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## Article

# Disparities and Outcomes in the First and Second Year of the Pandemic on Events of Acute Myocardial Infarction in COVID-19 Patient

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**Abstract:** Background: Coronavirus disease 2019 (COVID-19) caused several cardiovascular complications, including acute myocardial infarction(AMI) in infected patients. Our study aims to understand the overall trends of AMI among COVID-19 patients during the first two years of the pandemic and the disparities and outcomes between the first and second years. Methods: Our retrospective analysis via the 2020 and 2021 National Inpatient Sample(NIS) for hospitalizations between April 2020 and December 2021 analyzed adults with a primary diagnosis of COVID-19 who experienced events of AMI. We compared month-to-month events of AMI and mortality of AMI patients with COVID-19, patient characteristics, and outcomes between the 2020 and 2021 AMI samples. Results: There were 2,541,992 COVID-19 patients, with 3.55% experiencing AMI. The highest rate of AMI was in December 2021 (4.35%). No statistical differences in trends of AMI mortality were noted over the 21 months. AMI cases in 2021 had higher odds of undergoing PCI (aOR 1.627, p<0.01). They experienced higher risks of acute kidney injury (aOR 1.078, p<0.01), acute ischemic stroke (aOR 1.215, p<0.01), cardiac arrest (aOR 1.106, p<0.01), need for mechanical ventilation (aOR 1.133, p<0.01), and all-cause mortality (aOR 1.032, 95% CI 1.001-1.064, p=0.043). Conclusions: The incidence of AMI among COVID-19 patients fluctuated over the 21 months of our study, with a peak in December 2021. COVID-19 patients reporting AMI in 2021 experienced higher overall odds of multiple complications, which could relate to the exhaustive burden of the pandemic in 2021 on healthcare, the changing impact of the virus variants, and the hesitancy of infected patients to seek care.

**Keywords:** COVID-19; cardiovascular complications; national inpatient sample; United States; mortality; epidemiology

## Introduction

Since the initial outbreak of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in late December 2019, more than 703 million people have been infected with Coronavirus disease 2019 (COVID-19), which led to an estimated 6.9 million deaths.(1, 2) While the virus primarily targets the respiratory system, its impact on coagulopathy triggering thrombosis and the direct and indirect insult on the cardiovascular system can also provoke a higher risk of acute myocardial infarction (AMI).(3, 4)

Over the course of the pandemic, many drastic measures and changes were brought forward to reduce the impact of the virus, such as lockdown protocols and vaccinations. While past studies from the National Inpatient Sample(NIS) have evaluated different aspects of how the virus influenced the odds and outcomes of AMI patients in 2020(5-8), at present, there are none comparing how COVID-19 patients with AMI fared between the two years of the pandemic. Therefore, we propose a retrospective study to improve our understanding of potential differences.

## Materials and Methods

### *Data Source*

We evaluated patients with a primary diagnosis code for COVID-19 in 2020 and 2021 via the NIS. The NIS is produced each year under the supervision of the Healthcare Cost Utilization Project(HCUP) and the Agency for Healthcare Research and Quality(AHRQ). The de-identified data from the NIS covers around 20% of hospital records across 48 states in the United States. The use of the discharge code "DISCWT" allows users to estimate more than 97% of the population.(9, 10)

The 2021 NIS was released in 2024 and is, to date, the most recent national data covering COVID-19 hospitalization by HCUP. The NIS contains multiple patient records at a de-identified level, along with up to 40 clinical diagnoses and 25 procedures that can be evaluated using International Classification of Diseases (ICD) codes. For the NIS 2020 and 2021, users are required to use ICD-10 codes. In addition, the NIS also contains hospital characteristics such as location/teaching status, region, and bed size.(9)

### *Sample and Statistical Analysis*

The ICD-10 diagnosis code for COVID-19, "U071", was started on April 1<sup>st</sup>, 2020, and as per HCUP's recommendations, we only retained patients from April 1st, 2020, till December 31st, 2021, for our study.(9)

First, all cases of COVID-19 with a primary diagnosis were extracted. We excluded those of ages <18 years. The month-to-month event of AMI among COVID-19 hospitalizations was evaluated using linear-by-linear association.

