

Clinical Profile of ST-Elevation Myocardial Infarction Thrombolysed with Tenecteplase in Coronavirus Disease 2019 Pandemic: A Comparative Study

Kamal Kant Jena¹, MD, G Manohar¹, MD, DM, C Elamaram¹, MD, DM, A Rudrappa¹, MD, DM

¹Department of Cardiology, Government Stanley Medical College, Chennai, Tamil Nadu, India

Received: 01-11-2020
Revised: 14-11-2020
Accepted: 26-11-2020
Published: 22-06-2021

INTRODUCTION

The coronavirus disease 2019 (COVID-19) causing severe acute respiratory syndrome (SARS) is the pandemic of the century, with approximately 11 million cases and 560,000 deaths worldwide. India has 750,000 cases with a mortality of 20,000 as of July 2020.^[1] Cardiovascular complications, including myocardial injury, myocarditis, acute coronary syndromes, pulmonary embolism, stroke, arrhythmias, and heart failure, have been well described in COVID-19.^[2-5] COVID-19 may predispose to both venous and arterial thromboembolism due to excessive inflammation, hypercoagulability, hypoxia, immobilization, and diffuse intravascular coagulation,^[6] leading to increased risk of acute myocardial infarction (MI) in patients with COVID-19. Precise knowledge of the incidence, clinical features, and prognosis of ST-elevation MI (STEMI) in COVID-19 patients is important for decision-making and management of such patients, especially those who are admitted to the intensive care unit (ICU) bear high risk. In our study, we describe the impact of the COVID-19 outbreak on patients admitted in

ABSTRACT

Background: Coronavirus disease-2019 (COVID-19) pandemic has affected millions worldwide. The various complications of COVID-19 have been discussed in the recent studies. We would like to discuss about one such cardiovascular complication, ST elevation myocardial infarction (STEMI) in COVID-19, and its characteristics in this article. **Methodology:** An observational study was done from April 1, 2020, to July 15, 2020, selecting all STEMI patients admitted to a tertiary care center in Chennai and treated with tenecteplase were grouped in to COVID-19 positive and negative. Their presenting features and complications and outcome were studied. **Results:** A total of 300 patients were admitted with STEMI during the study period, of which 11.66% were COVID-19 positive. Atherosclerotic cardiovascular risk factors were much lower in COVID-19-positive STEMI patients when compared to non-COVID STEMI patients. Mean oxygen saturation at time of presentation in COVID-19 positive and negative patients was 85.1% and 97.5%, respectively ($P < 0.001$). COVID-19 group had significantly higher noncardiac complications than non-COVID patients ($P < 0.001$). The average duration of hospital stay in COVID-19 STEMI was 13.6 days, whereas in non-COVID group was 6.8 days ($P < 0.001$). Higher mortality was found in the COVID-19 positive group (14.28%) when compared to non-COVID STEMI (7.9%; $P < 0.001$). **Conclusion:** COVID-19 itself is a systemic inflammatory disease, which could increase the risk of coronary plaque rupture. Thrombosis has also been described as a mechanism underlying certain cases causing presentation of STEMI, because of endothelial dysfunction and hypercoagulable state.

KEYWORDS: Acute myocardial infarction, coronavirus disease-2019, fibrinolysis, hypercoagulability, risk factors

the cardiac ICU with STEMI in South India who underwent thrombolysis at our tertiary care center.

METHODOLOGY

This is a hospital-based observational study conducted from April 1, 2020, to July 15, 2020, at a Tertiary Care Medical College and Hospital in Chennai, India. We focused from April 1, 2020, when hospitals in the city started to institute emergency infection protocols to contain COVID-19. Our hospital has offered 24/7 service to all eligible patients presenting with acute STEMI as per the standard accident and emergency department protocol. Data on key time points in STEMI care were recorded in a clinical registry. STEMI

Address for correspondence: Dr. Kamal Kant Jena, MD, Department of Cardiology, Government Stanley Medical College, Chennai - 600 001, Tamil Nadu, India. E-mail: kamalkanth.jena92@gmail.com

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How to cite this article: Jena KK, Manohar G, Elamaram C, Rudrappa A. Clinical profile of ST-elevation myocardial infarction thrombolysed with tenecteplase in Coronavirus Disease 2019 Pandemic: A comparative study. J Clin Prev Cardiol 2021;10:58-62.

