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Nationwide Analysis of the Outcomes and Mortality of Hospitalized COVID-19 Patients

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Abstract: Introduction: The Coronavirus disease 2019 (COVID-19) pandemic has affected people worldwide with the United States (US) with the largest number of reported cases currently. Previous studies in hospitalized COVID-19 patients have been limited by sample size. **Methods:** The National Inpatient Sample database which is the largest inpatient database in the US was queried in the year 2020 for the diagnosis of COVID-19 based on ICD-10-CM U07.1 and associated outcomes. Multivariate logistic regression analysis was used to identify predictors of mortality. STATA 16.0 was used for statistical analysis. **Results:** A weighted total of 1,678,995 hospitalizations for COVID-19 were identified. Median age of admitted patients with COVID-19 was 65 year (51-77) with 47.9% female and 49.2% White. Majority of the patients admitted were > 65 years of age (49.3%). Hypertension and diabetes were the most common comorbidities (64.2% and 39.5%, respectively). Overall inpatient mortality was 13.2% and increasing to 55.9% in patients requiring mechanical ventilation. Trend of inpatient mortality was significantly decreasing over the year. Predictors of inpatient mortality included age, male sex, diabetes,

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chronic kidney disease, heart failure, arrhythmia, obesity, and coagulopathy. Despite a lower proportion of patients admitted to hospital with COVID-19, Black, Hispanic, and Native Americans were at an increased adjusted odds of inpatient mortality. Disparity was also noted in income, with low median household income associated with higher risk of mortality. *Conclusion:* In the largest US cohort with >1.6 million hospitalized COVID-19 patients in 2020, overall inpatient mortality was 13.6% with significantly higher mortality in ventilated patients. Significant socioeconomic and racial disparities were present with minorities at higher odds of mortality. (Curr Probl Cardiol 2023;48:101440.)

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has been an unprecedented challenge to global health and affected more than 600 million people worldwide.¹ SARS-CoV-2, the novel coronavirus that causes COVID-19, was first detected in the United States (US) in January 2020 with more than 96 million cases confirmed to date.¹

Comprehensive data on demographic characteristics and comorbidities, and clinical outcomes for hospitalized COVID-19 patients enables to apprise prevention and management strategies.

There have been few studies investigating clinical characteristics of patients admitted with COVID-19 and reports of in-hospital mortality of patients with COVID-19 has also varied widely.² Further, identification of patients with higher risk of death is critical for tailored allocation of treatment and prevention strategies. However, most studies have been limited to narrow geographic area and by sample size.² Metanalysis have tried to offset the limitations, however, sample size was still inadequate with amplified heterogeneity of the data from various countries.^{3,4}

We conducted a comprehensive analysis using a large national representative database with the primary objective of describing the characteristics and outcomes of adult patients hospitalized with COVID-19 in the United States. We also aimed to compare characteristics of patients who died in the hospital and ascertain predictors of adverse outcomes.

Methods

Data Source

We utilized the Healthcare Cost and Utilization Project (HCUP)—Nationwide Inpatient Sample (NIS) data set for the year 2020 which is the largest all-payer inpatient data set in the United States and is available publicly.⁵ The NIS represents 95% of US hospitalizations from 44 states participating in HCUP, provides a stratified sample of 20% of discharges, and includes up to 8 million hospital discharges per year. The NIS database has been demonstrated to correlate well with other discharge databases in the United States and has been validated in various studies to provide reliable estimates of admissions within the United States.⁷ Data collection methods and administration of NIS are detailed.⁵

Study Population

We included hospitalizations with diagnosis of COVID-19 using procedure International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) code U07.1 in the year 2020.

Outcomes

Our primary outcome was in-hospital mortality. Secondary outcomes included incidence of acute kidney injury (AKI), AKI requiring dialysis, acute respiratory failure, respiratory failure, sepsis, venous thrombosis, myocardial infarction, cardiac arrest, bleeding requiring transfusion, utilization of vasopressor and extracorporeal membrane oxygenation, and length of stay.

Statistical Analysis

Statistical analyses were performed using Stata 16.0 (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC). Since the HCUP database approximates only 20% of the stratified sample of US hospitals, the discharge weights provided by the Agency for Healthcare Research and Quality were applied to obtain weighted numbers to calculate regional and national estimates. Continuous variables are expressed as mean \pm standard deviation and categorical variables in percentage. All reported *P* values are 2-sided, with a value of < 0.05 considered significant. Logistic regression models were generated to

identify the independent multivariate predictors and is reported as adjusted odds ratio (aOR) with 95% confidence intervals (CI).

