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The correlations among racial/ethnic groups, hypertriglyceridemia, thrombosis, and mortality in hospitalized patients with COVID-19

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ABSTRACT

Reports of racial and ethnic disparities regarding both rates of infection of the SARS-CoV-2 virus and morbidity of the coronavirus disease-19 (COVID-19) contain profound differences depending on the population. Our previous study has shown that patients with COVID-19 who developed hypertriglyceridemia during hospitalization have a 2.3 times higher mortality rate. However, whether the correlation between hypertriglyceridemia and mortality has disparity among different racial and ethnic groups is unknown.

In this study, we investigated the impact of race/ethnicity on the correlation between hypertriglyceridemia and mortality in hospitalized patients with COVID-19. De-identified information from 904 hospitalized patients diagnosed with COVID-19 between March 2020 and June 2021 were extracted from the Medical College of Wisconsin Clinical Data Warehouse. A multivariable regression analysis suggested that the Asians and non-White Hispanics had 4 or 3.9 times higher mortality rate, respectively, after adjusting for age, morbid obesity (BMI $\geq$40), and gender. The hypertriglyceridemia ($\geq$150 mg/dL) was associated with higher mortality, after adjusting for age, gender, and morbid obesity. The baseline hypertriglyceridemia occurrence had relevantly more consistent percentages among all racial/ethnic groups. However, non-White Hispanic and Asian patients had the highest frequencies of peak hypertriglyceridemia occurrence during hospitalization. The peak hypertriglyceridemia developed during hospitalization correlates with the incidence of thrombosis after adjusting for morbid obesity, age, and sex. In summary, in this retrospective study of 904 hospitalized COVID-19 patients, Asians and non-White Hispanics had a greater likelihood of developing hypertriglyceridemia during hospitalization and mortality than White patients.

Abbreviations: COVID-19, coronavirus disease-19; VTE, venous thromboembolisms; FHSHB, Froedtert Health System Honest Broker Data extraction tool; BMI, body mass index; IQR, interquartile range; OR, Odds Ratio; CI, Confidence Interval; DIC, Disseminated intravascular coagulopathy; PAI-1, Plasminogen activator inhibitor-1; GWAS, Genome-wide association study; HLH, Hemophagocytic lymph histiocytosis.

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1. Introduction

The SARS-CoV-2 virus has infected hundreds of millions of people and caused millions of deaths worldwide [1]. The SARS-CoV-2 infection-associated coronavirus disease-19 (COVID-19) has a wide range of symptoms that range from loss of taste/smell to multi-organ system failure [1,2]. Recent studies showed a higher risk of thrombotic events in patients with COVID-19 infection [3,4] including heart attacks, strokes, pulmonary embolisms, and venous thromboembolisms (VTE) [5–7]. Reports of racial and ethnic disparities regarding both rates of SARS-CoV-2 infection and severity of COVID-19 have profound differences depending on the population [8]. Multiple studies have shown higher rates of positive testing and mortality are associated with Latinos and African Americans in the United States [9–11]. However, the underlying mechanism and the biological or socioeconomic factors that contributes to the racial/ethnic disparities are not well understood.

Our previous study has shown that in hospitalized patients with COVID-19, hypertriglyceridemia (triglyceride levels $\geq$150 mg/dL) developed during hospitalization independently associates with mortality after adjusting for age, gender, obesity, glucocorticoid treatment, history of hypertension and diabetes [12]. In the same study, we also found a correlation between hypertriglyceridemia and high leukocyte count, or C-reactive protein levels. Racial/ethnic minorities including Asians and non-White Hispanics, but not Black/African American, are known to be associated with hypertriglyceridemia [13], which increases risk for thrombotic events [13]. However, due to limitation on the study population in our previous study [12], we were unable to analyze the impact of race/ethnicity on hypertriglyceridemia and mortality at the time. Further investigation of triglyceride levels, thrombotic events-associated severity, and mortality of hospitalized patients with COVID-19 in a diverse population is required to understand the disease's racial and ethnic disparity.

In the current study, we aim to investigate the impact of racial/ethnic groups on hypertriglyceridemia, thrombosis, and mortality in hospitalized patients with COVID-19.

