Original article

Pattern of Admission, Management and In hospital Outcome of ACS Patients during COVID-19 pandemic - A study in Tertiary Care hospital

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Abstract:

Aim: This study aimed to evaluate the impact of coronavirus disease2019(Covid-19) outbreak on admissions for acute coronary syndrome (ACS) and related mortality, severity of presentation, major cardiac complications, and outcome in tertiary care hospital (NICVD).

Method: This is a cross sectional observational study on ACS admitted patients during the 1st and 2nd phase of COVID-19 from 1st June to 31st August in the year 2020 and 2021 who were COVID negative (RT PCR). Using a control of ACS admitted patients during corresponding period of year 2019 from registry.

Results: During the 1st phase of COVID (July to August 2020) 736 ACS patients were enrolled where as during 2nd phase (July to August 2021) 722 ACS patients were enrolled. Mean age were 52±8 vs 53±11 years. Demographic variables such as age, sex and risk factors are almost identical in all groups. Our study showed 46% decline in admission in ACS patients comparing same period of 2019. Though some inclination in 2021 still it showed 13% decline in ACS patient admission in comparison to 2019. There was substantial increase in percentage of patient suffering from STEMI in 2020(42% vs66% vs46%). Short time in hospital complications were more pronounced in 2020. During the study period average death rate was higher than the year 2019 (8.6% vs 5.8%). There was significant decline in numbers of interventions(CAG and PCI) for CAD during first phase of Covid which raised during second phase(429 vs 2151). Total number of interventions done of 1884 patients in 2019 whereas 2151 patients were undergone in the year 2021.

Conclusion: The Covid-19 outbreak affects hospital admission for acute coronary syndrome. During the first phase of the pandemic, significantly less patients with ACS admitted, but those admitted presented with a higher mortality, more complications and a worse short time outcome. Therefore ,our data indicate that Covid-19 had relevant impact on non-infectious disease status, such as acute coronary syndrome.

Key Word: *ACS, COVID-19, Admission pattern.*

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Introduction:

The coronavirus disease 2019 (Covid 19) pandemic has a significant impact on the health care systems with an enormous socio economic burden worldwide.[1] Since December 2019, the novel severe acute respiratory

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syndrome coronavirus 2 (SARS CoV 2) has spread around the globe starting from Wuhan, China.[2] The World Health Organization (WHO) confirmed mid of August 2020 that there are >5 million people infected with SARS CoV 2 and over 340 000 deaths worldwide.[4] Because of the exponential growth of infections in the early phase of the pandemic, hospitals from countries all over the world including China, the USA, Spain, and Italy were struggling to cope with Covid 19 patients.[3] In many places, there was a lack of intensive care unit resources including mechanical ventilators, personal protective equipment supplies, and medical staff.[4] As a result of the experience from these Covid 19 hotspots, many countries decreed a lockdown of public life with the goal of social distancing to control the expansion of the virus. [5] Many countries have reported a significant decline in the hospitalization rates for acute myocardial infarction (AMI) during the time of COVID-19 pandemic with average rate of decline ranging from 13 to 48%. [6]

Bangladesh is one of the affected countries in the world by COVID-19 pandemic with more than 1.95 million cases. The Government of Bangladesh implemented strict nationwide lockdown in phases starting from 25th March 2020 to limit the spread of the pandemic. The government directed different hospitals to focus on COVID-19 crisis. This approach may have resulted in unintended compromises in acute cardiac care across the country. The impact of COVID-19 on AMI admissions in low- and middle-income countries including Bangladesh is largely unknown. Observational studies from Northern Italy showed a significant decline in the number of ACS cases presenting to hospitals. The incidence rate ratio decreased by 30% as compared to the previous year and the decrease was seen in all forms of ACS admissions including STEMI, NSTEMI and unstable angina. [7] Recent studies from Europe, the USA, Asia, and New Zealand have not only shown a decrease in hospital admissions for AMI, but also an increase in time to medical contact, decrease in interventions, and increase in out of hospital cardiac arrest during the pandemic period. [8]

Possible Mechanisms Linking COVID-19 To AMI:

