ORIGINAL ARTICLE

Pattern of Chest Pain in Long COVID Syndrome

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Abstract

Introduction: The COVID-19 pandemic has persisted for over four years, resulting in numerous complications, including myocardial infarction, stroke, heart failure, and thromboembolism. These occur via various mechanisms, such as endothelitis, multisystem inflammatory syndrome, cytokine storm, and activation of the coagulation cascade. Despite recovery, many patients experience persisting symptoms, including chest pain and fatigue. However, the specific complications that arise and their underlying causes remain largely unclear. This study aimed to examine the frequency and pattern of chest pain in this population and thus unveiling the underlying pathophysiology.

Methods: This is an uni-center, prospective observational cohort study, conducted in Department of Cardiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), from July 2021-June 2023. Patients presenting within 7 days of positive RT-PCR COVID-19 report, were screened for this study. Among them, 382 patients were enrolled in the study, following inclusion and exclusion criteria. Relevant history (breathlessness, chestpain, palpitation, ankle edema, syncope,pulse, BP, JVP, lungbase, edema, NYHA Class, 6MWD) & cardiac investigations (Trop I, NT Pro-BNP, S.Creatinine, S.Electrolytes, S.Albumin, S.TSH, CBC, CRP, CXR, ECG, Echocardiography) were done at baseline. Patients were followed up in Cardiology OPD Clinic,BSMMU, after 3 months of enrollment, with same clinical, laboratory and cardiac investigations. Data were collected in a semi structured data sheet via personal interview. The variables included were, age, sex, chest pain, palpitation, breathlessness, ankle edema, syncope, pulse, systolic and diastolic blood pressure, raised JVP, lung base crackles and functional capacity (NYHA Classification and 6 Minute Walk Distance), S. Troponin-I, S. NT-proBNP, S. Creatinine, S. Albumin, TSH,FT_4, CXR P/A view, ECG, Resting Transthoracic Echocardiography. Data analysis was done using IBM SPSS® 29.0.

Results: The study showed, 59% of the populations presented with cardiac symptoms at 3 months follow up. Most of the symptomatic populations were between 60-69 years of age, male were more affected than female. Commonest cardiac manifestation were palpitation (79%), chest pain (53%) & breathlessness(48%). Chest pain was due to unstable angina (70%) and myocardial infarction (30%).

Conclusion: At the end of 3 months, a significant proportion of Long COVID-19 patients developed cardiac symptoms, specially chest pain due to coronary artery disease. So, further research in the field of Long COVID-19 is necessary to find out further impacts of this condition on cardiovascular syste.

Keywords: Long COVID-19, Chest Pain, Unstable angina, Myocardial Infarction, Chronic coronary syndrome, Cardiovascular effect

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Introduction:

Long COVID-19 is a complex condition with a range of symptoms that are not yet fully understood. A huge number of people are suffering from Long COVID-19. An estimated 150 million people worldwide, including 65 millions in Asia, have Long COVID-19. About 1 in 100 US children and 7 in 100 US adults are suffering from Long COVID-19. But still, research data are very limited in this field. Proper diagnostic tools, treatment plans, rehabilitation centers are also inadequate. Through multiple mechanisms, COVID-19 can affect the pulmonary, cardiovascular, digestive, urinary, hepatic, and central nervous systems.[1] Cardiovascular manifestations are one of the most critical factors affecting the morbidity and mortality caused by COVID-19. It's proven that, coronary artery disease (CAD), heart failure (HF), hypertension (HTN), and arrhythmias lead to a higher mortality rate in COVID-19 patients in short term.[2] Therefore, it seems there is a mutual relationship between COVID-19 and cardiovascular disease. . A meta-analysis indicated that 60% of COVID-19 patients were symptomatic after twelve weeks past the beginning of the infection[2]. But, what is mostly unknown is, exactly what manifestations and complications arises in this period, what the underlying pathophysiology is and what are the complications that may arise over the upcoming years. So, it is of utmost importance to know the full impact of COVID-19 on the cardiovascular system. This cohort study, aimed to investigate the cardiovascular manifestations of Long COVID-19 specially frequency & pattern of chest pain in these population. By analyzing the results of this study, we hoped to gain a better understanding on the pattern, frequency and pathophysiology of chest pain as a consequence of COVID-19. This will help us to develop appropriate treatment and rehabilitation plan for those who have been affected.

