BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-042042
Article Type:	Original research
Date Submitted by the Author:	23-Jun-2020
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Keywords:	INFECTIOUS DISEASES, Respiratory infections < THORACIC MEDICINE, Epidemiology < INFECTIOUS DISEASES

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Clinical Characteristics and Outcomes Among Hospitalized Patients with COVID19 in Southeast Michigan

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The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted

All authors declare no conflict of interest

Word count: 2543

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Abstract:

Introduction: There is limited information about the clinical characteristics and outcomes of patients hospitalized with COVID-19 in Southeast Michigan.

Methods: Retrospective cohort study included 3560 hospitalized patients with a positive SARS-CoV-2 infection by nasopharyngeal polymerase chain reaction (PCR) test from March 13 until April 29, 2020.

Results: During the study period 3,219 (90.4%) patients were discharged or died in the hospital. Median age was 65.2 (IQR 52.6 to 77.2) years, median length of stay in the hospital was 6.0 (IQR 3.2 to 10.1) days, and 51% were females**.** Hypertension was the most common chronic diseases occurring in 2,386 (74.1%) patients, followed by obesity in 1,642 (51.0%) patients. Overall mortality rate was 16.0%. Blacks represented 52.3% of the patients and had a mortality rate of 13.5%. Mortality was highest at 18.5% in the pre-peak hospital COVID-19 volume, decreasing to 15.3% during the peak period and to 10.8% in the post-peak period. Multivariable regression showed increasing odds of in-hospital death associated with older age (odds ratio 1.04, 95% CI 1.03 to 1.05; p<0.001) for every increase in year of age and being male (1.47 (95% CI 1.21 to 1.81; p<0.001). Chronic kidney disease, diabetes mellitus, heart failure, and obesity increased the odds of in-hospital mortality. Administration of hydroxychloroquine, azithromycin, therapeutic heparin, and systemic steroids in the hospital were associated with higher odds of death.

Discussion: In-hospital mortality was highest in early admissions and significantly improved as our knowledge and experience in treating COVID-19 patients increased. Black patients were more likely to get admitted to the hospital, and to receive mechanical ventilation, but less likely to die in the hospital

than Whites. Age, male sex, chronic kidney disease were found to increase the odds of in-hospital mortality.

Article Summary:

Patients hospitalized with COVID-19 in Southeast Michigan have a higher prevalence of comorbid conditions but lower mortality than other areas of the United States.

Chronic kidney disease, diabetes mellitus, heart failure, and obesity increased the odds of in-hospital mortality but hypertension did not

Mortality in patients with COVID-19 decreased significantly over time as therapies evolved and clinicians gained experience with the disease

Blacks were hospitalized and mechanically ventilated more often than Whites but had a lower in-hospital mortality rate

Coronavirus disease 2019 (COVID-19) was first reported as an outbreak of pneumonia of unknown cause in Wuhan, China in December 2019.[1] The virus responsible was subsequently named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The first confirmed case in the United States was reported January 31, 2020, and the first case in Michigan was reported March 10, 2020 [2]. As of June 1, 2020, 57,532 cases were confirmed in Michigan with 5,516 attributed deaths [2]. Southeast Michigan has been the epicenter of COVID-19 in the state [2].

As the pandemic spread, clinical characteristics of hospitalized COVID-19 patients were described in the medical literature from around the world, including China[3], Italy[4] New York City[5] and others. In this report we aim to describe the clinical characteristics of patients hospitalized with COVID-19 in Southeast Michigan, comparing those who did not survive hospitalization with those who were discharged alive between March 13, 2020 and April 29, 2020. We also report overall mortality rates during three periods of the COVID-19 surge, before, during and after the peak of COVID-19 hospital volumes.

Methods:

This study was conducted at an eight-hospital health system in Southeast Michigan. The study was approved by the Institutional Review Board. Patients were included in the study if they tested positive for SARS-CoV-2 infection by nasopharyngeal polymerase chain reaction (PCR) test and were admitted to one of the eight hospitals between March 13, 2020 and April 29, 2020. Data were collected retrospectively from the electronic health record (Epic). Data collected included date of admission and discharge, patient demographics, home medications, common chronic medical conditions, inpatient medications received for treatment of COVID19, oxygen therapy, and status at time of discharge from the hospital. Data were available for all patients during the study period. Patients who were still admitted at the end of the study period were not included in data analysis.

Race and ethnicity were available by self-reported status in the electronic health record (EHR). Home medications of interest were assessed based on medication reconciliation by the attending physician at the time of admission. Inpatient medications of interest were obtained from the medication administration record. Chronic medical conditions assessed include diabetes mellitus (DM), hypertension (HTN), heart failure (HF), coronary artery disease (CAD), chronic kidney disease (CKD), obesity (BMI $\geq$30), asthma, and chronic obstructive pulmonary disease (COPD). Documentation of these conditions in the medical history, problem list before admission, problem list during the admission, or discharge diagnoses in the EHR was used to evaluate the presence of these conditions. Patients were grouped as living or deceased based on status at the time of discharge from the hospital.

To evaluate the change in risk of mortality during the study, three periods were created: pre-peak, peak, and post-peak hospital COVID-19 volume. These periods were March 13 to March 30, 2020, March 31 to April 13, 2020, and April 14 to April 29, 2020. Peak was defined as the two-week period when the maximum number patients were admitted to the hospital system with a diagnosis of COVID-19.

Based on discharge status, groups were compared using Pearson's $\chi 2$ test for categorical variables and two-sample, unpaired t-test for continuous variables. Multivariate logistic regression was performed with death as the outcome of interest using age, gender, and chronic medical conditions and bivariate associations within the data. Interactions terms were used to evaluate interactions between independent variables. All statistical analyses were performed with Stata version 14.2 (Statacorp, College Station, TX).

Patient and public involvement: Due to the urgent need to publish data on the current pandemic patients or the public were not involved in the design, conduct or reporting of this research study.

Data Sharing Statement: no additional data available

Results:

During the study period 3,560 patients were admitted with a diagnosis of COVID-19; 3,219 patients (90.4%) were discharged or deceased and 341 patients (9.6%) were still hospitalized at the end of the study period (April 29, 2020). The demographic data for the 3,219 patients is shown in Table 1.

Overall mortality was 16.0%. Male patients had higher mortality than female patients (17.6% vs 14.5%, respectively). White patients had a mortality of 20.0% and Blacks had a mortality of 13.5%. Whites represented 37.8% of the patients who survived and 49.4% of those who died, while Blacks represented 54.8% of those patients who survived and 44.7% of those who died. For Arab or Middle Eastern patients' mortality was 9.5% and for Hispanic patients was 15.8%. The median length of hospital stay was 6.0 days, 5.6 days for the patients who were discharged alive and 8.6 days for the patients who died in the hospital.

Mortality increased with increasing age, reaching 28.1% for those patients 80 years of age and older. These results are shown in Table 2.

Comorbid medical conditions were common, with hypertension being the most common, followed by obesity, diabetes and chronic kidney disease. Each of the chronic medical conditions except asthma correlated with increased in-hospital mortality.

There were higher rates of hospital administration of hydroxychloroquine, azithromycin, therapeutic heparin, tocilizumab, and systemic corticosteroids in the group of patients who died. Use of remdesevir, prophylactic heparin, zinc and vitamin C did not differ between the two groups.

During hospitalization 571 (17.7%) received mechanical ventilation, 125 (3.9%) received BIPAP, and 848 (26.3%) received high flow oxygen. Black patients had higher rates of receiving mechanical ventilation than Whites, 19.6% vs. 15.2%, respectively. Rates of these oxygen therapies were higher in the group

that died in the hospital compared to those who were discharged alive. Specifically, 61.2% of the patients who died received mechanical ventilation compared to only 9.4% of those who survived.