Several mechanisms associated with COVID-19 may be involved in AMI. Type 1 AMI can be triggered in patients with COVID-19 by a pro-inflammatory state, which may promote destabilization of a coronary atherosclerotic plaque, a phenomenon already observed during influenza outbreaks. [9] Notably, viral infections have been shown to activate inflammatory cells of the coronary plaque and to upregulate metalloproteinases and peptidases, which, in turn, may disrupt plaque cap exposing the highly thrombogenic core to the blood [10] Another potential mechanism is the mismatch between reduced oxygen supply and increased myocardial oxygen demand due to sympathetic system activation, tachycardia, hypotension, and hypoxemia in the setting of acute respiratory insufficiency, which may be responsible for Type 2 AMI [11] Moreover, other mechanisms related to specific features of SARS-CoV-2 infection have been advocated to explain AMI in patients with COVID-19. In particular, the endothelial and microvascular injuries induced by SARS-CoV-2 may further enhance inflammation, resulting in coronary vasospasm, thrombosis, and myocardial perfusion defects. [12]Moreover, the low platelet count often described in patients with COVID-19 suggests an increased consumption due to great platelet activation and thrombus formation. Indeed, the cytokine storm associated with viral infection induces, together with the imbalance of endothelial function, significant activation of platelets, granulocytes, and microvesicles, which, in turn, produce tissue factors. Of note, it has also been demonstrated that plasma microvesicles-associated thrombin generation can still be present in patients with COVID-19 despite prophylactic anticoagulation. [13]

Another possible mechanism implicated in the association between SARS-CoV-2 and AMI is the pro-inflammatory state. Since the association between infection and acute coronary atherothrombosis has been established for a variety of pathogens and sites of infection, it is likely that the causal agent and the host response could have a crucial role in eliciting an inflammatory pattern that may trigger AMI. Atherosclerotic plaques contain inflammatory cells that proliferate, secrete cytokines, and stimulate smooth muscle cells to form a fibrous cap. Thus, an inflammatory status generates circulating cytokines that may activate inflammatory cells in atherosclerotic plaques, enhancing plaque vulnerability and the possibility of its rupture, leading to coronary thrombosis[14]. Of note, there are multiple reports of microvascular involvement in different organs of patients with COVID-19, leading to ischemic stroke, deep vein thrombosis, pulmonary embolism, and arterial thrombotic events. [14] The COVID-19 has more far-reaching cardiovascular implications than the pathophysiological effects of the disease per se. In fact, all countries have developed containment strategies based on social distancing, and it is well-known that the lack of human relationships and reduced interaction with other people are major risk factors for cardiovascular mortality. A previous meta-analysis includes 181,000 subjects demonstrated that the risk for AMI increases by almost 30% in lonely and socially isolated people. [15] The adult cohort studies reported initial evidence of a clinically meaningful increase in anxiety, depression, mental health disturbance, and disruption of well-being during the lockdown for SARS-CoV-2 spread containment, all of which have been associated with an increased AMI risk. [16]

Results:

During the 1st phase of Covid (July to August 2020) among 9693 admitted patients in NICVD 736 patients were

enrolled who were diagnosed as ACS patients. Similarly, during 2nd phase of Covid (July to August 2021) out of 15547 admitted in NICVD 922 ACS patients were enrolled. Highest patients stood in the age group of 40-60 years (47.6% vs 45.1%). Most of them were male 1458(84%) and female were 287(16%) which were almost similar in both phases. Patients were suffering from multiple comorbidities (Hypertension 50%, Smoking 41%, Diabetes 35%) during 1st phase. Comparing with the 1st phase during 2nd phase 52% ,40% and 37% were hypertensive, diabetic and smoker respectively.

