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Original Article

Others Section

An Outcome Analysis of Asymptomatic COVID-19 Patients Presenting with Angina- A Retrospective Study

DIPANKAR GHOSH DASTIDAR[1], RAKHI SANYAL[2], NANDITA GHOSH DASTIDAR[3], TIRNA HALDER[4]

ABSTRACT

Introduction: Cardiovascular disorders have long been considered as one of the leading causes of mortality in India, which when presented with concurrent Coronavirus Disease (COVID-19) infection becomes even more fatal. Evidence suggests that COVID-19 affects the cardiovascular system by causing exuberant cytokinaemia, which results in endothelial inflammation and microvascular thrombosis, leading to multiorgan failure.

Aim: To analyse the outcome of the asymptomatic COVID-19 patients presenting with cardiac angina during the second wave of COVID-19 in India.

Materials and Methods: This is a retrospective data analysis of asymptomatic COVID-19 patients hospitalised with angina that was conducted between April 2021 to June 2021 at Bardhhaman Medical College and Hospital located at Bardhdhaman district of West Bengal, India. A total of 1235 patients underwent all regular biochemical, haematological and cardiac investigations after undergoing test for COVID-19 test. Data was retrospectively collected. The outcome of these patients was analysed. Estimation of mean, standard deviation, percentage, p-value (from Pearson's correlation) was performed to establish the aim of the study.

Results: Seventy six out of 1235 patients tested positive for asymptomatic COVID-19. The mean age of this study population was 55.075±10.95 years, of which were 55 male and 21 female. Hypertension was the most prevalent co-morbidity followed by diabetes, 73 (96%) presented with chest pain. A total of 47 (62%) of these 76 patients had ST Elevated Myocardial Infarction (STEMI). 11 (14.4%) underwent Percutaneous Coronary Intervention (PCI) whereas 36 (47.3%) underwent fibrinolytic therapy with tenecteplase, followed by secondary PCI in 27 (75%) of them. Rest 29 (38%) were medically managed for unstable angina. Mortality rate was as low as 6.5%. Age and co-morbidity were the contributing factors for STEMI among asymptomatic COVID-19 patients.

Conclusion: The results indicate that age and co-morbidity are the factors, which lead to death or increases the life risk among patients with asymptomatic COVID-19. In this study, we have established that for the current patient population STEMI and age are negatively correlated. Medical management with thrombolytic agent became a lot more accepted in this scenario. PCI still remains the gold standard to treat myocardial infarction. It is recommended that there should be an ICMR guided protocol for the management of such cases with the concurrent COVID-19.

Keywords: Cardiovascular diseases, Coronavirus disease-2019, Myocardial infarction, Thrombolysis

INTRODUCTION

Epidemiological data suggests the global emergence of Non Communicable Diseases (NCD) is a threat to public health [1]. Among them, Cardio Vascular Disease (CVD) accounts for 17.9 million deaths worldwide followed by cancers (9.3 million), respiratory diseases (4.1 million) and diabetes (1.5 million) [2]. Global disease burden of CVD has significantly increased from 271 million in 1990 to 523 million in 2019 with a near 50% rise in death due to CVD as well from 12.1 million in 1990 to 18.6 million in 2019 [3]. The World Health Organisation (WHO)'s statistics suggests that NCDs accounts for 53% of total deaths in India of which 24% is attributed to CVD [4], making it the leading cause of mortality in India [5]. Though the mortality rate due to communicable diseases have been on a downward curve over the last 2 decades [6], the global emergence of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-COV-2) infection has rewritten all facts and numbers. As of May 2022, more than 539,795,635 confirmed cases of COVID-19 have been reported with 6,329,853 deaths [7].

Evidence suggests that COVID-19 effects the cardiovascular system [8,9] by causing exuberant cytokinaemia, which results in endothelial inflammation and microvascular thrombosis leading to multiorgan failure [10]. Prevalence of co-morbidities like hypertension and diabetes raises the risk factor for cardiac involvement among COVID-19 patients [11]. The association between systemic viral infection, acute myocardial infection and inflammation is well established [12,13]. Although the pathophysiology of cardiovascular complications due to COVID-19 infection has been established yet there is paucity of data on the characteristics, management and outcomes of asymptomatic COVID-19 patients presenting with cardiovascular complications. The aim of this retrospective study was to analyse the outcome of asymptomatic COVID-19 patients presenting with cardiac angina based on laboratory investigations and medical management provided.

