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COVID-19 infected ST-Elevation myocardial infarction in India (COSTA INDIA)

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ABSTRACT

Objective: To find out differences in the presentation, management and outcomes of COVID-19 infected STEMI patients compared to age and sex-matched non-infected STEMI patients treated during the same period.

Methods: This was a retrospective multicentre observational registry in which we collected data of COVID-19 positive STEMI patients from selected tertiary care hospitals across India**.** For every COVID-19 positive STEMI patient, two age and sex-matched COVID-19 negative STEMI patients were enrolled as control**.** The primary endpoint was a composite of in-hospital mortality, re-infarction, heart failure, and stroke.

Results: 410 COVID-19 positive STEMI cases were compared with 799 COVID-19 negative STEMI cases. The composite of death/reinfarction/stroke/heart failure was significantly higher among the COVID-19 positive STEMI patients compared with COVID-19 negative STEMI cases (27.1% vs 20.7% p value = 0.01); though mortality rate did not differ significantly (8.0% vs 5.8% p value = 0.13). Significantly lower proportion of COVID-19 positive STEMI patients received reperfusion treatment and primary PCI (60.7% vs 71.1% p value=< 0.001 and 15.4% vs 23.4% p value = 0.001 respectively). Rate of systematic early PCI (pharmaco-invasive treatment) was significantly lower in the COVID-19 positive group compared with COVID-19 negative group. There was no difference in the prevalence of high thrombus burden (14.5% and 12.0% p value = 0.55 among COVID-19 positive and negative patients respectively)

Conclusions: In this large registry of STEMI patients, we did not find significant excess in in-hospital mortality among COVID-19 co-infected patients compared with non-infected patients despite lower rate of primary PCI and reperfusion treatment, though composite of in-hospital mortality, re-infarction, stroke and heart failure was higher.

1. Introduction

Management of acute myocardial infarction (AMI), especially ST elevation myocardial infarction (STEMI), is challenging during the COVID-19 era due to disruption of health systems in different parts of the world. At the peak of the pandemic, many patients presenting with STEMI were positive for COVID-19 infection. Some reports suggested possibly higher in-hospital complications and mortality in these patients[1-3] . They had higher prevalence of thrombotic lesions and were more likely to receive GP IIb/IIIa inhibitors and undergo thrombus aspiration.[4] This is primarily attributed to the COVID-19 induced procoagulant state, which may also predispose to stent thrombosis.[5] There is lack of clarity regarding the most appropriate revascularization strategy in these cases, especially in resource-limited low-middle income countries (LMIC) such as India. Patients are often denied primary PCI due to either lack of resources or fear of spread of COVID-19 infection to the already burdened health care workers.[6]

There are limited data on clinical characteristics, management strategies, and in-hospital outcomes of COVID-19 infected STEMI patients, and no reports are available from India. Hence, the present study investigated the clinical presentation, management strategies, and in-hospital outcomes of COVID-19 infected STEMI patients.

2. Methods

2.1. Aims and objectives

Aim of the study was to determine whether the clinical presentation, management strategies, and in-hospital outcomes of COVID-19 infected STEMI patients differ from non-infected STEMI patients in India. The study's primary objective was to find out

differences in the composite of in-hospital mortality, re-infarction, stroke, and heart failure in COVID-19 infected STEMI patients as compared to age and sex-matched non-infected STEMI patients treated during the same period. Secondary objectives were to find out differences between the COVID-19 positive and negative patients in[1] initial management strategies for STEMI,[2] angiographic features,[3] thrombus burden and need for thrombus aspiration, and[4] in-hospital mortality.

2.2. Study design

The COSTA INDIA was a retrospective multicenter observational registry of hospitalized patients with STEMI and concomitant COVID-19 infection diagnosed by positive nucleic acid amplification test (NAAT) or rapid antigen test (RAT), either at admission or during the index hospitalization. We invited all tertiary care hospitals across India with at least two confirmed COVID-19 positive STEMI cases during the study period from May 1, 2020 to December 31, 2020 to participate. Data of all consecutive COVID-19 positive STEMI patients treated at the participating centers were collected in the prescribed proforma. For every COVID-19 positive STEMI patient, two age and sex matched COVID-19 negative STEMI patients admitted during the same period were enrolled as a control group. Twenty-seven tertiary care centers consented to participate. The study was conducted as per GCP guidelines and was registered under clinical trial registry of India (CTRI) (CTRI/2021/03/031757). The institutional review boards of all participating centers approved the protocol. All individual participating centers were required to take ethical approval at respective centers. The study was sponsored by Cardiological society of India.