Table-I

Baseline characteristics of patients admitted with Acute Coronary Syndrome (ACS)

characteristics	Year (2019) n=84	Year (2020) n=736	Year (2021) n=922
Age (in year) (mean ± SD)	56 ± 10	52 ± 8	53 ± 11
Male	707(84%)	618(84%)	747(81%)
Female	137(16%)	118(16%)	175(19%)
Diabetes	320(38%)	258(35%)	341(37%)
Hypertension	370(44%)	368(50%)	479(52%)
Dyslipidemia	320(38%)	302(41%)	369(40%)
Smoking	101(12%)	103(14%)	138(15%)

During both phases almost all patients presented with chest pain. Duration of chest pain less than 12 hours (56% vs 71%). Patients more than 12 hours were (44% vs 29%) while comparing in both groups. Raise of Troponinl >.1 ng/dl were 71% vs 69% whereas Troponinl <.1 ng/dl were 29% vs 31%. Among the enrolled patients during the 1st phase 66% were diagnosed as STEMI, 23% as NSTEMI and 11% as Unstable Angina. Whereas during 2nd phase 46% were diagnosed as STEMI, 29% as NSTEMI and 25% as unstable angina.

Table-II

Comparison of ACS admission during same time frame

	Year (2019)	Year (2020)	Year (2021)	P-value
STEMI	354(42%)	486(66%)	424(46%)	0.61
NSTEMI	278(33%)	169(23%)	267(29%)	0.43
Unstable Again	211(25%)	81(11%)	231(25%)	0.35

Regarding getting thrombolytics in STEMI significant difference in number of patients (70%vs 56%). All patients with NSTEMI, Unstable Angina and STEMI with delayed arrival were heparinized. In hospital complications such as left ventricular failure (38% vs 23%), cardiogenic shock (20% vs 7%), arrhythmia (4% vs 3%), complete heart block (6% vs 4%). Average death rate was higher in 1st phase (8.6% vs 5.8%)

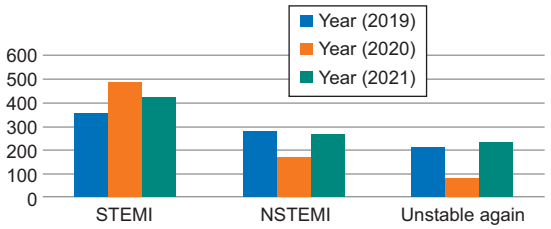

Fig.-1: *Comparison of ACS admission during same time frame*

Table-III

Comparison of outcome between patients admitted in 2019, 2020 and 2021 study period

	Year (2019)	Year (2020)	Year (2021)	P-value
Left ventricular failure	227(27%)	280(38%)	212(23%)	0.05
Cardiogenic shock	101(12%)	147(20%)	65(07%)	0.03
Arrhythmia	42(05%)	29(04%)	28(03%)	0.01
Complete heart block	59(07%)	44(06%)	37(04%)	0.08
Mortality	45(5.4%)	63(8.6%)	53(5.8%)	0.04

There was significant decline in numbers of interventions (CAG and PCI) for CAD during first phase of Covid which raised during second phase (429 vs 2151). Total number of interventions done of 1884 patients on 2019 whereas 2151 patients were undergone in the year 2021.

Table-IV

Comparison between cardiac intervention of ACS done on 2019, 2020 and 2021

	Year (2019)	Year (2020)	Year (2021)
CAG	1335	301	1495
PCI	509	128	656
Total	1844	429	2151

Comparing with the same duration in 2019 total number of admitted patients were 18067 which revealed 46% declined in admission during 1st phase and 13% declined in 2nd phase of Covid.

Table-V

Previous studies reporting about the deadline in ACS/MI admissions during covid-19 pandemic

Authors	Country	No of centres	No of patients	% Decline	Study duration (weeks)
Braiteh et al	USA	4	180	41% (ACS)	8
Metzler et al	Austria	19	725	39% (ACS)	4
Rodriguez et al	Spain	81	260	40% (PCI for STEMI)	1
Secco GG et al	Italy	3	84	52% (ACS)	4
Rattka M et al	Germany	1	52	25% (AMI)	4
Tsioufis K et al	Greece	1	39	P value - <0.001	8
De Rosa S et al	Italy	54	319	48% (AMI)	1
Filippo O D et al	Italy	15	547	50% (ACS)	6
Tam C Fet al	Hong Kong	1	7	STEMI	2
Garcia et al	USA	9	138	38% (STEMI activations)	12

Numbers not available

Discussion:

Though there were multiple reports from various countries about the decline in ACS admission during Covid-19 pandemic,[17] (table V) this is the first report from Bangladesh addressing this issue.