A logistic regression model was used to estimate the odds ratio of death when controlling for age, gender, race, current smoking, and chronic medical conditions. In this model, male patients had an increased odds of dying compared to female patients. The odds of dying were 1.04 for every increase in year of age. There was no difference in mortality based on race. The presence of diabetes mellitus, heart failure, obesity, and chronic kidney disease resulted in an increased odds of death, with chronic kidney disease having the highest effect. Hypertension, coronary artery disease, asthma, chronic obstructive pulmonary disease, and current smoking status were not associated with increased odds of dying. These results are shown in Figure 1.

A second logistic regression model was used to estimate the odds ratio of death with each of the ten home medications of interest when controlling for age, gender, smoking, and chronic medical conditions. None of the medications were associated with an increase in odds of mortality. Specifically, the odds ratio for angiotensin-converting enzymes inhibitors (ACEi) was 0.93 (CI: 0.74 to 1.18, P=0.971) and angiotensin receptor blockers (ARB) 1.00 (CI:0.79 to 1.28, P=0.566).

A third logistic regression model was used to estimate the odds of death when receiving the medications of interest in the hospital when controlling for age, gender, smoking, and chronic medical conditions. Administration of systemic corticosteroids, therapeutic heparin and vitamin C were associated with increased odds of dying in the hospital. Administration of zinc and novel oral anticoagulants were associated with decreased in odds of dying in the hospital. There was an increase in odds of dying with the administration of tocilizumab, although, only 30 patients received this drug during the study period. Similarly, only 8 patients received Remdesevir. These results are shown in Table 3.

Mortality was evaluated in three time periods, pre-peak, peak, and post-peak hospital COVID-19 volume. During the peak period there were over 800 COVID19 patients hospitalized each day. Overall mortality decreased significantly with each successive time period. These results are shown in Table 4.

A difference in the use of some treatment medications was noted in the pre-peak, peak, and post-peak periods. Specifically, hydroxychloroquine use decreased in the post-peak period but was still used in over 60% of patients. Similarly, azithromycin use decreased in the post-peak period to less than 35% compared to over 83% in the pre peak and peak periods.

Interaction terms were created in the logistic regression models to look for differing levels of effect for hospital administered medications at the three different time periods (pre-peak, peak, and post-peak). Hydroxychloroquine, azithromycin, and therapeutically dosed heparin all showed significant variation in their associated odds of death across time periods.

When controlling for other factors, use of hydroxychloroquine was associated with an increase in mortality when given in the pre-peak period (OR 2.72, CI 2.01 to 3.68, P<0.001) and a borderline increase in the peak period (OR 1.34, CI 1.00 to 1.79, P=0.051). When controlling for other factors, use of azithromycin was associated with a significant increase in mortality when given in the pre-peak time (OR 2.15, CI 1.62 to 2.86, P<0.001). When controlling for other factors, use of therapeutically dosed heparin was associated with an increase in mortality when given in the pre-peak (OR 5.72, CI 4.39 to 7.47, P<0.001) and peak timeframe (OR 2.76, CI 2.15 to 3.54, P<0.001) but no significant difference in the post-peak timeframe.

Discussion

This study describes the clinical characteristics of the patients who were hospitalized with COVID-19 in the largest health system in Southeast Michigan. Similar to other studies [3-7], we showed that age and

male gender are risk factors for increasing mortality with similar odds ratios of death. Mortality reached 28% in patients 80 years of age and older, and the risk of death was elevated (61.2%) in patients who received mechanical ventilation.

In-hospital COVID-19 mortality was 16%, which is lower than mortality rates reported in New York City area [5, 7]. This difference could be explained in several ways. First, the COVID-19 peak occurred earlier in New York City than Michigan which gave our hospitals and providers more lead time to prepare. Second, the number of patients admitted during the peak in New York City was greater than that seen in Southeast Michigan, causing comparatively less stress on hospitals in our area. Lastly, during the peak in Southeast Michigan, a small number of patients were redirected to other hospital systems after presentation to the emergency centers. This "load balancing" resulted in these patients not being admitted and therefore analyzed, which is a limitation to our study.

Mortality risk was highest in the first 2 weeks of the pandemic and subsequently decreased during the peak and post-peak time frames. This likely reflects improvement in the care provided to COVID-19 patients as hospitals and providers learned from the earlier cases. Hospital guidelines for care of COVID-19 patients were updated frequently and communicated broadly as outside studies and internal findings became available. Including prone positioning, delayed mechanical ventilation and broader use of anticoagulation.

Blacks represented over half of the admitted patients with a COVID-19 diagnosis, although, they only represent 17.4% of the population served by our health system. This is consistent with the Center for Disease Control and Prevention (CDC) reports showing overrepresentation of Blacks in hospitalized patients with COVID-19 [8]. Blacks in our study population had a lower mortality rate than Whites, 13.5% vs. 20%, although this difference was not statistically significant when controlling for other factors. This is not consistent with other reports showing higher COVID-19 mortality in non-hospitalized

and hospitalized Blacks in the US. [9, 10]. In Michigan 41.3% of COVID-19 related death are Blacks although they only represent 13.8% of the state population [11]. Another study of hospitalized patients with COVID-19 in State of Louisiana similarly reported lower in-hospital mortality in Blacks compared to Whites, 21.6% vs. 30.1% [12]. In our study hospitalized Blacks were younger on average than Whites, mean age 61.8 vs. 70.5 years. This difference in age and possibly the fact that our hospital system drew more suburban than urban patients could probably explain the lower rate of mortality in Blacks compared to the State reported rates.

Comorbid conditions were common in our patient population. Specifically, rates of hypertension, diabetes, and chronic kidney disease were much higher than previously reported by the CDC and similar studies in the United States [5, 7, 13]. This could be explained by many factors including the possibility that our patient population has more chronic disease compared to other areas in the U.S. Comorbid conditions that were associated with an increased risk of death were chronic kidney disease, heart failure, diabetes, and obesity which is similar to other studies. Interestingly, hypertension was not associated with worsening in-hospital survival as reported by other studies [14, 15].

Concerns exist that ACEi and ARB could increase the risk of death in COVID19 patients [16]. Although our study was not designed to answer this question, we found that use of these medications was not associated with an increased odds ratio of death. This was consistent with other retrospective studies [17].

The use of specific medications during the hospital stay was associated with an increased odds of death, especially systemic steroids. This may reflect provider overuse of corticosteroids in the sickest COVID-19 patients when other proven therapies were lacking. Hydroxychloroquine use was associated with an overall higher death rate but did not reach statistical significance. When broken down by study periods, however, there was an increase in odds of dying when hydroxychloroquine was administered during the

pre-peak period but no significant change in odds of dying in the post-peak period. This likely reflects a more judicious and evidence-based approach to COVID-19 treatment later in the study period as knowledge evolved. A similar pattern was seen with azithromycin.

The finding of increased mortality with therapeutically dosed heparin may be explained by several factors. In the pre-peak and peak period, therapeutic heparin use was primarily limited to patients with confirmed deep vein thromboses and pulmonary emboli. The odds ratio of death with the therapeutic use of heparin was 5.73 and 2.76 in the pre-peak and peak period, respectively. This likely reflects that these patients were sicker and would be expected to have higher mortality risk. As new data on thrombotic risk in COVID-19 patients emerged over time, local guidelines shifted at the end of the peak period to include the use of therapeutic heparin in patients with elevated oxygen requirements and elevated D-dimer levels, even in the absence of venous thromboembolism. The use of therapeutic heparin in the post peak period likely reflects use in a broader range of patients, contributing to the decrease in mortality in that period.

Limitations:

Our study has several limitations. First, this is a retrospective study with data collected from the EHR. Because of this, there is a risk of missing data points if they were not reported in a structured data element that can be queried. Second, although our health system cared for the largest share of COVID-19 patients in the area, the patients may not completely represent the entire population of Southeast Michigan. Third, as stated above, a few patients were transferred to other health systems during the peak period and their outcomes are not included in the analysis.

Conclusion:

We reported the characteristics of hospitalized COVID19 patients in this case series from Southeast Michigan. Comorbid conditions were more common than the national average. Black patients were more likely to get admitted to the hospital, and to receive mechanical ventilation, but less likely to die in the hospital than Whites. The reported improvement in survival during the 3 study periods is novel and needs to be evaluated further in similar studies.

