


# BMJ Open Influence of COVID-19 pandemic in India on coronary artery disease clinical presentation, angiography, interventions and in-hospital outcomes: a single centre prospective registry-based observational study

Rajeev Gupta <sup>1</sup>, Krishnakumar Sharma,<sup>2</sup> Raghubir Singh Khedar,<sup>1</sup> Sanjeev Kumar Sharma,<sup>3</sup> Jitender Singh Makkar,<sup>3</sup> Vishnu Natani,<sup>3</sup> Ajeet Bana,<sup>3</sup> Samin Sharma<sup>4</sup>

**To cite:** Gupta R, Sharma K, Khedar RS, *et al.* Influence of COVID-19 pandemic in India on coronary artery disease clinical presentation, angiography, interventions and in-hospital outcomes: a single centre prospective registry-based observational study. *BMJ Open* 2024;**14**:e078596. doi:10.1136/bmjopen-2023-078596

► Prepublication history for this paper is available online. To view these files, please visit the journal online (<https://doi.org/10.1136/bmjopen-2023-078596>).

Received 06 August 2023  
Accepted 08 March 2024



© Author(s) (or their employer(s)) 2024. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

## Correspondence to

Dr Rajeev Gupta;  
[rajeevgg@gmail.com](mailto:rajeevgg@gmail.com)

## ABSTRACT

**Objective** The study examined the influence of the COVID-19 pandemic in India on variation in clinical features, management and in-hospital outcomes in patients undergoing percutaneous coronary intervention (PCI).

**Design** Prospective registry-based observational study.

**Setting** A tertiary care hospital in India participant in the American College of Cardiology CathPCI Registry.

**Participants** 7089 successive patients who underwent PCI from April 2018 to March 2023 were enrolled (men 5627, women 1462). Details of risk factors, clinical presentation, coronary angiography, coronary interventions, clinical management and in-hospital outcomes were recorded. Annual data were classified into specific COVID-19 periods according to Government of India guidelines as pre-COVID-19 (April 2018 to March 2019, n=1563; April 2019 to March 2020, n=1594), COVID-19 (April 2020 to March 2020, n=1206; April 2021 to March 2022, n=1223) and post-COVID-19 (April 2022 to March 2023, n=1503).

**Results** Compared with the patients in pre-COVID-19 and post-COVID-19 periods, during the first COVID-19 year, patients had more hypertension, non-ST elevation myocardial infarction (NSTEMI), lower left ventricular ejection fraction (LVEF) and multivessel coronary artery disease (CAD). In the second COVID-19 year, patients had more STEMI, lower LVEF, multivessel CAD, primary PCI, multiple stents and more vasopressor and mechanical support. There were 99 (1.4%) in-hospital deaths which in the successive years were 1.2%, 1.4%, 0.8%, 2.4% and 1.3%, respectively (p=0.019). Compared with the baseline year, deaths were slightly lower in the first COVID-19-year (age-sex adjusted OR 0.68, 95% CI 0.31 to 1.47) but significantly more in the second COVID-19-year (OR 1.97, 95% CI 1.10 to 3.54). This variation attenuated following adjustment for clinical presentation, extent of CAD, in-hospital treatment and duration of hospitalisation.

**Conclusions** In-hospital mortality among patients with CAD undergoing PCI was significantly higher in the second

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The registry includes patients with coronary artery disease (CAD) before, during and following the COVID-19 pandemic in India.
- ⇒ More CAD deaths during the delta-wave of COVID-19 could partially explain the excess deaths in India during this period.
- ⇒ Data on prehospital pain-to-door time and door-to-balloon time are not available.
- ⇒ Extremely sick patients or those not suitable for coronary angioplasty have not been included.
- ⇒ This single hospital-based study may not be externally valid for the country.

year of the COVID-19 pandemic in India and could be one of the reasons for excess deaths in the country. These patients had more severe CAD, lower LVEF, and more vasopressor and mechanical support and duration of hospitalisation.

## INTRODUCTION

The pandemic of COVID-19 led to a large number of deaths at its peak during the years 2020–2022.<sup>1–4</sup> In developed countries, with robust healthcare systems and the availability of high-quality universal mortality statistics, these deaths were carefully enumerated and causes of excess deaths (incident deaths beyond the predicted usual) were provided.<sup>3</sup> It was estimated that while most of the excess deaths were directly related to COVID-19, a significant proportion was due to indirect effects of the pandemic due to non-availability or delays in seeking healthcare for medical emergencies such as acute coronary events, strokes and others.<sup>1</sup> In the UK it was estimated

**Table 1** Baseline characteristics of the study cohort

Variable	Total cohort (n-7089)
Age (years)	60.4±10.9
Men	5627 (79.4)
Women	1462 (20.6)
Risk factors	
Hypertension	3795 (53.5)
Diabetes	2763 (39.0)
Cholesterol >170 mg/dL	2481 (35.0)
Non-HDL, ≥100 mg/dL	4278 (60.3)
Smoking/tobacco(ever)	698 (9.8)
CKD, creatinine >2 mg/dL	154 (2.2)
BMI≥25 kg/m <sup>2</sup>	4551 (64.2)
CAD family history	1043 (14.7)
Uninsured status	3609 (50.9)
Previous cardiovascular status	
Coronary intervention (PCI)	945 (13.3)
Coronary bypass surgery	237 (3.3)
Congestive heart failure	40 (0.6)
Acute coronary syndromes	6735 (95.0)
STEMI	2801 (39.5)
Primary PCI	1091 (15.4)
Delayed/rescue PCI	1168 (16.5)
Pharmaco-invasive	542 (7.6)
NSTEMI/unstable angina	3934 (55.5)
Chronic coronary syndrome	354 (5.0)
Left ventricular ejection fraction (mean)	45.0±10.5
EF<30%	378 (5.3)
EF 30–45%	3735 (52.7)
EF>45%	2976 (42.0)
Coronary anatomy and extent	
Left main coronary artery	391 (5.5)
Right coronary artery	3647 (51.4)
Left anterior descending coronary artery	5633 (79.5)
Left circumflex coronary artery	3549 (50.1)
Single-vessel disease	2976 (42.0)
Double vessel disease	2378 (33.5)
Triple vessel disease	1699 (24.0)
Stents deployed	
Nil	148 (2.1)
1 stent	4661 (65.1)
2 stents	1774 (25.0)
≥3 stents	506 (7.1)
Pharmacological vasopressor support	756 (10.7)
Mechanical support	244 (3.4)

