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Sex and Ethnic Disparities during COVID-19 Pandemic among Acute Coronary Syndrome Patients

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Abstract: Introduction: The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) caused a global pandemic that emerged in 2019. During this period, a significant disparity in hospitalization and mortality rates emerged, particularly in terms of Ethnicity and sex. Notably, this study aims to examine the influence of sex and Ethnicity on acute coronary syndrome outcomes, specifically during the global SARS-CoV-2 pandemic. Methods: This retrospective observational study analyzed adult patients hospitalized with a primary diagnosis of acute coronary syndrome in the United States in 2020. Primary outcomes included inpatient mortality and the time from admission to percutaneous coronary intervention (PCI). Secondary outcomes encompassed the length of stay and hospital costs. The National Inpatient Sample (NIS) database was utilized to identify and study patients in our test group. Results: A total of 779,895 patients hospitalized with a primary diagnosis of acute coronary syndrome in the year 2020 and 935,975 patients in 2019 were included in this study. Baseline findings revealed that inpatient mortality was significantly higher in 2020 compared to 2019, regardless of sex and Ethnicity (adjusted odds ratio (aOR) 1.20, 95% confidence interval (CI) 1.12–1.23, p -value < 0.001). Concerning primary outcomes, there was no difference in inpatient mortality for hospitalized patients of different sexes between 2019 and 2020 (STEMI: aOR 1.05, 95% CI 0.96–1.14, p -value 0.22; NSTEMI/UA aOR 1.08, 95% CI 0.98–1.19, p -value 0.13). Regarding time to admission for PCI, NSTEMI/UA cases were found to be statistically significant in female patients compared to males (mean difference 0.06 days, 95% CI 0.02–0.10, p -value < 0.01) and African Americans compared to Caucasians (mean difference 0.13 days, 95% CI 0.06–0.19, p < 0.001). In terms of the length of stay, female patients had a shorter length of stay compared to males (mean difference –0.22, 95% CI –0.27 to –0.16, p -value < 0.01). Conclusions: As acute coronary syndrome is an urgent diagnosis, a global pandemic has the potential to exacerbate existing healthcare disparities related to sex and Ethnicity. This study did not reveal any difference in inpatient mortality, aligning with studies conducted prior to the pandemic. However, it highlighted significantly longer treatment times (admission to PCI) for NSTEMI/UA management in female and African American populations. These findings suggest that some disparities may have diminished during the pandemic year, warranting further research to confirm these trends in the years to come.

Keywords: gender; ethnicity; disparities; inpatient mortality



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1. Introduction

The COVID-19 pandemic has presented unprecedented challenges to healthcare systems worldwide, illuminating underlying disparities in patient outcomes across diverse demographic groups. Amidst the pandemic, individuals with acute coronary syndrome (ACS) have encountered distinctive challenges, with emerging evidence suggesting differential impacts based on sex and Ethnicity. In 2019, Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV-2) was discovered, causing widespread COVID-19 infections

that would result in a global pandemic. In the United States alone, the COVID-19 pandemic has been estimated to be responsible for 101 million cases and 1.1 million deaths [1]. Moreover, the pandemic has brought to the forefront known healthcare disparities specifically related to ethnicity and sex. The global crisis of COVID-19 has highlighted its impact on different sexes and Ethnicities. The intersection of COVID-19 and ACS has raised critical concerns. Studies have highlighted not only the direct cardiovascular implications of COVID-19 infection but also the secondary effects of the pandemic on the management and outcomes of ACS patients. Factors such as delayed presentation to healthcare facilities, altered treatment pathways, and variations in access to care have significantly influenced the landscape of ACS management during this crisis [2]. Studies have revealed that males and females experience varied susceptibility and severity levels, attributed to biological differences like immune response variations. For instance, females often exhibit stronger immune activity, potentially influencing their lower vulnerability to viral infections. Regarding ethnic groups, variations in COVID-19 susceptibility, access to healthcare resources, and cultural determinants have contributed to differential outcomes among various ethnic groups with ACS, warranting focused attention to address these inequalities. Studies have found that African Americans and Hispanics are about twice as likely to be hospitalized due to COVID-19 compared to Caucasians [3].

