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Research Article

Association of COVID-19 Infection with Acute Coronary Syndrome: A Case–Control Study

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ABSTRACT

Background: The coronavirus disease 2019 (COVID-19) pandemic has had profound cardiovascular implications, with emerging evidence linking it to acute coronary syndrome (ACS). However, data from low- and middle-income countries, particularly India, remain limited.

Objective: To investigate the association between prior COVID-19 infection and the occurrence of ACS in patients admitted to a tertiary care hospital in Kerala, India.

Methods: This hospital-based case–control study was conducted in the Department of Internal Medicine, Government Medical College, Thiruvananthapuram, over one year. Fifty cases with ACS (ST-elevation myocardial infarction, non-ST-elevation myocardial infarction, or unstable angina) were matched 1:1 by age and sex with 50 controls without ACS. Data on demographics, comorbidities, lifestyle factors, COVID-19 infection and vaccination history, and laboratory parameters were collected using a structured proforma. Statistical analysis included chi-square test, Student's t-test, and odds ratios (OR) with 95% confidence intervals (CI).

Results: The mean age of cases (50.9 ± 15.4 years) and controls (51.9 ± 16.2 years) did not differ significantly ($p = 0.738$). Dyslipidemia (48% vs. 18%, $p = 0.001$) and family history of coronary artery disease (44% vs. 24%, $p = 0.035$) were significantly more common among cases. Diabetes mellitus (56% vs. 38%, $p = 0.071$) and hypertension (46% vs. 32%, $p = 0.151$) were more frequent in cases but not statistically significant. Prior COVID-19 infection was reported in 36% of cases and 22% of controls ($p = 0.123$). Vaccination status did not differ significantly between groups (68% vs. 64%, $p = 0.673$).

Conclusion: Although prior COVID-19 infection was not significantly associated with ACS, a higher prevalence among cases suggests a possible contributory role. Dyslipidemia and family history of coronary artery disease were significant risk factors for ACS in this cohort. These findings highlight the importance of traditional cardiovascular risk factors in the post-COVID era and the need for larger multicentric studies to clarify the causal relationship between COVID-19 and ACS.

Keywords: *COVID-19, Acute Coronary Syndrome, Dyslipidemia, Risk factors, India.*

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has posed unprecedented challenges to global health, extending beyond respiratory illness to involve multiple organ systems. Increasing evidence highlights its significant cardiovascular effects, with patients frequently presenting with myocarditis, arrhythmias, acute coronary syndrome (ACS), and heart failure (1–3). These manifestations suggest that SARS-CoV-2 infection has profound implications for cardiovascular health, particularly in populations already burdened by high rates of coronary artery disease (CAD).

The pathophysiological mechanisms linking COVID-19 and ACS are complex and multifactorial. Viral entry via angiotensin-converting enzyme 2 (ACE2) receptors in cardiac and endothelial tissues facilitates direct myocardial injury (4). In parallel, systemic inflammation, cytokine storm, and endothelial dysfunction promote a hypercoagulable state that can destabilize atherosclerotic plaques and precipitate coronary thrombosis (5,6). Hypoxia -driven oxygen supply–demand imbalance may also trigger type 2 myocardia l infarction, further compounding the cardiovascular burden of COVID-19. Several epidemiological studies have demonstrated an elevated risk of acute myocardial infarction following COVID-19 infection. Katsoularis et al. reported a fourfold increase in myocardial infarction risk in a Swedish cohort (7), while Modin et al. showed a similar temporal association in Danish patients (8). Observational studies from China confirmed that cardiac injury was present in up to 20–30% of hospitalized COVID-19 patients and strongly correlated with higher mortality (2,9). A large meta-analysis also revealed that patients with COVID-19 and pre-existing CAD had worse outcomes, including higher rates of ACS and death (10).