Results

Baseline Characteristics

A total of 1,678,995 COVID-19 hospitalizations in the year 2020 were identified. The median age of the patients admitted with COVID-19 was 65 yrs. (51-77) with 805,515 (47.9%) female patients. A total of 826,975 (49.3%) were >65 years of age. The majority of the patients admitted to the hospital were non-Hispanic White (49.2%) followed by Hispanic (21.1%) and Black (18.5%). Hospitalizations for COVID-19 were primarily in the southern hospitals (41.1%).

Table 1 describes the distribution of co-morbidities among the patients. Hypertension was the most common pre-existing comorbidity identified, present in more than 60% of patients, followed by diabetes mellitus in over a third of patients. Chronic obstructive pulmonary disease was present in close to one fourth of the patients. Chronic kidney disease (CKD) was present in 20.8% patients, cardiac arrhythmias in 24.5%, atrial fibrillation in 12%, heart failure in 17.4%, and hypothyroidism in 13.1%. One in every 4 patients were also noted to be obese.

Outcomes

Among the 1,678,995 COVID-19 hospitalizations, 222,615 patients died in the hospital with overall inpatient mortality of 13.2%. Trends in hospitalizations as well mortality stratified by month is shown in **Figure 1**. Further, in patients with respiratory failure, mortality increased to 17.8% and was significantly higher in patients requiring mechanical ventilation (55.95%).

Table 2 describes the major complications during the hospital stay. Major complications included respiratory failure in more than half of the patients (n = 888,305, 52.9%), AKI in 476,290 (28.4%) patients and sepsis in 417,230 (24.85%) patients. Pulmonary embolism and deep vein thrombosis was present in 40,305 (2.4%) and 29,345 (1.75%) patients, respectively.

Cardiovascular complications included myocardial infarction in 32,510 (1.9%), ventricular tachycardia in 31315 (1.9%), and ventricular fibrillation in 5065 (0.3%). Hospital stay was complicated by cardiac arrest in 44,105 (2.63%) patients and prolonged intubation more than