Continued

**Table 1** Continued

Variable	Total cohort (n-7089)
IABP	229 (3.2)
Impella device	7 (0.1)
ECMO	2 (0.01)
Duration of hospitalisation: median duration (IQR) (hours)	68.1 (51.1–84.0)
Discharge medications	
Dual antiplatelets	6962 (98.2)
Anticoagulant	53 (0.7)
Statins	6951 (98.1)
Beta-blockers	4979 (70.2)
ACEI/ARB	3145 (44.4)
In-hospital deaths	99 (1.4)

Numbers±indicate 1 SD. Numbers in parenthesis are per cent.  
 ACEI, ACE inhibitor; ARB, angiotensin receptor blockers; BMI, body mass index; CAD, coronary artery disease; CKD, chronic kidney disease; ECMO, extracorporeal membrane oxygenation; EF, ejection fraction; HDL, high-density lipoprotein; IABP, intra-aortic balloon pump; LAD, left anterior descending; LCX, left circumflex; LDL, low-density lipoprotein; LMCA, left main coronary artery; NSTEMI, non-ST-segment elevation myocardial infarction; RCA, right coronary artery; STEMI, ST-segment elevation myocardial infarction.

that during the pandemic years about one-third of excessive deaths were due to non-COVID-19 reasons.<sup>5</sup> Similar data are available from the USA and many European countries.<sup>6–8</sup> In India and most developing countries real-time mortality statistics enumerating causes of death are not available.<sup>9–10</sup> In contrast to the official number of less than half a million deaths from COVID-19 in India, some estimates have reported more than 2.5 million deaths during the 2 years when COVID-19 was rampant.<sup>3 11–14</sup> Many of these estimates are based on extrapolations from locally available data.<sup>15–20</sup>

The COVID-19 pandemic in India led to severe disruptions in healthcare access, availability and quality of care for patients.<sup>21</sup> Excessive mortality beyond the official data was predicted.<sup>22</sup> In India, a proportion of excess deaths at the height of the COVID-19 pandemic could be due to hospitalisation delays leading to more advanced and complicated presentations in acutely ill patients without COVID-19 with coronary artery disease (CAD) or other cardiovascular, neurological, pulmonary and renal diseases.<sup>23–25</sup> CAD is the most important cause of death in India and delayed presentation following an acute coronary syndrome (ACS) is the most important cause of short-term and long-term mortality.<sup>26 27</sup> A proportion of excess deaths due to COVID-19 in India could have been due to such delays. As part of the American College of Cardiology (ACC) National Cardiovascular Disease Registry (NCDR) we have been systematically collecting data on

all patients who undergo percutaneous coronary intervention (PCI) at our hospital.<sup>28–30</sup> To evaluate variations in CAD risk factors, clinical presentation, disease severity and in-hospital outcomes among successive patients who underwent PCI before, during and after the COVID-19 pandemic years in India, we analysed our hospital data.

## METHODS

This single-centre registry-based study has been conducted at Eternal Heart Care Centre & Research Institute, Jaipur (India). The CathPCI Registry at the hospital is part of the ACC-NCDR Centre of Excellence programme.<sup>31</sup> Informed consent was obtained from each participant included in the registry with specific consent for inclusion of anonymised data. The protocol of the study and all the data are available at ACC-NCDR website at: <https://cvquality.acc.org/NCDR-Home/registries/hospital-registries/cathpci-registry>.

## Patients

Successive patients who underwent PCI at the hospital over a 60-month period, from April 2018 to March 2023, have been included. Clinical data were prospectively obtained at admission, coronary intervention and hospital discharge and entered into the NCDR database by research assistants. Details of the methodology have been previously reported.<sup>28</sup> Briefly, we obtained details regarding age and sex, risk factors- hypertension, diabetes, dyslipidaemias, tobacco use and chronic kidney disease, other laboratory investigations, clinical presentation (ST-segment myocardial infarction (STEMI) or non-STEMI (NSTEMI)/unstable angina and echocardiographic left ventricular ejection fraction (LVEF). We also recorded angiographic details of the location and extent of CAD and number of stents deployed. Almost all stents deployed (>99%) were drug-eluting. Details of in-hospital management with a specific focus on pharmacological vasopressors (norepinephrine, dopamine, vasopressin, etc), cardiac-support devices (intra-aortic balloon pump and miniature ventricular assist devices (mVAD) and post-discharge medications were also recorded.

## Outcomes

In-hospital follow-up were duration of hospitalisation (hours), cardiovascular deaths and all-cause deaths.

## Patient and public involvement

Patients were not involved in the study design, conduct, outcome measures or preparation of the manuscript.

## Statistical analyses

The patients have been divided into three periods according to Government of India guidelines<sup>32</sup>: Pre-COVID-19 period: first year - April 2018 to March 2019 and second year - April 2019 to March 2020; COVID-19 period: third year - April 2020 to March 2021 and fourth year - April 2021 to March 2022; and Post-COVID-19 period: fifth year - April 2022 to March 2023. Severe

restrictions and lockdowns in India started in the last week of March 2020, accordingly, the patients enrolled before 31st March 2020 have been included in pre-COVID-19 period. Lockdowns and restrictions continued for the next 2 years (COVID-19-phase) and were lifted in March 2022 when all restrictions were relaxed and international flights resumed. Therefore, the period from April 2022 to March 2023 has been categorised as post-COVID-19. Data have been downloaded from the ACC-NCDR website<sup>31</sup> and transferred to MS Excel worksheets. Data analyses have been performed using SPSS software (V.23). Continuous variables are reported as mean±1 SD and categorical variables as per cent. Non-normal data are presented as median with 25–75th percentile IQR. Inter-group differences have been determined using analysis of variance for continuous variables,  $\chi^2$  test for categorical variables and Kruskal-Wallis test for non-normal data. To identify the magnitude of inter-group difference in clinical presentation, angiographic findings, disease severity, clinical management, duration of hospitalisation and in-hospital outcomes in successive years, we calculated unadjusted; age-sex adjusted; age-sex, risk factors and presentation-adjusted; and multivariate-adjusted (age-sex, risk factors, presentation, left ventricular ejection fraction, extent of CAD, coronary stents, in-hospital therapies including vascular support and duration of hospitalisation) odds ratios (OR) and 95% confidence intervals (CIs) using stepwise logistic regression. The first year (April 2018 to March 2019) was the index. P values<0.05 are considered significant.

