Variation in clinical characteristics, outcomes, and mortality of hospitalized patients with COVID-19 during the second wave of the pandemic: a single-center experience

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ABSTRACT

As of February 2, 2021, the USA has 26,431,799 reported COVID-19 cases with 446,744 deaths. A high mortality rate (15%–40%) was reported among hospitalized patients with COVID-19 during the first wave of the pandemic. However, data regarding variation in COVID-19-related mortality and severity of illness among hospitalized patients with COVID-19 are heterogeneous. In this retrospective single-center study, we aimed to investigate the demographic characteristics, clinical presentations, disease severity, clinical outcomes, and in-hospital mortality of hospitalized patients with COVID-19 during the second wave of the pandemic. Adults with reverse transcription-PCR-confirmed SARS-CoV-2 infection were included. In-hospital mortality due to COVID-19 was the primary outcome, and intensive care unit admission, acute kidney injury, acute respiratory distress syndrome, respiratory failure requiring intubation, and septic shock were the secondary outcomes. A total of 101 adult patients were hospitalized with COVID-19 during the second wave study period. Of 101 patients, 8 were intubated and 6 died. The median duration of hospital stay was 6 days. Patients in the second wave were more likely to receive dexamethasone and remdesivir and less likely to require invasive mechanical ventilation. In-hospital mortality during the second wave was lower (5.9%) compared with the first wave (15.5%). At the last follow-up date, 86.1% were discharged alive from the hospital, 5.9% died and 7.9% were still in the hospital. Multivariate logistic regression showed higher odds of mortality were associated with higher age and elevated lactate dehydrogenase peak.

INTRODUCTION

Viral pandemics can occur in waves of illness, where a spike in the number of cases is observed after an initial decline. During the influenza pandemic of 1918, the second wave was the most fatal as it contributed to the majority of US deaths lost to the pandemic.[1] The first case of COVID-19 was reported on January 1, 2020, in the USA. As of February 2, 2021, the USA has 26,431,799 reported cases with 446,744 deaths.[2] A high mortality rate (15%–40%) was reported among hospitalized patients with COVID-19 during the first wave of the pandemic.[3] However, data regarding variation in COVID-19-related mortality and severity of illness among hospitalized patients with COVID-19 are heterogeneous. As supportive evidence accumulated, the utilization of dexamethasone and remdesivirhas opted as a standard of care for patients with severe COVID-19.[4 5] It is reasonable to assume that with the improvement in therapeutic intervention, the mortality rate may have decreased. In this single-center study, we aimed to investigate and compare the demographic characteristics, clinical presentations, disease severity, clinical outcomes, and in-hospital mortality of hospitalized patients with COVID-19 during the second wave of the pandemic and compare it with the first wave.

METHODS

This is a retrospective and single-center study. Adults (18 years of age or older) with reverse transcription-PCR-confirmed SARS-CoV-2 infection who were hospitalized at Monmouth Medical Center from October 20 until December 10, 2020 were included for the second wave. The first wave included the first 129 patients with COVID-19 admitted to Monmouth Medical Center from March 1 to April 25, 2020. Data were extracted manually using the hospital's electronic medical record. Continuous variables were presented as median and IQR, while categorical variables were expressed as percentages. Categorical variables were compared by conducting Chi-square (χ^2) test or Fisher's exact test, while continuous parameters were compared by conducting the median two-sample test, non-parametric Mood's median test. A bivariate analysis was conducted to compare the demographic characteristics, clinical presentations, disease severity, clinical outcomes, and in-hospital mortality of hospitalized patients with COVID-19 during the first and second waves. Multivariate logistic regression analysis was modeled (using age, gender, diabetes mellitus, coronary artery disease, peak D-dimer, peak lactate dehydrogenase (LDH), peak ferritin, nasal cannula, ventilator requirement, remdesivir, and anticoagulation) to choose the best possible predictors of in-hospital

Table 1 Comparison of demographics, clinical presentations, laboratory data, treatments, and outcomes between the first and second wave of COVID-19

