

A Hospital-Based Assessment of the Impact of the COVID-19 Pandemic on Gender Disparities in Acute Coronary Syndrome PatternsPramod¹, Aishwerya²¹Assistant Professor, Department of Cardiology, Narayan Medical College and Hospital, Sasaram, Rohtas, Bihar, India²Consultant, Radiologist, Bihar Diagnostics and Imaging, Patna, Bihar, India

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Conflict of interest: Nil

Abstract**Aim:** The aim of the present study was to evaluate the incidence of ACS before and after the onset of the COVID-19 pandemic and analyse differences in gender distribution, and type of presentation.**Material & Methods:** A retrospective, observational study performed in Department of Cardiology. In this study, 2250 consecutive patients were identified. Of these, 1750 patients without ACS were excluded from the analysis. Ultimately, 500 patients were included in this study. Based on these circumstances, we divided our study population into pre- (before the outbreak of COVID-19) and post-pandemic (after the outbreak of COVID-19) groups.**Results:** The median age was 64 years [interquartile range (IQR): 58–78], 75% were men, and 30%, 70%, and 65% had diabetes mellitus, hypertension, and dyslipidemia, respectively. There were no significant differences in gender, body mass index (BMI), past history, chief complaint, Killip classification, blood pressure, or heart rate between the groups. Patients in the post-pandemic group had higher levels of serum creatinine and longer time from an EMS call to hospital arrival than those in the pre-pandemic group. There were no significant differences between the groups in the number of patients with ACS receiving CABG. There were no significant differences in the use of intra-aortic balloon pumping or extra-corporeal membrane oxygenation between the groups. Overall, in-hospital death occurred in 20 patients (4%), including 18 with myocardial infarction (MI), one with bleeding, and one with sepsis. There was no significant difference in the in-hospital mortality between the groups.**Conclusion:** Patients presenting after the onset of the pandemic had elevated cardiac markers, representing higher severity and potentially presenting later in the disease course. The number of total ACS cases and percentage of females presenting to the catheterization lab before the COVID surge almost remained stable. This comparison data provides validity that the drop in ACS case volume and females is more likely due to the pandemic and not due to improvements in overall cardiovascular health metrics. Reasons for this disparity are likely multifaceted and deserve further investigation.**Keywords:** COVID, Myocardial Infarction, Acute Coronary Syndrome, Diagnosis, Sex Differences, Symptoms.This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.**Introduction**

The global coronavirus disease-2019 (COVID-19) pandemic has dramatically affected the health care system. The SARS-CoV-2 virus has largely and rapidly spread across the world, infecting more than 300 million people, with more than 5 million deaths. [1,2] The rapid increase in the number of patients with COVID19 requiring hospitalization and intensive care had made it difficult to accept patients with other diseases that require emergency treatment. Despite the maintenance of services for the management of urgent conditions, such as acute coronary syndromes, several previous reports have clearly shown a reduction in the number of treated acute coronary cases, mainly due to the fear of

contagion that prevents patient presentation to hospitals. [3,4,5] Additionally, the time from symptom onset to treatment has significantly risen, [6,7,8] secondary to the oversaturation of emergency departments, which contributes to explaining the higher mortality among STEMI patients observed in 2020. These results were confirmed by the recent International Study on Acute Coronary Syndromes—ST Elevation.

Ischemic heart disease (IHD) is the world's leading cause of death accounting for an estimated 9 million deaths in 2015. [9,10] Acute coronary syndrome (ACS) is an umbrella term for unstable angina (UA), non-ST-segment–elevation myocardial

infarction (NSTEMI) or ST-segment– elevation myocardial infarction (STEMI) and is a substantial component of IHD. [11]