TABLE 1. Baseline characteristics of patients admitted with COVID-19

Characteristics	All n = 1,678,995	Survivors n = 1,453,390	Non-survivors n = 222,130	P value
Age, median, years	65 (51-77)	63 (49-75)	74 (65-83)	<0.001
Age groups				<0.001
18-50	399,675 (23.8%)	386,055 (26.6%)	13,620 (6.1%)	
51-65	451,170 (26.9%)	406,240 (28.0%)	44,930 (20.2%)	
>65 years	826,975 (49.3%)	662,910 (45.6%)	164,065 (73.9%)	
Female	805,070 (47.9%)	712,605 (49.0%)	92,465 (41.6%)	<0.001
Race/Ethnicity				
White	825,135 (49.2%)	710,525 (48.9%)	114,610 (51.6%)	<0.001
Black	310,465 (18.5%)	272,910 (18.8%)	37,555 (16.9%)	
Hispanics	353,350 (21.1%)	309,745 (21.3%)	43,605 (19.6%)	
Asian or Pacific Islanders	52,810 (3.2%)	45,355 (3.1%)	7455 (3.4%)	
Native American	16,720 (1.0%)	14,000 (1.0%)	2720 (1.2%)	
Others	702,10 (4.2%)	60,410 (4.2%)	9800 (4.4%)	
Comorbidities				
Atrial fibrillation	201,290 (12.0%)	150,140 (10.3%)	51,150 (23.0%)	<0.001
Diabetes mellitus	661,965 (39.5%)	557,680 (38.4%)	104,285 (46.9%)	<0.001
Hypertension	1,076,220 (64.2%)	912,970 (62.8%)	163,250 (73.5%)	<0.001
Chronic kidney disease	348,965 (20.8%)	274,335 (18.9%)	74,630 (33.6%)	<0.001
CHF	291,595 (17.4%)	226,060 (15.6%)	65,535 (29.5%)	<0.001
Peripheral vascular disease	632,795 (4.7%)	561,680 (38.6%)	71,115 (32.0%)	<0.001
Dementia	198,780 (11.9%)	153,480 (10.6%)	45,300 (20.4%)	<0.001
COPD	367,350 (21.9%)	311,060 (21.4%)	56,290 (25.3%)	<0.001
Valvular heart disease	66,210 (4.0%)	53,570 (3.7%)	12,640 (5.7%)	<0.001
Arrhythmias	411,475 (24.5%)	315,720 (21.7%)	95,755 (43.1%)	<0.001
Liver disease	91,060 (5.4%)	69,060 (4.8%)	22,000 (9.9%)	<0.001
Hypothyroidism	219,040 (13.1%)	185,925 (12.8%)	33,115 (14.9%)	<0.001
Anemia	71,845 (4.3%)	61,550 (4.2%)	10,295 (4.6%)	0.005
Cancer	58,515 (3.5%)	46,700 (3.2%)	11,815 (5.3%)	<0.001
Rheumatological disorders	50,115 (3.0%)	43,015 (3.0%)	7100 (3.2%)	0.009
Weight loss	203,535 (3.0%)	151,845 (10.4%)	51,690 (23.3%)	<0.001
Coagulopathy	203,535 (12.1%)	151,845 (10.4%)	51,690 (23.3%)	<0.001
Obesity	427,305 (25.5%)	378,840 (26.1%)	48,465 (21.8%)	<0.001
Smoking history	104,815 (6.3%)	96,170 (6.6%)	8645 (3.9%)	<0.001
Coronary artery disease	297,930 (17.7%)	242,290 (16.7%)	55,640 (25.0%)	<0.001
Prior Stroke	139,990 (8.6%)	116,690 (8.0%)	23,300 (10.5%)	<0.001
Prior PCI	74,255 (4.4%)	63,150 (4.3%)	11,105 (5.0%)	<0.001
Prior CABG	57,685 (3.4%)	47,210 (3.2%)	10,475 (4.7%)	<0.001
Prior MI	69,015 (4.1%)	57,755 (4.0%)	11,260 (5.1%)	<0.001
Hospital location and teaching status				
Rural	162,866 (9.7%)	145,456 (10.0%)	17,410 (7.8%)	<0.001
Urban non-teaching	310,145 (18.5%)	270,675 (18.6%)	39,470 (17.8%)	
Urban teaching	1,204,809 (71.8%)	1,039,074 (71.5%)	165,735 (74.6%)	
Hospital region				
Northwest	308,205 (18.4%)	256,940 (17.7%)	51,265 (23.1%)	<0.001
Midwest	373,605 (22.3%)	328,550 (22.6%)	45,055 (20.3%)	
South	689,791 (41.1%)	604,326 (41.6%)	85,465 (38.5%)	
West	306,219 (18.3%)	265,389 (18.3%)	40,830 (18.4%)	
Expected primary payer				
Medicare	839,875 (50.1%)	689,540 (47.4%)	150,335 (67.7%)	<0.001

(continued)

TABLE 1. (continued)

Characteristics	All n = 1,678,995	Survivors n = 1,453,390	Non-survivors n = 222,130	P value
Medicaid	252,450 (15.1%)	232,480 (16.0%)	19,970 (9.0%)	
Private including HMO	441,235 (26.3%)	405,910 (27.9%)	35,325 (15.9%)	
Self pay	63,020 (3.8%)	57,755 (4.0%)	5,265 (2.4%)	
Median household income in percentile				
0-25th percentile	564,125 (33.6%)	486,340 (33.5%)	77,785 (35.0%)	<0.001
26-50th percentile	448,760 (26.7%)	390,265 (26.9%)	58,495 (26.3%)	0.0711
51-75th percentile	365,660 (21.8%)	319,115 (22.0%)	46,545 (21.0%)	0.0002
76-100th percentile	272,400 (16.2%)	236,130 (16.2%)	36,270 (16.3%)	0.8212
Hospital bed size				
Small	406,805 (24.2%)	357,370 (24.6%)	49,435 (22.3%)	<0.001
Intermediate	485,445 (28.9%)	417,455 (28.7%)	67,990 (30.6%)	<0.001
Large	785,570 (46.8%)	680,380 (46.8%)	105,190 (47.4%)	<0.001

CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; PCI, percutaneous coronary intervention, CABG, coronary artery bypass grafting; MI, myocardial infarction.

24 hours was needed in 172,625 (10.28%) patients. Extracorporeal membrane oxygenation was utilized in 480 (0.03%) patients.