Parameters	First wave (n=129)	Second wave (n=101)	P value
Demographics			
Median age, years (IQR)	63.0 (45.0–72.0)	58.0 (47.0–7.0)	0.1820
Male, n (%)	81 (62.8)	60 (59.4)	0.6009
Caucasian, n (%)	79 (61.2)	58 (57.4)	0.1165
Presentation, n (%)			
Fever	102 (79.1)	63 (62.4)	0.0053
Generalized weakness	51 (39.5)	58 (57.4)	0.0070
Shortness of breath	72 (55.8)	54 (53.5)	0.7225
Dry cough	80 (62.0)	36 (35.6)	<0.0001
Diarrhea	26 (20.2)	26 (25.7)	0.3147
Poor appetite	19 (14.7)	24 (23.8)	0.1140
Nausea	15 (11.6)	20 (19.8)	0.0867
Headache	31 (24.0)	14 (13.9)	0.0537
Productive cough	16 (12.4)	13 (12.9)	0.9155
Vomiting	8 (6.2)	12 (11.9)	0.1292
Sore throat	10 (7.8)	11 (10.9)	0.4121
Loss of taste or smell	2 (1.6)	5 (5.0)	0.2450
Altered mental status	6 (4.7)	5 (5.0)	1.0000
Comorbidities, n (%)			
Hypertension	56 (43.4)	49 (48.5)	0.4406
Diabetes mellitus	21 (16.3)	28 (27.7)	0.0354
Coronary artery disease	10 (7.8)	13 (12.9)	0.1990
Obesity	20 (56.1)	11 (10.9)	0.3093
Malignancy	9 (7.0)	10 (9.9)	0.4240
Heart failure	9 (7.0)	8 (7.9)	0.7859
Chronic kidney disease	13 (10.1)	5 (5.0)	0.1508
Chronic obstructive pulmonary disease	9 (7.0)	3 (3.0)	0.1751
Obstructive sleep apnea	5 (3.9)	3 (3.0)	0.7099
Admission			
Median systolic blood pressure, mm Hg (IQR)	130.0 (114.0–142.0)	127.0 (118.0–145.0)	0.4243
Median diastolic blood pressure, mm Hg (IQR)	76.0 (67.0–87.0)	80.0 (68.0–86.0)	0.2915
Respiratory rate >20, n (%)	66 (51.2)	34 (33.7)	0.0079
Oxygen saturation (without supplemental oxygen) <90%, n (%)	45 (35.2)	25 (24.8)	0.0897
Laboratory data at admission (within 24 hours of hospitalization)			
Median WCC, K/CMM (IQR)	6.9 (4.9–9.6)	6.3 (4.7–8.5)	0.1793
WCC <4.5, K/CMM, n (%)	27 (21.3)	24 (24.0)	0.6234
Median absolute lymphocyte count, n (IQR)	0.8 (0.5–1.1)	0.9 (0.6–1.3)	0.1130
Absolute lymphocyte <1, %	85 (66.9)	52 (51.5)	0.0180
Median platelet count, K/CMM (IQR)	196.0 (153.0–265.0)	197.0 (150.0–253.0)	0.8942
Platelet <140, K/CMM, n (%)	20 (15.8)	17 (16.8)	0.8255
Median CRP, mg/L (IQR)	136.1 (53.1–202.4)	44.7 (21.6–98.8)	<0.0001
Median LDH, IU/L (IQR)	408.0 (321.0–547.0)	316.0 (246.0–415.5)	<0.0001
Median ferritin, ng/mL (IQR)	848.0 (397.0–1606.0)	447.6 (225.8–763.0)	0.0001
Median IL-6, pg/mL (IQR)	73.82 (44.04–188.42)	14.0 (8.1–145.2)	0.1747
Median D-dimer, mg/L of FEU (IQR)	1.0 (0.5–1.7)	0.8 (0.5–1.3)	0.0495
Hospital course			
Median of peak CRP, mg/L (IQR)	154.7 (108.0–254.4)	76.8 (43.6–139.7)	<0.0001
Median of peak LDH, IU/L (IQR)	493.0 (369.0–686.0)	354.0 (281.0–538.0)	0.0002
Median of peak ferritin, ng/mL (IQR)	1379.0 (557.0–1908.0)	552.8 (423.9–1072.9)	<0.0001
Median of peak D-dimer, mg/L (FEU) (IQR)	2.3 (0.9–4.4)	1.3 (0.8–3.1)	0.0102
Medications, n (%)			
Dexamethasone	0	75 (74.3)	Data incomplete
Remdesivir	14 (10.9)	59 (58.4)	<0.0001
Antibiotics	83 (64.3)	20 (19.8)	<0.0001
Prednisolone/methylprednisolone	31 (24.03)	15 (14.9)	0.0841
Convalescent plasma	12 (9.3)	3 (3.0)	0.0536
IL-6 inhibitor	33 (25.6)	1 (1.0)	<0.0001
Anticoagulation during hospitalization, n (%)			
DVT PPx only	61 (47.3)	52 (51.5)	0.5273