## RESULTS

7089 successive patients (men 5627, women 1462) who underwent percutaneous coronary intervention from April 2018 to March 2023 have been enrolled. Mean age was 60.4±11 years (men 59.8±11 years, women 61.5±11). There was a significant prevalence of most coronary risk factors (table 1). Previous PCI was in 945 (13.3%) and coronary bypass surgery in 237 (3.3%). Clinical presentation was predominantly as ACS (n=6735, 95.0%) with more NSTEMI/unstable angina (n=3934, 55.5%) compared with STEMI (n=2801, 39.5%). Mean LVEF at admission was 45±11%, about half of the patients had LVEF 30–45%, while low LVEF (<30%) was in 378 (5.3%). Coronary angiography revealed that most patients had disease of the left anterior descending artery (n=5633, 79.5%). Single vessel disease was in 2976 (42.0%), double vessel disease in 2378 (33.5%) and triple vessel disease in 1699 (24.0%). Drug-eluting stents were deployed in almost all with single stents in the majority (4661, 65.1%) and 506 (7.1%) patients had >3 stents. During hospitalisation, pharmacological vasopressor support was in 756 (10.7%) and mechanical support in 244 (3.4%). The deployment of a mVAD or extracorporeal membrane oxygenation was minimal. Median duration of hospital stay was 68.1 hours (IQR 51.1–84.0). There were 99 (1.4%) in-hospital deaths.



**Table 2** Characteristics of patients undergoing PCI before, during and after COVID-19

Variable	Pre-COVID-19 period		COVID-19 period		Post-COVID-19 period	P value ( $\chi^2$ test)
	April 2018 to March 2019 N=1563	April 2019 to March 2020 N=1594	April 2020 to March 2021 N=1206	April 2021 to March 2022 N=1223	April 2022 to March 2023 N=1503	
Age	59.9±10.9	60.5±10.9	60.3±10.8	59.9±11.0	60.9±10.8	0.061*
Age <40 years	66 (4.2)	55 (3.5)	44 (3.6)	49 (4.0)	57 (3.8)	0.827
Men	1221 (78.1)	1294 (81.2)	964 (79.9)	950 (77.7)	1198 (79.7)	0.128
Risk factors						
Hypertension	843 (53.9)	872 (54.7)	704 (58.4)	647 (52.9)	729 (48.5)	<0.001
Diabetes	555 (35.5)	630 (39.5)	500 (41.5)	511 (41.8)	567 (37.7)	0.003
Cholesterol >170 mg/dL	486 (31.1)	515 (32.3)	365 (30.3)	507 (41.5)	608 (40.5)	<0.001
Non-HDL, ≥100 mg/dL	914 (58.5)	928 (58.2)	647 (53.6)	809 (66.1)	980 (65.2)	<0.001
Smoking/tobacco(ever)	269 (17.2)	170 (10.7)	110 (9.1)	99 (8.1)	50 (3.3)	<0.001
CKD, creatinine >2 mg/dL	28 (1.8)	38 (2.4)	24 (2.0)	28 (2.3)	36 (2.4)	0.732
BMI≥25 kg/m <sup>2</sup>	1054 (67.6)	1097 (69.0)	714 (59.5)	772 (63.2)	914 (60.8)	<0.001
CAD family history	74 (14.7)	290 (18.2)	205 (17.0)	291 (23.8)	183 (12.2)	<0.001
Uninsured status	861 (55.1)	870 (54.6)	760 (53.0)	594 (48.6)	524 (34.9)	<0.001
Cardiovascular status						
Previous PCI	161 (10.3)	198 (12.4)	180 (14.9)	178 (14.6)	228 (15.2)	<0.001
CABG surgery	42 (2.7)	58 (3.6)	47 (3.9)	35 (2.9)	55 (3.7)	0.286
CHF	13 (0.8)	09 (0.6)	17 (1.4)	0 (0.0)	01 (0.01)	<0.001
Aspirin	489 (31.3)	647 (40.6)	382 (31.7)	494 (40.4)	660 (43.9)	<0.001
Beta-blockers	369 (23.6)	480 (30.1)	316 (26.2)	379 (31.0)	450 (29.9)	<0.001
Statins	468 (29.9)	630 (39.5)	382 (31.7)	488 (39.9)	633 (42.1)	<0.001
Acute coronary syndrome						
STEMI	671 (42.9)	632 (39.6)	434 (36.0)	531 (43.4)	533 (35.5)	0.007
NSTEMI/UAP	824 (57.1)	873 (60.4)	689 (64.0)	619 (56.6)	929 (61.8)	0.017

Numbers±indicate 1 SD.

Numbers in parenthesis are per cent.

\*Analysis of variance test.

BMI, body mass index; CABG, coronary artery bypass graft; CAD, coronary artery disease; CHF, congestive heart failure; CKD, chronic kidney disease; DVD, double vessel disease; HDL, high-density lipoprotein; LAD, left anterior descending; LCX, left circumflex; LDL, low-density lipoprotein; LMCA, left main coronary artery; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery; STEMI, ST-segment elevation myocardial infarction; SVD, single vessel disease; TVD, triple vessel disease; UAP, unstable angina pectoris.