MATERIALS AND METHODS

This is retrospective data analysis of asymptomatic COVID-19 patients hospitalised with cardiac complications (like angina, shortness of breath, dizziness, heaviness in chest) at the Department of Cardiology of Bardhhaman Medical College and Hospital located at Bardhhaman district of West Bengal, India between April to June 2021. The symptoms included severe chest pain, shortness of breath, syncope, nausea and fatigue. Nasopharyngeal sample was collected for real-time Reverse Transcription-Polymerase Chain Reaction (RT-PCR) testing from all patients as they neither had any COVID-19 test report nor showed any symptom of COVID-19. They were also tested for COVID-19 with rapid antigen as the RT-PCR report came after 24 hours of sample collection.

The ethics committee of the institute was approached with retrospective study plan. The study received its ethical clearance from the Institutional Ethics Committee of Bardhhaman Medical

College. The ethical clearance letter number is BMC/I.E.C/470. Patients were called at site for follow-up after one month of discharge. Consent was obtained from all the participants.

Inclusion criteria: Patients who tested positive for COVID-19 but were symptomatic presenting with cardiac complications aged ≥18 years were included in the study.

Exclusion criteria: COVID-19 negative and or asymptomatic COVID-19 patients, unavailability of complete data set for analysis, patient's who did not consent were excluded from the study.

Among the 1235 patients who visited the cardiology department of the district superspecialty hospital during the second wave of COVID-19 in India between April to June 2021, 76 patients were found to be asymptomatic COVID-19 positive. As per the inclusion criteria only these 76 patients' data was included in the study.

Study Procedure

Data was retrospectively collected by on duty doctors in the hospitals from patients' medical notes when the project was conceived. It included demographics, co-morbidities, Echocardiography (ECG), laboratory investigations (biochemistry, haematology, serology, urine analysis), diagnosis, management, and outcomes.

The data was statistically analysed for the demographics (age, sex, ethnicity, marital status) of the study population, diagnosis (myocardial infarction, unstable angina, atrial fibrillation, atherosclerosis) rate of co-morbidities present and mortality outcome achieved by the patients.

As per the ICMR guidelines for management of MI [14], patients were managed medically by thrombolysis and/or PCI. When they tested COVID-19 negative or as per Cardiology Society of India guidelines for management of STEMI [15], PCI was performed with all safety measures. ICMR emergency surgical guidelines were followed in case of COVID-19 in patients with higher Thrombolysis In Myocardial Infarction (TIMI) risk score [16]. Successful thrombolysis was defined as reduced ST elevation by >50% within 90-120 minutes with relief from chest pain and haemodynamic stability [15]. Angiography was performed to assess the TIMI flow grade.

STATISTICAL ANALYSIS

Mean and standard deviation was estimated for quantitative parameters. Percentage was calculated for male, female, co-morbidity load and outcomes. Pearson's correlation test was performed between factors like co-morbidity, age, STEMI. Statistical analysis was performed by SPSS Version 28.

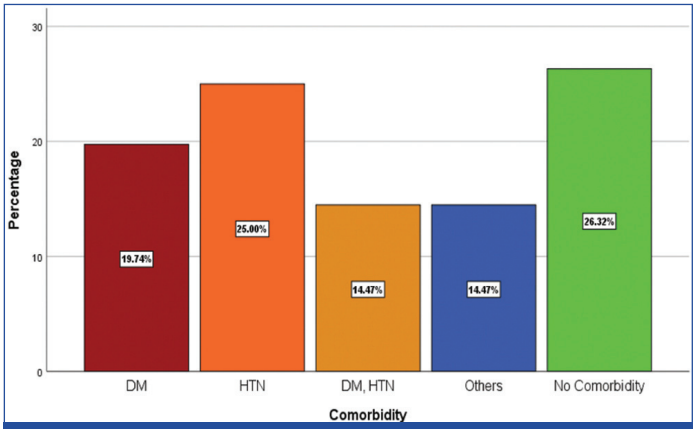
RESULTS

The number of male patients in the study population was 55 and that of female was 21. The mean age of the study patients was 55.075±10.95 years.

[Table/Fig-1] enlists the characteristics of 76 asymptomatic COVID-19 positive patients presenting with angina. Co-morbidity load of the study patients was high with 73.7% having at least one co-morbidity or more. Hypertension (HTN) (19, 25%) was the most common co-morbidity observed among the study patients, followed by Diabetes Mellitus (DM) (15,19.73%). Both DM and HTN were present among 14.47% of the study population. Strikingly 20 i.e., 26.31% patients did not have any known co-morbidity [Table/Fig-2].