The influence of Ethnicity on COVID-19 outcomes has been analyzed in numerous studies. The pandemic has shed light on ethnic disparities within the ACS patient population. Variations in COVID-19 susceptibility, access to healthcare resources, and cultural determinants have contributed to differential outcomes among various ethnic groups with ACS, warranting focused attention to address these inequalities. Studies have found that African Americans and Hispanics are about twice as likely to be hospitalized due to COVID-19 compared to Caucasians [4]. This discrepancy also extends to mortality rates, with African Americans being one and a half times more likely to die from a COVID-19 infection compared to Caucasians [4]. With respect to sex, a study conducted during the initial stages of the pandemic found that men with COVID-19 infection had a higher likelihood of death compared to women, regardless of age [5].

The COVID-19 pandemic has exacerbated adverse outcomes for acute coronary syndrome (ACS) patients. Studies indicate increased morbidity and mortality, often due to delays in seeking medical help driven by fears of COVID-19 exposure [6,7]. This hesitation in seeking timely care affected various demographic groups, potentially worsening outcome disparities. Understanding how Ethnicity and sex intersect with these delays is crucial to address health disparities and enhance care strategies for ACS patients during pandemics. There was a noticeable increase in the time before medical intervention during the early stages of the pandemic, likely aimed at reducing unwarranted COVID-19 exposure [5,8].

In this study, we aim to analyze the impact of sex and Ethnicity on acute coronary syndrome outcomes during the COVID-19 pandemic. Specifically, we aim to evaluate two key metrics: inpatient mortality rates and the duration from admission to percutaneous coronary intervention (PCI) among ACS patients during this critical period.

2. Methods

2.1. Study Design

The methodology employed in this study was a retrospective observational analysis encompassing adult patients admitted with the primary diagnosis of acute coronary syndrome (ACS) within the United States throughout the year 2020. This study's primary objective was to compare the outcomes of ACS patients based on their sex and Ethnicity during 2020 in contrast to 2019. The key endpoints under scrutiny were the rates of inpatient mortality and the duration from admission to PCI. Additionally, secondary endpoints included the duration of hospital stays and the overall cost of hospitalization. The study delved into independent variables such as sex and Ethnicity while accounting for potential confounders like age, hospital bed capacity, primary payer, hospital location, patient comor-

bidities assessed by the Charlson Comorbidity Index (CCI), hospital region, and teaching status.

2.2. Data Source and Sample

Analysis was conducted using the National Inpatient Sample (NIS) database of the Healthcare Utilization Project (HCUP), a database created by the Agency for Healthcare Research and Quality (AHRQ). NIS consists of discharge data from a 20% stratified sample of US hospitalizations designed to be representative of all nonfederal acute care inpatient hospitalizations nationwide. Patient identification was carried out using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD10-CM) coding system. Specific ICD10-CM codes were sought for primary diagnoses including STEMI (I21, I211, I212), NSTEMI (I214, I222), and UA (I25, I200, I222). Patients with diagnoses of shock (R571, R578, R579, R6521) and those requiring mechanical support (T884XXD, T88DXXS, T884XXA, T884,5A1522G) were excluded from the analysis (Supplemental File).

2.3. Statistical Analysis

Statistical analysis was performed using STATA version 17.0 software [9]. Categorical variables were presented as percentages, while continuous variables were expressed as mean \pm SD. Student's *t*-test was employed to compare continuous variables, while the chi-square test was used for categorical variables. Univariate regression analysis calculated unadjusted odds ratios for the study's outcomes. For further analysis, multivariate linear regression (for continuous outcomes) and logistic regression (for binary outcomes) were utilized to determine adjusted odds ratios (aORs). The construction of models involved the inclusion of significant variables associated with the outcomes of interest, as detailed in Table 1. All *p*-values were two-sided, with 0.05 considered the threshold for statistical significance.