The median total length of stay for this cohort was 5 days (IQR 3-10). Among survivors, 51.4% (n = 863,540) were discharged home and 3.01% (n = 50,505) to skilled nursing facility. The median cost of hospitalization for hospitalized COVID-19 patients was \$10,543 [6185-18,608] in survivors vs \$25,892 [11,403-53,656] in non-survivors, $P < 0.001$.

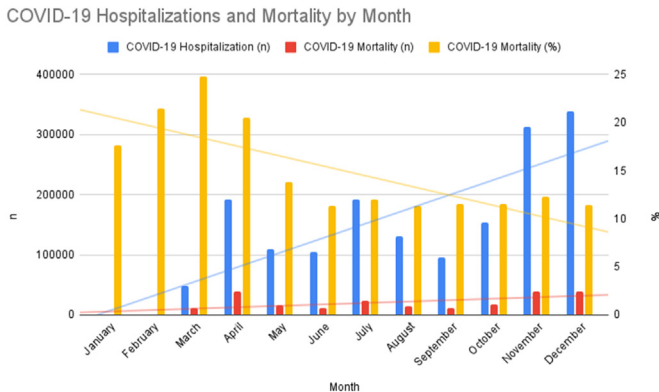


FIG 1. Trends in COVID-19 hospitalization and Mortality, n- absolute number (left vertical axis), % - percentage of COVID mortality (Number of COVID deaths/Number of COVID hospitalizations, in right vertical axis).

TABLE 2. Clinical outcomes of hospitalized COVID-19 patients stratified by death

Outcomes	All n = 1,678,995	Survivors n = 1,453,390	Non-survivors n = 222,130	P value
AKI	475,930 (28.4%)	337,975 (23.3%)	137,955 (62.1%)	<0.001
AKI leading to HD	40,895 (2.4%)	15,705 (1.1%)	25,190 (11.3%)	<0.001
Sepsis	416,995 (24.9%)	290,010 (20.0%)	126,985 (57.2%)	<0.001
Deep vein thrombosis	29,330 (1.8%)	21,565 (1.5%)	7765 (3.5%)	<0.001
Pulmonary embolism	40,285 (2.4%)	32,300 (2.2%)	7985 (3.6%)	<0.001
Stroke in-hospital	9975 (0.6%)	68,70 (0.5%)	3105 (1.4%)	<0.001
Bleeding requiring transfusion	60,900 (3.6%)	40,505 (2.8%)	20395 (9.2%)	<0.001
Vasopressors	43,050 (2.6%)	16,340 (1.1%)	26,710 (12.0%)	<0.001
Respiratory failure	887,735 (52.9%)	729,065 (50.2%)	158,670 (71.4%)	<0.001
Resp failure with intubation	109,265 (6.5%)	48,130 (3.3%)	61,135 (27.5%)	<0.001
Prolonged Intubations >24 hours	172,540 (10.3%)	74,525 (5.1%)	98,015 (44.1%)	<0.001
ECMO utilization	480 (0.03%)	235 (0.02%)	245 (0.1%)	<0.001
Cardiovascular Outcomes				
Myocardial infarction	32,510 (1.9%)	19,855 (1.4%)	12,655 (5.7%)	<0.001
Cardiogenic shock	10,590 (0.6%)	4080 (0.3%)	6510 (2.9%)	<0.001
Cardiac arrest	44,105 (2.6%)	5745 (0.4%)	38,360 (17.3%)	<0.001
Ventricular tachycardia	31,315 (1.9%)	19,100 (1.3%)	12,215 (5.5%)	<0.001
Ventricular fibrillation	5065 (0.3%)	1065 (0.1%)	4000 (1.8%)	<0.001

AKI, Acute kidney injury; RRT, renal replacement therapy; ECMO, extracorporeal membrane oxygenation.

Predictors of Mortality

Logistic regression analysis was used to identify independent predictors associated with increased odds of in-patient mortality. Age (aOR 1.04 [95% CI 1.04,1.04], $P < 0.001$), diabetes mellitus (aOR 1.17 [95% CI 1.14,1.20], $P < 0.001$), CKD (aOR 1.34 [95% CI 1.30,1.37], $P < 0.001$), heart failure [aOR 1.22 [95% CI 1.18, 1.25], $P < 0.001$], arrhythmia (aOR 1.78 [95% CI 1.77, 1.83], $P < 0.001$), and coagulopathy (aOR 2.22 [95% CI 2.14, 2.31], $P < 0.001$) were associated with increased odds of mortality. Obesity was also associated with an increased risk of mortality (aOR 1.17) 95% CI 1.17, 1.20], $P < 0.001$; [Table 3](#)).