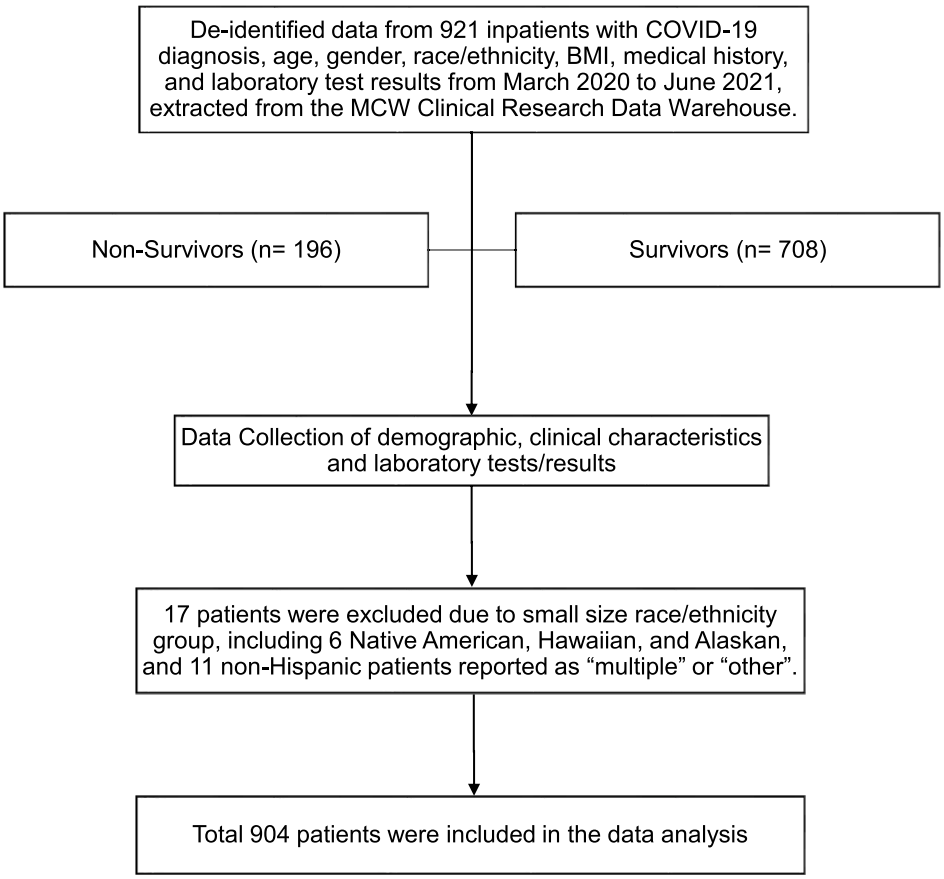


Fig. 1. Flowchart of the inclusion and exclusion for the study population. COVID-19, coronavirus 2019; BMI, body mass index; MCW, Medical College of Wisconsin.

2. Methods

2.1. Study design and population

We retrospectively reviewed hospitalized patients with a COVID-19 diagnosis and/or SARS-CoV-2 positive testing results during March 2020 to June 2021, at a large urban tertiary care academic center in Milwaukee, Wisconsin. Specifically, the positive SARS-CoV-2 testing results include RNA presence in respiratory specimen by nucleic acid amplification with probe detection and/or SARS-CoV-2 IgG Ab presence serum or plasma by immunoassay.

The patients' de-identified clinical information was extracted through the Froedtert Health System Honest Broker Data extraction tool (FHSHB), including diagnosis, diagnostic results, immunizations, demographics, and vitals. We extracted this data from a total of 921 hospitalized COVID-19 patients with complete de-identified information of age, gender, race/ethnicity, body mass index (BMI), medical history, laboratory test results, and admission dates between March 2020 and June 2021.

The de-identified patients were grouped into their respective race and ethnicity group based on self-report information as: non-White Hispanic, Asian, Black/African American, and White. Anyone that indicated that they were Hispanic and not White were included in the non-White Hispanic group, which was the only representation of ethnicity in this study. 17 patients were excluded from the study because of small sample size for powerful statistical analysis, including 6 Native American, Hawaiian, and Alaskan patients, and 11 non-Hispanic patients who documented 'Multiracial' or 'Other'. Therefore, a total of 904 hospitalized patients with were included in the study (Fig. 1). The study was approved by the Institutional Review Board at the Medical College of Wisconsin.

