Racial/ethnic Disparities on Inflammation and Response to Methylprednisolone in Severe Covid-19 Pneumonia

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Abstract

BACKGROUND

Racial/Ethnic minorities are at higher risk for Severe COVID-19. This may be related to social determinants that lead to chronic inflammatory states. The aims of the study were to determine if there are racial/ethnic differences between the inflammatory markers of survivors and non-survivors and if there was a dose dependent association of methylprednisolone to in hospital survival.

METHODS

This was a secondary analysis of a retrospective cohort. Patients were older than 18 years of age and admitted for severe COVID-19 Pneumonia Between March to June 2020 in 13 Hospitals in New Jersey, United States. Comparison of inflammatory markers used Kruskal-Wallis followed by pairwise comparison using two-sided Wilcoxon rank sum test. A Youden Index Method was used to determine the cut-off between low dose and high dose methylprednisolone. For each racial/ethnic group, cox regression was used to determine the association to survival between no methylprednisolone and methylprednisolone (high dose versus low dose).

RESULTS

Propensity matched sample (n=759) between no methylprednisolone (n=380) and methylprednisolone (n=379) had 338 Whites, 102 Blacks, 61 Asian/Indians, and 251 Non-Black Non-White Hispanics. Interleukin-6, C-reactive protein, ferritin, and d-dimer values were higher in non-survivors compared to survivors except in Asian/Indian survivors who had higher ferritin values compared to non-survivors (median: 1,265 vs 418 ug/L, P=0.0211). Black and Hispanic survivors had persistently elevated C-reactive protein, (10.2 mg/mL) and (13.70 mg/mL) respectively. Low dose methylprednisolone was associated with prolonged 60 days in hospital survival over no methylprednisolone in Whites (P<0.0001), Asian/Indians (P=0.0180), and Hispanics (P=0.0004). Regardless of dose, methylprednisolone was not associated with prolonged survival in Blacks. High dose methylprednisolone was associated with worse survival in Hispanics. (P=0.0181).

CONCLUSION

Racial/Ethnic disparities with inflammatory markers in survivors and non-survivors preclude the use of one marker as predictor of survival. Low dose methylprednisolone is associated with prolonged survival in Asian/Indians, Hispanics, and Whites. Methylprednisolone, regardless of dose, was not associated with prolonged survival in Blacks.

Introduction

As of July 2, 2021, there has been 182,319,261 coronavirus disease 2019 (COVID-19) cases and 3,954,324 deaths in worldwide (1), and the main cause of mortality is hyperinflammatory acute respiratory distress syndrome (ARDS). Advanced age, diabetes, cardiovascular disease, chronic lung disease, and racial/ethnic minorities are among the factors that appear to increase the risk for severe COVID-19.(2-4) Racial/ethnic minorities include non-black non-white Hispanics, Blacks, Native Americans, Native Hawaiians and other Pacific Islanders.(5) After age-related adjustments, mortality in Blacks, non-white non-black Hispanics, and Asians are higher compared to Whites in United States, United Kingdom, and Brazil.(1,6-8)

One explanation is social determinants (multi-generational homes, essential workers, low socio-economic status, lack of access to quality health care) predispose these minorities to higher COVID-19 exposure, and behaviors (depression, anxiety, smoking, alcoholism, high sugar, salt and fatty diet) that lead to chronic inflammatory states. These might influence the severe clinical presentation. (5) Inflammatory markers, such as IL-6 (>25 pg/mL), D-dimer ($\geq$ 2.0 mcg/ml), CRP ($\geq$ 10 mg/L) and/or ferritin $\geq$ 500 ug/L, are believed directly correlate with mortality in COVID-19.(9-17) There are racial/ethnic variability with inflammatory markers(18) but there has been no study comparing the variability between survivors and non-survivors.

Histologic studies show the sequalae of this inflammation, with severe endothelial damage, diffuse alveolar damage, thrombosis in situ, intussusceptive angio patterns of organizing pneumonia (OP) and / or acute fibrosing organizing pneumonia (AFOP).(19,20) Dexamethasone has been shown to improve mortality in patients requiring oxygen support including invasive mechanical ventilation.(21) Our initial study suggested that low dose methylprednisolone (< 1.36 mg/kg/d) given > 7 days from onset of symptoms for 7 days were associated with improved mortality and no additional benefit with duration > 14 days or high dose ($\geq$1.36 mg/kg/d). (22) Given that certain racial/ethnic minorities are predisposed to chronic inflammatory states, it is unknown if there is a methylprednisolone dose related association to in hospital survival.