Acute coronary syndrome (ACS), particularly ST-segment elevation myocardial infarction (STEMI), is an extremely serious disease that requires rapid transportation by the emergency medical system (EMS). Urgent coronary revascularization may be adversely affected by the COVID-19 pandemic, as the time from symptom onset to treatment and management strategies have a significant impact on patient outcomes. Male gender has been associated with a higher risk of COVID-19 infection compared to females, with higher rates of complications and worse outcomes. [12,13] Oppositely, among STEMI patients, females generally display more comorbidities and higher mortality. [14,15] Therefore, the aim of study was to evaluate the incidence of ACS before and after the onset of the COVID-19 pandemic and analyze differences in gender distribution, severity, and type of presentation

Material & Methods

A retrospective, observational study performed in Department of Cardiology, NMCH, Sasaram, Rohtas, Bihar, India. In this study, 2250 consecutive patients were identified. Of these, 1750 patients without ACS were excluded from the analysis. Ultimately, 500 patients were included in this study. Based on these circumstances, we divided our study population into pre- (before the outbreak of COVID-19) and post-pandemic (after the outbreak of COVID-19) groups.

In this study, because patient information was anonymised and de-identified prior to analysis, written informed consent was not obtained from each patient. Nevertheless, we posted a summary of the protocol (with an easily understood description) at each site; the notice clearly informed the patients of their right to refuse enrolment. These procedures for informed consent and enrolment were in accordance with the detailed regulations regarding informed consent described in the guidelines, and this study, including the procedure for enrolment, has been approved by the Ethics Committee of each participating hospital. [15]

Data collection and endpoint:

Individual clinical information was collected using a medical questionnaire. When an EMS team transported, they issued a medical questionnaire that included information on the vital signs, the situation at the onset, chief complaint, and past history and passed it to a cardiologist who received the patient. After treatment, the cardiologist completed the remaining questionnaire items, including treatment details, diagnosis, and in-hospital clinical outcomes. The completed questionnaire was mailed from the hospital. In this study, we extracted information on demographics, medical history, clinical data, clinical course, and the use of therapeutic interventions, such as PCI, surgery, and mechanical circulatory support. The study outcomes included the following: (1) the number of patients admitted by ambulance and diagnosed with ACS, (2) time from an EMS call to hospital arrival, (3) the proportion of patients receiving coronary angiography (CAG) and emergency PCI, and (4) in-hospital mortality. The daily numbers of patients with COVID-19 were obtained.

Statistical Analyses: Continuous variables are presented as mean \pm standard deviation (SD) when normally distributed and as medians and interquartile ranges (IQR) when non-normally distributed. Comparisons of differences between two groups were performed by an unpaired t-test or a Mann–Whitney U test for continuous variables and by a chi-squared test or Fisher’s exact test for dichotomous variables, when appropriate.¹⁵ Kolmogorov–Smirnov test was used to determine whether the distribution was normal or non-normal. For variables, including the number of patients with ACS via the EMS, time from an EMS call to hospital arrival, and the number and proportion of patients with ACS receiving PCI, linear mixed effects modelling was used to determine the longitudinal changes in these variables. A two-sided P value < 0.05 was considered statistically significant. All data were analysed using the Stata MP64 software (version 16; StataCorp, College Station, TX, USA).

Results

Table 1: Baseline patient characteristics

Variable	All patients (N = 500)	Pre pandemic (N = 300)	Post pandemic (N = 200)	P value
Age (years)	64 (58–78)	66 (58–78)	68 (59–79)	0.24
Male, n (%)	375 (75)	225	150	0.38
Body mass index (kg/m ²)	23.6 (22.1–27.2)	23.8 (22.1–26.9)	24.1 (22.1–27.4)	0.29
Medical history				
Diabetes, n (%)	150 (30)	90	60	0.96
Hypertension, n (%)	350 (70)	206	144	0.49
Hyperlipidemia, n (%)	325 (65)	195	130	0.79