We then proceeded to retain only COVID-19 cases with a coexisting code for AMI, and two groups were made: patients admitted in 2020 vs. those admitted in 2021. Additional comorbidities, diagnoses, and procedures were included via their ICD-10 codes.(10-22) Cells missing data for month or year were excluded from this study. The characteristics of the two groups were compared using Chi-Square tests for categorical variables (reported as frequency (%)) and T-tests(or Mann-Whitney U tests) for continuous variables (reported as mean  $\pm$  SD).(9)

Our primary outcome was the all-cause mortality among COVID-19 patients with AMI. We further explored the use of CABG, PCI, mechanical ventilation, IABP, and events of AKI, cardiogenic shock, cardiac arrest, and cardiac arrhythmias (atrial fibrillation, ventricular fibrillation, and supraventricular tachycardia) in these patients. The mean length of stay(LOS) and their mean hospital charges were also compared. The complications and outcomes were evaluated via multivariable regression analyses as an adjusted odds ratio (aOR), along with their 95% confidence interval (95% CI), and p-value. We retained statistical significance for  $p < 0.05$  throughout our study. The analyses were performed using SPSS 29.0 (IBM Corp., Armonk, New York, USA) and STATA 18.0 MP (StataCorp LLC).

As HCUP provided the data in de-identified form, we were exempted from any ethical or IRB approval. We also adhered strictly to the guidelines and rules of HCUP in the use of these databases. All cases <11 were not included in our results.(9)

Results

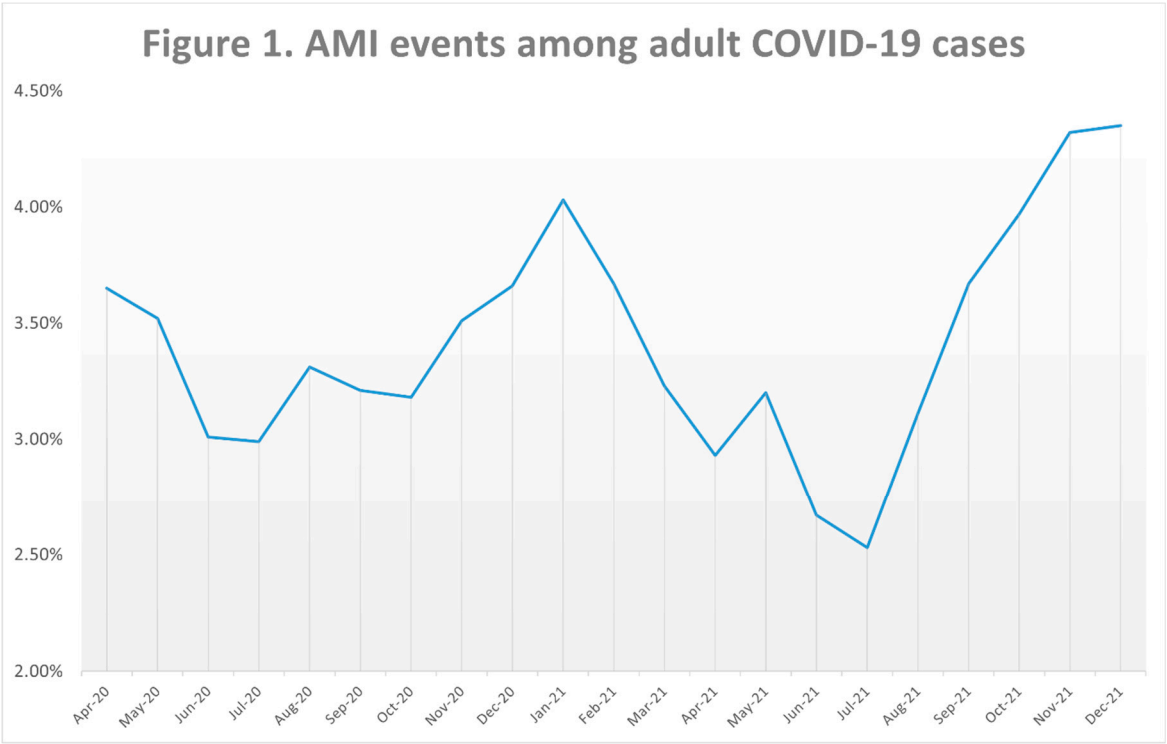
In the United States, an estimated 2,541,992 adult cases of COVID-19 were found between April 2020- December 2021, with 1,019,860 cases between April to December 2020 and 1,522,131 cases between January to December 2021.