Table 1. Baseline demographic and characteristics of patients who had a primary diagnosis of ACS. ACS: Acute coronary syndrome.

Variable	ACS Patients in 2020 (779,895)	ACS Patients in 2019 (935,975)
Mean age (years)	66.3 \pm 16	66.7 \pm 16
COVID-19	6245	-
Female Gender (%)	35%	35%
Ethnicity (%)		
Caucasian	74%	73%
African American	10.5%	11%
Hispanic	8.0%	8%
Asian or Pacific Islander	2.0%	3%
Native American	0.5%	0.5%
Others	3.0%	0.3%
Charlson comorbidity index (%) [10]		
0	5%	0%
1	24%	24%
2	24%	24%
3 or more	47%	52%
Hospital Bed size (%)		
Small	19%	19%
Medium	29%	30%

Table 1. *Cont.*

Variable	ACS Patients in 2020 (779,895)	ACS Patients in 2019 (935,975)
Large	52%	51%
Hospital Urban Location (%)		
Rural	7%	7%
Urban Non-Teaching	18%	18%
Primary Coronary Intervention (PCI)		
Caucasian	314,860 (73%)	359,535 (72%)
African American	40,085 (12%)	45,940 (12%)
Hispanic	34,959 (9%)	39,280 (9%)
Asian or Pacific islander	11,510 (3%)	13,820 (3%)
Native American	2650 (0.5%)	2915 (0.6%)
Others	14,230 (3%)	16,570 (3%)
Comorbidities		
Drug Abuse (%)	2.8%	2.6%
Hypertension (%)	42.2%	42.3%
Diabetes (%)	27.7%	27.5
Chronic Kidney Disease	12%	15%
Alcohol Abuse (%)	3.2%	3.0%
Obesity (%)	24.3%	22.6%
Peripheral Vascular Disease (%)	10.9%	11%
Chronic Pulmonary Disease (%)	21.4%	21.9%

3. Results

3.1. Baseline Demographics and Characteristics of Patient Population

In this study, the comparison between patients hospitalized with acute coronary syndrome (ACS) in 2019 and 2020 revealed several notable characteristics. In 2019, the total number of patients amounted to 935,975, while in 2020, it was 779,895. The mean age of admitted patients was similar in both years, averaging 66.7 years in 2019 and 66.3 years in 2020. Gender distribution showed that 35% of the patients were female in both years. When considering Ethnicity, Caucasians comprised the majority in both 2019 (73%) and 2020 (74%), followed by African Americans, Hispanics, Asians, Native Americans, and other ethnic groups, though there were slight variations in these proportions between the two years.

Regarding comorbidities, the Charlson Comorbidity Index demonstrated a shift in scores. In 2019, 52% of patients had a score of 3 or higher, while in 2020, this percentage decreased to 47%. Common comorbidities such as hypertension, diabetes, and obesity showed marginal changes between the years, with hypertension being the most prevalent at around 42–43%, diabetes at 27–28%, and obesity at 22–24%. However, chronic kidney disease exhibited a decline from 15% in 2019 to 12% in 2020. Other conditions like alcohol abuse, peripheral vascular disease, and chronic pulmonary disease maintained relatively stable prevalence rates between the two years. In terms of hospital characteristics, the distribution among bed sizes (small, medium, large) and urban locations (rural, urban non-teaching) remained quite consistent between 2019 and 2020 (Table 1).

3.2. Inpatient Mortality among Different Sexes and Ethnicities

Inpatient mortality for patients hospitalized with ACS was not different among different sexes during the year 2020, and likewise, there was no difference in mortality based on sexes in 2019 (2020: STEMI aOR 1.05 CI 0.96–1.14, *p*-value 0.22; NSTEMI/UA: aOR 1.08, CI 0.98–1.19, *p*-value 0.13) (Table 2).