Clinical characteristics and interventions among PCI patients during successive years of the study in pre-COVID-19, COVID-19 and post-COVID-19 periods are shown in [tables 2 and 3](#). No difference in mean age or sex distribution is observed. There is no difference in the proportion of young patients <40 years age in various groups ([table 2](#)). During COVID-19 years (April 2020 to March 2021 and April 2021 to March 2022) the prevalence of hypertension, diabetes, hypercholesterolaemia, kidney failure (creatinine >2mg/dL) and previous PCI were more ([table 2](#)). Presentation as STEMI was lower in the first year of COVID-19 and greater in the second ( $p<0.001$ ). Echocardiography at admission revealed lower mean LVEF with a greater presence of very low EF (<30%)

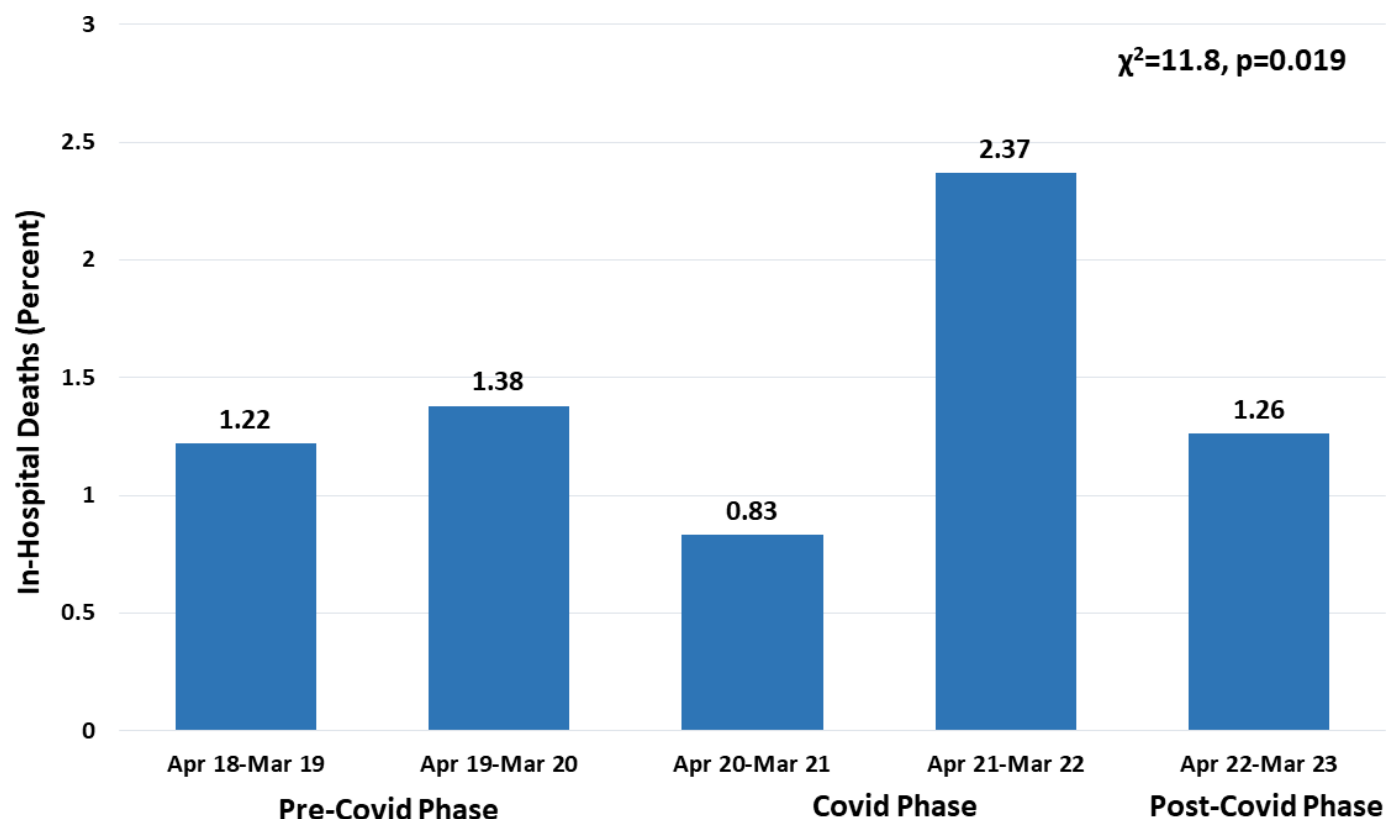
in the second year of COVID-19. Angiography revealed a greater prevalence of double and triple vessel disease during the COVID-19 and post-COVID-19 years. Primary PCI for STEMI was lower and pharmaco-invasive therapy was more during the first year of COVID-19. The pharmaco-invasive therapy was deployed according to Indian guidelines.<sup>33</sup> More coronary stents were deployed in the second year of COVID-19 ([table 3](#)). The use of pharmacological vasopressors (norepinephrine, dopamine, vasopressin, etc) and mechanical support was also more during the second year of COVID-19. Both the mean and median duration of hospitalisation were significantly greater during the first and second COVID-19 years ([table 3](#)).

**Table 3** Angiographic characteristics, interventions and outcomes of patients before, during and after COVID-19 pandemic