AMI Trend among COVID-19 Cases

The incidence of AMI among COVID-19 cases fluctuated across the 21 months of our study. Between April and July 2020, it dropped from 3.65% to 2.99%, followed by a rise till January 2021(4.03%). From January 2021 to July 2021, a drop was seen as it reached 2.53%, which was followed by a sharp rise till December 2021(4.35%) ( $p_{trend}<0.01$ ). The overall rate of AMI across these 21 months was 3.55% (Table 1, Figure 1).

**Table 1.** AMI cases among adult COVID-19 patients between April 2020 to December 2021 in the United States.

Time	AMI events among COVID-19 cases
Apr-20	3.65%
May-20	3.52%
Jun-20	3.01%
Jul-20	2.99%
Aug-20	3.31%
Sep-20	3.21%
Oct-20	3.18%
Nov-20	3.51%
Dec-20	3.66%
Jan-21	4.03%
Feb-21	3.67%
Mar-21	3.23%
Apr-21	2.93%
May-21	3.20%
Jun-21	2.67%
Jul-21	2.53%
Aug-21	3.11%
Sep-21	3.67%
Oct-21	3.97%
Nov-21	4.32%
Dec-21	4.35%
Overall	3.55%



Comparing AMI Cases in COVID-19 Patients in 2020 vs. 2021

We evaluated 90,180 AMI cases among COVID-19 patients. 34,735 were in our 2020 cohort, while 55,445 were in hospitalizations of COVID-19 cases in 2021.

Baseline Characteristics

AMI cases in COVID-19 patients were younger in 2021 as compared to 2020, with a mean age of 70.31 vs. 72.38 years( $p<0.01$ ) (Table 2).

**Table 2.** Characteristics of COVID-19 patients with AMI in 2020 vs 2021 in the United States.

Variable	AMI among COVID-19 patients in 2020 (n=34735)(%)	AMI among COVID-19 patients in 2021 (n=55445)(%)	p-value
Mean age (±SD)	72.38(13.31)	70.31(13.71)	<0.01
Weekend admission	26.8	26.7	0.766
Female	39.3	40.5	<0.01
Primary payer			<0.01
Medicare	69.9	66.1	
Medicaid	8.7	9.4	
Private	15.5	17.8	
Race			<0.01
White	55.6	65.0	
Black	17.8	16.1	
Hispanic	18.0	12.4	