Table 2. Inpatient mortality outcomes among ACS patients during 1st year of the pandemic 2020 and the pre-pandemic year 2019. Ethnicity is presented in comparison to white/Caucasian patients while Female is presented in comparison to male patients. *p*-value ≤ 0.05 indicates significance. STEMI: ST segment elevation myocardial infarction. NSTEMI: non-ST segment elevation myocardial infarction. UA: Unstable angina.

STEMI	2020		2019	
	Odds Ratio (95% Confidence Interval)	<i>p</i> Value	Odds Ratio (95% Confidence Interval)	<i>p</i> Value
African American	0.93 (0.85–1.13)	0.77	1.08 (0.94–1.24)	0.23
Hispanic	0.86 (0.73–1.00)	0.65	1.15 (1.00–1.34)	0.05
Asian or Pacific Islander	0.86 (0.66–1.11)	0.24	1.25 (1.01–1.54)	0.03
Native American	0.73 (0.38–1.37)	0.32	1.03 (0.61–1.76)	0.90
Other Ethnicities	1.01 (0.78–1.31)	0.89	1.08 (0.84–1.37)	0.55
Female	1.05 (0.96–1.14)	0.22	0.99 (0.91–1.09)	0.99
NSTEMI/UA				
African American	0.93 (0.78–1.10)	0.42	0.98 (0.83–1.16)	0.86
Hispanic	0.92(0.77–1.11)	0.40	1.09 (0.92–1.29)	0.31
Asian or Pacific Islander	0.78 (0.65–1.10)	0.16	1.48 (1.15–1.90)	<0.01
Native American	0.89 (0.48–1.65)	0.72	0.55 (0.24–1.27)	0.16
Other Ethnicities	0.78 (0.56–1.08)	0.14	0.87 (0.66–1.15)	0.34
Female	1.08 (0.98–1.19)	0.13	1.06 (0.96–1.17)	0.18

There was no difference in inpatient mortality based on Ethnicity for patients admitted with ACS during the year 2020. In 2019, inpatient mortality was higher for patients of Asian or Pacific Islander descent who were admitted with ACS when compared to Caucasians (Table 2).

For patients admitted with ACS, inpatient mortality was significantly higher in 2020 compared to 2019 regardless of sex and Ethnicity (aOR 1.20; 95% CI 1.12–1.23; *p*-value < 0.001).

3.3. Time from Admission to PCI Outcome among Different Sexes and Ethnicities

Although the time from admission to PCI for NSTEMI and UA was longer for females when compared to males in both 2020 and 2019, the small effect size makes the result clinically insignificant (2020 NSTEMI/UA: mean difference 0.06 days, 95% CI 0.02–0.10, *p*-value < 0.01) (Table 3 and Figure S1).

Similarly, African Americans with NSTEMI and UA were found to have a statistically significantly longer time from admission to PCI than Caucasians in both 2020 and 2019; the small effect size makes the results clinically insignificant (2020 NSTEMI/UA: mean difference 0.13 days, 95% CI 0.06–0.19, *p* < 0.001) (Table 3).

3.4. Resource Utilization among Different Sexes and Ethnicities

In 2020, female patients had a shorter average length of stay (LOS) for UA/NSTEMI admissions (NSTEMI/UA: mean difference −0.22, CI −0.27–−0.16, *p*-value < 0.01). Length

of stay was not different based on sex for STEMI admissions in both 2020 (p -value = 0.29) and 2019 (p -value = 0.55). In both years, patients who were Hispanic and Asian or Pacific Islander and admitted with STEMI had longer LOS compared to Caucasians (Supplementary Tables S1–S3).

Table 3. Admission to PCI time among NSTEMI/UA patients during 1st year of the pandemic 2020 and the pre-pandemic year 2019. Ethnicity is presented in comparison to white/Caucasian patients while Female is presented in comparison to male patients. p -value \leq 0.05 indicates significance.