Continued

Table 1 Continued

Parameters	First wave (n=129)	Second wave (n=101)	P value
Full-dose Lovenox	29 (22.5)	35 (34.7)	0.0409
DOACs	9 (7.0)	7 (6.9)	0.9891
Heparin drip	7 (5.4)	3 (3.0)	0.5190
Modes of respiratory support, n (%)			
Nasal cannula	74 (57.4)	46 (45.5)	0.0749
Hi-Flow	0	18 (17.8)	Data incomplete
Bilevel positive airway pressure (BiPAP)	0	6 (5.9)	Data incomplete
Ventilator	30 (23.3)	8 (7.9)	0.0019
Days on Hi-Flow (IQR)	0	5.0 (4.0–9.0)	Data incomplete
ICU care			
ICU level of care, n (%)	39 (30.2)	14 (13.9)	0.0034
Hospital admission to ICU upgrade, days (IQR)	1.0 (1.0–3.0)	1.0 (1.0–6.0)	0.5665
Length of ICU stay, days (IQR)	11.5 (5.0–23.0)	10.0 (4.0–21.0)	0.8126
Outcomes, n (%)			
AKI	14 (10.9)	25 (24.8)	0.0053
ARDS	42 (32.6)	14 (13.9)	0.0010
Septic shock	20 (15.5)	10 (9.9)	0.2105
New onset of arrhythmias	9 (7.0)	6 (5.9)	0.7521
Thrombotic event	3 (2.3)	2 (2.0)	1.0000
New onset of dialysis	3 (2.3)	1 (1.0)	0.6329
Discharged	95 (73.6)	87 (86.1)	0.0207
Died	20 (15.5)	6 (5.9)	0.0230
Still in the hospital	10 (7.8)	8 (7.9)	0.9623
Length of hospital stay	6.0 (3.0–10.0)	6.0 (4.0–9.0)	0.5464

AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; CRP, C reactive protein; DOACs, direct oral anticoagulants; DVT PPx, deep venous thrombosis prophylaxis; FEU, fibrinogen equivalent unit; ICU, intensive care unit; IL-6, interleukin 6; LDH, lactate dehydrogenase; WCC, white cell count.

mortality in hospitalized patients with COVID-19. Adjusted OR with 95% CI was calculated. In-hospital mortality due to COVID-19 was the primary outcome, and intensive care unit (ICU) admission, acute kidney injury (AKI), acute respiratory distress syndrome (ARDS), respiratory failure requiring intubation, and septic shock were the secondary outcomes. A p value of <0.05 was considered significant. Statistical analysis was done with SAS software (version 9.4, SAS Institute Inc., Cary, NC, USA).

RESULTS

First wave

During the first wave, 129 hospitalized patients with COVID-19 were included in the study. Of these, 98 got discharged home and 20 died in the hospital. At our last follow-up (April 25, 2020), 10 patients were still in the hospital and 1 patient was transferred to another hospital. In terms of baseline characteristics, the median age was 63.0 years (IQR 45.0–72.0), 62.8% were male, and 61.2% were Caucasian. Hypertension (43.4%) was the most common comorbidity, followed by diabetes mellitus (19.4%) and obesity (14.0%). In this patient population, fever was the most common presenting symptom (79.1%), followed by cough (62.8%) and shortness of breath in 55.8% of patients. Out of 129 patients, 23.25% (n=30) required invasive mechanical ventilation, 15 (11.6%) received remdesivir, 33 (25.6%) received full-dose anticoagulation, and 27 (20.9%) received steroids. ARDS was the most common complication (32.6%), followed by AKI (22.5%), septic shock (14.7%), suprainfection (10.1%), acute cardiac injury (7%), and new-onset cardiac arrhythmia (6.2%). A total of six patients had thromboembolic complications; one patient had bilateral pulmonary embolism, two patients had deep venous thrombosis (DVT), one patient had a cerebrovascular vascular accident, one patient developed acute popliteal artery occlusion, and one patient had an upper extremity DVT. Out of 129 patients, 39 (30.2%) were admitted to the ICU. The median duration from hospital admission to ICU upgrade in patients requiring mechanical ventilation was 1.0 day (IQR 1.0–2.0) for those initially admitted to the general medical floor or non-ICU level of care.[3]