Traditional risk factors such as diabetes, hypertension, dyslipidemia, smoking, and family history remain central to the development of ACS (11). However, the interaction between these factors and COVID-19 infection remains incompletely understood, especially in low- and middle-income countries. India, in particular, bears one of the world's highest burdens of cardiovascular disease (12,13). Recent Indian registry studies reported an increased incidence of ACS admissions during the pandemic and delays in ca re due to lockdowns (14,15), making it imperative to explore whether COVID-19 infection amplifies the risk of ACS in this setting.

MATERIAL AND METHOD

Study Design and Setting

This study was designed as a hospital-based case–control investigation to assess the association between prior COVID-19 infection and the occurrence of Acute Coronary Syndrome (ACS). It was conducted in the Department of Internal Medicine, Government Medical College, Thiruvananthapuram, Kerala. The study duration was one year, beginning immediately after obtaining approval from the Institutional Ethics Committee.

Study Population

The study population consisted of patients admitted to the Department of Internal Medicine during the study period. The **case group** included individuals diagnosed with ACS, comprising ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina. The **control group** included patients admitted without clinical or investigational evidence of ACS. To minimize confounding, cases and controls were matched for age and sex in a 1:1 ratio.

Eligibility Criteria

Inclusion criteria were:

- Male and female patients aged ≥13 years.
- For cases: diagnosis of ACS based on either (a) characteristic ST–T changes in the electrocardiogram (ECG), or (b) elevated cardiac troponin levels (Trop T >100 or Trop I >0.04).
- For controls: absence of clinical, electrocardiographic, or biomarker evidence of ACS.

Exclusion criteria were:

1) Previous history of ACS.
2) Presence of chronic kidney disease or chronic liver disease.
3) Pregnant and lactating women.
4) Patients who declined to provide informed consent.

Sample Size Determination

The required sample size was estimated using the standard formula for unmatched case–control studies. Based on a Swedish matched cohort study published in *The Lancet* (2021), the reported prevalence of COVID-19 exposure was 48.97% among ACS patients and 19.7% among controls, with an anticipated odds ratio (OR) of 4.06. Assuming a two -sided α of 0.05 and 80% power, the minimum required sample size was calculated as **50 cases and 50 controls**.

Sampling Strategy

Eligible participants who satisfied the inclusion and exclusion criteria were recruited consecutively until the sample size was achieved. Sampling was carried out simultaneously in both groups to avoid temporal bias.

Data Collection

A structured proforma was used for data collection. After obtaining informed consent, detailed history taking, physical examination, and relevant laboratory and imaging investigations were performed. Clinical and laboratory information was systematically recorded for all study participants.

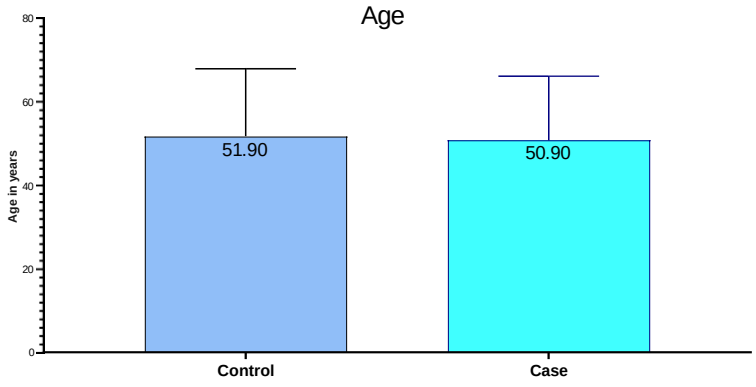
Statistical Analysis

Data entry was performed using Microsoft Excel, and statistical analysis was carried out using SPSS version 27. Continuous variables were expressed as mean ± standard deviation (SD) and compared using Student's *t*-test. Categorical variables were presented as frequencies and percentages and compared using the chi-square test. Odds ratios (OR) with 95% confidence intervals (CI) were calculated to assess the association between prior COVID-19 infection and ACS. A *p* value <0.05 was considered statistically significant.