Methodology

Eligibility criteria

Real world data was collected from Hackensack Meridian Health (HMH), a NJ health network comprising of thirteen hospitals on patients $\geq$ 18 years of age, and hospitalized for at least 2 days between March 1, 2020 and June 15, 2020 with severe COVID -19 Pneumonia.(22) These patients had a positive SARS-CoV-2 PCR and had SpO2 <94% on room air at sea level, a respiratory rate >30 breaths/min, PaO2/FiO2 <300 mm Hg, or lung infiltrates >50%. We excluded patients or had different corticosteroid regimen other than methylprednisolone. Approval was obtained by the Hackensack Meridian Health Institutional Review Board (study #Pro2020-0485) and the study was also registered on ClinicalTrials.Gov as a prospective observational database (NCT04347993).

Data collection process and data items

Demographic data such as age, gender, race, ethnicity, comorbidities, and sex were self-reported. Weight and height were measured. SARS-CoV-2 was detected in nasal swabs by RT-PCR. Routine blood tests included complete blood count (CBC), coagulation profile, complete metabolic profile (CMP), inflammatory markers [interleukin-6 (IL-6), C reactive protein (CRP), d-dimer, and ferritin], and arterial blood gas (ABG). Data was entered into Redcap and abstracted from June to December 2020.

Outcomes

The primary outcomes are the levels of the inflammatory markers of survivors and non-survivors and the association of methylprednisolone dose to in hospital survival for each racial/ethnic group.

Statistical Analysis

A one-to-one propensity score matched design of those treated with methylprednisolone and those without. (22) They were matched based variables associated with mortality such as age (age≥60 years vs. age <60 years), obesity (BMI ≥30.0 kg/m^2 vs. BMI <30.0 kg/ m^2), sex (M/F), diabetes (Yes/No), hypertension (Yes/No), cancer (Yes/No), respiratory rate (respiratory rate >22 vs <22), renal failure (Yes/No), low oxygen (oxygenation <94% vs. oxygenation ≥94%), CRP (CRP >20 mg/dL vs CRP ≤20 mg/dL), and qSOFA(score: 0,1,2,3).(22) A nearest-neighbor method (greedy match) was employed using a caliper of 0.20 to obtain the matched sample. We performed a post-match assessment of how distribution of propensity scores (or logit of propensity scores) and the adjusted variables are balanced between the no methylprednisolone (NMP) and methylprednisolone (MP) using standardized difference and variance ratio and graphical displays produced by the ASSESS statement of PROC PSMATCH in SAS 9.4. (22)

Categorical variables were presented as the frequency and percentage. Continuous variables were presented as the median and interquartile range (IQR). Shapiro-Wilk test was used to assess normality of continuous variables. A Youden Index Method was used to determine the cut-off between low dose (LD MP) and high dose methylprednisolone (HD MP). To examine association of risk factor of interest, methylprednisolone treatment, Cox proportional hazard regression analysis with robust covariance(23) (sandwich estimator) to account paired observations was used conducted and hazard ratios, (95% CIs) and p-values were reported in all univariable and multivariable analysis from PROC PHREG. The proportional hazard (PH) assumption, critical in Cox regression, was evaluated using a Kolmogorov-type supremum test (24) in ASSESS statement of PROC PHREG. If the PH assumption was violated, then a continuous variable which also violated the PH and its interaction with time were included in the model to adjust for the significant interaction with time to the risk of in-hospital mortality. (25)

The levels of inflammatory markers and age were compared between the race/ethnicity groups using Kruskal-Wallis followed by pairwise comparison using two-sided Wilcoxon rank sum test. Box plots were used to illustrate the difference between survivor versus non-survivor and the following variables: IL-6, CRP, D-dimer and ferritin.

Role of Funding

There was no external funding. The corresponding author had final responsibility for decision to submit for publication.

Results

Between March 4 and June 15, 2020, 2041 patients were flagged in the electronic health record with a diagnosis of COVID-19 and pneumonia. A total of 539 patients were excluded based on eligibility criteria (< 18 years of age, pregnant, received other formulations of corticosteroids, or hospitalized for less than 2 days) Thus, 1072 patients had their data abstracted. A propensity score matched sample was constructed out of 759 patients (381 in NMP and 378 in MP). **(Table 1)** An examination of the proportional hazard assumption, MP and Fractional inspired oxygen (FiO2) significantly violated it (both with P<0.0001). Data on P/F ratio was lacking; and FiO2 was used since 95% of patients had this data. The supremum test also indicated that non-proportionality was observed in other variables such as nursing home, lack of taste or smell, WBC<11,000 cells/ml, creatinine>1.5 ng/mL, respiratory rate >22 bpm, hydroxychloroquine (HCQ), MP, HD or LD MP, calcium, and initial diastolic blood pressure. All variables with non-proportional hazard were adjusted using FiO2, as indicated above. The Youden Index method yielded a MP dose cut- off 1.36 mg/kg/day. Low dose methylprednisolone (LDMP) was defined as < 1.36 mg/kg/day and high dose methylprednisolone (HDMP) was defined as ≥ 1.36 mg/kg/day. 215 received LDMP and 164 received HDMP. There were 102 Blacks, 338 Whites, 61 Asian/Indians, 251 Non-white / Non-black Hispanics and 7 unknown racial/ethnic group. For each racial/ethnic groups, there was no significant difference between no methylprednisolone and methylprednisolone. **(Table 2)**