2.2. Data collection

De-identified information of diagnosis and laboratory testing results were documented during each patient's hospital stay and were extracted from FHSHB. Hypertriglyceridemia was considered as triglyceride levels ≥150 mg/dL. To investigate a possible difference in baseline occurrence of hypertriglyceridemia and high triglyceride that developed during hospitalization, the first occurrence of hypertriglyceridemia during the hospital stay was considered as the "baseline" level; while the highest occurrence of hypertriglyceridemia of the same individual during the hospital stay was considered as the "peak" level. The BMI, age, and gender of the de-identified patients were included in the statistical analysis and considered as adjusted variables for the multivariable regression. BMI ≥40 was considered as morbid obesity [14]. Additionally, diagnosis information for the incidence of these thrombosis, and other occurrences of thrombosis were collected, with only one incidence of any type of thrombotic events was indicated for each patient.

2.3. Statistical analysis

Numerical variables were expressed as "median (interquartile range, IQR)". Categorical variables were expressed as "percentages (*n* numbers)". The multivariable binary logistic regression analyses were used for association analyses. The dependent variable was the vital status of the patient. Independent variables included were racial/ethnic groups, presence of baseline hypertriglyceridemia, presence of peak hypertriglyceridemia, incidence of thrombotic events, age, gender, morbid obesity (BMI ≥40), and race/ethnicity. All statistical analyses were performed using statistical software SPSS (Version 28.0.0.0; SPSS Inc. Cary, Chicago, USA). Two-tailed p values < 0.05 were considered statistically significant.

3. Results

3.1. Baseline characteristics of study population

A flow diagram is provided to illustrate the inclusion and exclusion criteria used in this study (Fig. 1). A total of 904 patients with a COVID-19 diagnosis and/or SARS-CoV-2 positive testing result with hospital admission dates between March 2020 and June 2021 were included in the statistical analysis of this study. The baseline characteristics of all participants were included in Table 1. This study cohort consisted of 456 males (50%), 514 patients over the age of 60 (56%), and 155 patients with a BMI ≥40 (17%). Median age was 64 (IQR, 52–75) years and median BMI was 30 (IQR, 25.9–36.9) kg/m^2. Of the 197 patients that died during hospitalization, 142

Table 1
Baseline characteristics of study population.

	Total (n = 904)	Non-survivors (n = 197)	Survivors (n = 707)	p
Age, years (IQR)	64 (52–75)	72 (58–81)	61 (50–73)	<0.001
Male percentage, % (n)	51.2 (456)	57.4 (113)	48.5 (343)	0.028
BMI, kg/m2 (IQR)	30.8 (25.9–36.9)	29.1 (23.9–35.8)	31.5 (26.7–37.3)	<0.001
Morbid obesity, % (n)	17.1 (155)	12.7 (25)	18.4 (130)	0.061
Triglyceride, mg/dl (IQR)	122 (89–181)	140 (95–234)	119 (88–170)	<0.001

Data are shown as median (IQR), or % (n) as appropriate. *P* values were from analyses of the Mann-Whitney *U* test, or Chi-Square test between non-survivors and survivors. Two-tailed $p < 0.05$ was considered statistically significant. IQR, interquartile range; BMI, body mass index; Morbid obesity, BMI >40.

of them (72% of the deceased patients) were older than the age of 60.

3.2. Racial/ethnic disparities of mortality in hospitalized patients with COVID-19

Non-White Hispanic and Asian patients had the highest percentage of mortality at 40.4% and 40.7%, respectively. The percentage of mortality was 20.3% in Black, and 19.8% in White. These results suggested that a disparity existed between racial/ethnic groups for mortality in this hospitalized patient cohort.

Previous studies have shown that morbid obesity, [15–17], the male gender, and people over the age of 60 or 65 [18–20] are more at risk to develop severe illness, hospital admission, and worse clinical outcomes, including death, from COVID-19 if contracted [21–23]. Therefore, we used a multivariable binary logistic regression to analyze the racial and ethnic impact on mortality, adjusting for age, gender, and morbid obesity. We found that non-White Hispanic and Asian patients with COVID-19 had a 3.9 (95% Confidence interval (CI),2.1–7.4, $p < 0.001$) and of 4.0 (95% CI,1.7–9.3, $p = 0.001$) times higher mortality than White patients, respectfully, after the adjustments for age, gender, and morbid obesity (Table 2).