Table 1. Overall COVID-19 Patients' Characteristics and by Hospital Discharge Outcome

	Total Discharged Patients n=3,219	**Discharged Alive n=2,703**	**Died in Hospital n=516**	**P value**
Demographic characteristics				
Age, median (IQR), years	65.2 (52.6 to 77.2)	63.4 (50.7 to 74.5)	75.7 (65.3 to 84.2)	<0.001
Length of Stay, median (IQR), days	6.0 (3.2 to 10.1)	5.6 (3.1 to 9.3)	8.6 (4.6 to 13.4)	<0.001
Gender				0.019
Male n (% of group)	1,576 (49.0)	1,299 (48.1)	277 (53.4)	
Female	1,643 (51.0)	1,404 (51.9)	239 (46.3)	
Race				<0.001
White	1,277 (39.7)	1,022 (37.8)	255 (49.4)	
Blacks	1,713 (53.2)	1,482 (54.8)	231 (44.7)	
Asian	67 (2.1)	59 (2.1)	8 (1.6)	
American Indian	5 (0.2)	5 (0.2)	0 (0.0)	
Pacific Islander	2 (0.1)	2 (0.1)	0 (0.0)	
Other	155 (4.8)	133 (4.9)	22 (4.3)	
Ethnicity				0.253
Arab or Middle Eastern	157 (4.9)	142 (5.3)	15 (2.9)	
Hispanic or Latino	82 (2.5)	69 (2.6)	13 (2.5)	
Non-Hispanic	2,776 (86.2)	2,319 (85.8)	457 (88.6)	
Other	170 (5.3)	146 (5.4)	24 (4.7)	
Unavailable	33 (1.0)	26 (1.0)	7 (1.4)	
Medical Condition				
Diabetes	1,329 (41.3)	1,073 (39.7)	256 (49.6)	<0.001
Hypertension	2,386 (74.1)	1,949 (72.1)	437 (84.7)	<0.001
Heart Failure	609 (18.9)	440 (16.3)	169 (32.8)	<0.001
Heart Disease	763 (23.7)	599 (22.2)	204 (39.5)	<0.001
Chronic Kidney Disease	1,299 (40.4)	929 (34.4)	300 (58.1)	<0.001
Asthma	429 (13.3)	362 (13.4)	67 (13.0)	0.803
COPD	568 (17.6)	428 (15.8)	140 (27.1)	<0.001
Obesity (BMI $\geq$30) [a]	1,642 (51.0)	1,405 (52.0)	237 (45.9)	0.036
Smoking [b]	133 (4.1)	115 (4.3)	18 (3.5)	<0.001
Health Insurance Payor				<0.001
Medicare	1,808 (56.2)	1,393 (51.5)	415 (80.4)	
Medicaid	460 (14.3)	429 (15.9)	31 (6.0)	

Commercial	897 (27.9)	836 (30.9)	61 (11.8)	
Military	7 (0.2)	5 (0.2)	2 (0.4)	
Exchange	41 (1.3)	37 (1.4)	4 (0.8)	
Unknown	6 (0.2)	3 (0.1)	3 (0.6)	
Home Medication				
Aspirin	1,354 (42.1)	1,054 (39.0)	300 (58.1)	<0.001
ACE Inhibitor	940 (29.2)	757 (28.0)	183 (35.5)	0.001
Angiotensin Receptor Blocker	676 (21.0)	533 (19.7)	143 (27.7)	<0.001
Metformin	688 (21.4)	565 (20.9)	123 (23.8)	0.136
Insulin	490 (15.2)	377 (14.0)	113 (21.9)	<0.001
Warfarin	230 (7.1)	173 (6.4)	57 (11.1)	<0.001
NOAC	347 (10.8)	271 (10.0)	76 (14.7)	0.002
Inhaled Corticosteroid	472 (14.7)	367 (13.6)	105 (20.4)	<0.001
LABA	318 (9.9)	240 (8.9)	78 (15.1)	<0.001
LAMA	197 (6.1)	150 (5.6)	47 (9.1)	0.002
Hospital Medication				
Hydroxychloroquine	2,496 (77.5)	2,061 (76.3)	435 (84.3)	<0.001
Azithromycin	2,463 (76.5)	2,046 (75.7)	417 (80.8)	0.012
Prophylactic Heparin	2,547 (79.1)	2,136 (79.0)	411 (79.7)	0.748
Therapeutic Heparin	1,257 (39.0)	916 (33.9)	341 (67.0)	<0.001
Tocilizumab	30 (0.9)	18 (0.7)	12 (2.3)	<0.001
Remdesevir	8 (0.2)	7 (0.3)	1 (0.2)	0.785
Systemic corticosteroids	1,631 (50.7)	1,265 (46.8)	366 (70.9)	<0.001
NOAC	340 (10.6)	291 (10.8)	49 (9.5)	0.390
Zinc	1,596 (49.6)	1,340 (49.6)	256 (49.6)	0.987
Vitamin C	794 (24.7)	637 (23.6)	157 (30.4)	0.001
Oxygen Therapy				
High Flow O2	848 (26.3)	534 (19.8)	314 (60.9)	<0.001
BiPAP	125 (3.9)	73 (2.7)	52 (10.1)	<0.001
CPAP	93 (2.9)	59 (2.2)	34 (6.6)	<0.001
Nonrebreather Mask	867 (26.9)	537 (19.9)	330 (64.0)	<0.001
Mechanical Ventilation	571 (17.7)	255 (9.4)	316 (61.2)	<0.001

Abbreviations: COVID-19, Coronavirus disease 2019; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NOAC, Non-vitamin K oral anticoagulation; LABA, Long-acting beta-agonist; LAMA, Long acting muscarinic antagonist; BiPAP, Bilevel positive airway pressure; CPAP, Continuous positive airway pressure. [a] BMI data available for 3135 patients. [b] smoking data available for 2517 patients.

Table 2. Overall Mortality by Age Category of Discharged Patients who were Admitted with a COVID-19 Diagnosis

Age Category, years	Total Patients	Alive at Discharge, n (%)	Deceased, n (%)
<18	8	7 (87.5)	1 (12.5)
19-40	295	285 (96.6)	10 (3.4)
41-50	370	350 (94.6)	20 (5.4)
51-60	554	510 (92.1)	44 (7.9)
61-70	737	631 (85.6)	106 (14.4)
71-80	621	464 (74.7)	157 (25.3)
>80	634	456 (71.9)	178 (28.1)

Table 3. Odds Ratio of Death from Logistic Regression Model for In-hospital Treatment Medications when Controlling for Age, Gender, and Chronic Medical Conditions