There was a statistically significant difference in age between all 4 groups (Kruskal-Wallis P<.0001). This difference was driven by the difference between Black and White patients (median age: 64 vs 68 years; P=0.0060), between White and Hispanic (median age: 68 vs 60 years; P=0.0005) and between Asian/Indian and Hispanic (median age: 69 vs 60 years; P= 0.0010), after adjusting for multiple tests using Hochberg method. The difference in age between Black and Hispanic patient was trending towards significance (64 vs 60; P=0.0846). Out of 102 Black COVID patients, 25 expired and the difference in age between survivors and non-survivors was significant (median: 60 vs 70 years, P=0.0002). 117 of the 338 White patients expired. The age in the patients that survived and those who did not survive was significantly different (median: 66 vs 74 years, P<0.0001). 23 of 61 Asian/Indian patients expired in the hospital. The age in patients that survived and patients that did not survive was significantly different (median: 64 vs 79 years, P=0.0001). 76 of 251 Hispanic patients expired in the hospital. The age of patients who survivor and patients who did not survive was significantly different (median: 55 vs 74 years, P<0.0001). [i.e. the median age non-survivors were clinically higher than the age in survivors in all other race/ethnicity groups].

For ferritin, the figure shows slightly elevated levels in the Asian/Indians (median=1,048 ug/L) compared to Blacks (median=743.0 ug/L), Whites (median=777.5 ug/L) and Hispanics (median=831.0ug/L), however, this did not translate into statistically significant difference between the groups (Kruskal-Wallis P=0.1689). **(Figure 1)** In Blacks with ferritin values (n=72), the difference in ferritin between survivors (n=21) and non-survivors (n=51) was not

significant (median: 745 vs 575 ug/L, P=0.9280). In Whites with ferritin values (n=338), the difference between survivors (n=243) and non-survivors (n=95) was significant (median: 641 vs 987 ug/L, P=0.0139). In Asian/Indians with ferritin values (n=56), the difference between survivors (n=38) and non-survivors (n=18) was significant (median: 1,265 vs 418 ug/L, P=0.0211). In Hispanics with ferritin values (n=226), the difference between survivors (n=158) and non-survivors (n=68) was not significant (median: 826.5 vs 897.5 years, P=0.0854).

For d-dimer, there were slightly elevated levels in Blacks (median=1.64 mcg/mL) compared to Whites (median=1.33 mcg/mL), Asian/Indians(median=1.21mcg/mL) and Hispanics (median=1.11 mcg/mL), however this did not translate into statistically significant difference between the groups (Kruskal-Wallis P=0.1240). In Blacks with d-dimer values (n=62), the difference between survivors (n=44) and non-survivors (n=18) was not significant (median: 1.91 mcg/mL vs 1.53 mcg/mL, P=0.9119). In Whites with d-dimer values (n=193), the difference between survivors (n=133) and non-survivors (n=60) was significant (median: 1.19 vs 1.76 mcgg/mL, P=0.0034). In Asian/Indians with d-dimer values (n=41), the difference between survivors (n=26) and patients that non-survivors (n=15) was trending towards significance (median: 1.10 vs. 1.51 mcg/mL, P=0.0784). In Hispanics with d-dimer values (n=172), the difference between survivors (n=116) and non-survivors (n=56) was significant (median: 0.89 vs 2.24 mcg/mL, P<0.0001). The d-dimer in non-survivors was significantly or trending higher than that in survivors in White, Asian/Indian and Hispanic groups while the order was reversed in the Black group; the median d-dimer in survivors was higher than the level in the non-survivors, albeit, not achieving statistical significance.

For CRP, the figure shows slightly elevated levels in Blacks (median=11.40 mg/mL), moderate to extremely elevated Asian/Indians (median=12.85 mg/mL) and Hispanics (median=14.32 mg/mL), compared to Whites (median=9.47 mg/mL), and this yielded a statistically significant difference between the groups (Kruskal-Wallis P<0.0001). This result was driven by the significant difference between Whites and Hispanics adjusting for multiple testing using Hochberg method. In Blacks with CRP values (n=85), the difference between survivors (n=63) and non-survivors (n=22) was not significant (median: 10.2 mg/mL vs 12.07 mg/mL, P=0.3586). In Whites with CRP values (n=276), the difference between survivors (n=183) and non-survivors (n=93) was significantly different (median: 7.71 vs 12.30 mg/mL, P=0.0004). In Asian/Indians (n=60), the difference between survivors (n=38) and non-survivors (n=22) was significantly different (median: 9.05 vs. 20.75 mg/mL, P<0.0001). In Hispanics with CRP values (n=228), the difference between survivors (n=158) and non-survivors (n=70) was trended towards being significantly different (median: 13.70 vs 16.70 mg/mL, P=0.0514).