Median household income			<0.01
0-25th percentile	36.8	36.8	
26th to 50th percentile (median)	<b>29.6</b>	27.4	
51st to 75th percentile	20.5	<b>21.7</b>	
76th to 100th percentile	13.1	<b>14.1</b>	
<b>Hospital characteristics</b>			
Hospital bed size			<0.01
Small	23.5	24.7	
Medium	29.9	30.7	
Large	46.6	44.6	
Location/Teaching status			<0.01
Rural	10.9	13.1	
Urban non-teaching	18.0	18.5	
Urban teaching	71.2	68.3	
Region of hospital			<0.01
Northeast	18.7	16.6	
Midwest	2.1	22.9	
South	38.7	42.8	
West	16.5	17.7	
<b>Comorbidities</b>			
Sarcoidosis	0.3	0.3	0.791
SLE	0.6	0.5	0.495
Rheumatoid arthritis	2.1	2.2	0.290
Hyperthyroidism	0.6	0.6	0.615
Hypothyroidism	<b>14.1</b>	13.2	<0.01
Hypertension	27.9	28.1	0.543
Dyslipidemia	<b>53.2</b>	49.4	<0.01
Smoking	28.1	<b>30.1</b>	<0.01
Diabetes	<b>49.0</b>	45.9	<0.01
CKD	<b>40.5</b>	39.2	<0.01
Prior CABG	<b>8.4</b>	7.6	<0.01
Prior PCI	<b>10.7</b>	9.2	<0.01
Family history of CAD	<b>4.5</b>	4.0	<0.01
Peripheral vascular disease	4.4	4.3	0.604
Prior stroke	<b>8.3</b>	7.6	<0.01
Cirrhosis	5.2	<b>5.8</b>	<0.01
Alcohol abuse	1.8	<b>2.4</b>	<0.01
Prior MI	<b>9.4</b>	8.8	<0.01
Obesity	20.4	<b>25.5</b>	<0.01
Drug abuse	2.0	<b>2.8</b>	<0.01
COPD	20.7	<b>21.9</b>	<0.01



Mean CCI Score	5.04(3.35)	4.91(3.36)	<0.01
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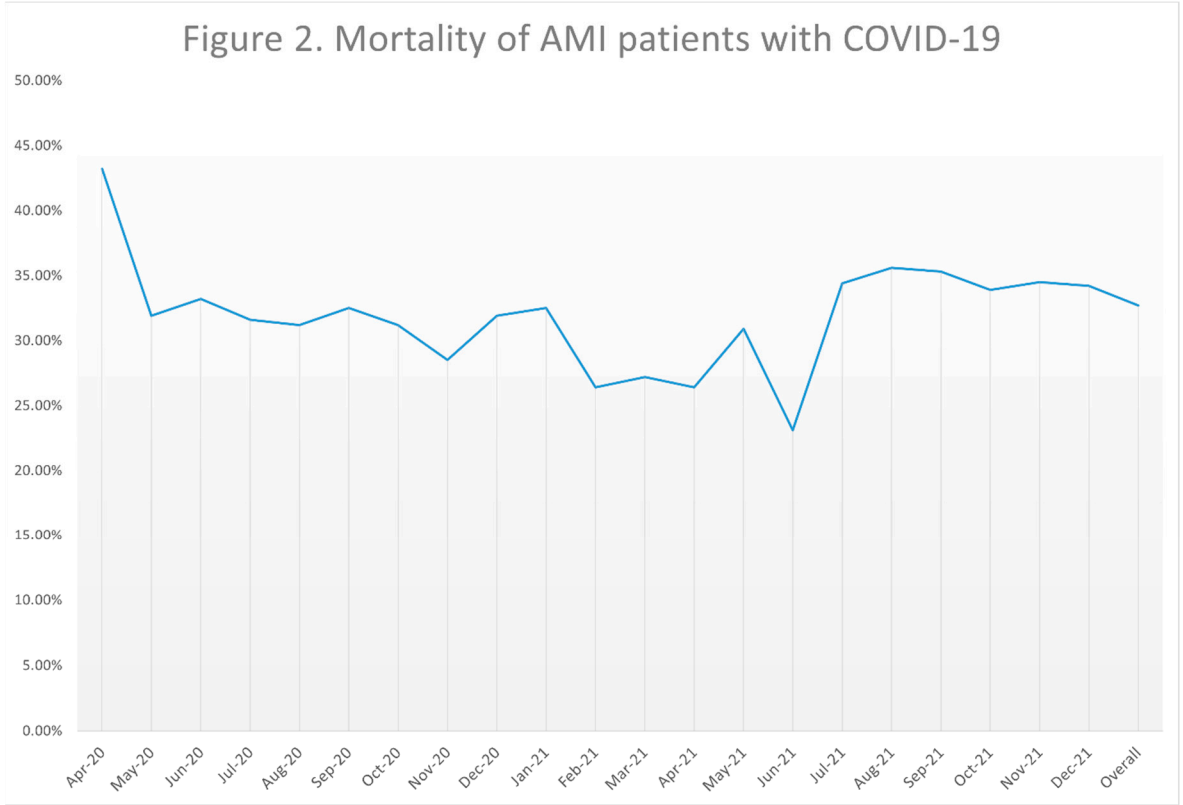
Both groups involved mostly males, with a slightly higher presence of females in 2021 vs. 2020 (40.5% vs. 39.3%,  $p<0.01$ ). In addition, we found that Medicare covered 69.9% of cases in 2020 and 66.1% of cases in 2021( $p<0.01$ ). Racially, Whites formed the biggest part of the AMI cases as 55.6% in 2020 and 65.0% in 2021 were Whites. Most cases were also in the 0-25<sup>th</sup> household income percentile in both groups (36.8% in 2020 and 36.8% in 2021,  $p<0.01$ ), and the patients were treated in large bed-size hospitals (46.6% in 2020 and 44.6% in 2021), and hospitals classified as urban teaching centers(71.2% in 2020, 68.3% in 2021,  $p<0.01$ ). Geographically, most cases were from the southern regions of the US(38.7% in 2020, 42.8% in 2021,  $p<0.01$ ).