RESULT

Age Distribution:

The study compared the average age of patients in the control group and the case group. The mean age for the control group was 51.9 years with a standard deviation of 16.2, while the case group had a mean age of 50.9 years with a standard deviation of 15.4. The t-test value was 0.336 with a p-value of 0.738, indicating no significant difference in age between the two groups.



Demographics Characteristics of Study Participants:

The demographic and clinical characteristics of the study participants are summarized in **Table 1**. Both groups were comparable in terms of sex distribution, with males comprising 52% in the control group and 54% in the case group (p = 0.841). The prevalence of diabetes mellitus (56% vs. 38%, p = 0.071) and hypertension (46% vs. 32%, p = 0.151) was higher among cases compared to controls, although the differences were not statistically significant.

Dyslipidemia was observed more frequently in the case group (48%) than in the control group (18%), and this difference was statistically significant (p = 0.001). Similarly, a positive family history of coronary artery disease (CAD) was significantly higher among cases (44%) compared to controls (24%) (p = 0.035).

In terms of lifestyle factors, smoking (30% vs. 28%, p = 0.826) and alcoholism (34% vs. 36%, p = 0.834) did not differ significantly between the two groups.

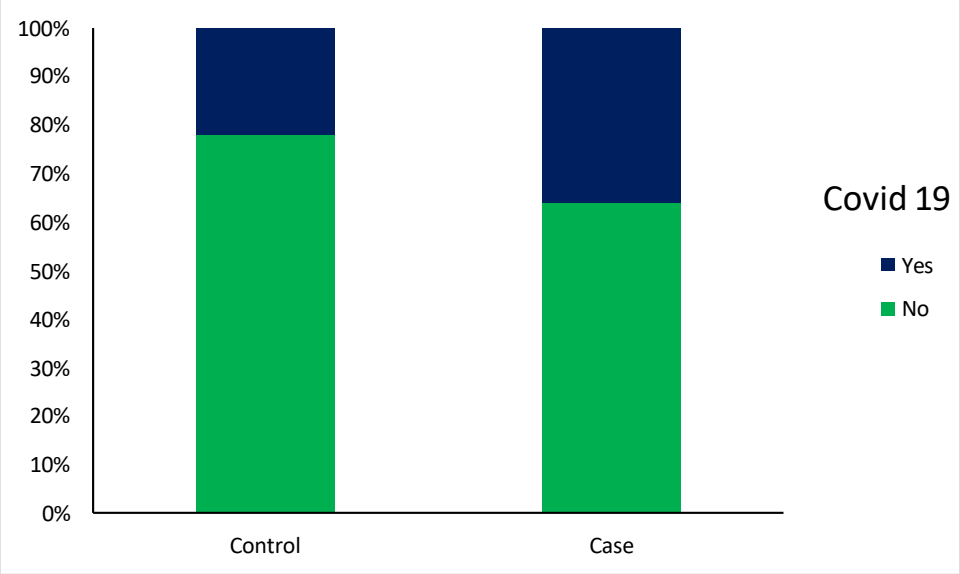
Table 1: Demographics Characteristics of Study Participant

Demographics Characteristics	Control		Case		χ^2	df	p
	N	%	N	%			

Male	26	52	27	54			
Female	24	48	23	46	0.04	1	0.841
Diabetes	19	38	28	56	3.252	1	0.071
Hypertension	16	32	23	46	2.06	1	0.151
Dyslipidemia	9	18	24	48	10.176	1	0.001
CAD in family	12	24	22	44	4.456	1	0.035
Smoking	14	28	15	30	0.049	1	0.826
Alcoholism	18	36	17	34	0.044	1	0.834

COVID-19 Infection:

The study also assessed prior exposure to COVID-19 infection among participants. In the control group, 11 individuals (22%) reported a history of COVID-19 infection, compared to 18 individuals (36%) in the case group. The chi-square test yielded a value of 2.38 with a p-value of 0.123, indicating that the difference between the groups was not statistically significant which is shows in figure 2



COVID-19 Vaccine:

The COVID-19 vaccination status was compared between the two groups. Among the controls, 18 participants (36%) were unvaccinated and 32 (64%) had received vaccination. In the case group, 16 participants (32%) were unvaccinated, while 34 (68%) were vaccinated. The chi-square test value was 0.178 with a p-value of 0.673, indicating no statistically significant difference in vaccination status between the groups.