For IL-6, there was no significant difference between the race/ethnicity groups (Kruskal- Wallis P=0.9843). Except for Asian/Indians with median IL-6 of 11 pg/ml, all of the other groups had a median IL-6 of 14.0 pg/ml. Blacks with IL-6 values (n=51), the difference between survivors (n=34) and non-survivors (n=17) was not significant(P=0.7868). Whites with IL-6 values (n=157), the difference between survivors (n=94) and non-survivors (n=63) was significant (median=11.0 pg/ml vs 27.0 pg/ml P=0.0005). In Asian/Indians with IL-6 values (n=65), the difference between survivors (n=42) and non-survivors (n=23) was trending towards significance(median 30.0 pg/ml vs 8.0 pg/ml P=0.0924). In Hispanics with IL-6 values (n=110) the difference between survivors (n=73) and non-survivors (n=37) was significant (median=19.0 pg/ml vs 11.0 pg/ml P=0.0168).

Overall, in hospital survival was significantly difference between the race/ethnicity groups (Wilcoxon P=0.0320). This result was driven by the significant difference between Whites and Blacks (P=0.0249) and Whites and Asian/Indian (P=0.0463), after adjusting for multiple testing. The 30-day in hospital survival rates amongst Asia/Indian, Blacks, Hispanics, and Whites were 54.4% (95% CI 35.6 to 72.5%), 37.9% (95% CI 19.8% to 57.8%), 33.4% (95%CI 22.9 to 44.7%), and 41.0% (95% CI 32.6 to 49.6%), respectively. These differences become less significant after 30 days. (Figure 2).

LDMP was associated with prolonged lhS compared to NMP in Whites (0.350 95% CI 0.217- 0.566 (P<0.0001), Asian/Indians (HR 0.083 95% CI 0.011-0.653) (P=0.0180), and Hispanics (HR 0.294 95% CI 0.149-0.581)(P0.0004). (**Table 3**) HDMP was associated with prolonged survival compared to NMP in Asian/Indian, and White but there was no significant difference between LDMP and HDMP (P<0.05). HDMP was not associated with prolonged lhS in Blacks [HR 1.336 (95% CI 0.455-3.926)(P 0.5979)] and Hispanics [HR 0.594 (95% CI 0.329- 1.075)(P=0.0851)]. HDMP was associated with prolonged lhS compared to NMP in Whites (HR 0.557 95% CI 0.353-0.881)(P=0.0122) and Asian/Indians (HR 0.294(95% CI 0.149- 0.581)(P=0.0004). There was no association with prolonged lhS in Blacks for LDMP (HR 0.612 95% CI 9.264-1.416)(P=0.2514) or HDMP (HR 1.336 95% CI 0.455-3.926)(P=.597). HDMP was associated with shorter survival than LDMP in Hispanics (HR 1.975 95% CI 1.123-3.473) (P=0.0181).

Due to the varying frequencies, we were not able to compare the association of NMP, LDMP, and HDMP between all racial/ethnic groups. We did compare NMP, LDMP, and HDMP and their association with survival between Whites and Hispanics and they were not significant. (P> 0.05). **(Figures S1-S3)**

Discussion

Black and Non-white Non-black Hispanic survivors had persistently elevated CRP and Asian/Indian survivors had persistently elevated ferritin. Weathering and/or allostatic load theory predisposes social determinants such as depression, anxiety, smoking, alcohol, lack of physical activity, and poor-quality diet can have biologic consequences of low grade chronic inflammation. (26,27) With lack of access to quality health care, co-morbidities such as diabetes and coronary artery disease can remain undiagnosed in these minority groups. Chronic inflammation predisposes these minorities to elevated inflammatory markers at baseline, particularly with CRP in Black and Hispanic. (26,27) This can explain why in our cohort, these markers were above the cut-off values for mortality even in survivors [median CRP n Black (10.2 mg/mL) and Hispanic (13.70 mg/mL)].

There may also be genetic influences to elevated inflammatory markers. F3 and sickle cell variant (HBB rs334) are associated with higher d-dimer levels in Blacks and thalassemia, iron overload, or HFE mutations are associated with elevated ferritin levels in Asian/Indians.(28,29) This can explain the elevated median d-dimer in Black survivors (1.91 pg/ml) and median Ferritin in Asian/Indian survivors (> 1265 ug/L).

