

A RETROSPECTIVE, OBSERVATIONAL STUDY EVALUATION OF THE IMPACT OF THE COVID-19 PANDEMIC ON GENDER DISPARITIES IN ACUTE CORONARY SYNDROME PATTERNS

Debjani Goswami¹, Sanjoy Sen², Chowdary Vivek Kumar²

¹Associate professor, Department of General Medicine IQ City Medical College, Durgapur, West Bengal, India.

²Assistant Professor, Department of General Medicine IQ City Medical College, Durgapur, West Bengal, India

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Corresponding Author:

Dr. Sanjoy Sen,
Email: sanjoys96@gmail.com

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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 analyze differences in gender distribution, and type of presentation. **Material & methods:** A retrospective, observational study performed among 3460 consecutive patients. Of these, 2460 patients without ACS were excluded from the analysis. Ultimately, 1000 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 65 [IQR: 58–78], 75% were men, and 30%, 70%, and 65% had diabetes, hypertension, and dyslipidaemia. Gender, BMI, previous history, principal complaint, Killip classification, blood pressure, and heart rate were similar between groups. Patients in the post-pandemic group had higher blood creatinine levels and longer EMS call-to-hospital times. The number of ACS patients getting CABG was similar between groups. Intra-aortic balloon pumping and extra-corporeal membrane oxygenation were similar between groups. Twenty patients (4%), including 18 with MI, one with haemorrhage, and one with infection, died at the hospital. In-hospital mortality was similar between groups. **Conclusion:** Patients arriving after the pandemic exhibited increased cardiac markers, indicating greater severity and perhaps later disease progression. Before the COVID-19 pandemic, ACS cases and female catheterisation lab visits were nearly steady. This comparative data supports the decline in ACS case numbers and females owing to the pandemic rather than cardiovascular health gains. This difference may have several causes and warrants additional examination.

INTRODUCTION

In the Western world, acute coronary syndrome (ACS) and myocardial infarction (MI) mortality has substantially decreased during the last decades.¹ During the Covid-19 pandemic and the associated lockdown period, the pattern of hospital admissions for conditions other than Covid-19 has been deeply influenced, with a tragic 40% average reduction in MI admissions.²⁻⁵ The pandemic may have reduced the possibility of screening for atypical or short-term symptoms, this behavior potentially leading to an increase in cardiovascular mortality and late complications, especially for women for whom late admission and longer time from symptoms onset were already more frequent before the pandemic.^{6,7} ACS events are well known to increase mortality and morbidity: they can lead to heart muscle

damage which in turn may evolve into heart failure, induce arrhythmic events and even lead to sudden cardiac death.⁸ To reduce such complications, efforts have been made on increasing people knowledge of cardiac symptoms and on the importance of shortening delay times, since a clear association between longer intervals from symptoms onset to treatment and a worse prognosis has been found.^{9,10}

Sex differences are the biological and physiological differences in the cardiovascular system that are a result of different gene expressions due to sex chromosomes. Some well-documented sex differences in ACS include that women are older and have more co-morbidities when compared to men.¹¹⁻¹³ Timely recognition of ACS is essential to the timely initiation of therapies and ultimately affects the outcomes of ACS. Delayed recognition

of ACS in both patients and providers has contributed to delays in treatment initiation and outcomes.¹⁴ The SEAR is home to a large population, additionally predisposed to the South Asian phenotype of CAD. The South Asian nations of India, Pakistan, Bangladesh, Sri Lanka, and Nepal account for about a quarter of the world's population and contribute the highest proportion of the world's CVD burden, many of whom are also young.¹⁵

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.^{16,17} Oppositely, among STEMI patients, females generally display more comorbidities and higher mortality.^{18,19} 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

MATERIALS AND METHODS

A retrospective, observational study performed among 3460 consecutive patients. Of these, 2460 patients without ACS were excluded from the analysis. Ultimately, 1000 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:

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).¹⁹

RESULTS

The median age was 65 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.

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.

Overall, in-hospital death occurred in 40 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.

Table 1: Baseline patient characteristics.

Variable	Allpatients(N=500)	Prepandemic(N=300)	Postpandemic(N=200)	P value
Age (years)	65(58–78)	67(58–78)	69(59–79)	0.32
Male,n	750(75)	450	300	0.48
Bodymassindex(kg/m2)	23.6 (22.1–27.2)	23.8 (22.1–26.9)	24.1 (22.1–27.4)	0.29
Medicalhistory				
Diabetes,n(%)	300(30)	180	120	0.86
Hypertension,n(%)	700(70)	412	288	0.38
Hyperlipidemia,n(%)	650(65)	195	130	0.79
Chiefcomplaint				
Chestpain,n(%)	850(85)	510	340	0.75
Dyspnoea,n(%)	50(5)	26	24	0.32
Killipclassification				
				0.110
ClassI,n(%)	800(80)	500	300	
ClassII,n(%)	100(10)	52	48	
ClassIII,n(%)	50(5)	30	20	
ClassIV,n(%)	50(5)	34	16	
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
Laboratoryfindings				
Haemoglobin(g/dL)	14.4 (12.8–15.6)	14.4 (12.6–15.6)	14.4 (12.9–15.6)	0.88
Serumcreatinine(mg/dL)	0.85 (0.76–1.08)	0.88 (0.74–1.04)	0.90 (0.79–1.12)	0.025
MaximumCPK(U/L)	846(160–2567)	759(134–2320)	1012(197–2819)	0.075
MaximumCK-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(%)	750(75)	430	320	0.089
TimefromEMScalltohospital(min)	30(25–37)	29(25–36)	32(26–39)	0.007