In this cohort, 5% of the hospitalized patients self-reported financial strain in their household and 36% of the hospitalized patients had Medicaid or were uninsured. The racial group with the highest percentage of Medicaid usage or absence of insurance was Black/African American (58%), followed by White (27.2%), non-White Hispanic (10.1%), whereas the Asian racial group had the lowest percentage (4.6%). We performed another multivariable logistic regression to include self-reported financial strain and usage of Medicaid, or absence of insurance to adjust the impact of race/ethnicity on mortality. In this analysis, self-reported financial resourc e strain (OR: 0.6, CI, 0.25–1.5, $p = 0.30$) and usage of Medicaid or absence of insurance (OR: 1.0, CI, 0.7–1.5, $p = 0.78$) were not statistically significant and did not impact mortality. Non-White Hispanic (OR: 3.9, CI, 2.0–7.5, $p < 0.001$) and Asian hospitalized patients (OR: 3.9, CI, 1.6–9.2, $p = 0.002$) continued to have significant correlation with mortality. These findings indicate that race and ethnicity independently associate with mortality, after adjusting for financial resource strain, usage of Medicaid or absence of insurance, age, gender, and morbid obesity.

3.3. Hypertriglyceridemia independently associates with mortality

Our previous study reported that hypertriglyceridemia developed during hospitalization of COVID-19 positive inpatients is independently associated with mortality [12]. Consistently, in this current study cohort, 61% of the deceased patients developed hypertriglyceridemia during hospitalization, which was associated with mortality, after adjusting for age, morbid obesity, and gender (OR: 2.0, 95% CI, 1.4–2.8, $p < 0.001$) (Table 3). Baseline hypertriglyceridemia was also associated with mortality with a slightly lower odds ratio (OR: 1.7, 95% CI, 1.2–2.5, $p < 0.001$).

Both baseline and peak hypertriglyceridemia associated with inpatient mortality independently and had significant correlation with one another. Although both variables correlated with one another and associated with inpatient mortality independently, the variables are kept separate to highlight the difference in impact of peak versus baseline hypertriglyceridemia among different racial and ethnic groups. The percentages of peak hypertriglyceridemia are different among all the racial/ethnic groups, while the baseline hypertriglyceridemia occurrence had relevantly more consistent percentages among groups (Fig. 2). Specifically, non-White Hispanics had the highest frequency of peak hypertriglyceridemia at 47%, whereas the White patients had the lowest frequency of 25%. These findings suggest that, in the hospitalized COVID-19 patients of this study cohort, Asians and non-White Hispanics had a greater likelihood of developing hypertriglyceridemia, which is associated with mortality, than White patients.

3.4. Association between thrombosis and hypertriglyceridemia developed during hospitalization

Previous studies showed that patients with severe COVID-19 have high risk of thrombotic events, including myocardial infarction, pulmonary embolism, deep vein thrombosis, portal vein thrombosis, ischemic stroke, disseminated intravascular coagulopathy (DIC) [3–7,24–26]. In the current study, 42% of the deceased patients had at least one thrombotic event (myocardial infarction, DIC, deep vein thrombosis, myocardial infarction, pulmonary embolism, or ischemic stroke). Therefore, a multivariable binary logistic regression was performed to test if thrombosis associates with mortality in hospitalized patients. We found that myocardial infarction (OR: 1.7, 95% CI, 1.1–2.8, $p = 0.01$) associated with increased mortality in the hospitalized patients (Table 4). DIC, deep vein thrombosis, and ischemic stroke did not have statistically significant results.

Previous studies have shown that dyslipidemia associates with increased platelet activity, coagulation factor activity, impaired fibrinolysis, and a higher risk of developing thrombotic events [27–36]. Additionally hypertriglyceridemia or thrombosis correlates

Table 2
Logistic analysis of the association between race/ethnicity and mortality during hospitalization in patients with COVID-19.

	OR (95% CI)	p
Non-white Hispanic (n = 52) vs White (n = 524)	3.9 (2.1–7.4)	<0.001
Asian (n = 27) vs White (n = 524)	4.0 (1.7–9.3)	0.001
Black/African American (n = 301) vs White (n = 524)	1.4 (0.9–2.0)	0.75

The p values are from the multivariable logistic regression analysis. Two-tailed $p < 0.05$ was considered statistically significant. OR, odds ratio.