These chronic inflammatory states are hypothesized to cause steroid desensitization, requiring higher doses of methylprednisolone to mount an effective response. However, LDMP, not HDMP was associated with prolonged lhS in Asian/Indian and Hispanic. HDMP was associated with worse survival in Hispanics. Lack of benefit of HDMP maybe due to a dose dependent increased severity of critical illness polyneuropathy, increased incidence of secondary

infections or practice of higher doses for patients who are very sick.(30) Methylprednisolone (LDMP and HDMP) was associated with worse mortality in Blacks. Explanation for this might be related to vitamin D deficiency that is common in Blacks. (31-34) Vitamin D sufficiency is often associated with efficacy of steroid response. (35) Non-steroidal anti-inflammatories such as tocilizumab maybe indicated sooner for these racial/ethnic minorities.(36) Baricitinib is promising although the studies had proportionally fewer racial/ethnic minorities.(37,38)

While racial/ethnic minorities are diagnosed and hospitalized with COVID-19 at a younger age compared to their White counterparts, age continues to be an important prognostic factor. In each racial/ethnic group, patients who survived were younger than those who did not.

Strengths of this study include the median days in both methylprednisolone and no methylprednisolone were 5 days, which is at the beginning stages of inflammatory phase of the disease and there were minimal number of patients on remdesivir, which has become standard of care for COVID-19. Therefore, focus there has been on the inflammatory phase and on anti-inflammatory medications.

Limitations

Our study has several limitations. First, since it is an observational study and there maybe known and unknown confounders. However, propensity matching was employed to limit the known confounders. Second, misclassification of data is possible due to manual extraction of structured and unstructured data from medical health records. Third, there was a higher prevalence of Whites and non-white / non-black Hispanics, which might have skewed the analysis. Fourth, methylprednisolone was used as a rescue, given to patients who were at a higher risk of death. During the initial pandemic surge, there were reservations on the use of methylprednisolone due to extrapolated data on prolonging viral shedding in SARS and MERS and worse mortality in Influenza. Therefore, it was used as a rescue and reserved for patients who are already on high oxygen supplementation requirements or on mechanical ventilation. Despite the possibility of corticosteroid resistance in certain racial/ethnic groups, the effect of corticosteroids in patients on lesser amounts of oxygen supplementation such as nasal cannula was not available.

Conclusions

Racial and ethnic disparities in inflammatory markers between survivors and non-survivors preclude the use of one marker as a solitary measure of mortality. Low dose methylprednisolone was associated with prolonged survival in Asian/Indians, Whites and non-white and non-black Hispanics. There was no added benefit with high dose methylprednisolone. Methylprednisolone regardless of dose, was not associated with prolonged survival in Blacks. Large randomized studies are needed to confirm these conclusions.

Declarations

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Tables

Table 1. Characteristics of hospitalized COVID-19 patients treated with or without Methylprednisolone (n=759)

	No Methylprednisolone (n=381)	Methylprednisolone (n=378)	
Level	Count (%)	Count (%)	P-Value
Age ≥60.0 years	254(66.67)	244(64.55)	0.2436
Male	237(62.20)	242(64.02)	0.5775
Black	58(15.30)	44(11.80)	0.2500
White	178(46.97)	160(42.90)	0.2500
Asian/Indian	25(6.60)	36(9.65)	0.2500
Hispanic	118(31.13)	133(35.66)	0.2500
BMI ≥30 kg/m^2	179(46.98)	181(47.88)	0.6767
Smoker (Former or Current)	77(21.69)	88(25.96)	0.2334
Fever	250(65.79)	294(77.78)	**0.0003**
Shortness of breath	248(65.09)	298(79.05)	**<.0001**
Cough	242(63.68)	270(71.43)	**0.0191**
Altered Mental Status	63(16.54)	41(10.85)	**0.0032**
GI	76(20.00)	81(21.49)	0.5211
Anosmia or Ageusia	6(1.59)	9(2.45)	0.5930
Duration of Symptoms PTA	5.00(2.00,7.00)	5.00(3.00,7.00)	0.0699
Duration>7 days	59(18.91)	75(21.99)	0.2864
Diabetes	143(37.53)	138(36.51)	0.6521
COPD	20(5.25)	28(7.41)	0.2482
Asthma	24(6.30)	37(9.81)	0.0741
Hypertension	225(59.06)	219(57.94)	0.5525
Cancer	43(11.29)	43(11.38)	0.9013
Cerebrovascular Accident	18(4.74)	14(3.70)	0.3692
Coronary Artery Disease	29(7.61)	28(7.41)	0.8886
Arrhythmia	41(10.79)	30(7.94)	0.1213
Renal Failure	28(7.35)	31(8.20)	0.6682
Rheumatologic disorder	10(2.62)	19(5.04)	0.0588
qSOFA 0	224(58.49)	222(58.42)	0.7647
qSOFA 1	130(33.94)	130(34.21)	0.7647
qSOFA 2	28(7.31)	26(6.84)	0.7647
qSOFA 3	1(0.26)	2(0.53)	0.7647
Temperature	98.80(97.70,100.40)	99.30(98.00,100.70)	0.1284
Heart Rate	95.00(84.00,108.00)	97.00(86.00,108.00)	0.1438
Arterial pressure	92.33(83.33,100.50)	90.67(81.83,99.33)	0.0870
Respiratory Rate	19.00(18.00,22.00)	20.00(18.00,22.00)	0.3231
O2 Sat <94%	215(56.43)	217(57.41)	0.6733
Nasal Cannula	160(82.05)	131(65.83)	0.2500
Venti mask	2(1.03)	3(1.51)	0.2500
High Flow	6(3.08)	15(7.54)	0.2500
CPAP	1(0.51)	2(1.01)	0.2500
BiPAP	0(0.00)	2(1.01)	0.2500
Non-rebreather	26(13.33)	46(23.12)	0.2500