Table 3: Comparison of covid-19 vaccination status in control and case group

Covid 19 vaccine	Control		Case		χ^2	df	P
	N	%	N	%			
No	18	36	16	32			
Yes	32	64	34	68	0.178	1	0.673
Total	50	100	50	100			

DISCUSSION

This study examined the association between prior COVID-19 infection and acute coronary syndrome (ACS) in a South Indian tertiary care setting. The demographic profile showed no significant age or sex differences between cases and controls, consistent with earlier findings where demographic distribution did not significantly alter ACS outcomes in COVID-19 patients (5,16).

Regarding comorbidities, dyslipidemia was significantly more frequent in the case group. This aligns with Madjid et al., who emphasized that systemic inflammation in COVID-19 may destabilize lipid-rich plaques (6). Similarly, registry-based data from Europe and India have demonstrated that patients with dyslipidemia were at greater risk of myocardial infarction during COVID-19 (14,17). Family history of CAD also emerged as an independent risk factor in this study, consistent with global data suggesting that genetic predisposition magnifies the cardiovascular impact of COVID-19 (7,18).

Diabetes and hypertension were more common among cases, although not statistically significant. However, multiple international studies, including Clerkin et al. and a meta -analysis by Wu et al., found both conditions to be predictors of poor cardiovascular outcomes in COVID-19 (1,19). The absence of significance in this study may reflect limited sample size rather than lack of association.

Lifestyle factors such as smoking and alcohol use showed no significant differences. This is consistent with findings from Stefanini et al. and Bangalore et al., who reported that acute infection and inflammation outweighed chronic exposures in precipitating ACS during COVID-19 (7,20).

Although prior COVID-19 infection was not significantly associated with ACS in this study, the higher prevalence among cases supports international data. Katsoularis et al. and Modin et al. reported clear temporal links between infection and ACS (7,8), while Guo et al. demonstrated elevated cardiac biomarkers in fatal COVID-19 cases (5). Large Indian studies, including ICMR reports, have similarly shown that COVID-19 survivors carry a higher long-term risk of major adverse cardiac events (15,21).

Vaccination status did not differ significantly between groups. While our study suggests no direct association, recent global evidence shows that vaccination indirectly reduces cardiovascular complications by lowering infection severity (22). Ongoing cohort studies are needed to validate this in Indian populations.

With respect to clinical parameters, cholesterol levels were significantly higher in ACS cases, reinforcing the importance of lipid control post-COVID. This is consistent with both Huang et al. and global guidelines emphasizing secondary prevention in post-COVID patients with dyslipidemia (8,23).

Overall, the findings suggest that while prior COVID-19 infection was not significantly associated with ACS in this study, the higher prevalence among cases, coupled with significant associations of dyslipidemia and family history of CAD, underscores the potential for COVID-19 to exacerbate cardiovascular risk in susceptible individuals. These results are consistent with global literature highlighting the interplay between infection-driven inflammation, genetic predisposition, and lipid abnormalities in ACS pathogenesis. Future prospective, multicenter studies with larger cohorts are necessary to validate these findings and inform preventive cardiology in the post-pandemic era.

CONCLUSION

This study indicates a possible association between prior COVID-19 infection and the risk of developing Acute Coronary Syndrome (ACS), although statistical significance was not achieved. The higher prevalence of dyslipidemia and family history of coronary artery disease (CAD) among ACS patients highlights the critical role of traditional cardiovascular risk factors in this context. These results emphasize the need for close cardiovascular surveillance and proactive risk management in patients with a history of COVID-19, particularly those with underlying susceptibility. Future large-scale, prospective studies are warranted to elucidate the biological mechanisms linking COVID-19 to ACS and to develop targeted preventive and therapeutic strategies in the post-pandemic era.

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