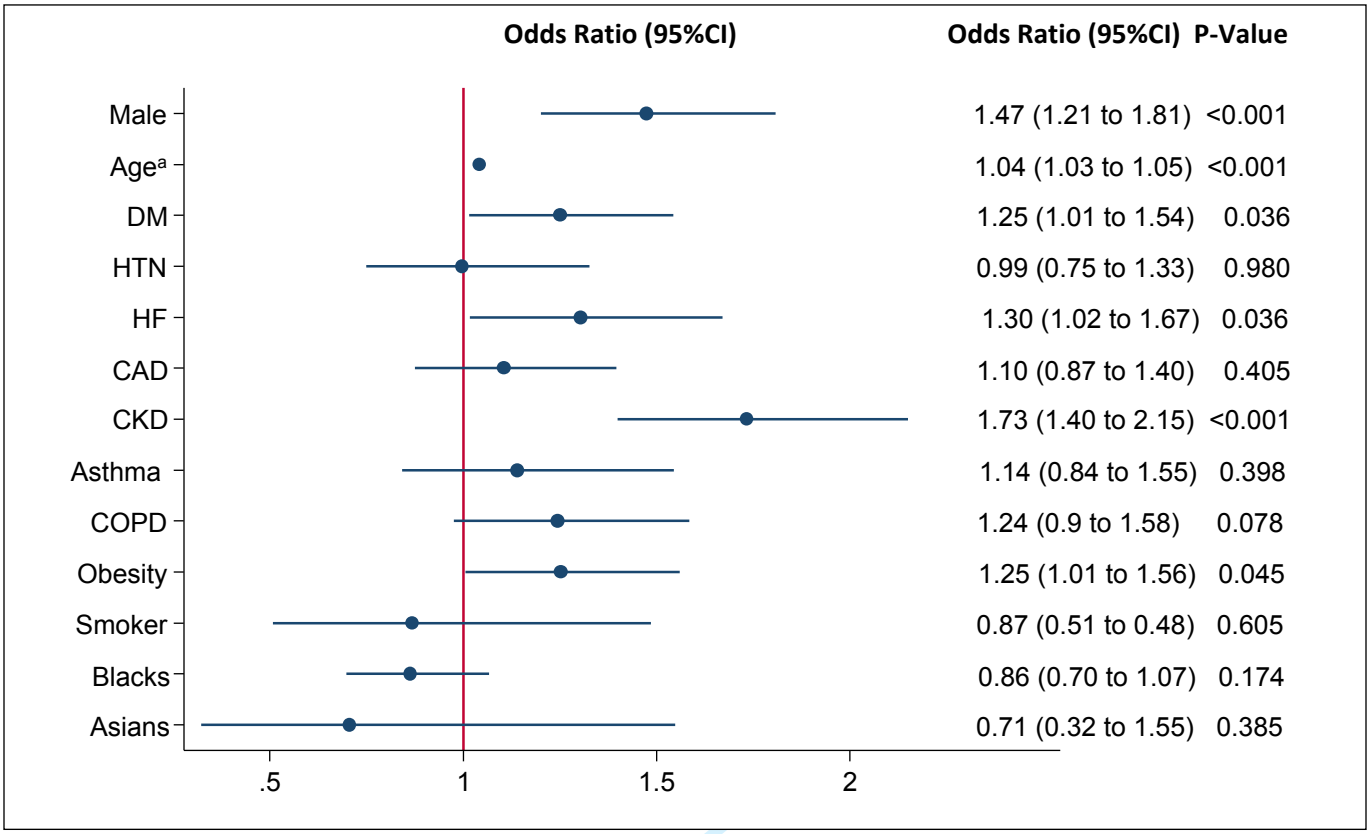
Medication	Odds Ratio of Death	Confidence Interval	P-Value
Hydroxychloroquine	1.33	0.95 to 1.88	0.102
Azithromycin	1.11	0.82 to 1.49	0.489
Vitamin C	1.40	1.08 to 1.81	0.011
Zinc	0.50	0.39 to 0.64	<0.001
Novel oral anticoagulants	0.42	0.29 to 0.60	<0.001
Systemic corticosteroids	2.45	1.91 to 3.12	<0.001
Remdesevir[a]	2.22	0.18 to 27.5	0.535
Tocilizumab[b]	2.23	0.99 to 5.02	0.052
Prophylactic heparin	0.76	0.57 to 1.02	0.071
Therapeutic heparin	3.06	2.44 to 3.83	<0.001

[a] only 8 patients received Remdesevir. [b] only 30 patients received Tocilizumab

Table 4. Overall Mortality by Time of Admission for Patients who were Discharged During Study Period. N=3.219

Time Frame	Total Hospital Admissions	Discharged Alive (%)	Died in the Hospital (%)
Pre-peak (3/13- 3/30/2020)	1,447	1,180 (81.5)	267 (18.5)
Peak (3/31- 4/13/2020)	1,279	1,083 (84.7)	196 (15.3)
Post-peak (4/14-4/29/2020)	493	440 (89.2)	53 (10.8)

Figure 1. Odds Ratio of Death from Logistic Regression Model when Controlling for Gender, Age, Race, Current Smoking, and Comorbidities.



Abbreviations: DM, Diabetes Mellitus; HTN, hypertension; HF, heart failure; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease. [a] Age: for every increase of one year in age

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BMJ Open

Retrospective Case Cohort Study of 3,219 Hospitalized Patients with COVID-19 in Southeast Michigan

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2020-042042.R1
Article Type:	Original research
Date Submitted by the Author:	10-Nov-2020
Complete List of Authors:	Mulhem, Elie; Oakland University William Beaumont School of Medicine, Family Medicine Oleszkowicz, Andrew; Oakland University William Beaumont School of Medicine, Family Medicine Lick, David; Oakland University William Beaumont School of Medicine, Family Medicine
Primary Subject Heading:	Infectious diseases
Secondary Subject Heading:	Public health, Respiratory medicine
Keywords:	INFECTIOUS DISEASES, Respiratory infections < THORACIC MEDICINE, Epidemiology < INFECTIOUS DISEASES

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Retrospective Case Cohort Study of 3,219 Hospitalized Patients with COVID-19 in Southeast Michigan

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Word count: 2784

Retrospective Case Cohort Study of 3,219 Hospitalized Patients with COVID-19 in Southeast Michigan

Abstract:

Objectives: To report the clinical characteristic of patients hospitalized with COVID-19 in Southeast Michigan.

Design: Retrospective cohort study

Setting: Eight hospitals in Southeast Michigan.

Participants: 3219 hospitalized patients with a positive SARS-CoV-2 infection by nasopharyngeal polymerase chain reaction (PCR) test from March 13,2020 until April 29, 2020.

Main outcomes measures: Outcomes were discharge from the hospital or in-hospital death. Examined predictors included patient demographics, chronic diseases, home medications, mechanical ventilation, in-hospital medications, and timeframe of hospital admission. Multivariable logistic regression was conducted to identify risk factors for in-hospital mortality.

Results: During the study period, 3,219 (90.4%) patients were discharged or died in the hospital. Median age was 65.2 (IQR 52.6 to 77.2) years, median length of stay in the hospital was 6.0 (IQR 3.2 to 10.1) days, and 51% were females**.** Hypertension was the most common chronic diseases occurring in 2,386 (74.1%) patients. Overall mortality rate was 16.0%. Blacks represented 52.3% of the patients and had a mortality rate of 13.5%. Mortality was highest at 18.5% in the pre-peak hospital COVID-19 volume, decreasing to 15.3% during the peak period and to 10.8% in the post-peak period. Multivariable regression showed increasing odds of in-hospital death associated with older age (odds ratio 1.04, 95% CI 1.03 to 1.05; p<0.001) for every increase in one year of age and being male (1.47 (95% CI 1.21 to 1.81; p<0.001). Certain chronic diseases increased the odds of in-hospital mortality especially chronic kidney

disease. Administration of vitamin C, corticosteroids, and therapeutic heparin in the hospital were associated with higher odds of death.

Conclusion: In-hospital mortality was highest in early admissions and improved as our experience in treating COVID-19 patients increased. Black were more likely to get admitted to the hospital, and to receive mechanical ventilation, but less likely to die in the hospital than Whites.

Strength and limitations:

- This is the largest study to date to describe the hospitalized patient population with SARS-CoV-2 in Southeast Michigan.
- The study population represents a large and diverse metropolitan area using data from the largest healthcare system in the region.
- This study relied on data collected from the EHR and thus there is risk of missing data points if they were not reported in a structured data element that could be queried.
- Although our health system cared for the largest share of patients with SARS-CoV-2 in the region, the patients may not completely represent the entire population of Southeast Michigan.
- Due to its retrospective design, results are subject to confounding factors.

Coronavirus disease 2019 (COVID-19) was first reported as an outbreak of pneumonia of unknown cause in Wuhan, China in December 2019.[1] The virus responsible was subsequently named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The first confirmed case in the United States was reported January 31, 2020, and the first case in Michigan was reported March 10, 2020 [2]. As of June 1, 2020, 57,532 cases were confirmed in Michigan with 5,516 attributed deaths [2]. Southeast Michigan has been the epicenter of COVID-19 in the state [2].