Methods:

This prospective observational study was conducted in Department of Cardiology,BSMMU, in Dhaka, Bangladesh, from July 2021 to June 2023. The study was initiated after receiving approval from the ithical review committee. During this period, patients who visited the outpatient department (OPD) within seven days of a positive RT-PCR COVID-19 report were screened for eligibility to participate in the study. To be included in the study, patients had to meet specific inclusion and exclusion criteria. Patients within 7 days of positive RT-PCR COVID-19 report and Adult of Both sexes and age more than 18 years. Patients suffering from cardiac problems before beginning of the study (Palpitation, Chestpain, Breathlessness, Ankle edema, Syncope), Patients suffering from Cardiovascular risk factors (DM, Hypertension, Dyslipidemia, Obesity, Smoking, Hypothyroidism, CKD, Connective Tissue Disease), Patients unwilling to get enrolled in this study. Total 382 samples were collected by purposive sampling method; data were collected in semi structured questionnaire by personal interview. All 382 patients who were enrolled in the study were eligible to participate. Before proceeding, the purpose of the study was explained in detail to each participant, and informed written consent was obtained. After obtaining consent, demographic data like age and sex, symptoms like typical cardiac chest pain and breathlessness, signs like pulse and blood pressure, and investigation results like serum troponin-I and ECG were recorded in a semi-structured data sheet. All patients were advised to notify the researchers via telephone call if they received a negative RT-PCR COVID-19 test result between the first and second visit. Interestingly, all patients became RT-PCR COVID-19 negative within two weeks of their first visit. The patients were then called back for a follow-up visit at cardiology OPD clinic. However, 9 patients refused to return for the follow-up visit, and 1 patient died after the initial visit. As a result, a total of 372 patients attended the follow-up visit at the cardiology OPD clinic after three months. Data from both the initial and follow-up visits were entered and analyzed using IBM SPSS 29.0. Descriptive analysis was performed, and the results were reported as frequency and percentage. Statistical analysis was conducted using Paired Samples Test and Chi-Square Tests. By comparing data from the baseline and after three months, final results were prepared.

Results:

Distribution of Presentations after 3 months among the Study Subjects: Following a three-month period, over 50 percent of the subjects exhibited various cardiovascular symptoms.

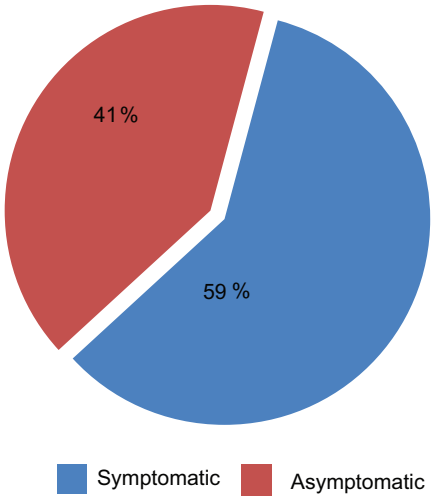

Fig. 1: Distribution of Presentations at 3 months

Distribution of Positive Symptoms after 3 months among the Study Subjects: Palpitation, Chest pain and breathlessness were statistically significant (p value < .05) positive symptoms observed after three months.

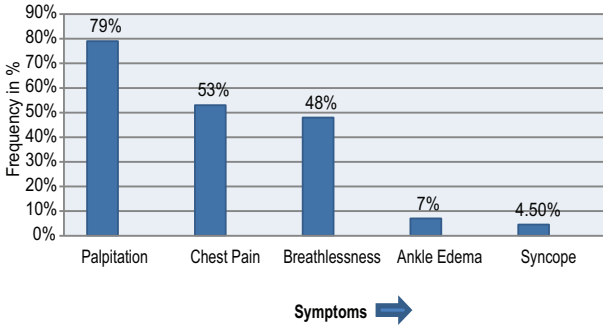

Fig. 2: *Distribution of presenting symptoms at 3 months*

Distribution of Age among the Study Subjects: The majority of the symptomatic group fell within the 60-69 years age range, while the asymptomatic group primarily consisted of individuals between 50-59 years old.

