID-19) pandemic and pregnancy. *American journal of obstetrics and gynecology* 2020; 222(6): 521-531.
- 2 WHO, 2020. General's opening remarks at the media briefing on COVID-19. Available at: <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-mediabriefing-on-covid-19---11-march-2020> (Accessed on 26 November 2020).
- 3 Cui J, Li F, Shi ZL. Origin and evolution of pathogenic coronaviruses. *Nature Reviews Microbiology* 2019; 17(3): 181-192.
- 4 Hui DS, Zumla A. Severe acute respiratory syndrome: historical, epidemiologic, and clinical features. *Infectious Disease Clinics* 2019; 33(4): 869-889.
- 5 Nassar M, Bakhrebah MA, Meo SA, Alsuabeyl MS, Zaher WA. Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection: epidemiology, pathogenesis and clinical characteristics. *Eur Rev Med Pharmacol Sci* 2018; 22(15): 4956-4961.
- 6 Yu P, Zhu J, Zhang Z, Han Y. A familial cluster of infection associated with the 2019 novel coronavirus indicating possible person-to-person transmission during the incubation period. *The Journal of infectious diseases* 2020; 221(11): 1757-1761.
- 7 Kotfis K, Skonieczna-Żydecka K. COVID-19: gastrointestinal symptoms and potential sources of SARS-CoV-2 transmission. *Anaesthesiology intensive therapy* 2020; 52(2): 171-172.
- 8 Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung KS, Lau EH, Wong JY, Xing X. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. *New England journal of medicine* 2020; 382: 1199-1207.
- 9 Gu J, Han B, Wang J. COVID-19: gastrointestinal manifestations and potential fecal-oral transmission. *Gastroenterology* 2020; 158(6): 1518-1519.
- 10 Oke J, Heneghan C. Global COVID-19 case fatality rates. *The Centre for Evidence-Based Medicine* 2020; Available at: <https://www.cebm.net/covid-19/global-covid-19-case-fatality-rates> (Accessed on 26 November 2020).
- 11 Boziki MK, Mentis AFA, Shumilina M, Makshakov G, Evdoshenko E, Grigoriadis N. COVID-19 immunopathology and the central nervous system: implication for multiple sclerosis and other autoimmune diseases with associated demyelination. *Brain sciences* 2020; 10(6): 345.
- 12 Mao L, Jin H, Wang M, Hu Y, Chen S, He Q, Chang J, Hong C, Zhou Y, Wang D, Miao X. Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA neurology* 2020; 77(6): 683-690.
- 13 Campbell A, Rodin R, Kropp R, Mao Y, Hong Z, Vachon J, Spika J, Pelletier L. Risk of severe outcomes among patients admitted to hospital with pandemic (H1N1) influenza. *CMAJ* 2010; 182(4): 349-355.
- 14 Hui DSC, Chan MCH, Wu AK, Ng PC. Severe acute respiratory syndrome (SARS): epidemiology and clinical features. *Postgraduate medical journal* 2004; 80(945): 373-381.
- 15 Moldofsky H, Patcai J. Chronic widespread musculoskeletal pain, fatigue, depression and disordered sleep in chronic post-SARS syndrome; a case-controlled study. *BMC neurology* 2011; 11(1): 1-7.
- 16 Clauw DJ, Hauser W, Cohen SP, Fitzcharles MA. Considering the potential for an increase in chronic pain after the COVID-19 pandemic. *Pain* 2020; 161(8): 1694-1697.
- 17 Hickie I, Davenport T, Wakefield D, Vollmer-Conna U, Cameron B, Vernon SD, Reeves WC, Lloyd A. Post-infective and chronic fatigue syndromes precipitated by viral and non-viral pathogens: prospective cohort study. *Bmj* 2006; 333(7568): 575.
- 18 Kamal MM, Rahman MM, Sharmin S, Bhowmick DK, Islam MS, Akhtaruzzaman AKM. Efficacy of amitriptyline and duloxetine in post-chikungunya neuropathic pain; a randomized, open-label, cross-over clinical trial. *Anaesthesia pain intensive care* 2021; 25(5): 647-652
- 19 Kamal MM, Afroz S, Zunaid M, Islam MS, Khan MSR, Akhtaruzzaman AKM. Neuropathic Pain Associated with Chikungunya: A Cross-Sectional Study. *Bangladesh J.Pain.* 2021; 1(1):16-21
- 20 Drozdal S, Rosik J, Lechowicz K, Machaj F, Szostak B, Majewski P, Rotter I, Kotfis K. COVID-19: Pain management in patients with SARS-CoV-2 infection-molecular mechanisms, challenges, and perspectives. *Brain sciences* 2020; 10(7): 465.