Despite a lower proportion of patients admitted to hospital with COVID-19, Black and Hispanic patients were at increased odds of mortality compared to White patients (aOR 1.20 [95% CI 1,15,1.25] and aOR 1.51 [95% CI 1.44, 1.57], respectively). Patients identifying as Native Americans have ~ 2 times increased odds of mortality compared to White patients.

Further, patients in the low median household income group were at higher odds of increased mortality compared to the high-income group (aOR 1.11 [95% CI 1.01,1.22]).

TABLE 3. Independent predictors of mortality in patients admitted with COVID-19

	aOR	95% CI		P value
Age	1.04	1.04	1.04	<0.001
Female sex	0.74	0.72	0.76	<0.001
Diabetes	1.17	1.14	1.20	<0.001
Chronic kidney disease	1.34	1.30	1.37	<0.001
Congestive heart failure	1.22	1.18	1.25	<0.001
Peripheral vascular disease	1.38	1.32	1.44	<0.001
Dementia	1.07	1.03	1.11	<0.001
COPD	1.06	1.03	1.08	<0.001
Arrhythmia	1.78	1.73	1.83	<0.001
Cancer	1.17	1.13	1.20	<0.001
Obesity	1.17	1.13	1.20	<0.001
Coagulopathy	2.22	2.14	2.31	<0.001
Rheumatological disorder	1.68	1.61	1.76	0.001
Based on income				
Lowest income	1.11	1.02	1.22	0.021
Highest income	0.85	0.77	0.94	0.002
Intermediate low	0.98	0.89	1.08	0.696
Intermediate high	0.90	0.82	0.99	0.031
Based on Race/Ethnicity (white as reference)				
Black	1.12	1.08	1.17	<0.001
Hispanic	1.42	1.36	1.48	<0.001
Asian	1.24	1.15	1.33	<0.001
Native Americans	2.14	1.87	2.46	<0.001

PVD, peripheral vascular disease; COPD, chronic obstructive pulmonary disease; aOR, adjusted odds ratio; CI, confidence interval.

Discussion

This real-word study describes the characteristics of hospitalized patients with COVID-19 in a large inpatient database during the peak of the pandemic in the year of 2020. To the best of our knowledge, this is the largest series of hospitalized patients with more than 1.6 million patients.

The main findings of our study are that (Figure 2):

1. Overall in-patient mortality was 13.2%, increasing up to 17.8% in patients with respiratory failure and more than 50% mortality in mechanically ventilated patients.
2. Among ~1.6 million patients hospitalized for COVID-19, most common co-morbidity was hypertension, followed by diabetes. Age, male gender, diabetes, obesity, CKD, cardiac arrhythmia, and cancer were the predictive of greater odds of mortality.