2.3. Inclusion criteria

All consecutive patients, 18 years or above with STEMI or new LBBB on 12 lead ECG with a diagnosis of AMI as per the fourth universal definition of MI and positive for COVID-19 infection by NAAT or RAT test were enrolled. The cases could be those found to be COVID-19 positive during routine screening after admission for STEMI, those referred from elsewhere as COVID-19 positive STEMI or those who developed STEMI while admitted for treatment of COVID-19 infection.

2.4. Data collection

Data was collected using a standard electronic case record form (eCRF). Patient anonymity was maintained. The entries were checked by the regional and state coordinators of the study, and random verification with source documentation was conducted to ensure data quality. The data coordinating centre at Lisie Hospital, Kochi, India, supervised the eCRF entries and its verification.

Patient demographics, risk factors, and relevant comorbidities were documented. History of prior MI, heart failure, COPD, CVA, CKD, CABG/PTCA and symptoms due to STEMI and COVID-19 infection were recorded along with COVID test details, findings of Chest X-ray and CT scan chest. We also captured information about the type of reperfusion, its outcome, time windows and procedural and angiographic characteristics including thrombus burden by TIMI thrombus grade (when PCI was done). Pharmacotherapy administered for STEMI and COVID-19, was also documented.

2.5. Outcomes

The primary endpoint was a composite of in-hospital mortality, re-infarction, heart failure, and stroke. The secondary endpoints were in-hospital mortality, angiographic features like number of vessels involved and the success of angioplasty, and thrombus load as evidenced by grade of thrombus burden, need for thrombus aspiration and use of glycoprotein 11b111a inhibitors.

2.6. Statistical analyses

All the categorical variables were summarized using frequency and percentages and continuous variables were summarised using median along with quartiles (Q1, Q3). The statistical assumption of normality was tested using the Kolmogorov–Smirnov test. Comparison of baseline demographics and procedural characteristics, angiographic and procedural characteristics, in-hospital outcome between the study (COVID-19 positive STEMI and Control) groups were done using Chi-square test/Fisher's exact test. A p-value less than 0.05 was considered to be statistically significant. Mann–Whitney *U* test was carried out to compare the median ER to Wire Time, Heart Rate at admission, etc., across the study groups. Robust Poisson regression with log-link function under the generalised linear model was used to identify the factors associated with mortality among COVID-19 positive STEMI patients. The factors associated with mortality among COVID-19 positive STEMI patients, which were significant in the univariate with a predefined cut-off of p-value <0.10, were used to build the multivariable robust poisson regression model. Both unadjusted and adjusted Relative Risks (RR and aRR), along with their 95% Confidence Intervals (CI), were reported. All the statistical analyses were carried out using SPSS version 19.

3. Results

A total of 410 COVID-19 confirmed STEMI cases (COVID-19 +) were retrospectively enrolled from twenty seven tertiary care hospitals in India with 799 age and sex-matched COVID-19 negative STEMI control cases. Of the COVID-19 positive STEMI patients 49.3% came with a positive report on admission itself, and the others were found to be COVID-19 positive during the hospital stay. A large proportion of STEMI patients (57.0%) with COVID-19 infection had no COVID-19 related symptoms.

Baseline characteristics of the patients are presented in Table 1. The median age of the participants and the proportion of women was comparable in both the groups. Hypertension and Diabetes were equally present in both groups, while smoking was more prevalent among the patients in the control group. There was no difference between the two groups with respect to previous history of PCI/CAG/CABG/CVA. There was no significant difference in the proportion of patients with low EF (<40%). Abnormal findings and lung consolidation in the Chest X-ray and abnormal CT scan were more frequent in the active group.

Table 2 shows the initial reperfusion strategy and angiographic characteristics of COVID-19 positive and negative patients with STEMI. COVID-19 negative STEMI patients were more likely to undergo primary PTCA (23.4% vs 15.4% p-value = 0.001) as compared to COVID-19 positive STEMI patients. Among the active group, 5 patients underwent delayed PCI and 3 patients rescue PCI whereas, in control group only one patient underwent rescue PCI and seven underwent delayed PCI. There was no difference in the rate of thrombolytic therapy in the two groups. A larger proportion of COVID-19 positive patients did not receive any kind of reperfusion therapy (thrombolysis or primary PTCA) (39.3% vs. 28.9%). Systematic early PCI (pharmaco-invasive strategy) was performed only in a very small proportion of COVID-19 positive STEMI patients compared to COVID-19 negative patients (1.2% vs 14.3% p=< 0.001). The number of vessels involved and the thrombus burden was similar in both the groups. However, thrombus aspiration was more frequently done in the active cases (44.0% vs. 31.5% p-value 0.04).