Table 3
Logistic regression analysis of the association between peak hypertriglyceridemia and mortality during hospitalization in patients with COVID-19.

	OR (95% CI)	p
Peak hypertriglyceridemia (n = 447)	2.0 (1.4–2.8)	<0.001
Ages over 60 Years Old (n = 514)	2.4 (1.7–3.5)	<0.001
Morbid obesity (n = 155)	0.7 (0.4–1.2)	0.27

The p values are from the multivariable logistic regression analysis. Two-tailed $p < 0.05$ was considered statistically significant. OR, odds ratio; BMI, body mass index. Hypertriglyceridemia quantified as triglyceride levels ≥150 mg/dL. BMI ≥40 was considered morbid obesity. Peak is the highest occurrence of hypertriglyceridemia during the hospital stay.

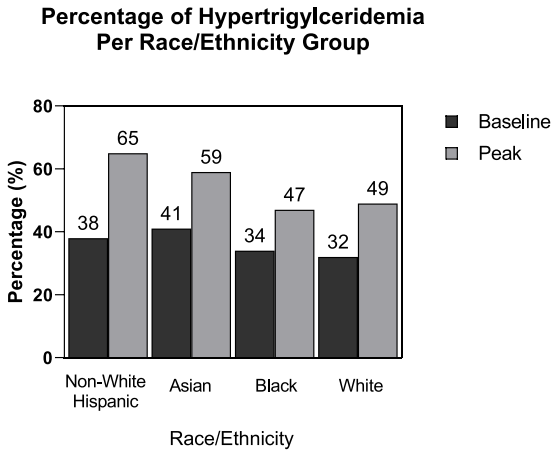


Fig. 2. Percentage of hypertriglyceridemia per race/ethnicity group at baseline and peak during hospitalization. n = 904. Hypertriglyceridemia was defined as triglyceride levels ≥150 mg/dL "Baseline" is the first occurrence of hypertriglyceridemia, and "peak" is the highest occurrence of hypertriglyceridemia during the hospital stay.

Table 4
Logistic Regression Analysis of the association between different types of thrombosis and mortality during hospitalization in patients with COVID-19.

	OR (95% CI)	p
Disseminated intravascular coagulopathy (DIC, n = 15)	3.1 (0.8–11.5)	0.07
Deep Vein Thrombosis (DVT, n = 100)	1.2 (0.7–2.3)	0.39
Myocardial Infarction (MI, n = 183)	1.7 (1.1–2.8)	0.01
Pulmonary Embolism (PE, n = 86)	1.8 (0.9–3.5)	0.06
Ischemic Stroke (IS, n = 34)	1.4 (0.5–3.7)	0.48

The p values are from the multivariable logistic regression analysis. Two-tailed $p < 0.05$ was considered statistically significant. OR, odds ratio.

with severity and mortality of COVID-19 [3,4,12]. Therefore, we aimed to investigate whether hypertriglyceridemia associates with an increased prevalence of thrombosis. In our study, 121 of the deceased patients had hypertriglyceridemia that developed during hospitalization (61% of the deceased patients). Additionally, 83 of the deceased patients experienced at least one form of thrombosis during hospitalization. To investigate the impact of presence of peak hypertriglyceridemia on thrombotic event, we performed another binary multivariable logistic regression. We found that hypertriglyceridemia developed during hospitalization associated with the prevalence of thrombosis (OR: 1.3, 95% CI, 1.0–1.8, p = 0.02), after adjusting for age, sex, and morbid obesity.

Contradictory findings have been published regarding the correlation between aspirin use and thrombotic outcomes. In several studies, patients who received aspirin had a low risk of thrombotic incidence; whereas in COVID-19, a study documented an association between thrombosis and aspirin use [37–39]. In our study, aspirin was used by 257 (28%) of the hospitalized patients. The distribution of patients who received aspirin by racial and ethnic category was for non-White Hispanic = 23%, Asian = 25%, Black = 29%, and White = 28%. Dexamethasone was used by 342 (38%) of patients in this cohort, with similar percentages per race which were for non-White Hispanic = 40%, Asian = 44%, Black = 30%, and White = 42%. When performing a logistic regression to investigate the impact of peak hypertriglyceridemia on prevalence of thrombosis after adjusting for Aspirin and dexamethasone use,

peak hypertriglyceridemia is still associated with inpatient mortality (OR = 1.3, CI 1.0–1.7, p = 0.045) (Table 5).