Parameters		Outcome			
		Death	Medically managed	PCI	Total
Sex	M	5	21	29	55
	F	0	8	13	21
Co-morbidities	DM	0	6	9	15
	HTN	0	7	12	19
	DM, HTN	1	2	8	11
	DM, HTN, COPD; Hypothyroid	4	2	5	11
	No co-morbidity	0	14	6	20
Age (years)	Mean	75.60	49.10	57.08	NA

[Table/Fig-1]: Characteristics of 76 asymptomatic COVID-19 positive patients with presenting with angina.
COPD: Chronic obstructive pulmonary disease; DM: Diabetes mellitus; HTN: Hypertension

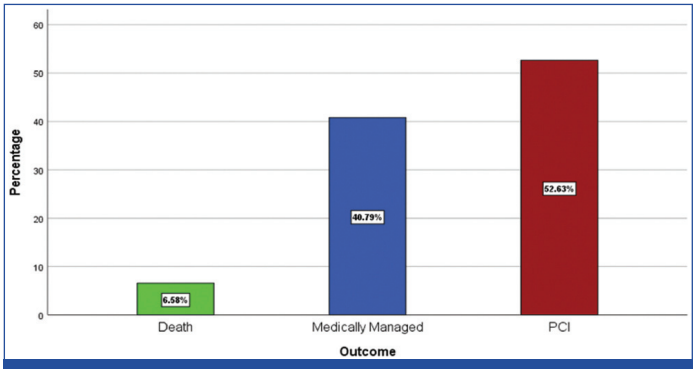


[Table/Fig-2]: Graphical representation of co-morbidity among asymptomatic COVID-19 patients presented with cardiac angina.

ECG was performed as primary investigation for all 76 patients and ST elevation was observed among 47 patients i.e., 61.8%. Non ST elevation patients, 29 (38.15%) were treated for unstable angina, atrial fibrillation, hypertropic cardiomyopathy, atherosclerosis and managed medically but had a mean hospital stay of 5±1.2 days. Laboratory investigations such as sodium (136-145 mEq/L), potassium (3.5-5.1 mEq/L), liver function test (AST and ALT <32 U/L), urea (21-43 mg/dL), creatinine (<1.2 mg/dL), lipid profile, complete blood culture, thyroid profile, urine analysis of patients in all subgroups (death, PCI and medical management) based on their outcomes showed similar characteristics with a p-value which was not statistically significant.

Out of 76, 73 (96%) presented with chest pain and 3 (4%) presented with shortness of breath. The ECG conducted confirmed 47 patients of having ST elevation. Among these 47 patients, 37 patients underwent PCI, either primary or secondary. As the hospital was in a rural setting, only 11 patients underwent primary PCI as their door to balloon time was less than 120 minutes. Others (36) underwent thrombolysis with hospital supplied tenecteplase of which 27 underwent secondary PCI after recovering from COVID-19. The dose of thrombolytic agent tenecteplase was calculated based on the body weight of the patients.

Out of 76, 71 patients reported recovered either with medicine, thrombolysis or PCI. Death was the outcome for five patients whose mean age was 75.60±16.22 and strikingly all of them were male with more than 2 co-morbidities. The mean hospital stay was 7.8±2.3 and 10.32±3.68 days for patients undergoing thrombolysis and PCI, respectively. Mechanical ventilation was given to two patients who underwent primary PCI but ultimately resulted in death. [Table/Fig-3] graphically represents the final outcome of the study population.



[Table/Fig-3]: Final outcome of the study population.

Statistically significant correlation was found to exist between co-morbidity, age and STEMI as represented in [Table/Fig-4,5].

Variables	STEMI			Co-morbidities		
	Pearson correlation	Sig. (2-tailed)	N	Pearson correlation	Sig. (2-tailed)	N
STEMI	1	-	76	0.566	0.000	76
Co-morbidities	0.566	0.000	76	1	-	76

[Table/Fig-4]: Correlation between co-morbidities and STEMI.
(STEMI and co-morbidities have positive correlation as indicated by Pearson Correlation Coefficient, r=0.566; Correlation between STEMI and co-morbidities is significant as indicated by p-value=<0.0001)

Variables	STEMI			Age		
	Pearson correlation	Sig. (2-tailed)	N	Pearson correlation	Sig. (2-tailed)	N
STEMI	1	-	76	-0.432	0.000	76
Age	-0.432	0.000	76	1	-	76

[Table/Fig-5]: Correlation between AGE and STEMI.
STEMI and age have negative correlation as indicated by Pearson Correlation Coefficient, (r=-0.432; Correlation between STEMI and AGE is significant as indicated by p-value=<0.0001)