Table 1
Baseline demographics, risk factor profile, clinical presentation and details of COVID test done of STEMI patients in the active (COVID-19 positive) and control group (COVID-19 negative). Values are n (%) or median (Q_1,Q_3).

Characteristics	COVID-19 positive STEMI (n = 410)	Control(n = 799)	P-value
Age Group			
<60 years	242(59.0)	474(59.3)	0.92
≥60 years	168(41.0)	325(40.7)	
Age median (years)	56(49,65)	56(48,65)	0.73
Sex			
Male (%)	330(80.5)	651(81.5)	0.68
Medical History			
Hypertension (%)	146/400(36.5)	287/769(37.3)	0.78
Diabetes	164/400(41.0)	277/769(36.0)	0.10
Smoking	119/400 (29.8)	283/769(36.8)	0.02
Previous PCI/CAG	25/380(6.6)	29/739(3.9)	0.05
Previous CABG	4/380(1.1)	4/739(0.5)	0.46[a]
History of CVA	11/380(2.9)	11/739(1.5)	0.11
History of CKD	8/369(2.2)	9/732(1.2)	0.23
History of COPD	16/369(4.3)	39/732(5.3)	0.48
Type of COVID Test			
rt PCR/TRUENAT/CBNAAT	346(84.4)	610(76.3)	0.001
Rapid Antigen Test	64(15.6)	189(23.7)	
Clinical Presentation			
SBP on Admission	120(110,130)	120(110,132)	0.73
Heart Rate on admission	82(72,93.25)	80(72,90)	0.06
LVEF, <40%	162(39.5)	311(38.9)	0.84
Imaging findings			
Abnormal Chest X ray	117/299 (39.1)	15/414 (3.6)	<0.001
Lung consolidation[b]	34/117 (29.1)	0/15(0)	0.02[a]
Abnormal CT	63/85 (74.1)	12/95 (12.6)	<0.001

[a] Fisher's exact test; denominators are provided for those variables having missing data.
[b] Denominator is those patients having abnormal Chest X ray.

Table 2
Initial reperfusion strategy and angiographic characteristics of COVID-19 positive and negative patients with STEMI. Values are n (%) or median (Q_1,Q_3).

Parameter	COVID-19 positive STEMI (Active) N 410	COVID-19 negative STEMI (Control) N 799	p-value
No Reperfusion Treatment	161(39.3)	231(28.9)	<0.001
Thrombolysis	186 (45.4)	381(47.7)	0.44
Primary PCI	63(15.4)	187(23.4)	0.001
Systematic early PCI	5(1.2)	114(14.3)	<0.001
ER to Wire Time	75(59,103) n = 58	60(40,75) n = 166	0.001
LAD as culprit artery[a]	47/76 (61.8)	172/309 (55.7)	0.33
Multi vessel disease[a]	27/76 (35.5)	136/309 (44.0)	0.18
High Thrombus Burden (TIMI Grade 4/5[a]	11/76(14.5)	37/309(12.0)	0.55
DES use[a]	74/76 (97.4)	306/309(99.0)	0.26[b]
Thrombus aspiration[a]	33/75 (44.0)	97/308 (31.5)	0.04
TIMI 3 flow[a]	58/76 (76.3)	288/308 (93.5)	<0.001

[a] Denominator consist of subjects undergone Primary PCI, Systematic early PCI, delayed PCI and rescue PCI.
[b] Fisher's exact test; denominators are provided for those variables having missing data.

TIMI 3 flow after angioplasty was achieved in a larger number of patients in the control arm compared to COVID-19 positive arm.

Table 3 shows in-hospital medical treatment and outcomes in the two groups of patients with STEMI. The frequency of use of aspirin and heparins was comparable in both groups but beta-blockers, angiotensin converting enzyme inhibitors (ACE-I)/angiotensin receptor blockers (ARB)/, angiotensin receptor blocker neprilysin inhibitor (ARNI), prasugrel, and ticagrelor were more commonly used in the control group.