4. Discussion

In this current retrospective study of hospitalized patients with COVID-19, non-White Hispanic and Asian patients had a higher mortality rate than White patients. Additionally, hypertriglyceridemia developed during hospitalization is associated with mortality in hospitalized COVID-19 patients. Importantly, non-White Hispanic and Asian patients with COVID-19 had higher frequencies to develop hypertriglyceridemia during hospitalization. These findings contribute to the growing assessment of mortality risk for hospitalized COVID-19 patients with consideration of racial and ethnic disparities.

The association between dyslipidemia and risk for thrombotic and thromboembolic events have been investigated. Mechanistically, dyslipidemia, specifically hypertriglyceridemia, independently increases the risk of the incidences of these thrombotic events by increased platelet activation, pro-coagulation factors, and reduced fibrinolysis [27–36]. High triglyceride levels associated with procoagulant factors II, VII, IX, X, XI, as well as endogenous thrombin potential and increased platelet activation [28–35]. Fibrinolysis is also impaired by dyslipidemia by increased levels of plasminogen activator inhibitor-1 (PAI-1) [27,34,36], which inhibits the breakdown of fibrin clots. The dyslipidemia-associated increased coagulation, platelet activation, and decreased fibrinolysis further contribute to the manifestation of thrombotic events. Previous clinical observations have shown that triglyceride-rich lipoproteins have an association with myocardial infarction and ischemic stroke [40,41]. Specifically, an article reported that there was an association between triglyceride-rich lipoproteins and atherosclerotic cardiovascular disease [41]. Another study consisting of 12,510 middle aged men in an urban hospital in Sweden, found that there was an increasing association between high serum triglycerides and cholesterol with myocardial infarction [42]. Similarly, in a study involving 1,462 adult women in Sweden, they found that in postmenopausal women, high serum triglyceride concentration was a risk factor for myocardial infarction [43]. However, investigation in thrombotic events and dyslipidemia are needed in COVID-19, especially in different racial and ethnic populations.

Our findings regarding the racial/ethnic distribution of hypertriglyceridemia are consistent with other reports. Accumulated clinical observations have showed that the frequencies of dyslipidemia in population vary in different racial/ethnic groups. One study reported that racial/ethnic minorities, including non-White Hispanics and Asians, but not Black/African American were more likely to have high triglyceride dyslipidemia than other ethnic groups [13]. Whereas, other reports showed that Black/African American patients are less likely to have elevated triglyceride levels [44,45]. Consistently, our study found that non-White Hispanics and Asians had the highest frequencies of developing hypertriglyceridemia during the hospital stay. Black/African American and White patients had lower frequencies of developing hypertriglyceridemia during the hospital stay. The frequencies of hypertriglyceridemia at baseline were more relevantly consistent among all race/ethnicity groups. Future studies are needed to further investigate the underlying mechanism that is potentially more prevalent in non-White Hispanic and Asian COVID-19 patients that drives the increase of triglyceride and mortality. Additionally, whether the opportunity for getting immediate healthcare and laboratory testing is equally accessible among different racial and ethnic groups, and the associated impact on hypertriglyceridemia and mortality requires further investigation. Racial disparities regarding the incidence and outcome of COVID-19 have been recorded both nationally and regionally. However, prospective studies to investigate the association between hypertriglyceridemia and mortality in non-White Hispanic and Asian patients and the underlying mechanism are needed.

In this study, myocardial infarction, pulmonary embolism, and hypertriglyceridemia was correlated with mortality in hospitalized COVID-19 patients. We also found that hypertriglyceridemia that manifested during the hospital stay increased the likelihood of developing adverse thrombotic events. Non-White Hispanic and Black/African American groups have higher prevalence of chronic diseases, such as diabetes, cardiovascular diseases, and cancer, which can contribute to a worsened outcome of infectious diseases [46,47]. In the current study, non-white Hispanics had a higher frequency of peak hypertriglyceridemia, suggesting potential hypertriglyceridemia-associated mechanisms contribute to mortality in the non-White Hispanic patients.