Chief complaint				
Chest pain, n (%)	425 (85)	255	170	0.85
Dyspnoea, n (%)	25 (5)	13	12	0.40
Killip classification				0.110
Class I, n (%)	400 (80)	250	150	
Class II, n (%)	50 (10)	26	24	
Class III, n (%)	25 (5)	15	10	
Class IV, n (%)	25 (5)	17	8	
SBP (mmHg)	136 (120–160)	138 (120–160)	140 (119–159)	0.55
HR (beats/min)	74 (60–86)	75 (60–84)	77 (61–89)	0.064
Laboratory findings				
Haemoglobin (g/dL)	14.4 (12.8–15.6)	14.4 (12.6–15.6)	14.4 (12.9–15.6)	0.88
Serum creatinine (mg/dL)	0.85 (0.76–1.08)	0.88 (0.74–1.04)	0.90 (0.79–1.12)	0.025
Maximum CPK (U/L)	846 (160–2567)	759 (134–2320)	1012 (197–2819)	0.075
Maximum CK-MB (U/L)	72.2 (11.0–244.0)	60.0 (11.0–231.7)	83.2 (12.9–268.9)	0.32
ST-segment elevation, n (%)	375 (75)	215	160	0.089
Time from EMS call to hospital (min)	30 (25–37)	29 (25–36)	32 (26–39)	0.007

The median age was 64 years [interquartile range (IQR): 58–78], 75% were men, and 30%, 70%, and 65% had diabetes mellitus, hypertension, and dyslipidemia, respectively. There were no significant differences in gender, body mass index (BMI), past history, chief complaint, Killip

classification, blood pressure, or heart rate between the groups. Patients in the post-pandemic group had higher levels of serum creatinine and longer time from an EMS call to hospital arrival than those in the pre-pandemic group.

Table 2: Angiographic findings and invasive procedures

Variable	All patients (N = 500)	Pre pandemic (N = 300)	Post pandemic (N = 200)	P value
Emergency CAG, n (%)	450 (90)	266	184	0.138
Access site				
Conventional radial approach, n (%)	300 (60)	170	130	0.070
Femoral approach, n (%)	200 (40)	128	72	0.064
Location of culprit lesion				
RCA, n (%)	200 (40)	120	80	0.48
LMT, n (%)	15 (3)	9	6	0.82
LAD, n (%)	225 (45)	129	96	0.64
LCX, n (%)	75 (15)	45	30	0.99
Treatment				
Emergency PCI, n (%)	440 (88)	264	176	0.57
TIMI grade 3 flow post PCI, n (%)	460 (92)	276	184	0.43
Door to balloon time (min)	79 (61–106)	74 (58–102)	85 (65–115)	0.002
Door to balloon time under 90 min, n (%)	325 (65)	205	120	0.076
CABG, n (%)	10 (2)	6	4	0.85
IABP, n (%)	40 (8)	22	18	0.54
ECMO, n (%)	10 (2)	6	4	0.92

Although the absolute number of patients in the post-pandemic period who underwent emergency CAG and PCI decreased, the proportion of patients with ACS receiving CAG and PCI on the day of admission slightly increased compared to that in

the pre-pandemic period. The reduction in admissions by ambulance for AMI and STEMI was accompanied by a slight increase in the proportion of patients admitted to the hospital and receiving PCI on the day of admission. The proportion of

patients with NSTEMI or UAP receiving PCI on the day of admission tended to decrease in response to the COVID-19 pandemic wave. There were no significant differences between the groups in the

number of patients with ACS receiving CABG. There were no significant differences in the use of intra-aortic balloon pumping or extra-corporeal membrane oxygenation between the groups.

Table 3: Clinical outcomes

Variable	All patients (N = 500)	Pre pandemic (N = 300)	Post pandemic (N = 200)	P value
In-hospital death, n (%)	20 (4)	12	8	0.64
Cause of death				
Myocardial infarction, n (%)	18	9	9	0.178
Bleeding, n (%)	1	1	0	0.36
Sepsis, n (%)	1	1	0	0.39

Overall, in-hospital death occurred in 20 patients (4%), including 18 with myocardial infarction (MI), one with bleeding, and one with sepsis. There was no significant difference in the in-hospital mortality between the groups.