The in-hospital outcome of death/re-infarction/stroke/heart failure was significantly higher among the COVID-19 positive STEMI patients. There was non-significant trend towards higher mortality in the COVID-19 positive group. Reinfarction was significantly higher and there was a trend towards higher heart failure in COVID-19 positive STEMI compared to COVID-19 negative controls. There were no differences between the groups regarding other complications like systemic embolization, cardiogenic shock, acute MR, mechanical complications, stroke or major bleeding.

Table 4 shows the determinants of in-hospital mortality in COVID-19 positive STEMI patients. In univariate analysis, in-hospital mortality was significantly higher in the elderly (12.5% vs 5.0% p value = 0.01), those who were COVID-19 positive on admission (12.9% vs 3.4% p value = 0.001), patients with COVID-19 related symptoms on admission (14.2% vs 3.4% p value < 0.001), patients with abnormal chest x ray findings (20.5% vs 0.5% p value < 0.001) and those with achieved TIMI flow less than grade 3 (27.8% vs 3.4% p value = 0.01). When adjusted for confounding variables, risk for mortality was found to be significantly higher for the elderly, those who were COVID-19 positive on admission and those with abnormal chest X ray (Fig. 1).

4. Discussion

Our study showed that the primary composite outcome of death, MI, heart failure and stroke occurred in significantly larger number of COVID-19 infected STEMI patients than COVID-19

Table 3
In-hospital medical treatment and outcomes. Values are n (%) or median (Q_1,Q_3).

Parameter	Active group (N = 410)	Control group (N = 799)	P value
Length of hospital stay (days)	5(3,8)	5(4,6)	0.29
In-hospital medical treatment			
Aspirin	379 (92.4)	745 (93.2)	0.61
Clopidogrel/Ticagrelor/Prasugrel	390 (95.1)	770(96.4)	0.30
Heparin/LMH/Fondaparinux	353(86.1)	671(84.0)	0.33
NOAC/VKA	18 (4.4)	17 (2.1)	0.03
ACE/ARB/ARNI	261(63.7)	583(73.0)	0.001
Betablockers	260(63.4)	554(69.3)	0.04
In-hospital outcomes			
Death	33 (8.0)	46 (5.8)	0.13
Re infarction	12(2.9)	10(1.3)	0.04
Stroke	2(0.5)	1(0.1)	0.27[a]
Heart failure	77(18.8)	119(14.9)	0.08
Cardiogenic shock	38(9.3)	69(8.6)	0.71
Acute MR	17(4.1)	23(2.9)	0.24
Systemic embolization	1(0.2)	0(0)	0.34[a]
Major bleeding	11/406 (2.7)	15/782 (1.9)	0.38
Death/Re-infarction/Stroke/HF	111(27.1)	165(20.7)	0.01

[a] Fisher's exact test; denominators are provided for those variables having missing data.

Table 4
Determinants of In-hospital mortality in COVID-19 positive STEMI patients.

Variables		Mortality n (%)		Unadjusted RR (95% CI)	P-value	Adjusted RR (95% CI)	P-value
		Yes 33 (8.0)	No 377(92.0)				
Age categories	≥60 years	21(12.5)	147(87.5)	2.52(1.28,4.98) ref	0.01	2.14(0.99,4.62) ref	0.05
	<60 years	12(5.0)	230(95.0)				
Diabetes	Yes	16(9.8)	148(90.2)	1.44(0.74,2.79) ref	0.28		
	No	16(6.8)	220(93.2)				
COVID-19 positivity	On admission	26(12.9)	176(87.1)	3.83(1.70,8.61) ref	0.001	2.91(1.18,7.22) ref	0.02
	During hospitalization	7(3.4)	201(96.6)				
COVID-19 related symptoms	Yes	25(14.2)	151(85.8)	4.14(1.91,8.95) ref	<0.001	2.06(0.79,5.33) ref	0.14
	No	8(3.4)	225(96.6)				
Chest X ray	Abnormal	24(20.5)	93(79.5)	37.33(5.12,272.26) ref	<0.001	22.66(2.78,184.5) ref	0.004
	Normal	1(0.5)	181(99.5)				
Reperfusion	Thrombolysis	18(9.7)	168(90.3)	1.73(0.80,3.75) ref	0.16		
	Primary PCI	6(9.5)	57(90.5)				
Thrombus Burden[a]	TIMI Grade 4–5	3(27.3)	8(72.7)	4.43(1.15,17.16) ref	0.03		
	TIMI Grade 0/1/2/3	4(6.2)	61(93.8)				
TIMI Flow[a]	2–3 vessel	2 (3.4)	56(96.6)	0.12 (0.03, 0.58) ref	0.01		
	1 vessel	5 (27.8)	13(72.2)				
CAG	2–3 vessel	2(7.4)	25(92.6)	0.73(0.15,3.49) ref	0.69		
	1 Vessel	5(10.2)	44(89.8)				