Variable	Pre-COVID-19 period		COVID-19 period		Post-COVID-19 period	P value ( $\chi^2$ test)
	April 2018 to March 2019	April 2019 to March 2020	April 2020 to March 2021	April 2021 to March 2022	April 2022 to March 2023	
	N=1563	N=1594	N=1206	N=1223	N=1503	
LVEF (mean)	45.1±10.8	45.8±10.2	44.6±10.8	44.1±10.5	45.0±10.3	<0.001
EF<30%	91 (5.8)	56 (3.5)	71 (5.9)	78 (6.4)	82 (5.5)	<0.001
EF 30–45%	826 (52.8)	841 (52.8)	656 (54.4)	665 (54.4)	747 (49.7)	0.062
Coronary angio						
LMCA	83 (5.3)	100 (6.3)	89 (7.4)	45 (3.7)	74 (4.9)	0.001
RCA	733 (46.9)	869 (54.5)	658 (54.6)	678 (55.4)	709 (47.2)	<0.001
LAD	1218 (77.9)	1309 (82.1)	982 (81.4)	973 (79.6)	1151 (76.6)	0.001
LCX	724 (46.3)	801 (50.3)	679 (56.3)	648 (53.0)	697 (46.4)	<0.001
SVD	704 (45.0)	615 (38.6)	435 (36.1)	461 (37.7)	761 (50.6)	<0.001
DVD	570 (36.5)	564 (35.4)	414 (34.3)	430 (35.2)	400 (26.6)	0.003
TVD	2774 (17.7)	412 (25.8)	352 (29.2)	326 (26.7)	332 (22.1)	<0.001
STEMI PCI						
Primary PCI	230 (14.7)	242 (15.2)	83 (6.8)	277 (22.6)	259 (17.2)	<0.001
Delayed PCI	297 (19.0)	275 (17.2)	202 (16.7)	191 (15.6)	203 (13.5)	0.001
Pharmaco-invasive	144 (9.2)	115 (7.2)	149 (12.3)	63 (5.1)	71 (4.7)	<0.001
Stents deployed						
Nil	05 (0.3)	44 (2.8)	41 (3.4)	25 (2.0)	33 (2.2)	<0.001
1 stent	987 (62.1)	1037 (65.1)	885 (73.4)	779 (63.7)	973 (64.7)	<0.001
2 stents	429 (27.4)	411 (25.8)	244 (20.2)	302 (24.7)	388 (25.8)	<0.001
≥3 stents	142 (9.0)	102 (6.4)	36 (3.0)	117 (9.5)	109 (7.2)	<0.001
Vasopressor use	140 (8.9)	162 (10.1)	145 (12.0)	202 (16.5)	207 (13.8)	<0.001
Mechanical support	47 (3.0)	46 (2.9)	37 (3.1)	69 (5.6)	40 (3.1)	<0.001
IABP	45 (2.9)	42 (2.6)	37 (3.1)	66 (5.4)	40 (3.1)	<0.001
Impella	2 (0.1)	4 (0.2)	0 (0.0)	1 (0.08)	0 (0.0)	0.190
ECMO	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.24)	0 (0.0)	0.056
Hospitalisation (hours)						
Mean duration	73.4±48.7	75.8±50.7	89.0±68.7	85.5±72.7	72.7±47.5	<0.001*
Median (IQR)	65.2 (50.0–77.0)	66.5 (50.1–83.3)	66.5 (50.1–83.3)	72.3 (56.1–94.3)	64.5 (49.0–79.0)	<0.001†
Discharge meds						
Dual antiplatelets	1536 (98.3)	1564 (98.1)	1196 (99.2)	1188 (97.1)	1478 (98.3)	0.006
Anticoagulant	3 (0.2)	6 (0.4)	7 (0.6)	14 (1.2)	18 (1.2)	0.003
Statins	1532 (98.5)	1559 (99.7)	1196 (99.2)	1186 (99.8)	1478 (99.7)	<0.001
Beta-blockers	703 (45.0)	1255 (78.7)	976 (80.9)	915 (74.8)	1130 (75.2)	<0.001
ACEI/ARB	732 (46.8)	679 (42.6)	678 (56.2)	512 (41.9)	544 (36.2)	<0.001
In-hospital deaths	19 (1.2)	22 (1.4)	10 (0.8)	29 (2.4)	19 (1.3)	0.019

Numbers±indicate 1 SD.  
 Numbers in parenthesis are per cent.  
 \*Analysis of variance test.  
 †Kruskal-Wallis test.

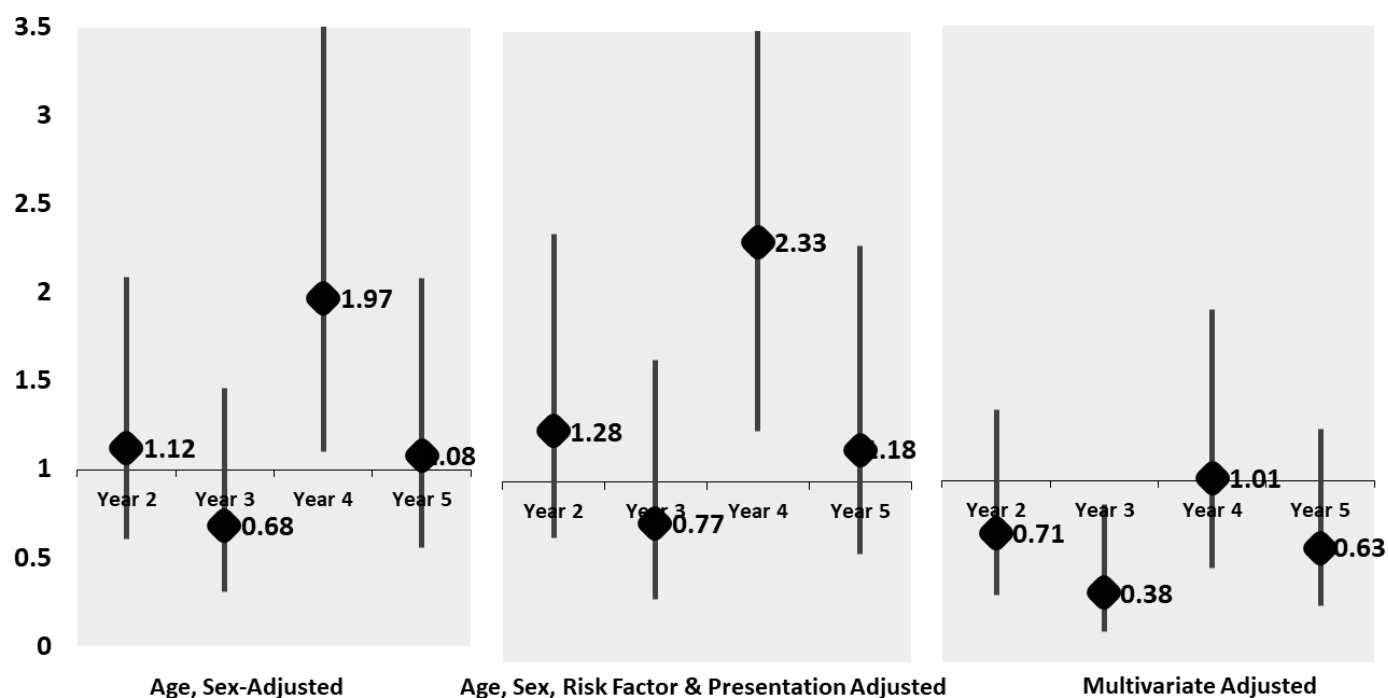
ACEI, ACE inhibitors; ARB, angiotensin receptor blockers; CAD, coronary artery disease; CKD, chronic kidney disease; ECMO, extra-corporeal membrane oxygenation; EF, ejection fraction; HDL, high-density lipoprotein; IABP, intra-aortic balloon pump; LAD, left anterior descending; LCX, left circumflex; LDL, low-density lipoprotein; LMCA, left main coronary artery; LVEF, left ventricular ejection fraction; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; RCA, right coronary artery; STEMI, ST-segment elevation myocardial infarction.