As the pandemic spread, clinical characteristics of hospitalized COVID-19 patients were described in the medical literature from around the world, including China[3], Italy[4] New York City[5], Louisiana[6], and Michigan[7]. These studies indicated that increase age, male sex, and presence of chronic medical conditions increase risk of death during hospitalization. In this report we aim to describe the clinical characteristics of a large cohort of patients hospitalized with COVID-19 in Southeast Michigan. Understanding the clinical characteristics of hospitalized COVID-19 patients in the Midwest region of the United States will help to provide a more complete description of this population on a national level. We compared those who did not survive hospitalization with those who were discharged alive between March 13, 2020 and April 29, 2020. We also report overall mortality rates during three periods of the COVID-19 surge, before, during and after the peak of COVID-19 hospital volumes.

Methods:

This study was conducted at an eight-hospital health system in Southeast Michigan. Southeast Michigan is the Metro area of Detroit and is home to 4.5 Million people, almost half of the population of the State of Michigan. The study was approved by the Institutional Review Board. Patients were included in the study if they tested positive for SARS-CoV-2 infection by nasopharyngeal polymerase chain reaction (PCR) test and were admitted to one of the eight hospitals between March 13, 2020 and April 29, 2020. Data were collected retrospectively from the electronic health record (Epic). Data collected included

date of admission and discharge, patient demographics, home medications, common chronic medical conditions, inpatient medications received for treatment of COVID19, oxygen therapy, and status at time of discharge from the hospital. Data were available for all patients during the study period. Patients who were still admitted at the end of the study period were not included in data analysis.

Race and ethnicity were available by self-reported status in the electronic health record (EHR). White patients tend to live in suburban communities while Black patients tend to live in urban and poorer communities. Home medications of interest were assessed based on medication reconciliation by the attending physician at the time of admission. Inpatient medications of interest were obtained from the medication administration record. Chronic medical conditions assessed include diabetes mellitus (DM), hypertension (HTN), heart failure (HF), coronary artery disease (CAD), chronic kidney disease (CKD), obesity (BMI $\geq$30), asthma, and chronic obstructive pulmonary disease (COPD). Documentation of these conditions in the medical history, problem list before admission, problem list during the admission, or discharge diagnoses in the EHR was used to evaluate the presence of these conditions. Patients were grouped as living or deceased based on status at the time of discharge from the hospital.

To evaluate the change in risk of mortality during the study, three periods were created: pre-peak, peak, and post-peak hospital COVID-19 volume. These periods were March 13,2020 to March 30, 2020, March 31,2020 to April 13, 2020, and April 14,2020 to April 29, 2020. Peak was defined as the two-week period when the maximum number patients were admitted to the hospital system with a diagnosis of COVID-19.

Based on discharge status, groups were compared using Pearson's $\chi 2$ test for categorical variables and two-sample, unpaired t-test for continuous variables. Multivariate logistic regression was performed with death as the outcome of interest using age, gender, and chronic medical conditions and bivariate associations within the data. Four separate models were created and are described in further detail in

the Supplement. All variables were added to the models a priori.. All statistical analyses were performed with Stata version 14.2 (Statacorp, College Station, TX).

Patient and public involvement: Due to the urgent need to publish data on the current pandemic patients or the public were not involved in the design, conduct or reporting of this research study.

Data Sharing Statement: no additional data available

Results:

During the study period 3,560 patients were admitted with a diagnosis of COVID-19; 3,219 patients (90.4%) were discharged or deceased and 341 patients (9.6%) were still hospitalized at the end of the study period (April 29, 2020). The demographic data for the 3,219 patients is shown in Table 1.

Overall mortality was 16.0%. Male patients had higher mortality than female patients (17.6% vs 14.5%, respectively). White patients had a mortality of 20.0% and Blacks had a mortality of 13.5%. Whites represented 37.8% of the patients who survived and 49.4% of those who died, while Blacks represented 54.8% of those patients who survived and 44.7% of those who died. For Arab or Middle Eastern patients' mortality was 9.5% and for Hispanic patients was 15.8%. The median length of hospital stay was 6.0 days, 5.6 days for patients who were discharged alive and 8.6 days for the patients who died in the hospital.

Mortality increased with increasing age, reaching 28.1% for those patients 80 years of age and older. These results are shown in Table 2.

Comorbid medical conditions were common, with hypertension being the most common, followed by obesity, diabetes and chronic kidney disease. Each of the chronic medical conditions except asthma correlated with increased in-hospital mortality.

There were higher rates of hospital administration of hydroxychloroquine, azithromycin, therapeutic heparin, tocilizumab, and systemic corticosteroids in the group of patients who died. Use of remdesevir, prophylactic heparin, zinc and vitamin C did not differ between the two groups.

During hospitalization 571 (17.7%) received mechanical ventilation, 125 (3.9%) received BIPAP, and 848 (26.3%) received high flow oxygen. Black patients had higher rates of receiving mechanical ventilation than Whites, 19.6% vs. 15.2%, respectively. Rates of these oxygen therapies were higher in the group that died in the hospital compared to those who were discharged alive. Specifically, 61.2% of the patients who died received mechanical ventilation compared to only 9.4% of those who survived.

Mortality was evaluated in three time periods, pre-peak, peak, and post-peak hospital COVID-19 volume. During the peak period there were over 800 COVID-19 patients hospitalized each day. Overall mortality decreased significantly with each successive time period. These results are shown in Table 3.

A difference in the use of some treatment medications was noted in the pre-peak, peak, and post-peak periods. Specifically, hydroxychloroquine use decreased in the post-peak period but was still used in over 60% of patients. Similarly, azithromycin use decreased in the post-peak period to less than 35% compared to over 83% in the pre peak and peak periods. A logistic regression model was used to estimate the odds ratio of death when controlling for age, gender, race, current smoking, and chronic medical conditions. In this model, male patients had an increased odds of dying compared to female patients. The odds of dying were 1.04 for every increase in year of age. There was no difference in mortality based on race. The presence of diabetes mellitus, heart failure, obesity, and chronic kidney disease resulted in increased odds of death, with chronic kidney disease having the highest effect. Hypertension, coronary artery disease, asthma, chronic obstructive pulmonary disease, and current smoking status were not associated with increased odds of dying. These results are shown in Figure 1.

A second logistic regression model was used to estimate the odds ratio of death with each of the ten home medications of interest when controlling for age, gender, smoking, and chronic medical conditions. None of the medications were associated with an increase in odds of mortality. Specifically, the odds ratio for angiotensin-converting enzymes inhibitors (ACEi) was 0.93 (CI: 0.74 to 1.18, P=0.971) and angiotensin receptor blockers (ARBs) was 1.00 (CI:0.79 to 1.28, P=0.566). The full results of this model are found in Table S1 in the Supplement.

A third logistic regression model was used to estimate the odds of death when receiving the medications of interest in the hospital when controlling for age, gender, smoking, and chronic medical conditions. Administration of systemic corticosteroids, therapeutic heparin and vitamin C were associated with increased odds of dying in the hospital. Administration of zinc and novel oral anticoagulants were associated with decreased in odds of dying in the hospital. There was an increase in odds of dying with the administration of tocilizumab, although, only 30 patients received this drug during the study period. Similarly, only 8 patients received Remdesevir. These results are shown in Table 4.

Categorical variables were created in the fourth logistic regression models to look for differing levels of effect for hospital administered hydroxychloroquine, azithromycin, and therapeutically dosed heparin at the three different time periods (pre-peak, peak, and post-peak). All three medications showed significant variation in their associated odds of death across time periods.

When controlling for other factors, use of hydroxychloroquine was associated with an increase in mortality when given in the pre-peak period (OR 2.36, CI 1.39 to 4.00, P=0.018), but nonsignificant changes in mortality in the other two time periods. When controlling for other factors, use of azithromycin was not associated with significant differences in mortality over the three time periods. When controlling for other factors, use of therapeutically dosed heparin was associated with an increase in mortality when given in the pre-peak (OR 3.97, CI 2.90 to 5.44, P<0.001) and peak timeframe (OR

3.38, CI 2.47 to 4.61, P<0.001) but no significant difference in the post-peak timeframe. The full results of this model are found in Table S2 in the Supplement.