Table 2: Angiographic findings and invasive procedures

Variable	Allpatients(N=1000)	Prepandemic(N=600)	Postpandemic(N=400)	P value
EmergencyCAG,n(%)	900 (90)	532	368	0.138
Accesssite				
Conventional radialapproach,n(%)	600(60)	340	260	0.070
Femoralapproach,n(%)	400(40)	256	144	0.064
Locationofculpritlesion				
RCA,n(%)	400(40)	240	160	0.48
LMT,n(%)	30(3)	18	12	0.82
LAD, n (%)	450(45)	258	192	0.64
LCX,n(%)	150(15)	90	60	0.99
Treatment				
EmergencyPCI,n(%)	880(88)	528	352	0.57
TIMIgrade3flowpostPCI,n(%)	920(92)	552	368	0.43
Doortoballoontime(min)	79(61–106)	74(58–102)	85(65–115)	0.002
Doortoballoontimeunder90min,n(%)	650(65)	410	240	0.076
CABG,n(%)	20(2)	12	8	0.85
IABP,n(%)	80(8)	44	36	0.54
ECMO,n(%)	20(2)	12	8	0.92

Table 3: Clinical outcomes

Variable	Allpatients(N=1000)	Prepandemic(N=600)	Postpandemic(N=400)	P value
In-hospitaldeath,n	40	24	16	0.54
Causeofdeath				
Myocardialinfarction,n	36	18	18	0.178
Bleeding,n	2	2	0	0.36
Sepsis,n	2	2	0	0.39

DISCUSSION

Ischemic heart disease (IHD) is the world's biggest cause of mortality accounting for an estimated 9 million fatalities in 2015.^{20,21} Acute coronary syndrome (ACS) is an umbrella term covering unstable angina (UA), non-ST-segment-elevation myocardial infarction (NSTEMI) or ST-segment-elevation myocardial infarction (STEMI) and is a prominent component of IHD.²² In recent decades ACS mortality has dropped, owing of breakthroughs in therapy, lifestyle modifications, and an emphasis on primary prevention, but rates remain high.^{20,23} Symptoms reported by women with ACS are typically classified as "atypical" if these are dissimilar to those encountered by males. Previous systematic evaluations of sex differences in symptoms of individuals with ACS have been inconsistent, with different inclusion and exclusion criteria and studies missing uniform data collecting.^{24,25} Recent research have sought to alleviate these challenges, with the establishment of standardized data gathering surveys.^{26,27}

The median age was 65 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 variations in gender, body mass index (BMI), prior history, major complaint, Killip classification, blood pressure, or heart rate across the groups. Patients in the post-pandemic group had greater 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 induced fast changes in social, economic, and healthcare systems, and has had substantial indirect consequences on the clinical course and management of individuals with ACS. Research from Italy found that the COVID-19 pandemic led to a substantial rise in the proportion of myocardial infarction patients presenting to the hospital late from onset (50.0% vs 4.8%; $p < 0.01$) and lowered the incidence of primary PCI (80.8% vs 100%; $p = 0.06$).⁹ In the United States and Spain, there was an estimated 40% drop in PCI done in patients with STEMI during the early phases of the COVID-19 epidemic.^{28,29} In another survey in China, the overall number of hospitalized STEMI patients countrywide fell by roughly 26% every week, and by nearly 62% in Hubei province, the core of the COVID-19 outbreak. In Hubei, the median period from symptom start 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.³⁰ Numerous studies indicate that the duration for transporting STEMI patients to a hospital was markedly prolonged during the COVID-19 epidemic.^{31,32}

No notable variations were between the groups for the number of patients with ACS undergoing CABG. No substantial variations were seen in the

use of intra-aortic balloon pumping or extracorporeal membrane oxygenation across the groups. A total of 40 patients (4%) experienced in-hospital mortality, comprising 18 due to myocardial infarction (MI), one from haemorrhage, and one from sepsis. No substantial difference in in-hospital mortality was seen across the groups. A significant number of cardiovascular facilities and cardiologists exist per capita, enabling them to swiftly conduct emergency PCI during the COVID-19 epidemic. Consequently, the frequency of PCI operations for ACS remained unchanged, and in-hospital mortality did not rise in the post-pandemic era. Additionally, we discovered that the COVID-19 pandemic correlated with a markedly extended duration from the EMS call to hospital arrival. This might be ascribed to the rise of patients denied by EMS due to the restricted capacity of hospitals to admit emergency cases during the COVID-19 epidemic. Prompt diagnosis and efficient therapy of ACS are essential to save considerable morbidity and death, particularly for individuals presenting with ACS, including STEMI. A prior study indicated that the duration from initial medical contact to primary PCI is a significant predictor of negative outcomes, with each 10-minute delay correlating with heightened mortality in patients presenting with STEMI.³³

CONCLUSION

Patients who came after the pandemic's commencement exhibited increased cardiac markers, indicating greater severity and probably later presentation in the illness progression. The total number of ACS cases and the percentage of females presenting to the catheterisation lab prior to the COVID spike remained rather steady. This comparative data substantiates that the decline in ACS case volume and female cases is more likely attributable to the pandemic rather than enhancements in overall cardiovascular health indicators. The causes of this difference are likely complex and warrant additional examination.

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