Mechanical Ventilation	35(11.15)	129(39.33)	**<.0001**
WBC	6.65(5.10,9.20)	6.50(5.10,9.50)	1.0000
HGB	13.40(12.30,14.50)	13.50(12.20,14.70)	0.6746
PLT	203.00(161.00,257.00)	189.00(147.00,252.00)	0.2736
ALC	0.90(0.60,1.30)	0.80(0.60,1.10)	**0.0031**
IL6	12.00(5.00,39.00)	15.00(5.00,36.00)	0.2678
CRP	9.88(4.99,17.31)	12.67(6.84,19.08)	**0.0047**
D-dimer	1.09(0.65,2.20)	1.44(0.72,3.13)	0.1155
Ferritin	729.50(325.50,1404.00)	867.00(418.00,1548.00)	0.0675
Creatinine	1.01(0.80,1.50)	1.01(0.80,1.35)	0.2630
Troponin	0.03(0.01,0.30)	0.02(0.01,0.09)	0.0732
BNP	131.85(40.30,1000.55)	88.80(26.20,362.00)	0.2110
Hydroxychloroquine	269(71.93)	317(88.55)	**<.0001**
Azithromycin	255(68.55)	264(73.54)	0.0728
Remdesivir	3(0.82)	10(2.82)	**0.0196**
Tocilizumab	13(3.53)	63(17.65)	**<.0001**

Table 2. Comparison of Age and inflammatory markers between the race/ethnicity groups in hospitalized COVID-19 patients

Variable	Black (n=102)	White (n=338)	Asian/Indian (n=61)	Hispanic (n=251)	P-Value
Diagnosis age	64.00(56.00,71.00)	68.50(60.00,79.00)	69.00(58.00,79.00)	60.00(49.00,71.00)	**<.0001**
(min, max)	(37.00,100.00)	(27.00,100.00)	(31.00,96.00)	(20.00,96.00)	
IL-6, pg/mL	14.00(5.00,35.00)	14.00(4.00,41.00)	11.50(5.00,36.00)	14.50(5.00,38.00)	0.9843
(min, max)	(4.00,781.00)	(4.00,3170.00)	(4.00,164.00)	(4.00,996.00)	
D-dimer	1.64(0.71,3.50)	1.33(0.72,3.08)	1.21(0.87,3.12)	1.11(0.59,2.29)	0.1240
(min, max)	(0.18,87.80)	(0.23,109.15)	(0.24,67.00)	(0.11,116.00)	
Ferritin	743.00(318.00,1481.00)	777.50(350.00,1457.00)	1048.50(403.50,2212.00)	831.50(391.00,1500.00)	0.1689
(min, max)	(51.10,13833.00)	(13.50,11229.00)	(193.00,33511.00)	(40.00,27548.00)	
CRP	11.40(5.66,19.21)	9.47(4.93,16.24)	12.85(6.29,19.08)	14.32(7.06,20.77)	**<.0001**
(min, max)	(0.04,38.00)	(0.30,38.00)	(0.41,41.40)	(0.11,42.50)	
Creatinine	1.15(0.90,1.86)	1.10(0.85,1.48)	1.09(0.80,1.53)	0.90(0.73,1.13)	**<.0001**
(min, max)	(0.30,11.20)	(0.40,16.20)	(0.56,7.09)	(0.40,15.80)	
Troponin	0.04(0.01,0.30)	0.02(0.01,0.10)	0.03(0.01,0.17)	0.02(0.01,0.11)	0.6241
(min, max)	(0.00,0.80)	(0.00,7.19)	(0.00,0.62)	(0.00,30.00)	
Fio2	28.00(21.00,44.00)	32.00(21.00,44.00)	28.00(21.00,44.00)	28.00(21.00,100.00)	0.9277
(min, max)	(21.00,100.00)	(21.00,100.00)	(21.00,100.00)	(21.00,100.00)	
Symptoms Dur.	5.00(2.00,7.00)	5.00(2.00,7.00)	5.00(3.00,7.00)	5.00(3.00,7.00)	0.1747
(min, max)	(1.00,21.00)	(1.00,30.00)	(1.00,14.00)	(1.00,30.00)	