CENTRAL ILLUSTRATION: COVID-19 Hospitalizations in the United States 2020

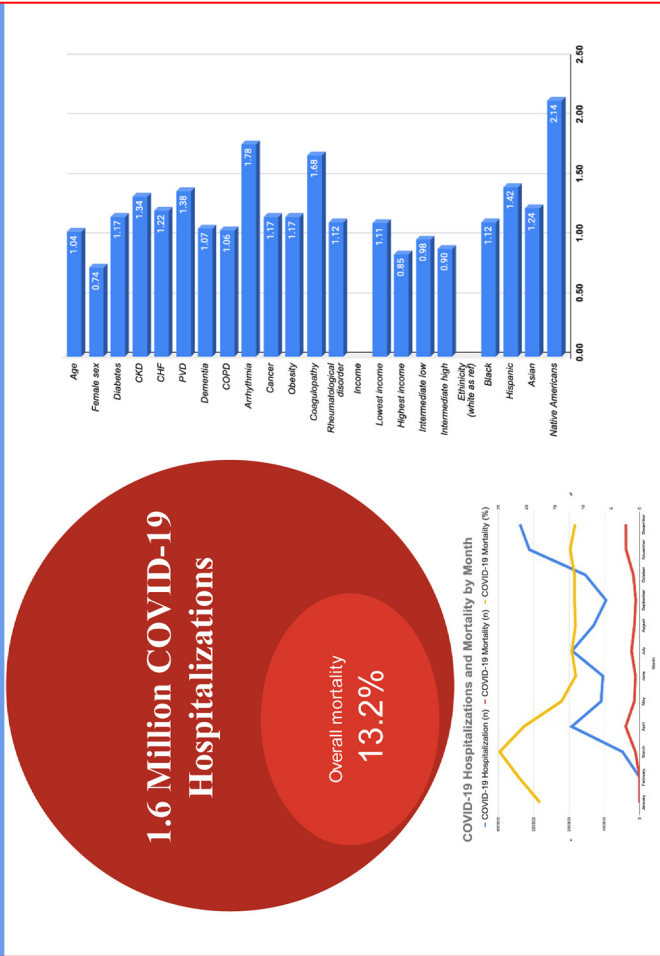


FIG 2. Central illustration.

3. Significant disparities based on race and socioeconomic status were present in COVID-19 hospitalizations and mortality.

The previous largest retrospective report by Nguyen et al² of 192,550 hospitalized COVID-19 patients in the United States using an administrative database reported an inpatient mortality of 13.6%. Previous reports from the United States have revealed in-hospital mortality ranging from 13.6% to 23.5%.^{2,6-8} Our cohort study of more than 1.6 million hospitalized COVID-19 patients demonstrated an in-patient mortality of 13.2%. We also further stratified the mortality by month and there was significantly decreasing mortality noted after the initial rise in the first few months. This was likely due to a host of factors including advancing diagnostic and management strategies, seasonal effects, and evolving strains of the virus.

Various studies have shown that patients with underlying cardiovascular disease are at a higher risk of adverse outcomes of COVID-19 including mortality.^{9,10} The etiology of association between cardiovascular comorbidities and increased COVID-19 mortality is likely multifaceted.^{9,10} Infection related demand ischemia, inflammatory storm causing shock and ischemia as well as direct myocardial injury has been proposed as underlying mechanisms, however, needs to be further elucidated to differentiate association vs causation.¹⁰ In our study, diabetes, cardiovascular comorbidities such as arrhythmias and heart failure were associated with an increased odds of mortality. Also, hospitalized COVID-19 patients also developed cardiovascular complications such as myocardial infarction and ventricular arrhythmias. Pillarisetti et al¹¹ reported an incidence of 1.3% for acute coronary syndrome, and 0.5% for ventricular tachycardia which was similar to our reports.

Further, increasing age as well as male gender was associated with an increased risk of mortality confirming previous reports.^{12,13} The gender difference in risk of mortality has been postulated to be related with the differential expression of angiotensin converting enzyme-2 expression.¹³

Patients hospitalized with COVID-19 were primarily White however, Black, Hispanic, and Native American populations were associated with a higher odds of mortality with as high as 2 times in Native Americans. Further, patients with the lowest household income also had an increased odds of mortality compared to the higher income patients. This builds on the prior work which has demonstrated similar disparities in mortality outcomes of COVID-19 in the general population.^{14,15} An ecological study by Abedi et al¹⁶ demonstrated African Americans as well as counties with poor median income were associated with higher rate of mortality

from COVID-19. Policy makers and health care professionals need to work together to further investigate and mitigate factors that contribute to inequity and disparities in hospital mortality.

Our study is best interpreted in the context of its limitations. First, NIS is an administrative claim-based database that uses ICD-10-CM codes for identification of disease processes and thus, COVID-19 diagnosis might be subjected to misclassification. The hard-clinical points, such as death, complications, and discharge disposition, are less prone to error. Management of COVID-19 was rapidly changing in the initial phase of the pandemic, and this study did not compare treatment modalities, radiologic and laboratory clinical findings which were not available. The influence of vaccination status on outcomes could also not be studied as that information is not included in the NIS database. Despite these limitations, the HCUP-NIS attempts to mitigate potential errors by internal and external quality control measures and is a well validated representation with good generalizability to the US population. The large sample size of the NIS database also increases the power of the study and allows to compensate for residual confounders which is the inherent limitation of observational studies.

Conclusion

Our study confirms age, male gender, co-existing obesity, diabetes, cardiovascular comorbidities, are the independent predictors of mortality in hospitalized COVID-19 patients and can help identify high risk patients with COVID-19. Further, significant socioeconomic and racial disparities exist with non-white patients at a higher risk of inpatient mortality.

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