An earlier study conducted in Milwaukee, WI, during the initial one month of the COVID-19 pandemic (March 1st to March 31st, 2020) reported that people who were enrolled in Medicaid had a higher likelihood of hospital admission [48]. Other reports also described significant healthcare inequity for Black/African American and Hispanic/Latino communities, which include a disparity in healthcare or insurance access [49]. Similarly, patients with low socioeconomic status seek healthcare less frequently or only during an

Table 5
Logistic Regression Analysis of the association between peak hypertriglyceridemia and any one incidence of thrombosis during hospitalization in patients with COVID-19.

	OR (95% CI)	P
Peak Hypertriglyceridemia (n = 447)	1.3 (1.0–1.7)	0.045
Aspirin (n = 257)	2.6 (1.9–3.6)	<0.001
Dexamethasone (n = 342)	0.76 (0.5–1.0)	0.89
Age over 60 years old (n = 514)	1.2 (0.9–1.7)	0.09
Female (n = 448)	0.9 (0.6–1.2)	0.51
Morbid Obesity (n = 155)	1.2 (0.8–1.7)	0.29

The p values are from the multivariable logistic regression analysis. Two-tailed $p < 0.05$ was considered statistically significant. OR, odds ratio; BMI, body mass index. Hypertriglyceridemia quantified as triglyceride levels greater than 150 mg/dL. BMI greater than 40 was considered extreme obesity. Peak is the highest occurrence of hypertriglyceridemia during the hospital stay.

emergency, which could lead to worsened outcomes during hospitalization [50,51]. In the current study, we used self-reported financial resource strain and usage of Medicaid/absence of insurance as indicators of possible socioeconomic status to attempt analyzing whether financial status has an impact on mortality. We found that 61% of the patients who self-reported financial income strain where racial/ethnic minorities (Black/African American, non-White Hispanic, or Asian). Absence of insurance or Medicaid usage were the variables we investigated because Medicaid is the insurance generally provided to people who are defined as "low income" in their respective state and family size. Despite usage of Medicaid or absence of insurance, there was no correlation with mortality. We then investigated whether our findings of hospitalized non-White Hispanic and Asian COVID-19 patients being correlated with mortality were driven by financial status. We found that non-White Hispanic and Asian hospitalized patients continued to correlate with mortality, after adjusting for age, gender, morbid obesity, self-reported financial resource strain, and Medicaid usage/absence of insurance. We acknowledge the limitation of using self-reported financial resource strain and Medicaid usage/absence of insurance as qualitative measures of financial status. Future prospective studies that consider the socioeconomic statuses in assessing the hospitalized patient mortality in COVID-19 are needed.

Our findings for non-White Hispanic and Asian hospitalized patients with COVID-19 being associated with mortality are not entirely consistent with the findings of other reports. In a systematic review and meta-analysis of 50 research articles regarding the ethnic and racial outcomes of COVID-19, they found that Black, Asian, and Hispanic patients were more likely to contract SARS-CoV-2. Furthermore, they found that Asian people had a higher risk of death related to COVID-19 than other racial/ethnic groups [52]. This study included both inpatients and outpatients with COVID-19. With these previous findings in mind, we initially hypothesized that Black/African American, Asians, and non-White Hispanics would have a greater likelihood for worsened outcome of COVID-19 than the White patients in the de-identified patient cohort. However, the Asian and non-White Hispanic hospitalized patients in this cohort was associated with higher mortality, but not Black patients. Additionally, the Asian population in Wisconsin is unique as the Hmong Americans are the largest Asian ethnic group. In our current study, the percentage of Hmong speaking Asian patients in the whole Asian group is 51.8%, which is higher than the percentage of Hmong people in whole Asians in Wisconsin, which is about 29% in 2019 [53]. Nationally, the Hmong population has even much smaller percentage among all Asians in 2020 [54,55]. The Hmong American populations are known to practice traditional remedies as preference, rather than seeking immediate modern medical treatments [56–58].