Discussion

This study describes the clinical characteristics of the patients who were hospitalized with COVID-19 in the largest health system in Southeast Michigan. Similar to other studies [3-5, 8, 9], we showed that age and male gender are risk factors for increasing mortality with similar odds ratios of death. Mortality reached 28% in patients 80 years of age and older, and the risk of death was elevated (61.2%) in patients who received mechanical ventilation.

In-hospital COVID-19 mortality was 16%, which is lower than mortality rates reported in the New York City area [5, 9]. This difference could be explained in several ways. First, the COVID-19 peak occurred earlier in New York City than Michigan which gave our hospitals and providers more lead time to prepare. Second, the number of patients admitted during the peak in New York City was greater than that seen in Southeast Michigan, causing comparatively less stress on hospitals in our area. Lastly, during the peak in Southeast Michigan, a small number of patients were redirected to other hospital systems after presentation to the emergency centers. This “load balancing” resulted in these patients not being admitted and therefore analyzed, which is a limitation to our study.

Mortality risk was highest in the first 2 weeks of the pandemic and subsequently decreased during the peak and post-peak time frames. This likely reflects improvement in the care provided to COVID-19 patients as hospitals and providers learned from the earlier cases. Hospital guidelines for care of COVID-19 patients were updated frequently and communicated broadly as outside studies and internal findings became available. Changes instituted including prone positioning, delayed mechanical ventilation and broader use of anticoagulation.

Blacks represented over half of the admitted patients with a COVID-19 diagnosis, although, they only represent 17.4% of the population served by our health system. This is consistent with the Center for Disease Control and Prevention (CDC) reports showing overrepresentation of Blacks in hospitalized patients with COVID-19 [10]. Blacks in our study population had a lower mortality rate than Whites, 13.5% vs. 20%, although this difference was not statistically significant when controlling for other factors. This is not consistent with other reports showing higher COVID-19 mortality in non-hospitalized and hospitalized Blacks in the US. [11, 12]. In Michigan, 41.3% of COVID-19 related death are Blacks although they only represent 13.8% of the state population [13]. Another study of hospitalized patients with COVID-19 in the State of Louisiana similarly reported lower in-hospital mortality in Blacks compared to Whites, 21.6% vs. 30.1% [6]. In our study hospitalized Blacks were younger on average than Whites, mean age 61.8 vs. 70.5 years. Further evaluation of the data showed 26.7% of Blacks in the study were 50 years of age or younger compared to 12.5% of Whites while only 11.6% of Blacks were over the age of 80 years compared to 30.4% of Whites. This difference in age distribution is significant, the model did control for age, so this difference in age canno9t entirely explain the lower rate of mortality in Blacks.

Comorbid conditions were common in our patient population. Specifically, rates of hypertension, diabetes, and chronic kidney disease were much higher than previously reported by the CDC and similar studies in the United States[5, 6, 9, 10]. This could be explained by many factors including the possibility that our patient population has more chronic disease compared to other areas in the U.S. Comorbid conditions that were associated with an increased risk of death were chronic kidney disease, heart failure, diabetes, and obesity which is similar to other studies. Interestingly, hypertension was not associated with worsening in-hospital survival as reported by other studies [14, 15].

Concerns exist that ACEi and ARBs could increase the risk of death in COVID19 patients [16]. Although our study was not designed to answer this question, we found that use of these medications was not

associated with an increased odds ratio of death. This was consistent with other retrospective studies [17].

The use of specific medications during the hospital stay was associated with increased odds of death, especially systemic steroids. This may reflect provider overuse of corticosteroids in the sickest COVID-19 patients when other proven therapies were lacking. Hydroxychloroquine use was associated with an overall higher death rate but did not reach statistical significance. When broken down by study periods, however, there was an increase in odds of dying when hydroxychloroquine was administered during the pre-peak period but no significant change in odds of dying in the post-peak period. This likely reflects a more judicious and evidence-based approach to COVID-19 treatment later in the study period as knowledge evolved. A similar pattern was seen with azithromycin.

The finding of increased mortality with therapeutically dosed heparin may be explained by several factors. In the pre-peak and peak period, therapeutic heparin use was primarily limited to patients with confirmed deep vein thromboses and pulmonary emboli. The odds ratio of death with the therapeutic use of heparin was 5.73 and 2.76 in the pre-peak and peak period, respectively. This likely reflects that these patients were sicker and would be expected to have higher mortality risk. As new data on thrombotic risk in COVID-19 patients emerged over time, local guidelines shifted at the end of the peak period to include the use of therapeutic heparin in patients with elevated oxygen requirements and elevated D-dimer levels, even in the absence of venous thromboembolism. The use of therapeutic heparin in the post peak period likely reflects use in a broader range of patients, contributing to the decrease in mortality in that period.

Strength of the study includes that it is the largest report of hospitalized COVID-19 patients in Southeast Michigan; and we included diverse population form the largest health system in the Detroit metropolitan area.

Limitations:

Our study has several limitations. First, this is a retrospective study with data collected from the EHR. Because of this, there is a risk of missing data points if they were not reported in a structured data element that can be queried. Second, although our health system cared for the largest share of COVID-19 patients in the area, the patients may not completely represent the entire population of Southeast Michigan. Third, as stated above, a few patients were transferred to other health systems during the peak period and their outcomes are not included in this analysis.

Conclusion:

We reported the characteristics of the largest cohort of hospitalized COVID19 patients in Southeast Michigan. As the coronavirus pandemic continues to progress across the United States, understanding of the medical comorbidities and sociodemographic factors associated with hospitalization and mortality will aid in identifying populations at elevated risk. In this cohort, comorbid conditions were more common than the national average. Black patients were more likely to get admitted to the hospital, and to receive mechanical ventilation, but less likely to die in the hospital than Whites. The reported significant improvement in survival during the 3 study periods is novel and needs to be evaluated further in similar studies.

Table 1. Overall COVID-19 Patients' Characteristics and by Hospital Discharge Outcome

	Total Discharged Patients n=3,219	**Discharged Alive n=2,703**	**Died in Hospital n=516**	**P value***
Demographic characteristics				
Age, median (IQR), years	65.2 (52.6 to 77.2)	63.4 (50.7 to 74.5)	75.7 (65.3 to 84.2)	<0.001
Length of Stay, median (IQR), days	6.0 (3.2 to 10.1)	5.6 (3.1 to 9.3)	8.6 (4.6 to 13.4)	<0.001
Gender				0.019
Male n (% of group)	1,576 (49.0)	1,299 (48.1)	277 (53.4)	
Female	1,643 (51.0)	1,404 (51.9)	239 (46.3)	
Race				<0.001
White	1,277 (39.7)	1,022 (37.8)	255 (49.4)	
Blacks	1,713 (53.2)	1,482 (54.8)	231 (44.7)	
Asian	67 (2.1)	59 (2.1)	8 (1.6)	
American Indian	5 (0.2)	5 (0.2)	0 (0.0)	
Pacific Islander	2 (0.1)	2 (0.1)	0 (0.0)	
Other	155 (4.8)	133 (4.9)	22 (4.3)	
Ethnicity				0.253
Arab or Middle Eastern	157 (4.9)	142 (5.3)	15 (2.9)	
Hispanic or Latino	82 (2.5)	69 (2.6)	13 (2.5)	
Non-Hispanic	2,776 (86.2)	2,319 (85.8)	457 (88.6)	
Other	170 (5.3)	146 (5.4)	24 (4.7)	
Unavailable	33 (1.0)	26 (1.0)	7 (1.4)	
Medical Condition				
Diabetes	1,329 (41.3)	1,073 (39.7)	256 (49.6)	<0.001
Hypertension	2,386 (74.1)	1,949 (72.1)	437 (84.7)	<0.001
Heart Failure	609 (18.9)	440 (16.3)	169 (32.8)	<0.001
Heart Disease	763 (23.7)	599 (22.2)	204 (39.5)	<0.001
Chronic Kidney Disease	1,299 (40.4)	929 (34.4)	300 (58.1)	<0.001
Asthma	429 (13.3)	362 (13.4)	67 (13.0)	0.803
COPD	568 (17.6)	428 (15.8)	140 (27.1)	<0.001
Obesity (BMI $\geq$30) [a]	1,642 (51.0)	1,405 (52.0)	237 (45.9)	0.036
Smoking [b]	133 (4.1)	115 (4.3)	18 (3.5)	<0.001
Health Insurance Payor				<0.001
Medicare	1,808 (56.2)	1,393 (51.5)	415 (80.4)	
Medicaid	460 (14.3)	429 (15.9)	31 (6.0)	