The Italian society of Cardiology multicenter register, which compared acute MI incidence in a week with the equivalent period in 2019, observed a drastic reduction of 48.4% (p< 0.001) and complications (RR = 1.8; 1.1–2.8; p = 0.009) during the pandemic, compared to 2019. [18] Then, Metzler et al. conducted an Austrian nationwide retrospective survey involving 17 primary PCI centers for 27 days during COVID-19 outbreak, founding a relative reduction from the beginning to the end of this period of 39.4% in admission for all subtypes of ACS. [19] Interestingly, the decline in hospital admissions for STEMI was seen in all geographic areas of the United States, irrespective of COVID-19 incidence, implementation of lockdown, and level of SARS-CoV2 testing.[20] Later on, nationwide analysis of acute coronary syndrome admissions conducted in other geographical areas that had lockdown restrictions, such as England, France, Greece, and California showed the same concerning trend. Finally, Mohammad et al. [21] recorded a nationwide significant decline in AMI presentation during the COVID-19 pandemic as compared to the corresponding period of previous years (2015–2019) also in Sweden.

During the study period in 2020 ,9693 patients were admitted (age58±12 years) which is 46% decline in admission compared to same period in previous year. On the other hand, during second phase of Covid in 2021 declined in admission was 13% comparing to year 2019. Several hypotheses has been postulated to explain this decline in admission for cardiac emergencies. NICVD is a tertiary care hospital and it is not only center of treatment of heart disease of capital city but lots of patients are referred from different divisions of Bangladesh. As Dhaka was the mostly infected zone of Covid, patients from different zones were fear of getting in contact Covid-19 infected patients for seeking acute medical care. Due to lockdown scarcity of transport also played a key role. Significant decrease in air pollution and less job stress were implicated for the decrease in ACS admissions. On the other hand, comparing to 1st phase during the 2nd phase some inclination in the admission rate was due to improvement of knowledge about Covid, its complications and management. Moreover, though increase in infection rate, there was some relaxation of lockdown during 2nd phase.

There was no significant difference between the baseline characteristics of patients admitted in 2019 and 2020 (Table I). Highest patients stood in the age group of 40-60 years (47.6% vs 45.1%). Most of them were male 618 (84%) and female were 287(16%) which were almost similar in both phases. Patients were suffering from multiple comorbidities (Hypertension 50%, Smoking 41%, Diabetes 35%) during 1st phase. Comparing with the 1st phase 52%, 40% and 37% were hypertensive, diabetic and smoker respectively. Clinical observations made in England about the characteristics of patients with AMI during the pandemic lockdown showed that they were younger, less frequently diabetics, and less likely to have a history of prior cerebrovascular disease, as compared to those admitted during the previous year. [22] On the other hand, a Swedish registry reported no difference (both at a nationwide level and in Stockholm) in age, gender, and comorbidities in patients with AMI

during the pandemic. [21]In line with the Swedish observation, both a French registry by Mesnier et al. [23] and a single-center German study by Primessnig et al. [24] showed that age, gender, and prevalence of risk factors did not differ between the pre-pandemic and pandemic period in patients with AMI.

An observation common to studies was that during the pandemic a higher percentage of patients were admitted with STEMI as compared to NSTEMI.A large database of 99 English hospitals showed that, on average, hospitalization for NSTEMI was reduced by 50% and by 25% for STEMI. [25] Likewise, a multicenter observational survey examining 319 consecutive patients with AMI in the week with the highest peak of COVID-19 spread in Italy reported a decrease in hospital admission by 27% for STEMI and by 65% for NSTEMI. [26] Among the enrolled patients during the 1st phase 66% were diagnosed as STEMI,23% as NSTEMI and 11% as Unstable Angina. Whereas during 2nd phase 46% were diagnosed as STEMI,29% as NSTEMI and 25% as unstable angina. The greater reduction in NSTEMI admissions might have several explanations. There is the chance that patients with NSTEMI did not seek medical help because their symptoms were less severe precordial pain or chest discomfort, thus increasing their reluctance to expose themselves to the in-hospital risk of COVID-19 infection. In addition, an association between increasing age and pre-existing comorbidities and a poorer outcome following COVID-19 infection was largely emphasized by the media at the start of the pandemic, affecting the choice of some patients with NSTEMI to remain at home, since they considered themselves at high risk in case of infection due of their older age and concomitant illnesses.