**Figure 1** In-hospital deaths (%) during the pre-COVID-19, COVID-19 and post-COVID-19 years.

The incidence of in-hospital deaths in the five successive years was 1.2%, 1.4%, 0.8%, 2.4% and 1.3%, respectively, ( $\chi^2$  test,  $p=0.019$ ) (figure 1). Compared with pre-COVID-19 years, the deaths were lower in the first

year of COVID-19 (0.8%) and significantly more during the second year (2.4%). Age and sex-adjusted, age, sex, risk factor and clinical presentation-adjusted and multivariate-adjusted logistic regression for in-hospital



**Figure 2** Age and sex adjusted; age, sex, risk factor and clinical presentation adjusted; and multivariate-adjusted ORs and 95% CIs for in-hospital deaths in pre-COVID-19 period (year 2), COVID-19 period (years 3 and 4) and post-COVID-19 period (year 5) compared with the baseline pre-COVID-19 year.

deaths at years 2, 3, 4 and 5 compared with the first year are shown in [figure 2](#). This shows that in the age-sex-adjusted model, compared with the baseline year, deaths were slightly lower in the first year of COVID-19 (age-sex adjusted OR 0.68, 95% CI 0.31 to 1.47) and significantly more in the second year (age-sex adjusted OR 1.97, 95% CI 1.10 to 3.54). The OR for deaths in the second year of COVID-19 increased further following adjustment for risk factors and clinical presentation (OR 2.33, 95% CI 1.28 to 4.22). This variation is completely attenuated following adjustment for age, sex, risk factors, clinical presentation, LVEF, extent of CAD, stents, in-hospital treatments and duration of hospitalisation (OR 1.00, 95% CI 0.52 to 1.94) ([figure 2](#)).

## DISCUSSION

This single-hospital-based prospective percutaneous coronary intervention registry in India among patients with ACS from April 2018 to March 2023 shows that there was a doubling of in-hospital deaths during the second phase of COVID-19 (SARS-CoV-2 delta variant wave)<sup>14</sup> as compared with the pre-COVID-19 years. A higher death rate in the second COVID-19 year was associated with patients having more coronary risk factors, STEMI, lower LVEF, multivessel CAD, deployment of >3 coronary stents, higher use of pharmacological and mechanical vasopressor support and longer duration of hospitalisation. These findings suggest more severe cases with complex CAD. We cannot comment on delayed presentation as we do not have data on symptom-to-hospital, door-to-needle or door-to-balloon times.

Studies in the UK, Europe and the USA have reported considerable disruption of acute coronary care and cardiovascular services during the COVID-19 pandemic.<sup>23 24 34–36</sup> This was also associated with delays in seeking care following acute coronary events due to multiple factors including over-burdened ambulance services, less availability of trained emergency care personnel (who were deployed for COVID-19 patient care), greater use of pharmacological therapies for STEMIs and lower use of primary PCI.<sup>35 36</sup> All such data are available for high-income countries with limited data from lower-income countries such as India.<sup>37 38</sup> The present study shows that in the first year of the pandemic in India, there was a slight decline in COVID-19-related deaths suggesting a lack of access to healthcare for patients with ACS due to prolonged lockdowns.<sup>39 40</sup> The patients who reached the hospital were less sick resulting in slightly lower (though not significant) deaths following PCI. On the other hand, during the second wave of the pandemic in India (delta-variant wave in 2021), a doubling of deaths is observed ([figure 2](#)). Patients with CAD who underwent PCI at the hospital during the second wave of the pandemic in India were sicker at presentation with more hypertension and diabetes, lower LVEF, more multivessel disease and had a greater need for multivessel stenting and pharmacological and mechanical circulatory support

([table 3](#)). This is similar to studies from UK and USA.<sup>24 36</sup> Higher in-hospital deaths during the second wave attenuated after adjustment of these clinical variables. In India, the second COVID-19 wave was associated with a doubling of the pandemic-associated deaths compared with the first and subsequent waves.<sup>41 42</sup> The doubling of deaths following PCI in the present study suggests that many of the excess deaths due to COVID-19 in India could be related to non-COVID-19 reasons. However, the estimation of the excess deaths due to non-COVID-19 reasons in India shall require a comprehensive modelling exercise. More data from across the country are needed to model the contribution of CAD events for excess deaths as there is a large state-level variation in CAD incidence.<sup>43</sup>

There are many reasons for variability in CAD deaths during COVID-19 as observed in the present study. Apart from healthcare-seeking delays for acute coronary events, a substantial decline in control of important cardiovascular risk factors (hypertension, hypercholesterolaemia and diabetes), more sedentariness, confined indoor activities and exposure to indoor pollution, mental stress, increased tobacco and alcohol use, etc could be responsible.<sup>44</sup> The biological effects of acute COVID-19 infection on the vascular system (endothelialitis, thrombosis, etc) as well as long-term influence on vascular reactivity and plaque destabilisation are also important.<sup>45</sup> All these factors need more studies.

Limitations of the study include a tertiary care location of the study and our data is not nationally representative. A large number of patients with private health insurance (40%) also suggests a skewed sample and is not representative of India, where only 10–15% have such insurance.<sup>28</sup> We also did not include all the patients with ACS presenting to the hospital as patients who do not undergo PCI were not enrolled in the ACC-NCDR CathPCI Registry. More sick patients or those with severe CAD, not suitable for PCI have not been included. There is no information regarding symptom-to-hospital, door-to-needle or door-to-balloon times and this is an important study limitation. Studies have reported that COVID-19 pandemic led to delayed presentation following ACS.<sup>23</sup> We have no data on geographic, social, economic and other determinants that influence prehospital delays,<sup>27</sup> especially during the COVID-19 pandemic.<sup>36 38</sup> We also do not have data on the status of cardiovascular risk factor control at admission. A low representation of women is also an important limitation, but the data are similar to other Indian CAD registries.<sup>27</sup> The lack of long-term follow-up data is also an important limitation as in-hospital events are likely an underestimate of the true influence of the pandemic on cardiovascular outcomes.<sup>3</sup> On the other hand, this is one of the larger prospective CAD intervention registries from lower-middle income countries. We enrolled patients with CAD before, during and following the COVID-19 pandemic and could identify variations in the characteristics of the patients with CAD and in-hospital outcomes. Standardised and comparable data have been obtained as part of the ACC-NCDR CathPCI Registry.