[a] There were not enough cases in each category of Thrombus Burden and TIMI Flow variables to be included in the final model.

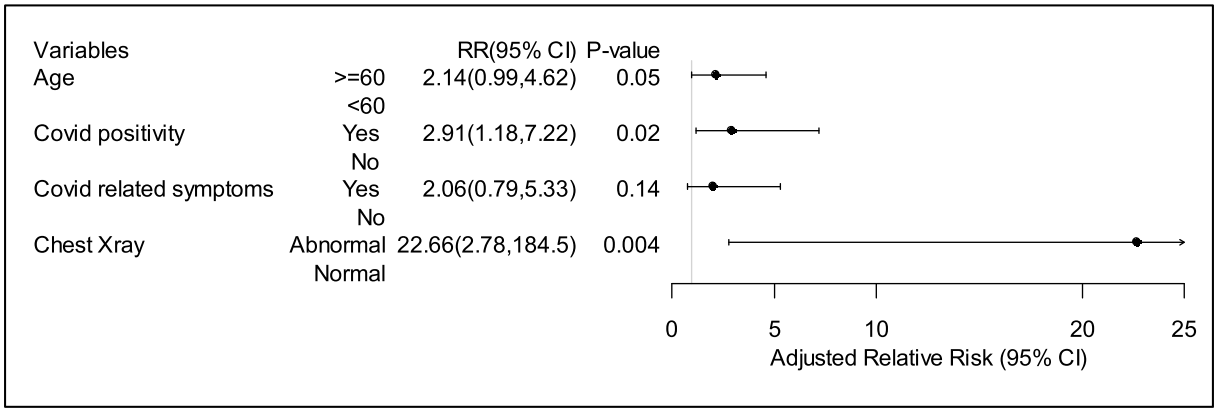

Fig. 1. Plot of adjusted Relative Risk (aRR) and 95% confidence intervals(CI) for factors associated with mortality obtained from multivariable Robust Poisson regression.

negative STEMI controls. However, individual components of the primary composite endpoint other than MI did not show significant differences between the two groups. It is difficult to compare our results with other similar studies because the primary endpoint was different for the various studies. The primary end-point of NACMI registry, a composite of in-hospital death, stroke, recurrent

MI, and repeat unplanned revascularization occurred in 36% of COVID-19 positive STEMI patients compared with 5% in the control group. This was mainly driven by 33% in-hospital mortality. In our study, there was a trend towards higher in-hospital mortality in the COVID-19 positive STEMI patients. Most of the studies have reported a very high in-hospital mortality (12%–34%) among COVID-19 positive STEMI patients[1-3, 7-12] . One possible explanation for the relatively lower in-hospital mortality in our study is the younger age of our study population (mean age 57 years), 8–10 years lower than patients in the above studies. Another factor is the severity of the COVID-19 infection. Many deaths in these patients could be due to COVID-19 related complications rather than the severity of STEMI. In the ISACS-STEMI COVID-19 registry 55.6% of deaths were related to COVID-19.[2] In the study by Rodrigues et al non-cardiovascular mortality was nearly half of the total in-hospital mortality. Unfortunately most studies including ours did not distinguish between cardiovascular and non-cardiovascular deaths. In the NACMI registry which reported one of the highest mortality rates for COVID-19 positive STEMI patients (33%), there was no difference in the LVEF between COVID-19 positive and negative patients and most likely, the excess deaths were attributable to COVID-19 rather than STEMI. Mean number of COVID-19 positive STEMI cases per site in the NACMI registry during the nearly one year period of the study was 4.1 and it was possible that patients had more severe COVID-19 infection. The most recent report from the NACMI registry noted that significant changes occurred in the outcomes during the course of the pandemic and mortality decreased by 25% in 2021 compared to 2020.[13] Mortality was zero for vaccinated patients with STEMI suggesting that the excess mortality was due to severity of COVID-19 infection. In our study, patients with COVID-19 related symptoms and abnormal chest X-ray had higher mortality compared to those without (14.2% vs. 3.4% p value < 0.001 and 20.5% vs. 0.5% p value < 0.001 respectively). Patients who were COVID-19 positive on admission had higher mortality rate compared with those who turned positive for COVID-19 during hospital stay.