During both phases almost all patients presented with chest pain. In STEMI patients, duration of chest pain less than 12 hours (56% vs 71%). Patients with chest pain more than 12 hours were (44% vs 29%) while comparing both groups. Time from symptom onset to first medical contact was substantially delayed in STEMI and NSTEMI patients during e COV compared with pre COV. Forty three per cent of STEMI patients presented within the first 12 h from symptom onset to first medical contact in the pre COV time, while only 23% of STEMI patients did that in the e COV period. However, in pre COV, only 6% of STEMI patients presented after 72 h, while in e COV, 27% did, which was an increase of 21% (p = 0.04). In NSTEMI patients, 33% presented within the first 12 h to the hospital in pre COV, while only 16% of them did in e COV. Indeed, 28% of NSTEMI patients presented after 72 h during e COV compared with only 6% in pre COV, which was again an increase of >20%[28]. This delay in symptom onset to first medical contact may due to patient·s reluctance to come to hospital for medical care, fear of getting infected with COVID and scarcity of transport in lockdown. Raise of Troponinl >.1 ng/dl were 71% vs 69% where Troponinl <.1 ng/dl were 29% vs 31%. Regarding getting thrombolytics in STEMI significant difference in number of patients (70% vs 56%).

An important observation made during the COVID-19 pandemic was that patients with STEMI had greater enzymatic infarct size, as assessed by the peak of troponin or creatine kinase levels (lower left ventricular ejection fraction [28], higher intracoronary thrombotic burden and, therefore, more frequent in-hospital complications.[29] Indeed, a higher rate of cardiogenic shock, need for inotropic and mechanical hemodynamic support, and an increased incidence of life-threatening ventricular arrhythmias after successful revascularization of the culprit artery were found in patients with AMI admitted during the COVID-19 pandemic, with higher early mortality.[25] In particular, De Rosa et al. [25] found that in-hospital mortality for STEMI increased to 14% during the pandemic as compared to a 4% rate in the same period of 2019. In their work, De Rosa et al. found that major complications (cardiogenic shock, left ventricular failure, life-threatening arrhythmias cardiac rupture, and severe mitral regurgitation) were also increased from 10% of the previous year to 19%). Our study shows, In hospital complications such as left ventricular failure (38% vs 23%), cardiogenic shock (20% vs7%), arrhythmia (4% vs 3%), complete heart block (6% vs 4%). Moreover, a study carried out in London found that not only higher in hospital mortality in patients with STEMI but also a raised length of stay during the peak of the pandemic (1 march to 30 April 2020) compared to those observed during the corresponding 2019 period.[30] In our study average death rate was higher in 1st phase (8.6% vs 5.8%) and it was also higher than the year 2019 (8.6% vs 5.8%). According to Showkathali. R, et al. there was no difference in in-hospital mortality (IHM) between the two-study period of 2020 and 2019 respectively (8.7% vs 6.3%). However, the duration of hospital stay is longer (4.5 vs 4 days) and patients were discharged with more cardiac medications (5.6 ± 1.9 vs 4.6 ± 1.6) compared to last year. [31] The significant delay in hospital presentation of patients with STEMI reported during COVID-19 may have resulted in a higher rate of complications and, consequently, in-hospital mortality. There was significant decline in numbers of interventions for CAD during first phase of Covid which raised during second phase (929

vs 2151). Total number of interventions done of 1844 patients on 2019 whereas 2151 patients were undergone in the year 2021. A single-center study from Hong Kong showed a decrease in the number of primary PCI as well as an increase in the time to first medical contact and time to revascularization. [32] A recent large analysis from 9 high volume centers across the United States of America also suggested a 38% reduction in cardiac catheterization laboratory activations for STEMI during the pandemic period. [33]

Conclusion:

The Covid-19 outbreak affects hospital admission for acute coronary syndromes. During the first phase of the pandemic, significantly less patients with ACS admitted, but those admitted presented with a higher mortality, more complications and a worse short time outcome. Therefore, our data indicate that Covid-19 had relevant impact on non-infectious disease status, such as acute coronary syndrome.

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