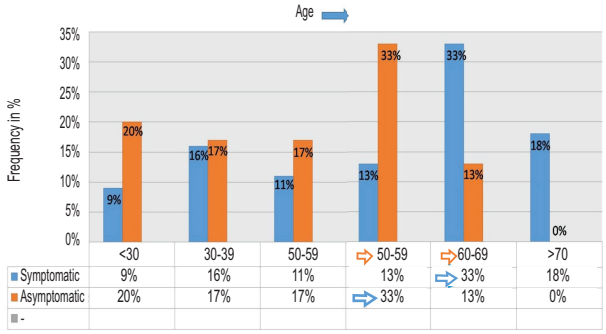

Fig. 3: *Distribution of Age among Symptomatic and Asymptomatic group of study subjects*

Distribution of Sex among the Study Subjects: The majority of the study population in both symptomatic and asymptomatic groups were male.

Characteristics of Subjects Presenting with Chest Pain at 3 months: Almost two third (70%) of the chest pain population were unstable angina and chronic coronary syndrome evidenced by normal Trop I. Remaining one-third (30%) of the subjects experiencing chest pain had acute myocardial infarction, as evidenced by elevated Troponin I. Among the myocardial infarction population, most (17%) presented with ST-elevation myocardial infarction. 13% presented with NSTMI. Among the ST-elevation myocardial infarction subjects, 8 percent were below 30 years of age.

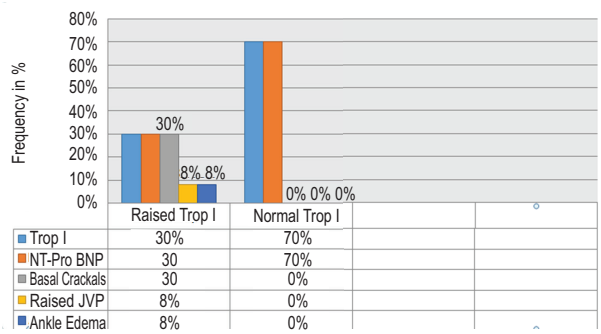

Fig. 4: *Clinical Characteristics of Chest Pain in symptomatic Subject*

Characteristics of ECG in Study Subjects after 3 months: The most common ECG presentations among symptomatic subjects were non specific ST-T changes (37%), followed by, ST depression (26%), ST elevation (17%) .

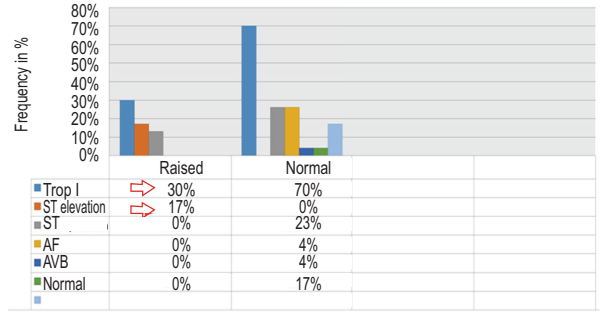

Fig. 5: *ECG patterns among subjects presenting with Chest Pain at 3 months follow up*

Characteristics of 2D Resting TTE Findings among Symptomatic Subjects: Most subjects (70%) presented with preserved ejection fraction, no regional wall motion abnormalities, Grade I diastolic dysfunction, and absence of pulmonary hypertension, again indicating unstable angina and chronic coronary syndrome as the main cause of chest pain in this population.