When out of hospital STEMI (patients admitted with STEMI and found to be COVID-19 positive) and in-hospital STEMI (patients admitted in the hospital for COVID-19 infection and developed STEMI), were compared, mortality was grossly different as shown in the study by Saad et al (15.2% vs 76.6%).[12] Hence total mortality in COVID-19 positive STEMI will depend on the proportion of the patients with in-hospital STEMI which however is not reported in most studies including ours.

Many large studies, used data of patients treated during the pre-COVID-19 era as control. However, in many parts of Europe and USA, acute MI admissions came down during COVID-19 era because of fear of getting infection from the hospital and this resulted in excess in-hospital mortality during the COVID-19 era. In the report by Rosa et al from Italy, the STEMI in-hospital mortality rate during the pandemic substantially increased to 13.7% compared with the 4.1% in 2019.[14] In a previous study, we had shown that AMI admissions during the initial period of the COVID-19 pandemic came down in India, similar to many other parts of the world, but picked up when lockdown was relaxed.[15] Present study was undertaken in patients with STEMI admitted after June 2020, a period when patients did not hesitate to approach hospitals for symptoms of AMI in India, which could have contributed to the lower in-hospital mortality.

4.1. Reperfusion strategy for STEMI

We found that only 15.4% of COVID-19 positive STEMI patients received primary PCI compared with 23.4% of COVID-19 negative STEMI patients. We had already reported that the rate of primary PCI during COVID-19 pandemic in India was 30.4% which was not significantly different from the rate noted during the pre-pandemic period (2019).[15] The decrease in rate of primary PCI among COVID-19 positive STEMI patients reflected the strategy adopted by most hospitals in India during the study period for the management of COVID-19 positive STEMI patients. The low rates of reperfusion including primary PCI in COVID-19 positive STEMI patients could be one of the reasons for the worse outcomes in these patients noted in our study. No reperfusion treatment was provided to a sizable proportion of COVID-19 positive STEMI patients compared to COVID-19 negative STEMI patients probably because of late presentation, details of which were not captured in our study. In contrast, reports from the developed world indicate that most centres followed an aggressive approach during the pandemic, adopting primary PCI for both COVID-19 positive and COVID-19 negative patients.[12] We expected higher rates of pharmaco-invasive strategy in COVID-19 positive cases considering the logistic issues during the pandemic. However, unexpectedly this was not the case. One possible explanation is that during COVID-era, the reperfusion strategy varied considerably across the hosptials and despite the guidelines, the hospitals were following different strategies. The findings only reflect the policy adopted by the participating hospitals in the present study.

4.2. Time windows

Being a retrospective study, we were not able to record symptom onset to door time in our patients. However, the ER to wire time in those who underwent primary PCI was significantly prolonged in COVID-19 positive cases compared with COVID-19 negative cases (75 min vs 60 min respectively). Most studies reported a similar pattern with prolonged door to balloon time in COVID-19 positive STEMI cases undergoing primary PCI[3,10] . This also reiterates the world wide experience of prolonged door to wire time in COVID-19 positive STEMI cases due to logistic issues.