Commercial	897 (27.9)	836 (30.9)	61 (11.8)	
Military	7 (0.2)	5 (0.2)	2 (0.4)	
Exchange	41 (1.3)	37 (1.4)	4 (0.8)	
Unknown	6 (0.2)	3 (0.1)	3 (0.6)	
Home Medication				
Aspirin	1,354 (42.1)	1,054 (39.0)	300 (58.1)	<0.001
ACE Inhibitor	940 (29.2)	757 (28.0)	183 (35.5)	0.001
Angiotensin Receptor Blocker	676 (21.0)	533 (19.7)	143 (27.7)	<0.001
Metformin	688 (21.4)	565 (20.9)	123 (23.8)	0.136
Insulin	490 (15.2)	377 (14.0)	113 (21.9)	<0.001
Warfarin	230 (7.1)	173 (6.4)	57 (11.1)	<0.001
NOAC	347 (10.8)	271 (10.0)	76 (14.7)	0.002
Inhaled Corticosteroid	472 (14.7)	367 (13.6)	105 (20.4)	<0.001
LABA	318 (9.9)	240 (8.9)	78 (15.1)	<0.001
LAMA	197 (6.1)	150 (5.6)	47 (9.1)	0.002
Hospital Medication				
Hydroxychloroquine	2,496 (77.5)	2,061 (76.3)	435 (84.3)	<0.001
Azithromycin	2,463 (76.5)	2,046 (75.7)	417 (80.8)	0.012
Prophylactic Heparin	2,547 (79.1)	2,136 (79.0)	411 (79.7)	0.748
Therapeutic Heparin	1,257 (39.0)	916 (33.9)	341 (67.0)	<0.001
Tocilizumab	30 (0.9)	18 (0.7)	12 (2.3)	<0.001
Remdesevir	8 (0.2)	7 (0.3)	1 (0.2)	0.785
Systemic corticosteroids	1,631 (50.7)	1,265 (46.8)	366 (70.9)	<0.001
NOAC	340 (10.6)	291 (10.8)	49 (9.5)	0.390
Zinc	1,596 (49.6)	1,340 (49.6)	256 (49.6)	0.987
Vitamin C	794 (24.7)	637 (23.6)	157 (30.4)	0.001
Oxygen Therapy				
High Flow O2	848 (26.3)	534 (19.8)	314 (60.9)	<0.001
BiPAP	125 (3.9)	73 (2.7)	52 (10.1)	<0.001
CPAP	93 (2.9)	59 (2.2)	34 (6.6)	<0.001
Nonrebreather Mask	867 (26.9)	537 (19.9)	330 (64.0)	<0.001
Mechanical Ventilation	571 (17.7)	255 (9.4)	316 (61.2)	<0.001

Abbreviations: COVID-19, Coronavirus disease 2019; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NOAC, Non-vitamin K oral anticoagulation; LABA, Long-acting beta-agonist; LAMA, Long acting muscarinic antagonist; BiPAP, Bilevel positive airway pressure; CPAP, Continuous positive airway pressure. [a] BMI data available for 3135 patients. [b] smoking data available for 2517 patients. * P value for the difference between discharged alive and died in the hospital groups

Table 2. Overall Mortality by Age Category of Discharged Patients who were Admitted with a COVID-19 Diagnosis

Age Category, years	Total Patients	Alive at Discharge, n (%)	Deceased, n (%)
<18	8	7 (87.5)	1 (12.5)
19-40	295	285 (96.6)	10 (3.4)
41-50	370	350 (94.6)	20 (5.4)
51-60	554	510 (92.1)	44 (7.9)
61-70	737	631 (85.6)	106 (14.4)
71-80	621	464 (74.7)	157 (25.3)
>80	634	456 (71.9)	178 (28.1)

Table 3. Overall Mortality by Time of Admission for Patients who were Discharged During Study Period. N=3.219

Time Frame	Total Hospital Admissions	Discharged Alive (%)	Died in the Hospital (%)
Pre-peak (3/13- 3/30/2020)	1,447	1,180 (81.5)	267 (18.5)
Peak (3/31- 4/13/2020)	1,279	1,083 (84.7)	196 (15.3)
Post-peak (4/14-4/29/2020)	493	440 (89.2)	53 (10.8)

Table 4. Odds Ratio of Death from Logistic Regression Model for In-hospital Treatment Medications when Controlling for Age, Gender, and Chronic Medical Conditions

Medication	Odds Ratio of Death	Confidence Interval	P-Value
Hydroxychloroquine	1.33	0.95 to 1.88	0.102
Azithromycin	1.11	0.82 to 1.50	0.489
Vitamin C	1.40	1.08 to 1.81	0.011
Zinc	0.50	0.39 to 0.64	<0.001
Novel oral anticoagulants	0.42	0.29 to 0.60	<0.001
Systemic corticosteroids	2.45	1.91 to 3.12	<0.001
Remdesevir[a]	2.22	0.18 to 27.5	0.535
Tocilizumab[b]	2.23	0.99 to 5.02	0.052
Prophylactic heparin	0.76	0.57 to 1.02	0.071
Therapeutic heparin	3.06	2.44 to 3.83	<0.001

[a] only 8 patients received Remdesevir. [b] only 30 patients received Tocilizumab

Figure 1. Odds Ratio of Death from Logistic Regression Model when Controlling for Gender, Age, Race, Current Smoking, and Comorbidities.

Ethics Statement:

Study was approved by Beaumont IRB, Study ID: 2020-161

Funding Statement: this research received no grant from any funding agency in the public, commercial, or not for profit sectors.

Competing Interest: none declared by all authors.

Contributorship statement:

EM contributed to design of the study, data interpretation, drafting the article, critical revision and final approval of the manuscript

AO contributed to design of the study, data interpretation, drafting the article, critical revision and final approval of the manuscript

DL contributed to design of the study, data analysis and interpretation, drafting the article, critical revision and final approval of the manuscript