We found that cases in 2020 had higher prevalence of hypothyroidism (14.1%vs. 13.2%,  $p<0.01$ ), dyslipidemia (53.2% vs. 49.4%,  $p<0.01$ ), diabetes (49.0% vs. 45.9%,  $p<0.01$ ), chronic kidney disease (40.5% vs. 39.2%,  $p<0.01$ ), prior CABG (8.4% vs. 7.6%,  $p<0.01$ ), prior PCI (10.7% vs. 9.2%,  $p<0.01$ ), family history of CAD (4.5% vs. 4.0%,  $p<0.01$ ), prior stroke (8.3% vs. 7.6%,  $p<0.01$ ), and prior myocardial infarction(9.4% vs. 8.8%,  $p<0.01$ ). On the contrary, 2020 cases had fewer smokers (28.1% vs. 30.1%,  $p<0.01$ ), cases with liver cirrhosis (5.2% vs. 5.8%,  $p<0.01$ ), alcohol abuse (1.8% vs. 2.4%,  $p<0.01$ ), obesity (20.4% vs. 25.5%,  $p<0.01$ ), drug abuse (2.0% vs. 2.8%,  $p<0.01$ ), and COPD (20.7% vs. 21.9%,  $p<0.01$ ).

The overall mean Charlson Comorbidity (CCI) score was higher in the 2020 cohort (5.04 vs. 4.91.  $p<0.01$ ). 2021 admissions were longer (11.20 days vs. 9.95 days,  $p<0.01$ ), with a higher mean hospital charge (\$155587 vs. \$130538,  $p<0.01$ ).

Trends in Mortality

The overall mortality rate fluctuated between the 21 months of our study, with a maximum of 43.2% observed in April 2020 and a minimum of 23.1% in June 2021. The trend was not statistically significant ( $p_{trend}=0.103$ )(Table 3, Figure 2).



**Table 3.** Mortality rates among AMI events in COVID-19 patients between April 2020 to December 2021 in the United States.