4.3. Thrombus burden and need for thrombus aspiration

We didn't find significantly higher thrombus burden in COVID-19 positive STEMI patients compared with COVID-19 negative patients. However, there was significantly higher requirement for thrombus aspiration in COVID-19 positive cases. These findings have to be interpreted cautiously because only fewer patients underwent primary PCI in our series (15.4% and 23.4% in COVID-19 positive and negative STEMI patients respectively). The NACMI registry did not report thrombus burden and the need for thrombus aspiration. In the international prospective registry of COVID-19 co-infected patients with ACS, high grade thrombus (TIMI grade 5) was observed in 5% of the patients with STEMI and COVID-19 infection (prevalence of high thrombus burden was not reported in the control group) but no patient underwent thrombus aspiration. In the ISACS-STEMI COVID-19 registry, more COVID-19 positive STEMI patients received thrombectomy and were treated with glycoprotein (GP) 11 b-111a antagonists compared to COVID-19 negative controls (37.1% vs 20.6%, p value = 0.05 and 33.9% vs 22.9%, p value = 0.07 respectively) suggesting higher thrombus burden even though they did not report thrombus TIMI grade. The study also noted higher in-hospital definite in-stent thrombosis (8.1% vs 1.6%, p value = 0.0001). High rate of stent thrombosis was also reported by Hamadeh el (21% of 19 patients treated with primary PCI). In the study by Rodriguez-Leor et al, 91 STEMI patients positive for COVID-19, compared with 919 STEMI patients negative for COVID-19, were found to require more frequent mechanical thrombectomy (44% vs 33.5%, p value = 0.046), higher rate of use of GP 11 b/111a inhibitors (20.9% vs 11.2%, p value = 0.007) and higher rate of stent

thrombosis (3.3% vs 0.8%, p value = 0.020). Little CD, et al, also noted higher use of GP 11 b/111a inhibitors (56.5% vs 38.7% p value = 0.022) and aspiration thrombectomy (30.4% vs. 17.9%, p value = 0.046) in COVID-19 positive cases compared with COVID-19 negative cases.[16] These reports including ours suggest the possibility that there is higher thrombus load in COVID-19 positive STEMI patients. However, the studies vary considerably as to the number of COVID-19 positive cases included, nature of the comparator group, reporting of GP11b-111a inhibitors use, requirement of thrombus aspiration, and thrombus grading and firm conclusions cannot be drawn on this aspect.

Nonobstructive coronary artery disease: We did not find any case of STEMI without clear culprit lesion or MI with normal coronary arteries (MINOCA) probably because only confirmed STEMI cases were included and only a smaller proportion of the patients underwent coronary angiography. In the NACMI registry, 23% of patients with STEMI with COVID-19 co-infection had no culprit artery involved, compared to 1% in the control group. The study by Kite et al found that 18.2% of the patients had non obstructive CAD (comparative figures for patients in the control group were not available). In the study from India, Pandit et al found that among those who underwent coronary angiography, 12% of patients with COVID-19 co-infection had non obstructive coronary artery disease compared 1.1% in those without COVID-19 infection. However, in the observational cohort study using multisource data from all acute NHS hospitals in England, out of 517 (4%) COVID-19 positive ACS patients, only 1.7% had angiographically normal coronaries, compared to 4.8% among the 12441 patients with COVID-19 negative ACS. It appears that there is no clear pattern of higher frequency of nonobstructive coronary artery disease in COVID-19 positive STEMI cases when care is taken to exclude cases of COVID-19 myocarditis and stress cardiomyopathy.

4.4. Does COVID-19 positive STEMI behave differently?

It has been argued that COVID-19 positive STEMI is a different disease altogether, with high rate of nonobstructive CAD, high rate of thrombus burden requiring thrombus aspiration and high rate of in-stent thrombosis causing very high in-hospital mortality.[17] However as discussed above, prevalence of nonobstructive CAD, high thrombus burden, need for thrombus aspiration, and use of GP 11 b/111a inhibitors have varied considerably in the various studies and it is difficult to draw firm conclusions. It seems likely that the increased risk of in-hospital mortality of COVID-19 co-infected STEMI is related to the mortality directly associated with COVID-19 and the inability to provide appropriate STEMI management to all patients with COVID-19.[18]

4.5. Heart failure, stroke and re-infarction

We found higher rate of re-infarction and a trend towards higher frequency of heart failure, though there were no differences in the occurrence of stroke in COVID-19 positive STEMI patients compared with COVID-19 negative STEMI cases. Overall, the studies showed no consistent pattern regarding the frequency of heart failure, stroke and re-infarction.[1](3)[2](12).

4.6. Limitations

The retrospective observational study design has its own inherent limitations which is applicable to our study also. It is possible that some patients who died quite early after admission were not included in the study which can influence the mortality rate. We randomly checked the case records, but may have missed these omissions due limitations of EMR/case chart review during the COVID-19 pandemic period due to logistic issues in many participating hospitals. Some COVID-19 positive patients may have got transferred to COVID exclusive care centres and managed by a different multidisciplinary team and the site investigator may have failed to enrol these patients. All the participating centres were tertiary care hospitals and our results might not represent the true picture of countrywide COVID-19 positive STEMI management and outcomes.

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