Access this article online

Quick Response Code:



Website: www.jcpconline.org

DOI: 10.4103/jpcp.jpcp_64_20

was defined according to criteria proposed in the most recent international guidelines.^[7]

We included all patients with STEMI, irrespective of their COVID status, admitted through the Accident and Emergency Department, who were re-vascularized by fibrinolysis. Fibrinolysis was done using intravenous tenecteplase based on international standard protocol.^[8] Nasal/throat swab for reverse transcription–polymerase chain reaction was sent for all patients admitted in our cardiac ICU. They were categorized into two groups based on their COVID-19 status into COVID-19 positive and negative groups. These two groups were analyzed and compared based on the demographic details, comorbidities, duration of hospital stay, morbidity, and mortality using the SPSS software (Chi-square test). Two-sided $P < 0.05$ was considered significant. The COVID-19 positive patients were treated according to the Indian Council of Medical Research guidelines.^[9]

RESULTS

A total of 300 patients were admitted with STEMI to our cardiac ICU from April 2020 to July 15, 2020, among which 35 (11.66%) patients were COVID-19 positive [Table 1]. Majority of COVID-19 positive STEMI patients were male (82.9%) and presented between 41 and 60 years ($n = 19$, 54.3%), with a mean age of 55 ± 12 years. The risk factors were observed to be more in non-COVID group compared

to COVID group. Diabetes and hypertension were found in 25.7% and 54.3% of COVID-19 positive patients, respectively when compared to 66.8% ($P < 0.001$) and 63.7% ($P = 0.742$) of non-COVID 19 patients. 37.1% were smokers in COVID-19 positive group, whereas it was 54.7% in non-COVID 19 group ($P = 0.215$). Dyslipidemia was found to a risk factor in only 22.8% of COVID-19 positive patients had, whereas it was found in 76.2% of non-COVID-19 patients ($P < 0.001$).

In both the groups, anterior wall MI was the most common presentation [Table 1]. In COVID-positive group, 20 patients presented with anterior wall STEMI and 15 with inferior wall STEMI [Table 1]. Thrombolysis could not be done in 14.3% ($n = 5$) of COVID-19 positive STEMI patients and 10.9% ($n = 29$) non-COVID patients as they presented after 12 h after onset of symptoms.

Acute STEMI was the first clinical manifestation in 69.4% of the COVID-19 positive patients [Table 2]. Chest pain was the most common presenting feature in both the groups, although lesser than the non-COVID group (77.1% in COVID group and 97.3% in non-COVID group; $P = 0.049$). The second most common being breathlessness (54.3%) in COVID-positive group and around 36% only in non-COVID group ($P = 0.043$). Analysis of other clinical presentations [Table 2] revealed 9 (25.7%) patients with fever and 17 (48.6%) with cough in COVID positive group, whereas only 2 (0.7%) and 14 (5.3%) had fever and cough, respectively, in the non-COVID group

Table 1: Characteristics of coronavirus disease-2019 positive and noncoronavirus disease ST-elevation myocardial infarction patients

| Demographic characters | Total STEMI patients admitted ($n=300$) | | <i>P</i> |
|---|--|---|----------|
| | COVID-19 positive ($n=35$; 11.66%), <i>n</i> (%) | COVID-19 negative ($n=265$; 88.33%), <i>n</i> (%) | |
| Age groups (years) | | | |
| 21-40 | 5 (14.3) | 28 (10.6) | 0.915 |
| 41-60 | 19 (54.3) | 126 (47.5) | 0.983 |
| 61-80 | 10 (28.6) | 107 (40.4) | 0.198 |
| 81-100 | 1 (2.8) | 4 (1.5) | 0.018 |
| Sex | | | |
| Male | 29 (82.9) | 187 (70.56) | 0.045 |
| Female | 6 (17.1) | 78 (29.44) | 0.023 |
| Risk factors | | | |
| Diabetes mellitus | 9 (25.7) | 177 (66.8) | <0.001 |
| Hypertension | 19 (54.3) | 169 (63.7) | 0.242 |
| Smoking | 13 (37.1) | 145 (54.7) | 0.215 |
| Dyslipidemia | 8 (22.8) | 202 (76.2) | <0.001 |
| Alcoholism | 8 (22.8) | 139 (52.4) | <0.001 |
| STEMI | | | |
| Anterior wall MI | 20 (57.1) | 162 (61.1) | 0.877 |
| Inferior wall MI | 15 (42.9) | 103 (38.9) | 0.981 |
| Late presentation >12 h | 5 (14.3) | 29 (10.9) | 0.012 |
| Mean SpO ₂ at time of presentation (%) | 85.1 | 97.5 | <0.001 |
| Mechanical ventilation (NIV + IV) | 18 (51.42) | 34 (12.8) | <0.001 |
| Average duration of hospital stay (days) | 13.6 | 6.8 | <0.001 |
| Mortality | 5 (14.28) | 21 (7.9) | <0.001 |

STEMI=ST-elevation myocardial infarction, MI=Myocardial infarction, IV=Invasive ventilation, NIV=Non-IV, COVID-19=Coronavirus disease 2019, SpO₂=Oxygen saturation

with a $P < 0.001$. Pneumonia was present in 54.3% of patients in COVID-19-positive group when compared to 1.1% in non-COVID group ($P < 0.001$).