In conclusion, the present study that used annual data of patients with CAD undergoing PCI shows a lower death rate (possibly related to reduced access to care) during the first year of the COVID-19 pandemic in India and a doubling of in-hospital mortality during the second year. The latter was associated with more severe disease at presentation, more multivessel CAD and greater deployment of coronary stents. These patients also required more pharmacological and mechanical vascular support. COVID-19-like pandemics are likely to recur. Increased cardiovascular mortality as demonstrated in the present study can be ameliorated by multiple health system interventions.<sup>46</sup> Development of well-equipped healthcare infrastructure trained to function during an infectious disease pandemic is required. Strategies include widespread availability of pandemic-proof ambulances and supply chain logistics; well-trained healthcare workers, nurses and clinicians; provision of acute coronary care including invasive care during an epidemic with the deployment of multidisciplinary teams.<sup>46</sup> Technology has a huge role in disease surveillance, monitoring of healthcare workers and managing logistics during such an epidemic.<sup>47</sup> Artificial intelligence-based systems can provide seamless care to the needy.<sup>47</sup> All these initiatives are important to reduce excess deaths from cardiovascular events during infectious disease pandemics.

#### Author affiliations

<sup>1</sup>Medicine, Eternal Heart Care Centre and Research Institute, Jaipur, Rajasthan, India

<sup>2</sup>Pharmacy, LBS College of Pharmacy, Rajasthan University of Health Sciences, Jaipur, Rajasthan, India

<sup>3</sup>Cardiology, Eternal Heart Care Centre and Research Institute, Jaipur, Rajasthan, India

<sup>4</sup>Cardiology, Mount Sinai Health System, New York, New York, USA

**Twitter** Rajeev Gupta @rajeevvg

**Contributors** RG, SKS and SS initiated the study. RG, KS, RSK and VN contributed to project administration, supervision and analyses. SKS, JSM, AB and SS supervised the study conduct and contributed to the study with patient management. RG and KS performed the statistical analyses. RG wrote the first and revised all the subsequent drafts. All the authors reviewed and provided critical inputs to the manuscript. RG is responsible for the overall content and is the guarantor.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not applicable.

**Ethics approval** This study involves human participants and was approved by Institutional Ethics Committee, Eternal Heart Care Centre & Research Institute, Jaipur, Government of India, Registration No. ECR/615/Inst/RJ/2014/RR-20. Participants gave informed consent to participate in the study before taking part.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data are available upon reasonable request. Data may be obtained from a third party and are not publicly available. The data are available at ACC CathPCI website and are available to site investigators and other researchers upon reasonable request.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially,

and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

#### ORCID iD

Rajeev Gupta <http://orcid.org/0000-0002-8356-3137>

#### REFERENCES

- Ioannidis JPA. Reconciling estimates of global spread and infection fatality rates of COVID-19: an overview of systematic evaluations. *Eur J Clin Invest* 2021;51:e13554.
- COVID-19 Cumulative Infection Collaborators. Estimating global, regional and national daily and cumulative infections with SARS-CoV-2 through Nov 14, 2021: a statistical analysis. *Lancet* 2022;399:2351–80.
- COVID-19 Excess Mortality Collaborators. Estimating excess mortality due to COVID-19 pandemic: a systematic analysis of COVID-19 related mortality, 2020–21. *Lancet* 2022;399:1513–36.
- Schöley J, Aburto JM, Kashnitsky I, et al. Life expectancy changes since COVID-19. *Nat Hum Behav* 2022;6:1649–59.
- Aburto JM, Kashyap R, Schöley J, et al. Estimating the burden of COVID-19 pandemic on mortality, life expectancy and lifespan inequality in England and Wales: a population level analysis. *J Epidemiol Community Health* 2021;75:735–40.
- Woolf SH, Masters RK, Aron LY. Effect of the COVID-19 pandemic on 2020 on life expectancy across populations in the USA and other high income countries: simulations of provisional mortality data. *BMJ* 2021;373:n1343.
- Silva S, Goosby E, Reid MJA. Assessing the impact of one million COVID-19 deaths in America: economic and life expectancy losses. *Sci Rep* 2023;13:3065.
- Aburto JM, Schöley J, Kashnitsky I, et al. Quantifying impacts of COVID-19 pandemic through life-expectancy losses: a population level study of 29 countries. *Int J Epidemiol* 2022;51:63–74.
- Gomes M, Begum R, Sati P, et al. Nationwide mortality studies to quantify causes of death: relevant lessons from India's million death study. *Health Aff (Millwood)* 2017;36:1887–95.
- Jha P. Reliable direct measurements of causes of deaths in low- and middle-income countries. *BMC Med* 2014;12:19.
- Zimmermann LV, Salvatore M, Babu GR, et al. Estimating COVID-19 related mortality in India: an epidemiological challenge with insufficient data. *Am J Public Health* 2021;111:S59–62.
- Jha P, Deshmukh Y, Tumbe C, et al. Covid mortality in India: national survey data and health facility deaths. *Science* 2022;375:667–71.
- Guilmoto CZ. An alternative estimation of the death toll of the COVID-19 pandemic in India. *PLoS One* 2022;17:e0263187.
- The Lancet. India's COVID-19 emergency. *Lancet* 2021;397.
- Banaji M, Gupta A. Estimates of pandemic excess mortality in India based on civil registration data. *PLOS Glob Public Health* 2022;2:e0000803.
- Cai R, Novosad P, Tandel V, et al. Representative estimates for COVID-19 infection fatality rates from four locations in India: cross sectional study. *BMJ Open* 2021;11:e050920.
- Sharma AK, Gupta R, Baig VN, et al. Educational status and COVID-19 related outcomes in India: hospital based cross-sectional study. *BMJ Open* 2022;12:e055403.
- Lewnard JA, Mahmud A, Narayan T, et al. All-cause mortality during the COVID-19 pandemic in Chennai, India: an observational study. *Lancet Infect Dis* 2022;22:463–72.
- Beaney T, Clarke JM, Jain V, et al. Excess mortality: the gold standard in measuring the impact of COVID-19 worldwide? *J R Soc Med* 2020;113:329–34.
- India State-Level Disease Burden Initiative Collaborators. Nations within a nation: variations in epidemiological transition across the States in India 1990–2016, in the global burden of disease study. *Lancet* 2017;390:2437–60.
- Sundaraman T, Ranjan A, Rajendran P, et al. India and the world: response to COVID-19 pandemic. In: Jain Y, Nabia S, eds. *COVID-19: a view from the margins*. New Delhi: Manohar Publishers, 2022: 89–119.
- Muniyandi M, Singh PK, Aanandh Y, et al. A national level analysis of life expectancy associated with the COVID-19 pandemic in India. *Front Public Health* 2022;10:1000933.
- Kontopantelis E, Mamas MA, Webb RT, et al. Excess deaths from COVID-19 and other causes by region, neighborhood deprivation level and place of death during the 30 weeks of the pandemic in England and Wales: a retrospective registry study. *Lancet Reg Health Eur* 2021;7:100144.