Discussion

Ischemic heart disease (IHD) is the world's leading cause of death accounting for an estimated 9 million deaths in 2015. [16,17] Acute coronary syndrome (ACS) is an umbrella term for unstable angina (UA), non-ST-segment-elevation myocardial infarction (NSTEMI) or ST-segment-elevation myocardial infarction (STEMI) and is a substantial component of IHD. [18] In recent decades ACS mortality has decreased, because of advancements in treatment, lifestyle changes, and a focus on primary prevention, but rates remain high. [16,19] Symptoms experienced by women with ACS are often labelled as "atypical" if these are different to those experienced by men. Previous systematic reviews of sex differences in symptoms of patients with ACS have been inconsistent, with varying inclusion and exclusion criteria and studies lacking standardized data collection. [20,21] Recent studies have attempted to solve these issues, with the development of standardized data collection surveys. [22,23]

The median age was 64 years [interquartile range (IQR): 58–78], 75% were men, and 30%, 70%, and 65% had diabetes mellitus, hypertension, and dyslipidemia, respectively. There were no significant differences in gender, body mass index (BMI), past history, chief complaint, Killip classification, blood pressure, or heart rate between the groups. Patients in the post-pandemic group had higher levels of serum creatinine and longer time from an EMS call to hospital arrival than those in the pre-pandemic group. The COVID-19 pandemic has caused rapid changes in social, economic, and healthcare systems, and has had significant indirect impacts on the clinical course and management of patients with ACS. A study from Italy showed that the COVID-19 pandemic led to a significant increase in the proportion of myocardial infarction patients arriving at the hospital late from onset

(50.0% vs 4.8%; $p < 0.01$) and decreased the rate of primary PCI (80.8% vs 100%; $p = 0.06$). In the United States and Spain, there was an estimated 40% reduction in PCI performed in patients with STEMI during the early stages of the COVID-19 pandemic. [24,25] In another survey in China, the total number of hospitalized STEMI patients nationwide declined by about 26% per week, and by about 62% in Hubei province, the epicentre of the COVID-19 outbreak. In Hubei, the median time from symptom onset to first medical contact during the COVID-19 pandemic was 6.75 (IQR 5.66–7.89) hours, compared to 5.66 (IQR 4.99–6.32) hours before the pandemic. [26] Similarly, several reports have suggested that the time for taking patients with STEMI to a hospital was significantly longer after the COVID-19 pandemic. [27,28]

There were no significant differences between the groups in the number of patients with ACS receiving CABG. There were no significant differences in the use of intra-aortic balloon pumping or extra-corporeal membrane oxygenation between the groups. Overall, in-hospital death occurred in 20 patients (4%), including 18 with myocardial infarction (MI), one with bleeding, and one with sepsis. There was no significant difference in the in-hospital mortality between the groups. There are a considerable number of cardiovascular hospitals and cardiologists per population; therefore, they would be able to promptly perform emergency PCI during the COVID-19 pandemic. As a result, the rate of PCI procedures for ACS did not decrease, and in-hospital mortality did not increase in the post-pandemic period. Furthermore, we found that the COVID-19 pandemic was associated with a significantly longer time from an EMS call to hospital arrival. This may be attributed to the fact that the number of patients who were refused by the EMS increased owing to the limited number of hospitals that could accept emergency patients during the COVID-19 pandemic. Timely diagnosis and effective management of ACS are required to prevent significant morbidity and mortality, with the greatest benefit in patients presenting with ACS, especially STEMI. A previous study reported that the time from first

medical contact to primary PCI is a strong predictor of adverse outcomes with every 10-min delay associated with increased mortality in patients presenting with STEMI. [29]

Conclusion

Patients presenting after the onset of the pandemic had elevated cardiac markers, representing higher severity and potentially presenting later in the disease course. The number of total ACS cases and percentage of females presenting to the catheterization lab before the COVID surge almost remained stable. This comparison data provides validity that the drop in ACS case volume and females is more likely due to the pandemic and not due to improvements in overall cardiovascular health metrics. Reasons for this disparity are likely multifaceted and deserve further investigation.

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