Time	Mortality of AMI patients with COVID-19
Apr-20	43.20%
May-20	31.90%
Jun-20	33.20%
Jul-20	31.60%
Aug-20	31.20%
Sep-20	32.50%
Oct-20	31.20%
Nov-20	28.50%
Dec-20	31.90%
Jan-21	32.50%
Feb-21	26.40%
Mar-21	27.20%
Apr-21	26.40%
May-21	30.90%
Jun-21	23.10%
Jul-21	34.40%
Aug-21	35.60%
Sep-21	35.30%
Oct-21	33.90%
Nov-21	34.50%
Dec-21	34.20%
Overall	32.70%

*Events of Cardiac Arrhythmias*

Multivariable regression models for cardiac arrhythmias found that in 2021, there were higher odds of events of ventricular tachycardia (aOR1.126, 95% CI 1.062-1.194,  $p<0.01$ ) among COVID-19-positive patients who experienced AMI than those in 2020. No differences were seen for atrial fibrillation or supraventricular tachycardia (Table 4).

**Table 4.** Arrhythmias, procedures, and complications among COVID-19 patients with AMI in 2021 vs. 2020(reference).

Cardiac arrhythmias				
Variable	p-value	aOR	Lower 95% CI	Upper 95% CI
Atrial fibrillation	.424	1.013	.982	1.045
Supraventricular tachycardia	.527	1.023	.954	1.096
Ventricular tachycardia	<.001	1.126	1.062	1.194
Complications				
Variable	p-value	aOR	Lower 95% CI	Upper 95% CI



PCI	<.001	1.627	1.454	1.822
Cardiogenic shock	.841	1.008	.931	1.092
IABP	.565	.902	.636	1.281
AKI	<.001	1.078	1.047	1.110
AIS	<.001	1.215	1.113	1.328
Cardiac arrest	<.001	1.106	1.050	1.166
Invasive mechanical ventilation	<.001	1.133	1.096	1.172
Died	.043	1.032	1.001	1.064

### *Complications and Outcomes*

Our study found several differences in outcomes between the two years of the pandemic. In 2021, patients with AMI while admitted for COVID-19 had a higher likelihood of having a PCI (aOR 1.627, 95% CI 1.454-1.822,  $p<0.01$ ), while also reporting more complications such as acute kidney injury (aOR 1.078, 95% CI 1.047-1.110,  $p<0.01$ ), acute ischemic stroke (aOR 1.215, 95% CI 1.113-1.328,  $p<0.01$ ), events of cardiac arrest (aOR 1.106, 95% CI 1.050-1.166,  $p<0.01$ ), need for mechanical ventilation (aOR 1.133, 95% CI 1.096-1.172,  $p<0.01$ ), and all-cause mortality (aOR 1.032, 95% CI 1.001-1.064,  $p=0.043$ ). We found no statistically significant results for events of cardiogenic shock and the need for IABP between these two years. (Table 3).

### **Discussions**

In our study, there were several key differences in incidence of AMI among COVID-19 patients, patient characteristics, and outcomes of the AMI cases between the first two years of the pandemic in the United States.

We found that AMI events among COVID-19 cases reached an initial peak during January 2021. This corresponds to another peak previously reported among the daily deaths during that same month, which to date was the highest number of COVID-related deaths reported in the United States and worldwide.(23, 24) Our analysis also confirmed a continuous drop in AMI cases between January to July 2021, which could also correlate to the introduction of vaccination access to the general public and expansion of vaccination campaigns in the United States. However, we further noticed that from July 2021, the incidence of AMI among COVID-19 patients rose constantly till the end of our study (December 2021). This may be linked to the waning levels of antibodies following vaccination, the changes in preventive protocols to prevent infection in at-risk groups, and the impact of viral mutations(such as Delta, Omicron, Alpha, Gamma, and Beta) and their pathophysiological impact on the cardiovascular system.(25-32) Further studies exploring the hesitancy of patients with AMI symptoms to seek medical care due to fear of being infected with COVID-19 while being hospitalized should also be explored.(33, 34)