- 24 Banerjee A, Chen S, Pasea L, *et al.* Excess deaths in people with cardiovascular diseases during the COVID-19 pandemic. *Eur J Prev Cardiol* 2021;28:1599–609.
- 25 Han L, Zhao S, Li S, *et al.* Excess cardiovascular mortality across multiple COVID-19 waves in the United States from March 2020 to March 2022. *Nat Cardiovasc Res* 2020;2:322–33.
- 26 Gupta R, Gaur K. Epidemiology of ischemic heart disease and diabetes in India: an overview of the twin pandemic. *Curr Diabetes Rev* 2021;17:e100620186664.
- 27 Gupta R, Khedar RS, Gaur K, *et al.* Low quality cardiovascular care is important coronary risk factor in India. *Indian Heart J* 2018;70:S419–30.
- 28 Gupta R, Makkar JS, Sharma SK, *et al.* Association of health insurance status with cardiovascular risk factors, coronary artery disease, coronary interventions, and outcomes in India. *Int J Cardiol Cardiovasc Risk Prev* 2022;14:200146.
- 29 Sharma SK, Makkar JS, Bana A, *et al.* Premature coronary artery disease, risk factors, coronary angiography and interventions: a hospital-based registry in India. *Indian Heart J* 2022;74:391–7.
- 30 Gupta R, Lodha S, Sharma KK, *et al.* Association of diabetes with coronary artery disease, risk factors, clinical presentation, angiography, interventions, and outcomes: a prospective registry in India. *Diabetes Metab Syndr* 2023;17:102709.
- 31 American College of Cardiology's CathPCI registry. Available: <https://cvquality.acc.org/NCDR-Home/registries/hospital-registries/cathpci-registry> [Accessed 30 Apr 2023].
- 32 COVID-19 pandemic in India. Available: [https://en.wikipedia.org/wiki/COVID-19\\_pandemic\\_in\\_India](https://en.wikipedia.org/wiki/COVID-19_pandemic_in_India) [Accessed 18 Feb 2024].
- 33 Kerkar PG, Naik N, Alexander T, *et al.* Cardiological society of India: document on acute MI care during COVID-19. *Indian Heart J* 2020;72:70–4.
- 34 Mathieu E, Ritchie H, Rodas-Guirao LR, *et al.* Coronavirus pandemic (COVID-19). Available: <https://ourworldindata.org/coronavirus> [Accessed 30 Apr 2023].
- 35 Mattiuzzi C, Lippi G. Excess mortality is not synonymous with COVID-19 related deaths. *Am J Trop Med Hyg* 2022;107:217.
- 36 Czeisler MÉ, Marynak K, Clarke KEN, *et al.* Delay or avoidance of medical care because of COVID-19 related concerns: United States June 2020. *MMWR Morb Mortal Wkly Rep* 2020;69:1250–7.
- 37 Jabir A, Zachariah G, Mohanan PP, *et al.* COVID-19 infected ST-elevation myocardial infarction in India (COSTA-India). *Indian Heart J* 2023;75:243–50.
- 38 Singh K, Xin Y, Xiao Y, *et al.* Impact of COVID-19 pandemic on chronic disease care in India, China, Hong Kong, Korea, and Vietnam. *Asia Pac J Public Health* 2022;34:392–400.
- 39 Dutt B. *Humans of COVID: to hell and back*. New Delhi: Juggernaut, 2022.
- 40 Ghosh A. *Billions under lockdown: the inside story of India's fight against COVID-19*. New Delhi: Bloomsbury, 2021.
- 41 Kumar G, Mukherjee A, Sharma RK, *et al.* Clinical profile of hospitalized COVID-19 patients in the first and second wave of the pandemic: insights from an India registry based observational study. *Indian J Med Res* 2021;153:619–28.
- 42 Khedar RS, Gupta R, Mittal K, *et al.* Greater COVID-19 severity and mortality in hospitalised patients in the delta-wave compared to the other two waves: single centre prospective registry. *J Assoc Physicians India* 2023;71:11–2.
- 43 Ke C, Gupta R, Xavier D, *et al.* Divergent trends in ischemic heart disease and stroke mortality in India from 2000 to 2015: a nationally representative mortality survey. *Lancet Glob Health* 2018;6:e914–23.
- 44 Singh K, Kaushik A, Johnson L, *et al.* Patient experiences and perceptions of chronic disease care during the COVID-19 pandemic in India; qualitative study. *BMJ Open* 2021;11:e048926.
- 45 Su Y, Yuan D, Chen DG, *et al.* Multiple early factors anticipate post-acute COVID-19 sequelae. *Cell* 2022;185:881–95.
- 46 Gupta R. Health systems in the post-COVID-19 era: strengthening primary care and district hospitals. *RUHS J Health Sciences* 2020;5:61–5.
- 47 Singh J. *Future care: sensors, artificial intelligence, and the reinvention of medicine*. Rochester, MN: Mayo Clinic Press, 2023.