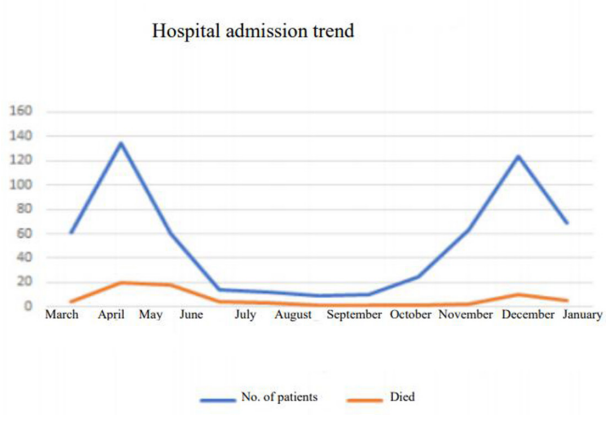

Figure 1 Admission and mortality trends.

Second wave

A total of 101 adult patients were hospitalized with COVID-19 from October 20, 2020 to December 10, 2020. The median age was 58 (47.0–70.0) years, 59.4% were male, and 57.4% were Caucasians. The most common symptoms were fever

(62.3%), generalized weakness (57.4%), and shortness of breath (53.5%). The most common comorbidities were hypertension (48.5%), diabetes mellitus (27.7%), and coronary artery disease (12.9%). The most common complication was AKI (24.8%), followed by ARDS (13.9%) and septic shock (9.9%). Of 101 patients, 8 were intubated and 6 died. In-hospital mortality in hospitalized patients with COVID-19 during the second wave was 5.9%. The median duration of hospital stay was 6 days. Other clinical characteristics, vital signs, and laboratory findings are mentioned in table 1. Inflammation markers (C reactive protein, LDH, ferritin, D-dimer) at admission and their peak values during the hospital course are tabulated and compared with the first wave ($p<0.05$). Patients in the second wave were more likely to receive dexamethasone and remdesivir and less likely to require invasive mechanical ventilation. At the last follow-up date, 86.1% were discharged alive from the hospital, 5.9% died and 7.9% were still in the hospital. Multivariable logistic regression showed higher odds of in-hospital mortality were associated with increased age (OR=1.191, 95%CI 1.051 to 1.350, p=0.0063) and peak LDH level (OR=1.005, 95% CI 1.001 to 1.009, p=0.0063). The hospital admission and mortality trends are shown in figure 1.

DISCUSSION

This study reviews and compares the demographic characteristics, clinical presentation, and disease severity of the second wave of COVID-19 with the first wave in the USA. During the second wave, the baseline characteristics of hospitalized patients with COVID-19 remained the same; however, laboratory findings have shown significant differences in bivariate analysis. As suggested by Puja Mehta *et al*, cytokine storm or hyperinflammatory state, quantified by inflammatory markers, indicates disease severity.[6 7] Patients during the second wave were more likely to have lower inflammatory markers than the first wave ($p<0.05$), which may indicate a difference in disease severity of COVID-19 between the two waves. Lower values of inflammatory markers may co-relate with milder disease severity due to early presentation. These findings are consistent with comparative studies from Europe.[8] It is also reasonable to presume that evolving therapeutic interventions and prevention of known complications of COVID-19 (AKI, ARDS, and septic shock) may lead to an improvement in primary and secondary outcomes (table 1). Older age, comorbid conditions, and severe hypoxemia at presentation are known risk factors for severe COVID-19.[3] Conversely, the bivariate analysis showed that there is no statistically significant difference in age, major comorbid conditions (except diabetes mellitus), and hypoxemia in both waves. Patients who received early invasive mechanical ventilation had poor outcomes and a high mortality rate during the first wave; this led to a strategy to use intubation as a last resort and more inclination toward non-invasive (high-flow nasal cannula and Bilevel positive airway pressure) oxygen therapy.[9] Our data may indicate that patients in the second wave were more likely to receive non-invasive mechanical ventilation than the first wave, which may have contributed to a lower mortality rate. However, in a multivariable logistic regression model, treatment modalities (remdesivir, invasive mechanical ventilation, high-dose anticoagulation) did not show independent association with outcomes. Limitations of our study include its small sample size, retrospective study design, and single-center data. Even though the mortality rate is lower, it is important to adhere to public health measures to limit community spread to end this pandemic.

CONCLUSIONS

To our knowledge, this is the first study in the USA that compares hospitalized patients with COVID-19 between the first and second waves of the pandemic. Inpatient mortality in hospitalized patients with COVID-19 was higher during the first wave at 15.5% vs 5.9% during the second wave. Odds of in-hospital mortality were higher with increased age and elevated LDH peak level per unit (IU/L).

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