Table 3. Association of MP dose and In-hospital Survival within each Race/Ethnicity				
Race/Ethnicity	Comparison	PH Supremum Test	HR (95% CI)	P-value
Black	LD MP vs. NMP	0.3780	0.612 (0.264 – 1.416)	0.2514
White	LD MP vs. NMP	**0.0100**	0.350 (0.217 – 0.566)	**<.0001**
Asian/Indian	LD MP vs. NMP	0.3210	0.083 (0.011 – 0.653)	**0.0180**
Hispanic	LD MP vs. NMP	0.2300	0.294 (0.149 – 0.581)	**0.0004**
Black	HD MP vs. NMP	0.8060	1.336 (0.455 – 3.926)	0.5979
White	HD MP vs. NMP	**0.0010**	0.557 (0.353 – 0.881)	**0.0122**
Asian/Indian	HD MP vs. NMP	0.0590	0.356 (0.127 – 0.993)	**0.0485**
Hispanic	HD MP vs. NMP	0.6980	0.594 (0.329 – 1.075)	**0.0851**
Black	HD MP vs. LD MP	0.2550	2.645 (0.881 – 7.935)	0.0828
White	HD MP vs. LD MP	0.9080	1.536 (0.925 – 2.550)	0.0969
Asian/Indian	HD MP vs. LD MP	0.3530	1.476 (0.490 – 4.449)	0.4888
Hispanic	HD MP vs. LD MP	0.4310	1.975 (1.123 – 3.473)	**0.0181**