Mean oxygen saturation at the time of presentation in COVID-19 positive and negative patients was 85.1% and 97.5%, respectively ($P < 0.001$) [Table 1]. Among COVID-19 positive group, 5 were clinically asymptomatic, 9 patients required high flow oxygen, 13 patients required noninvasive ventilation, and 5 were on invasive mechanical ventilation. A total of 51.42% in the COVID group required mechanical ventilation (invasive or noninvasive ventilation), which is significantly higher compared to non-COVID 19 group which was only 12.8% ($P < 0.001$).

Comparing the complications of both the groups [Table 3], we observed that acute respiratory distress syndrome (25.7%), acute kidney injury (22.6%), acute pulmonary edema (11.4%), shock (17.1%), and arrhythmias (14.28%) were more in COVID-positive group. Heart failure (38.1%) was the predominant complication in non-COVID group. Though only 35 COVID-19-positive STEMI patients were studied, it was found that patients with COVID 19 had higher rate of noncardiac complications than non-COVID 19 patients. The duration of hospitalization for COVID-19 positive patients was 13.6 days which significantly more than non-COVID 19 patients who were hospitalized for an average of 6.8 days ($P < 0.001$). The mortality rate was much higher in COVID group (14.2%) when compared with non-COVID STEMI patients which was 7.9%; $P < 0.001$).

DISCUSSION

SARS-coronavirus-2 causing COVID-19 has presented a new challenge for the health-care community worldwide. It has become a pandemic due to its high infectivity and ability to get transmitted even during asymptomatic phase, resulting in the rapid transmission of this virus beyond the geographic regions. As of now, we know that majority of the people present with respiratory involvement ranging from mild flu-like illness to potentially lethal acute respiratory distress syndrome or fulminant pneumonia. Although lots of cardiovascular complications with high mortality and morbidity have also been described lately in some recent studies,^[2] we would like to discuss about STEMI in COVID-19 era in our hospital and its clinical presentations and its disease course.

In the present study, we screened 300 patients presenting with STEMI. Of which the incidence of COVID-19-positive patients presenting with STEMI was 11.66%. The overall incidence of acute cardiac injury reported till now has been variable but roughly 8%–12% of the positive cases.^[10] A study by Showkathali *et al.* described the incidence of STEMI in COVID-19 to be 7%.^[8]

The mean age of presentation for COVID-positive STEMI in our study was 55 ± 12 years in a similar study by Showkathali *et al.* and Stefanini *et al.*, the mean age was 59 ± 13 and 68 ± 11 years, respectively.^[8,11] Majority of the study group were males (82.9% in COVID group and 70.56% in non-COVID group), which was consistent with a study done by Bangalore *et al.*^[12]

Table 2: Comparison of clinical presentation coronavirus disease-2019 positive and noncoronavirus disease ST elevation myocardial infarction patients (n=300)

| Clinical presentation | COVID-19 positive (n=35; 11.66%), n (%) | COVID-19 negative (n=265; 88.33%), n (%) | P |
|-----------------------|---|--|--------|
| Fever | 9 (25.7) | 2 (0.7) | <0.001 |
| Cough | 17 (48.6) | 14 (5.3) | <0.001 |
| Sore throat | 11 (31.4) | 0 | - |
| Rhinorrhoea | 5 (14.3) | 0 | - |
| Headache | 7 (20) | 0 | - |
| Myalgia | 10 (28.6) | 0 | - |
| Pneumonia | 19 (54.3) | 3 (1.1) | <0.001 |
| Breathlessness | 19 (54.3) | 98 (36) | 0.043 |
| Chest pain | 27 (77.1) | 258 (97.3) | 0.049 |

COVID-19=Coronavirus disease-2019

Table 3: Comparison of complications in coronavirus disease-2019 positive and negative ST elevation myocardial infarction (n=300)

| Complications | COVID-19 positive (n=35; 11.66%), n (%) | COVID-19 negative (n=265; 88.33%), n (%) | P |
|-----------------------------|---|--|--------|
| AKI | 8 (22.6) | 21 (7.9) | <0.001 |
| Heart failure | 4 (11.42) | 101 (38.1) | <0.001 |
| ARDS | 9 (25.7) | 5 (1.8) | <0.001 |
| MOF | 5 (14.3) | 2 (0.7) | <0.001 |
| Neurological manifestations | 1 (2.8) | 0 | - |
| Shock | 6 (17.1) | 23 (8.6) | <0.001 |
| Acute pulmonary edema | 4 (11.4) | 82 (30.9) | <0.001 |
| Mechanical complications | 2 (5.7) | 13 (4.9) | 0.589 |
| Arrhythmias | 5 (14.28) | 35 (13) | 0.634 |