In our study, we found that hypertriglyceridemia that developed during the hospital stay was associated with mortality. These findings are consistent with two other reports regarding hypertriglyceridemia in patients with COVID-19. Our previous study conducted during earlier period of the pandemic showed that hypertriglyceridemia during hospitalization in patients with COVID-19 was correlated with mortality [12], consistent with the findings of the current study. Additionally, based on a genome-wide association study (GWAS), a consistent result was found that genetic variants that associate with hypertriglyceridemia were associated with COVID-19 severity in both inpatients and outpatients [49]. Likewise, investigation in the genetic variants related to Hemophagocytic lymph histiocytosis (HLH), such as the perforin gene, in Asian and non-White Hispanic patients are needed to assess the increased prevalence of hypertriglyceridemia. Due to the limitation of the current retrospective study, we are unable to investigate the prevalence of permissive mutations in HLH in patients with hypertriglyceridemia. Prospective studies with diverse patient population are needed to investigate the genetic impact of the incidence and outcome of hypertriglyceridemia in hospitalized patients with COVID-19.

Strategies of risk mitigation are essential in the assessment of patients presenting with high triglyceride levels during admission. Our retrospective study showed that non-White Hispanic and Asian hospitalized patients with COVID-19 between March 2020 and June 2021 had a higher association with mortality than White patients. Prospective studies with a racially and ethnically diverse population are needed to investigate risk mitigation in patients who have hypertriglyceridemia at admission or during the hospital stay.

Our study included hospitalized patients who received care at a large urban tertiary care academic center in Milwaukee, Wisconsin. According to 2021 Census data, of the Wisconsin population, 86.6% is White, 6.8% is African American, 3.2% is Asian, and 7.5% [59] is Hispanic/Latino. Although Hispanic/Latino ethnic category has a higher population than African American in the Census data, it is important to note that this category also includes White Hispanic, Black Hispanic, and other non-White Hispanic populations in their count. The small sample sizes of Asian and non-White Hispanics in our cohort are representative of the small population sizes of those racial/ethnic communities in the surrounding areas of our tertiary academic center in Milwaukee, Wisconsin, from which we extracted our de-identified patient data.

Limitations of this study. Our findings provided valuable insight on the potential racial/ethnic disparity in the COVID-19-associated hypertriglyceridemia and mortality. This single-center retrospective study included hospitalized COVID-19 patients from Milwaukee, Wisconsin, with good sample sizes for minorities including Black/African Americans, non-White Hispanics, and Asians, but not Native American, Hawaiian, and Alaskan patients. Additionally, only self-reported race/ethnicity information was collected. Furthermore, socioeconomic status information was limited. Additionally, the information regarding administration method, dose, and duration of medication use was limited in the current study. Therefore, multicenter-based prospective studies with geographic and racial/ethnic diversity are needed to consider the impact of all race/ethnicity groups and socioeconomic status, and medication use on the COVID-19 severity and mortality.

In summary, in this retrospective study, we found that hospitalized non-White Hispanic and Asian COVID-19 patients had a higher likelihood for mortality than White patients. We also found that hypertriglyceridemia developed during the hospital stay was associated with mortality. The non-White Hispanics and Asians had the highest frequencies of developing hypertriglyceridemia during hospitalization.

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Authorship contributions

MR and ZZ designed the research; MR, HL, KO, and ZZ obtained the de-identified clinical research data; MR, WD, ZYZ and ZZ analyzed the data; RLS provided critical advice related to study design and data interpretation; and MR and ZZ wrote the manuscript. All authors read and approved the final manuscript.

Data availability

Restrictions apply to the availability of some, or all data generated or analyzed during this study to preserve patient confidentiality or because they were used under license. The corresponding author will on request detail the restrictions and any conditions under which access to some data may be provided.

Practice points

- In hospitalized COVID-19 patients, Asians and non-White Hispanics had 4 or 3.9 times higher mortality, respectively, after adjusting for age, morbid obesity, and gender.
- The hypertriglyceridemia developed during hospitalization correlates with mortality after adjusting for morbid obesity, age, and gender.
- Non-White Hispanic and Asian COVID-19 patients had the highest frequencies of peak hypertriglyceridemia occurrence during hospitalization.
- The peak hypertriglyceridemia developed during hospitalization correlates with the incidence of thrombosis and mortality after adjusting for morbid obesity, age, and gender.

Research agenda

- The impact of racial/ethnic disparity on the thrombosis and mortality of hospitalized patients with COVID-19 requires more multicenter-based studies with geographic and racial/ethnic diversity.
- Hypertriglyceridemia developed during hospitalization associates with thrombosis and mortality in COVID-19 patients.

Declaration of competing interest

The authors have no conflicts of interest to declare.

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