DISCUSSION

Management of any coronary disease or event presents a great challenge as it can be fatal if not addressed in time. When such events are added with concurrent asymptomatic COVID-19, it presents an even greater threat than the prepandemic management of such events. In this scenario, the use of fibrinolytic therapy has gained momentum [17]. Stable patients who report at hospital within 12 hours of experiencing STEMI can be administered with this therapy. In COVID-19 patients', fibrinolytic therapy is chosen over primary PCI by experts in China [18] if the patient is stable and presents within 12 hours of experiencing angina or cardiac complications which can fall under this category of coronary events. Though patients are successfully being managed with fibrinolytic therapy, many questions still remain unanswered and unaddressed. The guidelines available for management of coronary events in COVID-19 patients are still not enough to address various situations encountered in real life settings. Different hospitals have different SOP based on the country's medical guidelines for such scenarios. The mortality rates vary across different populations, such as a 19 patient case series in New York [19] and a 28 patient case series in Italy [20] reported much higher mortality rates than observed in the study population of 76 patients. However, the long term follow-up of the cases may report differently as the far-fetched effects of the pandemic are still unknown. Coronary diseases or events are categorised as highly morbid and there is a plethora of condition which influences mortality. In this study, death was the outcome for patients who were male and their average age was 75.60±19.28 years. Patients without any co-morbidity recovered faster than patients with one or more co-morbidity. It can be concluded that presence or absence of co-morbidity influenced the patient outcome in case of this study as all patients who experienced death had two or more co-morbidities, whereas 13 of 20 patients with no co-morbidity could be medically managed with thrombolysis.

Fibrinolytic therapy has been recommended as the first line of treatment for stable patients with myocardial infarction and COVID-19 infections by many experts from USA and China [18], however, no such ICMR guideline is available yet for the same. Also, it is reported that since COVID-19 has approximately 31% [21] thrombotic complications, fibrinolytic therapy and anticoagulants can improve outcomes in patients who have high levels of D-dimer. Elevated level of cytokines and D-dimer is a result of COVID-10 infection which in turn increases the prothrombin time [22]. This can also lead to endothelial damage, thus exposing the patient to a hypercoagulable state [23]. It is suggested by Schoenhagen P et al., that change in the coagulable state may result in the plaques to weaken, rupture and finally lead to thrombosis [24]. Kumar N et al., also suggests the use of anticoagulant therapy in such cases [22]. There are also several studies suggesting that COVID-19 patients are prone to thrombosis or thrombotic events and co-morbidities like diabetes and hypertension can act as a prognostic factor [25-27]. The present study also reports the same. Several protocol changes can be suggested to treat patients in such scenarios but we are yet to appear at a structured guideline to counter such situations. The research available on COVID-19 and its cardiac manifestation is very less to understand and manage patients in such emergency conditions.

Limitation(s)

Due to the rural setting, it is one of the limitations that the D-dimer of the patient population could not be estimated. The other limitations include the fact that this study was performed retrospectively during the second wave of COVID-19 so it was not possible to collect more data from patients due to the shortage of staff and facilities in our settings. Second, patients in cardiogenic shock could not be taken to OT due to the unavailability of ventricular assist device and Intra-Aortic Balloon Pump at the hospital. The study population is very small which limits us from performing many relevant statistical analyses. Lastly, there was no control group to match the data and perform case control analysis at the then emergency situation along with the dearth of proper guidelines to treat patients in the pandemic scenario.

CONCLUSION(S)

The present study concludes that there is a positive correlation between STEMI and co-morbidities. This study also shows multiple outcomes in case of asymptomatic COVID-19 patients. The analysis of the outcome reports the mortality rate to be low and concludes that patients can be saved if diagnosed in time but the unavailability of proper guidelines had worsened the situation during the second wave. The results establish the need for proper guidelines from ICMR and cardiology society of India in such emergency situation.

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PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Cardiology, Burdwan Medical College, Kolkata, West Bengal, India.
2. Associate Professor, Department of Internal Medicine, JIMSH, Kolkata, West Bengal, India.
3. Consultant, Department of Pulmonology, South Eastern Railway Hospital, Kolkata, West Bengal, India.
4. Director, Department of Clinical Operations, OrciVita Sciences and Research Pvt. Ltd., Kolkata, West Bengal, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dipankar Ghosh Datidar,
5/2, Gobindo Auddy Road, Kolkata-700027, West Bengal, India.
E-mail: dr.dgd1972@gmail.com

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