AKI=Acute kidney injury, ARDS=Acute respiratory distress, MOF=Multiorgan failure, COVID-19=Coronavirus disease-2019

In our study, we observed that the risk factors such as hypertension, diabetes, and smoking were more in non-COVID group compared to COVID group. There are no studies as of now comparing the risk factors in COVID positive and negative groups, but studies on COVID-19 positive STEMI patients by Alaarag *et al.* in their study also found that the incidence of diabetes, hypertension, current smoking status, and dyslipidemia were 38.5%, 42.3%, 50.0%, and 38.5%, respectively, which was almost consistent with our study.^[13] In a similar study by Stefanini *et al.* found that 71.4% had hypertension, 32.1% had diabetes mellitus, and Bangalore *et al.* found 86% to have hypertension, 43% to have diabetes mellitus, and 14% were smokers.^[11,12] The reason behind having lower risk factors in COVID group when compared to non-COVID group is probably because COVID-19 itself might trigger an intense inflammatory response, which could also increase the risk of coronary plaque rupture and also micro-vascular thrombosis has also been described as a mechanism underlying certain cases mimicking presentation of STEMI without obstructive CAD, given the endothelial dysfunction and hypercoagulable state associated with COVID-19.^[14]

Studies till now have indicated that fever and cough are the dominant symptoms in COVID-positive patients.^[15,16] Few studies have also reported that some severely or critically ill patients may have moderate, low, or even no significant fever,^[16] even our study showed only 25.7% patients with fever but 54.3% of the COVID-positive patients had pneumonia and breathlessness. In addition, a few COVID-19 patients also showed gastrointestinal symptoms, i.e., diarrhea (3.8%) and vomiting (5.0%) in the study by Guan *et al.* which was not seen in our study. In our study, 77.1% patients presented with chest pain which was lower compared to non-COVID group (97.3%). Stefanini *et al.* in their study found an incidence of 78.6% with chest pain in COVID-19 STEMI.^[11]

Alaarag *et al.* in their study highlighted a mortality rate of 15.4% which was almost similar to our study (14.28%).^[13] Although our case fatality rate in COVID-positive group was almost half of Stefanini *et al.*'s study,^[11] it was twice when compared to non-COVID STEMI group (7.9%). In our study, 51.42% of COVID-19 positive patients required mechanical ventilation including endotracheal as well as noninvasive, which was similar to a cohort study conducted by Yang *et al.* where he found 56% were given noninvasive ventilation at ICU admission, of whom 76% required further oro-tracheal intubation and invasive mechanical ventilation.^[17]

Similar to our study, Yang *et al.* also observed that most of his patients had organ function damage, including 35 (67%) with acute respiratory distress, 15 (29%) with acute kidney injury, 12 (23%) with cardiac injury, and 15 (29%) with liver dysfunction.^[17] The incidence of cardiac complications such as arrhythmias in COVID-19 positive group was 14.28%, Guo *et al.* and Wang *et al.* in a similar kind of study reported an incidence of 19.6% and 16.7% of arrhythmia, respectively.^[18,19]

Study limitations

The small COVID-19 positive sample size may limit the generalizability of the findings and the power to detect

associations. Data such as echocardiography, biomarkers, and coronary angiograms were not done in our patients. Primary percutaneous coronary intervention was not preferred due the COVID-19 pandemic which may have altered the outcome. Angiographic assessments were not done due high COVID-19 burden in our institute and the man power was diverted for managing COVID-19 patients. Long-term follow-up could not be done.

CONCLUSION

COVID-19 has profoundly reshaped usual pathways of care of both elective and acute cardiac patients. Further research is needed to define the pathophysiology of COVID-19 precisely and its effects on other systems. Although respiratory illness is the dominant clinical manifestation of COVID-19, the sheer burden of the illness implies that a large number of patients with COVID-19 would present with new-onset cardiac dysfunction during the course of the illness. Considering this, there is a huge vacuum in knowledge regarding the current understanding about the interplay between cardiovascular disease and COVID-19. It is therefore highly desirable that the future studies on COVID-19 specifically describe the incidence, mechanisms, clinical presentation, and outcomes of various cardiovascular manifestations in these patients. The diagnostic and therapeutic challenges posed by the concurrence of these two illnesses also need to be adequately studied.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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