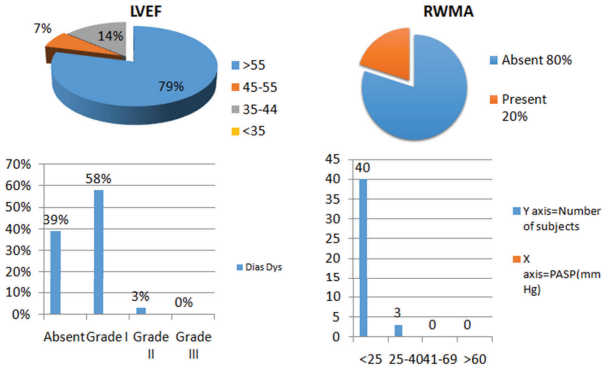

Fig. 6: *Characteristics 2D Resting TTE findings among symptomatic subjects at 3 months*

Discussion:

Three months into our study, a striking 59% of our participants exhibited symptoms of Long COVID-19. This mirrors the findings of Püntmann et al. (2020)[3], who reported that 60% of patients developed cardiovascular manifestations of Long COVID-19 within the same timeframe. This prevalence underscores the commonality of cardiovascular issues in Long COVID-19 patients.

Delving deeper, we discovered that chest pain , breathlessness and palpitation were the most prevalent symptoms in our study. Notably, the elderly were more susceptible to developing cardiac manifestations of Long COVID-19. Our data showed that a substantial 33% of symptomatic subjects fell within the 60-69 age group, echoing the findings of Huang et al. (2020)[4], who observed that cardiac manifestations are more common above 60 years of age.

However, our study showed that, there was no significant (p= >0.05) correlation between age and individual symptoms, except palpitation and chest pain. Hossain et al. (2021),[5] also found that, there was no significant correlation between age & individual symptoms.

While there was no significant correlation between age and individual symptoms, except for palpitation and chest pain, our study revealed that males were more affected by Long COVID-19 than females. This aligns with the results of Nasserie et al. (2021)[6] in Bangladesh. However, a contrasting study by Pelà et al. (2022)[7] in Italy found that females were more likely to develop symptoms. This disparity may be attributed to the disparity in tertiary healthcare facilities available to female populations in our country.

Despite this, our study did not uncover any significant sex-related differences in individual symptoms of Long COVID-19, a finding supported by Di Toro et al. (2021).[8]

Chest pain emerged as a common symptom, affecting 53% of our population, a figure corroborated by other studies, which reported 48% of Long COVID-19 patients experiencing chest pain.[9]

Further analysis revealed that 30% of our chest pain population had myocardial infarction. We also found that chest pain was a significant positive symptom, closely correlated with age but not sex differences.

Our study characterized chest pain as largely non-specific, with myocardial infarction being uncommon. Among the non-infarction population, ST depression was the most common ECG feature. Moreover, our data showed that the most frequent ECG presentation was non specific ST-T changes, echoing the findings of Long et al. (2020b).[10]

The majority (70%) of our subjects presented with preserved ejection fraction, no RWMA, normal LV diameter, and Grade 1 diastolic dysfunction. This mirrors the findings of Huang et al. (2023)[4], who reported that 55% of Long COVID-19 syndrome patients presented with preserved ejection fraction. The higher percentage in our study may be attributed to our smaller sample size.

Among the myocardial infarction population, STEMI was more common than NSTMI. Notably, 8% of the STEMI subjects were below 30 years of age, suggesting possible thrombotic manifestations causing MI in the Long COVID-19 population, rather than atherosclerosis. This is is often due to the activation of coagulation cascades and thrombosis.[11,12]

Conclusion:

This study revealed a significant correlation between Long COVID-19 and cardiovascular manifestations, particularly chest pain. The elderly and male populations exhibited a higher likelihood of experiencing these manifestations. Recent studies provide emerging evidence that suggests the burden of Long COVID-19 patients will increase in the future. Therefore, we recommend conducting further research on Long COVID-19 to determine the exact pathophysiology, which can provide valuable insights and facilitate the identification of novel therapeutic targets.

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Author Contributions : All authors participated in idea generation, data collection, data processing, manuscript preparation, revising and drafting.

Conflict Of Interest: The authors have none to declare.

Data & Materials: Available from the corresponding author, on reasonable request.

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