	2020		2019	
African American	0.13 (0.06–0.19)	<0.01	0.16 (0.09–0.22)	<0.01
Hispanic	0.05 (−0.01–0.13)	0.14	0.07 (−0.01–0.14)	0.08
Asian or Pacific Islander	0.01 (−0.11–0.14)	0.82	−0.07 (−0.17–0.03)	0.20
Native American	−0.02 (−0.32–0.27)	0.87	−0.03(−0.23–0.18)	0.77
Others	0.006 (−0.12–0.13)	0.93	−0.003 (−0.17–0.16)	0.97
Female	0.06 (0.02–0.10)	<0.01	0.06 (0.02–0.09)	<0.01

4. Discussion

Given the time-sensitive nature of ACS management, a global pandemic like the COVID-19 pandemic has the potential to worsen existing healthcare disparities in sex and Ethnicity. The rationale behind this investigation is rooted in the recognition of the multifaceted impact of demographic variables, notably sex and Ethnicity, on the trajectory and prognosis of ACS patients during the COVID-19 pandemic. Acknowledging the emerging data that indicate potential disparities in outcomes among different demographic groups, our study seeks to provide a comprehensive assessment of inpatient mortality rates and the temporal aspect of PCI initiation, shedding light on potential variations influenced by sex and Ethnicity. This study showed that first, during the COVID-19 pandemic in the year 2020, there was no difference in inpatient mortality, with respect to sex and Ethnicity in ACS patients. Prior to the pandemic, in the year 2019, inpatient mortality for ACS admissions among patients of Hispanic, Asian, or Pacific Islander Ethnicity was higher compared to those of Caucasian Ethnicity. Second, among patients admitted with NSTEMI and UA, the time from admission to PCI was significantly longer for females and African Americans when compared to males and Caucasians, respectively in both 2019 and 2020, although the effect size was small. Third, female patients admitted with UA and NSTEMI in 2020 had a shorter length of hospital stay compared to male patients.

The inconsistency in the evaluation and management of suspected acute coronary events in females has been assessed considerably in the literature. Studies have revealed a higher mortality for women with acute coronary syndrome compared to men. This is particularly seen in the case of ST-elevation myocardial infarction [8,11,12]. The higher mortality in women may be explained in part by the higher prevalence of comorbid conditions, longer system delays to appropriate care, decreased use of guideline-directed medical therapy, and older age at presentation [13–16].

Numerous studies have been performed to compare inpatient mortality and survival rates among different Ethnicities. In the Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BCBS-MICC) study, the Ethnicity of the patients was not found to affect inpatient mortality in coronary artery disease [17]. Similarly, in an analysis of 12,555 acute myocardial infarction patients in New York City, investigators found no significant difference in survival rates among African Americans compared to Whites [18]. However, a retrospective analysis by Yong et al. of 689,238 hospitalizations for ACS from 2008 to 2011 in the United States found that patients of Asian descent had the highest inpatient mortality rates when compared to other Ethnicities. In contrast, African American patients had the lowest inpatient mortality rates when admitted with STEMI and NSTEMI [19].

Our study attempted to determine whether the pre-existing sex and Ethnicity disparities in the management of acute coronary syndrome were influenced by the COVID-19 pandemic. Inpatient mortality for patients admitted with ACS was significantly higher in 2020 compared to 2019 regardless of sex and Ethnicity and it is reasonable to infer that inpatient mortality in ACS during the pandemic was determined primarily by the clinical characteristics of patients. This contrasts with the pre-pandemic data from 2019, which showed increased inpatient mortality for ACS admissions among Asians and Hispanics compared to Caucasians. Notably, we found that African American and Hispanic ACS patients experienced slight delays in appropriate and timely interventions during the COVID-19 pandemic, although the effect size was small and likely not clinically significant.