There were also some discrepancies in the patient demographics between the AMI patients in our two groups. AMI patients were younger in 2021, with varying differences in several comorbidities between the two groups, and expressed a lower mean CCI score in 2021 as compared to 2020. Based on the data provided by the CDC, the mortality rates of all COVID-19 cases among various younger adult groups also rose in 2021; for example the mortality among COVID-19 patients of ages 35-44 and 45-54 rose from 16.0 and 45.2 per 100,000 standard population to 40.6 and 97.9 per 100,000 standard population in 2021, while the rise in much older groups was less drastic; from 644.4 to 649.3 among patients ages 75-84.(35) Furthermore, vaccination hesitancy among younger population may have predisposed them to worse outcomes following COVID-19.(36) We therefore encourage additional retrospective studies to identify the factors associated with the differences seen, as it can be utilized as a model to improve the outcomes in any future pandemics.(37)

Finally, our study also found several differences in the outcomes between the 2021 and 2020 AMI cases in COVID-19 patients. The CDC has confirmed that there was a higher mortality rate among COVID-19 patients in 2021, as the overall deaths rose from 93.2 per 100,000 individuals to 111.4 per 100,000 individuals. A similar rise was seen as 2021 AMI cases reported higher odds of death in our study.(35) Furthermore, we also found various complications such as events of cardiac arrest, ventricular tachycardia, acute ischemic stroke, acute kidney injury and need for mechanical ventilation, which can predispose to a higher mortality rate.(38) The higher use of PCI in 2021 could correlate with the improvement in the access of care and distribution of resources as compared to the first year of the pandemic.(39, 40)

As our study relies on the NIS, there are several associated limitations that can be addressed in future studies. The 2021 NIS does not have data on the vaccination status of the patients, which could influence outcomes. In addition, the NIS does not include details about their medication history and treatment plans during their hospitalization. Our study could not include critical physical examination, laboratory test results, and radiographic findings that could help categorize and study the patients based on severity. Mistakes in codes and inputs at physician level may also influence our results.(6, 41)

## Conclusion

Our retrospective study, via one of the biggest hospitalization records, has shown that incidence of AMI among COVID-19 patients between April 2020 to July 2021 was highest in January 2021, and from July 2021 the numbers rose constantly till December to reach a new peak. Differences in the comorbidities and characteristics existed in the COVID-19 positive adults with AMI between the two years, who also experienced more complications in 2021, and a higher adjusted odds ratio of mortality.

**Author Contributions:** Conceptualization, Jasninder Dhaliwal, Manraj S Sekhon, Arush Rajotia, Ashujot K Dang, 5. Prabh Partap Singh, Hemamalini Sakthivel, Raheel Ahmed, Renuka Verma, Kamleshun Ramphul and Prabhdeep S Sethi; Methodology, Hemamalini Sakthivel; Validation, Kamleshun Ramphul; Formal analysis, Hemamalini Sakthivel, Renuka Verma and Kamleshun Ramphul; Investigation, Jasninder Dhaliwal, Manraj S Sekhon, Kamleshun Ramphul and Prabhdeep S Sethi; Data curation, Hemamalini Sakthivel, Renuka Verma and Kamleshun Ramphul; Writing – original draft, Jasninder Dhaliwal, Manraj S Sekhon, Arush Rajotia, Ashujot K Dang and Prabhdeep S Sethi; Writing – review & editing, Jasninder Dhaliwal, Arush Rajotia, 5. Prabh Partap Singh, Hemamalini Sakthivel, Raheel Ahmed, Renuka Verma, Kamleshun Ramphul and Prabhdeep S Sethi; Supervision, Kamleshun Ramphul and Prabhdeep S Sethi. All authors read and approved the final draft.

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**Informed Consent Statement:** Not applicable

**Data Availability Statement:** The authors are not allowed to share the database. However, anyone interested in the database can contact HCUP <https://hcup-us.ahrq.gov/nisoverview.jsp>.

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**Conflicts of Interest:** The authors declare no conflict of interest.

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