- 21 Jagodic HK, Jagodic K, Podbregar M. Long-term outcome and quality of life of patients treated in surgical intensive care: a comparison between sepsis and trauma. *Critical Care* 2006; 10(1): R134.
- 22 Schelling G, Stoll C, Haller M, Briegel J, Manert W, Hummel T, Lenhart A, Heyduck M, Polasek J, Meier M, Preu B U. Health-related quality of life and posttraumatic stress disorder in survivors of the acute respiratory distress syndrome. *Critical care medicine* 1998; 26(4): 651-659.
- 23 Timmers TK, Verhofstad MH, Moons KG, van Beeck EF, Leenen LP. Long-term quality of life after surgical intensive care admission. *Archives of surgery* 2011; 146(4): 412-418.

- 24 Lee AM, Wong JG, McAlonan GM, Cheung V, Cheung C, Sham PC, Chu CM, Wong PC, Tsang KW, Chua SE. Stress and psychological distress among SARS survivors 1 year after the outbreak. *The Canadian Journal of Psychiatry* 2007; 52(4): 233-240.
- 25 Maunder RG. Was SARS a mental health catastrophe?. *General hospital psychiatry* 2009; 31(4): 316-17.
- 26 Karos K, McParland JL, Bunzli S, Devan H, Hirsh A, Kapos FP, Keogh E, Moore D, Tracy LM, Ashton-James CE. The social threats of COVID-19 for people with chronic pain. *Pain* 2020; 161(10): 2229-2235.
- 27 Holt-Lunstad J, Smith TB, Baker M, Harris T, Stephenson D. Loneliness and social isolation as risk factors for mortality: a meta-analytic review. *Perspectives on psychological science* 2015; 10(2): 227-237.
- 28 Carfi A, Bernabei R, Landi F. Persistent symptoms in patients after acute COVID-19. *JAMA* 2020; 324(6): 603-605.
- 29 Cleeland CS, Ryan K. Pain assessment: global use of the Brief Pain Inventory. *Annals, academy of medicine* 1994; 23(2): 129-138.
- 30 Ferreira KA, Teixeira MJ, Mendonza TR, Cleeland CS. Validation of brief pain inventory to Brazilian patients with pain. *Supportive Care in Cancer* 2011; 19(4): 505-511.
- 31 Centers for Disease Control and Prevention-CDC, U.S. 6 April 2020.
- 32 Cascella M, Del Gaudio A, Vittori A, Bimonte S, Del Prete P, Forte CA, Cuomo A, De Blasio E. COVID-Pain: Acute and Late-Onset Painful Clinical Manifestations in COVID-19—Molecular Mechanisms and Research Perspectives. *Journal of Pain Research* 2021; 14: 2403.
- 33 Norrefalk JR, Kristian BORG, Bileviciute-Ljungar I. Self-scored impairments in functioning and disability in post-COVID syndrome following mild COVID-19 infection. *Journal of Rehabilitation Medicine* 2021; 53(11): 1-8.
- 34 Fiala K, Martens J, Abd-Elsayed A. Post-COVID Pain Syndromes. *Current Pain and Headache Reports* 2022; 26(5): 379-383.
- 35 Fernández-de-Las-Peñas C, Rodríguez-Jiménez J, Fuensalida-Novo S, Palacios-Ceña M, Gómez-Mayordomo V, Florencio LL, Hernández-Barrera V, Arendt-Nielsen L. Myalgia as a symptom at hospital admission by severe acute respiratory syndrome coronavirus 2 infection is associated with persistent musculoskeletal pain as long-term post-COVID sequelae: a case-control study. *Pain* 2021; 162(12): 2832-2840.
- 36 Mandal S, Barnett J, Brill SE, Brown JS, Denny EK, Hare SS, Heightman M, Hillman TE, Jacob J, Jarvis HC, Lipman MC. 'Long-COVID': a cross-sectional study of persisting symptoms, biomarker and imaging abnormalities following hospitalisation for COVID-19. *Thorax* 2021; 76(4): 396-398.
- 37 Islam MR, Rahman T, Ahmed SM, Khan MSH, Azad MR, Alam D, Habib R. Neurological presentation of COVID-19: experience from a tertiary care hospital of Bangladesh. *BIRDEM Medical Journal* 2020; 10: 33-40.
- 38 Mahmud R, Rahman MM, Rassel MA, Monayem FB, Sayeed SJB, Islam MS, Islam MM. Post-COVID-19 syndrome among symptomatic COVID-19 patients: A prospective cohort study in a tertiary care center of Bangladesh. *PLoS One* 2021; 16(4): e0249644.