Figures

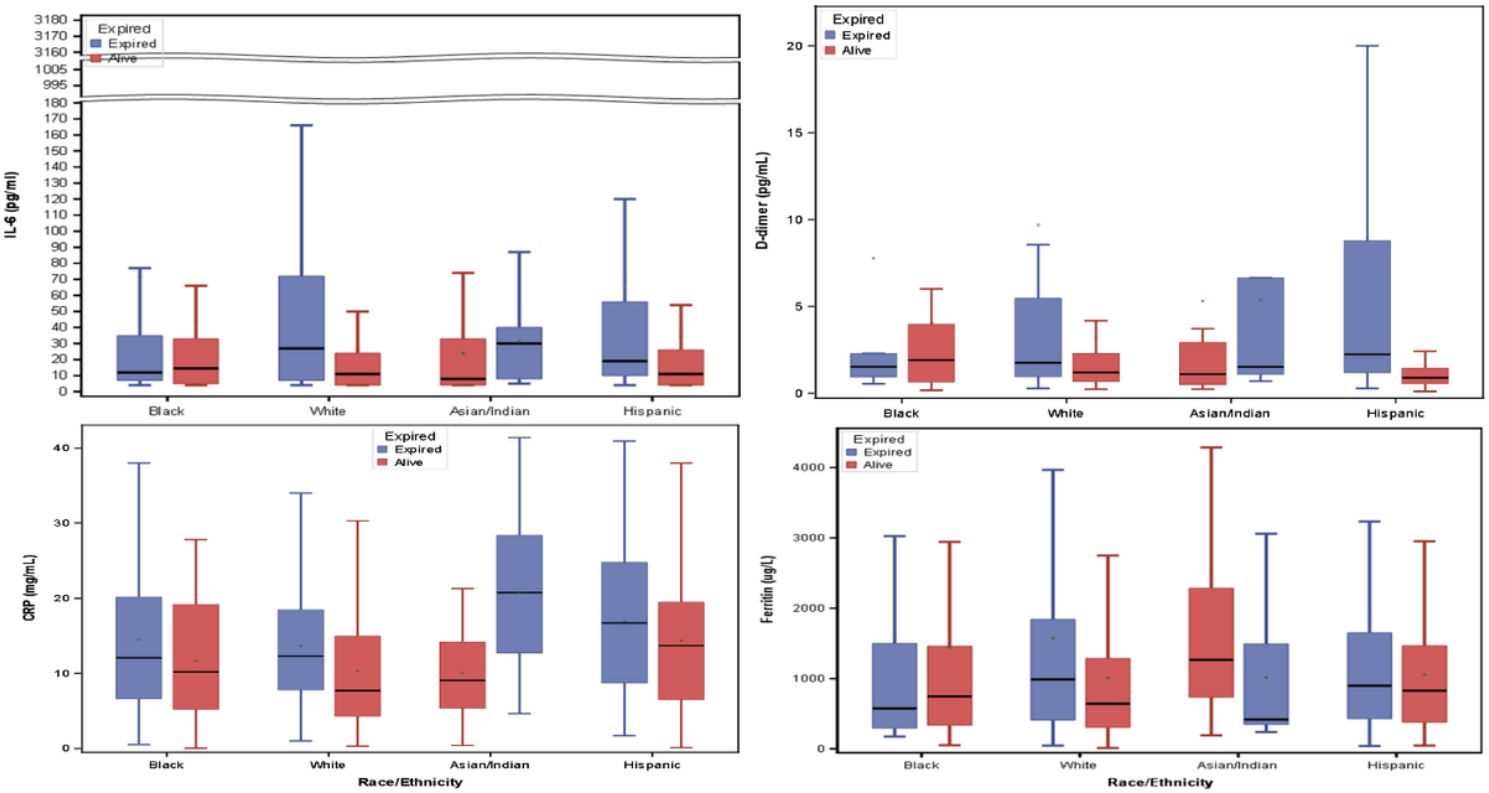

Figure 1

Race/Ethnicity and Inflammatory Markers between Survivors and Non-Survivors

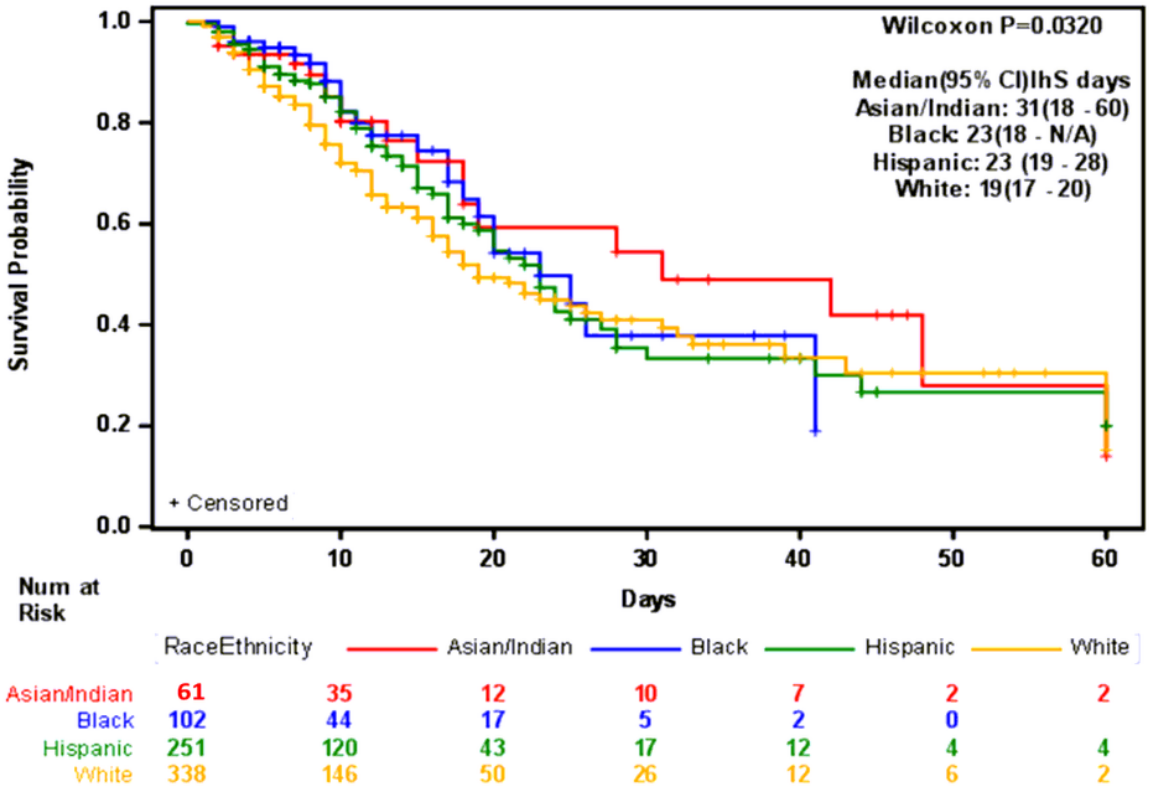

Figure 2

KM plot for overall in-hospital survival (IhS) for COVID-19 admitted for Asian/Indian (n=61), Blacks (n=102), Hispanics (n=251), and Whites (n=338) groups. IhS was significantly difference between the race/ethnicity groups (Wilcoxon P=0.0320). This result was driven by the significant difference between Whites and AA (P=0.0249) and Whites and Asian/Indian (P=0.0463), after adjusting for multiple testing. The 30-day IhS rates amongst Asia/Indian, AA, Hispanics, and Whites were 54.4% (95% CI 35.6 to 72.5%), 37.9% (95% CI 19.8% to 57.8%), 33.4% (95%CI 22.9 to 44.7%), and 41.0% (95% CI 32.6 to 49.6%), respectively.

Supplementary Files

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