Multiple studies have attempted to analyze the impact of sex and Ethnicity on timely curative intervention in the setting of acute coronary syndrome [18,20,21]. The ACTION Registry-GWTG study, which studied 46,245 STEMI patients in the United States, showed remarkable delays in terms of reperfusion interventions specifically among Hispanic STEMI patients compared to Caucasians [20]. Another study by Bradley et al. revealed significantly longer door-to-drug and door-to-balloon times for Hispanic and African American myocardial infarction patients compared to Caucasian [22]. Another study based in China found that, compared to men, women with ACS were less likely to receive adequate initial treatment, including PCI. The current study focused on patients with ACS admissions in the United States and included 779,895 patients during the first year of the COVID-19 pandemic, yielding a study with a higher power and more precise estimate of the magnitude of the effect.

5. Limitations

Our study leveraged one of the largest available databases in the United States, the NIS database, to conduct our research. However, inherent limitations accompany its use. Coding and documentation errors within the database raise concerns about the representativeness of all subjects in our study concerning the broader study population. Furthermore, the database's structure provides admission length in days but lacks granularity by not offering time in hours. It also lacks patient-specific data like individual lab results, medications, and imaging outcomes, which could significantly impact our findings. To address potential biases from the observational nature of the database, we conducted a comprehensive multivariable analysis.

Nevertheless, our study faced certain limitations. Firstly, crucial patient-level data essential for analysis, including laboratory results, oncologic status, angiograms, coronary lesion descriptions, imaging studies, medications, and procedural details, were unattainable. Secondly, the database's administrative design, reliant on coding for diagnosing conditions and procedures, introduces a susceptibility to documentation errors. Thirdly, the retrospective observational approach introduces the potential for selection and unmeasured biases. However, our efforts included a robust multivariable analysis to mitigate allocation bias. Finally, important information regarding out-of-hospital mortality, short-term non-hospitalized outcomes, and long-term results was unavailable within the NIS database.

6. Conclusions

Our study during the COVID-19 pandemic found no differences in inpatient mortality among ACS patients based on ethnicity and sex. However, there was an overall increase in inpatient mortality in 2020 compared to 2019. Females with UA and NSTEMI had shorter hospital stays than males. No significant delays in time to PCI were observed based on ethnicity or sex. Importantly, disparities seen before the pandemic in 2019, particularly increased inpatient mortality among Hispanic, Asian, or Pacific Islander patients with ACS, were eliminated in 2020. Future research should explore underlying factors contributing to and further minimizing these disparities.

COVID-19's intersection with ACS has raised concerns, impacting not just cardiovascular implications but also treatment pathways, access to care, and patient outcomes.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/hearts5010004/s1>, Table S1: Clinical Modification (ICD10-CM) coding system. Table S2: Inpatient length of stay outcomes among ACS patients during 1st year of the pandemic 2020 and the pre-pandemic year 2019. Table S3: Inpatient hospital cost outcomes among ACS patients during 1st year of the pandemic 2020 and the pre-pandemic year 2019. Figure S1: Predictors of time from admission to PCI among UA/NSTEMI patients during 1st year of the pandemic 2020.

Author Contributions: A.A., A.E. and A.J. conceptualized the study, developed the methodology, performed the formal analysis, conducted the investigation, curated data, prepared the original draft, conducted the review and editing, visualized the results, supervised the project, and administered the project. M.S. (Mohammad Safi), M.S. (Momin Shah) and H.A. contributed to the conceptualization, validation, and funding acquisition. M.S. (Mohammad Safi) and M.S. (Momin Shah) participated in the validation. H.A., Z.H., A.J. and E.E. were involved in conceptualization. All authors have read and agreed to the published version of the manuscript.

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Informed Consent Statement: Not applicable.

Data Availability Statement: The data supporting the reported results are publicly available through the HCUP (Healthcare Cost and Utilization Project) database at <https://hcup-us.ahrq.gov/nisoverview.jsp> (accessed on 10 October 2023). We have utilized this database for the analysis presented in this study.

Conflicts of Interest: The authors declare no conflicts of interest. The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties. Peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

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