The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted

All authors declare no conflict of interest

Data sharing statement: study data are available upon reasonable request

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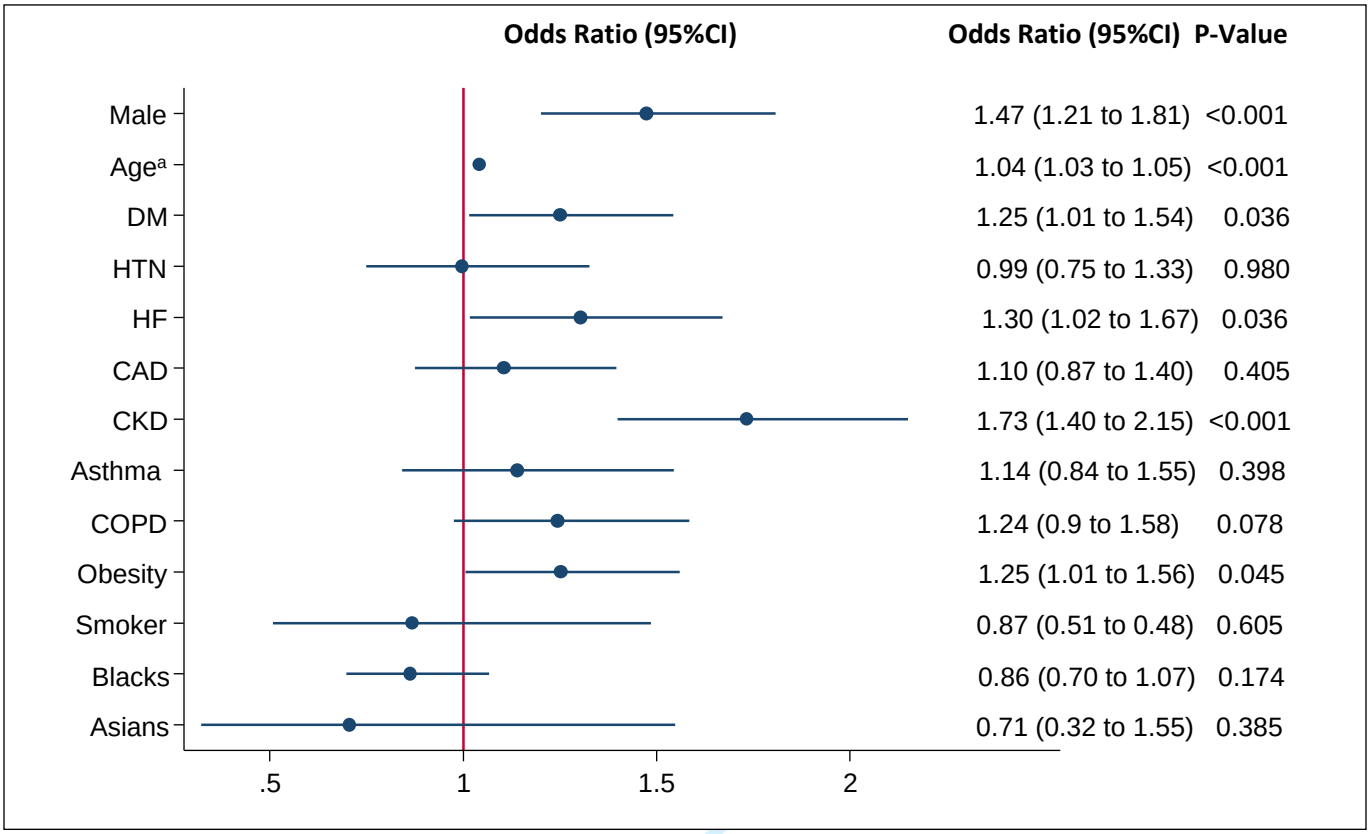
Figure 1. Odds Ratio of Death from Logistic Regression Model when Controlling for Gender, Age, Race, Current Smoking, and Comorbidities.



Abbreviations: DM, Diabetes Mellitus; HTN, hypertension; HF, heart failure; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease. [a] Age: for every increase of one year in age

Retrospective Case Cohort Study of 3219 Hospitalized Patients with COVID19 in Southeast Michigan

Supplement

Four multivariate logistic regression models were created with death as the outcome of interest using age, gender, and chronic medical conditions and bivariate associations within the data. The first model calculated the odds ratio of death when controlling for age, gender, race, current smoking, diabetes mellitus (DM), hypertension (HTN), heart failure (HF), coronary artery disease (CAD), chronic kidney disease (CKD), obesity (BMI >30), asthma, and chronic obstructive pulmonary disease (COPD) . The second model used the same variables as the first model with the addition of ten home medications of interest (angiotensin converting enzyme inhibitors, angiotensin receptor blockers, aspirin, insulin, metformin, warfarin, novel oral anticoagulants, inhaled corticosteroids, inhaled long-acting muscarinic antagonists, and inhaled long-acting beta agonists). The third model used the same variables as the first model with the addition of ten hospital-administered medications of interest (hydroxychloroquine, azithromycin, vitamin C, novel oral anticoagulants, remdesevir, tocilizumab, subcutaneous prophylactic heparin, and therapeutic heparin). The fourth model used the same variables as the first model with the addition of use of hydroxychloroquine, azithromycin, and therapeutically dosed heparin as categorical variables based on time period. All variables were retained in the final models other than the fourth model where highly nonsignificant medical conditions were excluded to increase model stability.

Table S1. Odds Ratio of Death from Logistic Regression Model with Home Medications when Controlling for Age, Gender, and Chronic Medical Conditions

Variable	Odds Ratio of Death	Confidence Interval	P-Value
Male gender	1.47	1.20 to 1.80	<0.001
Age (per year)[a]	1.04	1.03 to 1.05	<0.001
Diabetes	1.18	0.90 to 1.54	0.229
Hypertension	0.99	0.73 to 1.33	0.922
Heart Failure	1.32	1.03 to 1.70	0.031
Coronary Artery Disease	1.08	0.85 to 1.37	0.62
Chronic Kidney Disease	1.66	1.34 to 2.07	<0.001
Asthma	1.13	0.81 to 1.56	0.475
COPD	1.23	0.93 to 1.61	0.137
Ace Inhibitor	0.93	0.74 to 1.18	0.552
Angiotensin Receptor Blocker	1.01	0.80 to 1.29	0.906
Aspirin	1.16	0.92 to 1.48	0.214
Insulin	1.24	0.92 to 1.67	0.161
Metformin	0.98	0.73 to 1.31	0.884
Warfarin	1.05	0.74 to 1.48	0.785
Novel Oral Anticoagulant	0.85	0.62 to1.15	0.281
Inhaled corticosteroid	0.86	0.54 to 1.35	0.500
Heparin Post-peak	1.08	0.56 to 2.09	0.830
LAMA	0.85	0.54 to 1.34	0.487
LABA	1.45	0.87 to 2.41	0.157

Abbreviations: COPD, chronic obstructive pulmonary disease; LAMA, long-acting muscarinic antagonist; LABA, long-acting beta agonist [a] Age: for every increase of one year in age

Table S2. Odds Ratio of Death from Logistic Regression Model with Administration of Azithromycin, Hydroxychloroquine, and Therapeutically Dosed Heparin in Three Time Periods when Controlling for Age, Gender, and Chronic Medical Conditions

Variable	Odds Ratio of Death	Confidence Interval	P-Value
Male gender	1.34	1.08 to 1.65	0.007
Age[a]	1.05	1.04 to 1.06	<0.001
DM	1.14	0.91 to 1.41	0.237
Heart Failure	1.35	1.05 to 1.73	0.017
CKD	1.54	1.24 to 1.93	<0.001
COPD	1.19	0.93 to 1.52	0.176
Azithromycin Pre-peak	0.68	0.40 to 1.16	0.158
Azithromycin Peak	0.89	0.58 to 1.34	0.568
Azithromycin Post-peak	0.90	0.39 to 2.09	0.806
Hydroxychloroquine Pre-peak	1.90	1.11 to 3.24	0.018
Hydroxychloroquine Peak	0.71	0.46 to 1.09	0.118
Hydroxychloroquine Post-peak	0.69	0.34 to 1.32	0.246
Heparin Pre-peak	3.41	2.47 to 4.70	<0.001
Heparin Peak	2.99	2.20 to 4.08	< 0.001
Heparin Post-peak	1.08	0.56 to 2.09	0.830

Abbreviations: DM, Diabetes Mellitus; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease. a Age: for every increase of one year in age

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3: 5 3:2-4:5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6:7-6:16
Objectives	3	State specific objectives, including any prespecified hypotheses	6:10-6:16
Methods			
Study design	4	Present key elements of study design early in the paper	6:20-8:2
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6:18-7:18
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up (*b*) For matched studies, give matching criteria and number of exposed and unexposed	6:20-7:22
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7:1-8:1
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	6:20-6:22
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding (*b*) Describe any methods used to examine subgroups and interactions (*c*) Explain how missing data were addressed (*d*) If applicable, explain how loss to follow-up was addressed (*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9:14-17; 13:23-14:6
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11:5-13:22
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.