- 39 Badawi A, Ryoo SG. Prevalence of comorbidities in the Middle East respiratory syndrome coronavirus (MERS-CoV): a systematic review and meta-analysis. *International Journal of Infectious Diseases* 2016; 49: 129-133.
- 40 Channappanavar R, Fett C, Mack M, Ten Eyck PP, Meyerholz DK, Perlman S. Sex-based differences in susceptibility to severe acute respiratory syndrome coronavirus infection. *The Journal of Immunology* 2017; 198(10): 4046-4053.
- 41 Jaillon S, Berthenet K, Garlanda C. Sexual dimorphism in innate immunity. *Clinical reviews in allergy & immunology* 2019; 56(3): 308-321.
- 42 Soares FHC, Kubota GT, Fernandes AM, Hojo B, Couras C, Costa BV, Lapa JDDS, Braga LM, Almeida MMD, Cunha PHMD, Pereira VHH. Prevalence and characteristics of new-onset pain in COVID-19 survivors, a controlled study. *European Journal of Pain* 2021; 25(6): 1342-1354.
- 43 Bileviciute-Ljungar I, Norrefalk JR, Borg K. Pain Burden in Post-COVID-19 Syndrome following Mild COVID-19 Infection. *Journal of Clinical Medicine* 2022; 11(3): 771.
- 44 Gewandter JS, Dworkin RH, Turk DC, Farrar JT, Fillingim RB, Gilron I, Markman JD, Oaklander AL, Polydefkis MJ, Raja SN, Robinson JP. Research design considerations for chronic pain prevention clinical trials: IMMPACT recommendations. *Pain* 2015; 156(7): 1184.
- 45 Ghetti MI. Functional Assessment of Pain in Post-COVID-19 Patients. *Biomedical Sciences* 2022; 8: 6-9.
- 46 Ojeda A, Calvo A, Cuñat T, Artigas RM, Comino-Trinidad O, Aliaga J, Arias M, Ahuir M, Ferrando C, Dürsteler C. Rationale and study design of an early care, therapeutic education, and psychological intervention program for the management of post-intensive care syndrome and chronic pain after COVID-19 infection (PAIN-COVID): study protocol for a randomized controlled trial. *Trials* 2021; 22(1): 1-9.
- 47 Khasru MR, Haseen F, Khan MM, Naz R, Marzen T, Siddiq AB, Hasan M, Khan S, Islam MJ, Ullah MA, Salek AKM. Musculoskeletal pain and physical health status among

- confirmed COVID-19 patients of Bangladesh. *Bangabandhu Sheikh Mujib Medical University Journal* 2021; 114: 1-7.
- 48 Yang J, Zheng YA, Gou X, Pu K, Chen Z, Guo Q, Ji R, Wang H, Wang Y, Zhou Y. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. *International journal of infectious diseases* 2020; 94: 91-95.
- 49 Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y, Shi J, Zhou M, Wu B, Yang Z, Zhang C. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. *Journal of Allergy and Clinical Immunology* 2020; 146(1): 110-118.
- 50 Zhang J, Wang X, Jia X, Li J, Hu K, Chen G, Wei J, Gong Z, Zhou C, Yu H, Yu M. Risk factors for disease severity, unimprovement, and mortality in COVID-19 patients in Wuhan, China. *Clinical microbiology and infection* 2020; 26(6): 767-772.
- 51 Ganesh R, Grach SL, Ghosh AK, Bierle DM, Salonen BR, Collins NM, Joshi AY, Boeder ND, Anstine CV, Mueller MR, Wight EC. The female-predominant persistent immune dysregulation of the post-COVID syndrome. *Mayo Clinic Proceedings* 2022; 97(3): 454-464.
- 52 Kemp HI, Corner E, Colvin LA. Chronic pain after COVID-19: implications for rehabilitation. *British Journal of Anaesthesia* 2020; 125(4): 436-449.
- 53 Puntillo KA, Max A, Timsit JF, Vignoud L, Chanques G, Robleda G, Roche-Campo F, Mancebo J, Divatia JV, Soares M, Ionescu DC. Determinants of procedural pain intensity in the intensive care unit. *American journal of respiratory and critical care medicine* 2014; 189(1): 39-47.
- 54 Gustafson OD, Rowland MJ, Watkinson PJ, McKechnie S, Igo S. Shoulder impairment following critical illness: a prospective cohort study. *Critical care medicine* 2018; 46(11): 1769-74.