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Clinical Characteristics and Inpatient Treatment Outcome of Critically Ill Covid-19 Patients in St Paul's Hospital Millennium Medical College

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Abstract **Background**: The world is facing unprecedented health crisis that is caused by pandemic novel coronavirus, known as severe acute respiratory syndrome coronavirus disease 2. The numbers of patients with coronavirus disease 2019 admitted to intensive care unit is escalating in Ethiopia. The main objective of the study was to identify the clinical characteristics and inpatient treatment outcome of critically ill patients of coronavirus disease 2019 at St. Paul's Hospital Millennium Medical College. **Method**: A five-month retrospective cross-sectional study was be employed at covid intensive care unit of St. Paul's hospital millennium medical college. Review of records of all patients admitted from January 1, 2021, to May 30, 2021, was carried out. Information on socio-demographic characters, characteristic of patients, comorbidities, and laboratory investigations on admission and throughout their stay, and outcomes was be documented. Data was compiled and analyzed using SPSS Statistics Version 26. **Results**: One hundred and eighty-five COVID-19 positive patients were admitted to St. Paul's Medical Millennium Medical College during the study period. Of these, 132 (71.35%) were managed with invasive mechanical ventilation. 77.3% had died and 22.7% were discharged after improvement. Male gender had a significantly higher rate of death when compared with female p=0.044 (OR=0.173, 95% CI=0.33-0.93). Deceased patients were older (63.91 ± 13.33 Vs 49.55 ± 12.91 years, p <0.001) and had coexisting medical illness (114 (79.7%) Vs 12 (28.6%), p <0.001), a lower level of lymphocytes (5.10 ± 4.75 Vs 7.29 ± 5.27, p=0.023) and peak Alanine aminotransferase, neutrophils and potassium levels compared to survivors. 86.4% of patients who received mechanical ventilation had died. Compared to the survivors, deceased patients received mechanical ventilation significantly p<0.001. Conversely, 67.4% of patients aged 70 or younger survived to hospital discharge. Older age, male gender, tachycardia at admission, history of co-existing illness, need for mechanical ventilation, increased serum potassium and ALT, decreased lymphocyte levels were associated with high risk of mortality.

Keywords: *COVID-19, SARS-CoV-2 infection, coronavirus, intensive care unit, treatment outcome*

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1. Introduction

In December 2019, human infection with novel coronavirus, known as syndrome coronavirus disease (SARS-CoV-2) was identified in Wuhan, China as the cause of severe respiratory failure in a larger number of hospitalized patients now named coronavirus disease 2019 (COVID-19). It is the third coronavirus infection in two

decades that was originally described in Asia, after severe acute respiratory syndrome (SARS) in 2003 and Middle East respiratory syndrome (MERS) in 2012 [1].

The SARS-CoV-2 belongs to a group of viruses that cause COVID-19 which affects the respiratory, gastrointestinal, liver, and central nervous system of humans, livestock, Bats, mice and other wild animal [2,3]. It primarily spreads through droplets of saliva or discharge from the nose when an infected person coughs or sneezes and by contact rout of infected person or contaminated surfaces [4]. It can be transmitted from symptomatic person, during its incubation period and from asymptomatic people [5]. The incubation period of COVID-19, in which, is the time between exposure to the virus and symptom onset, is approximately 7–12 days with median time of 5.2 days [1]. However, it can be up to 14 days in some cases [4,5].

The best way to prevent and slow down transmission deemed to be well informed about the virus and its way of transmission and protecting oneself and others by washing hands or using an alcohol-based rub frequently and not touching one's face and wearing personal protective devices like face masks and getting vaccinated. Several COVID-19 vaccines have demonstrated efficacy as high as 95% in preventing symptomatic COVID-19 infections [6] and as of May 2021, a total of 1,489,727,128 vaccine doses have been administered globally [7].

Despite measures to contain the virus, COVID-19 spread widely across all continents and a pandemic was declared on March 11, 2020, by the world health organization (WHO) [8,9]. By June 2021, a total of 173,005,553 cases of COVID-19 is confirmed with 3,727,605 deaths (2.15% of total cases), according to world health organization [7].

The infection mainly affects the respiratory system of the human host and causes, in susceptible individuals, an unrestrained response of the immune system, respiratory failure, cardiovascular system damage, neuropsychiatric manifestations, and multiple organ injuries [2,3] Most infected individuals with the COVID-19 virus experience mild to moderate influenza like symptoms of fever, rhinorrhea, sneezing, nonproductive cough, anosmia, myalgia, shortness of breath and gastrointestinal symptoms like diarrhea. Patients will have a normal or decrease leukocyte counts and recover without requiring special treatment or hospitalization in many of the cases. But there might be also severe cases of infection causing pneumonia, severe acute respiratory syndrome (ARDS), acute kidney injury (AKI) and acute cardiac injury that may leads to death.

Severe disease may present with severe acute respiratory infection i.e., severe pneumonia and ARDS which is reported in 60%– 70% of patients; sepsis and septic shock reported in 30%; myocarditis, arrhythmia, and cardiogenic shock in 20%– 30%; and AKI in 10%–30% of patients [1,10]. Although respiratory failure is often hypoxemic, hypercapnic respiratory failure might also be seen mainly due to mucus plugs. The most at risk groups of developing severe disease include older patients with age above 60 years and patients with comorbidities such as diabetes, coronary heart disease, chronic kidney disease (CKD), autoimmune conditions, cancer and hypertension [4,5].

Though the need for intensive care might differ according to institutions or even countries, depending on the demand and supply ranging from 5% to 32% [10,11,12], respiratory rate ≥30, shortness of breath and increased work of breathing, SpO2 < 90% on oxygen supplement more than 5 liters per min, lactate > 2 mmol/L, hypotension and organ dysfunction such as confusion, kidney and liver tests abnormalities, thrombocytopenia, elevated troponin level and arrhythmia are the commonest indications for ICU admissions.

The first COVID-19 case in Ethiopia was reported on March 13, 2020, in a 48-year-old Japanese man reported to have traveled from Japan to Burkina Faso and who then arrived in Ethiopia on March 4 [13,14] and soon thereafter patients with COVID-19 were admitted to Ethiopia hospitals and intensive care units. Since then, the Ethiopian government swiftly responded to minimize the impact of COVID-19 by using different strategies like school closures, social distancing, and limiting public gathering. However, the situation is becoming unstoppable [4]. Several cases have been reported daily. The cases have been escalated reaching to 272,914 confirmed cases of COVID-19 with 4,209 deaths (1.5% of total cases) as of June 7, 2021 [7].

In Ethiopia, though the government took several measures ranging from public health emergency response to the state of emergency and implement several policies to prevent the spread, there is marked failure to adhere to physical distancing and other preventions advice among the public. Such negligence among the public and related factors undermined the preparedness and responses towards COVID-19 in Ethiopia [15]. Therefore, the spreading of COVID-19 is increasing making new cases and deaths non-stoppable which might create overwhelming of the already overstretched health care service [5].

Initially, On January 7, 2020, the virus was identified as a new strain and named COVID-19 by WHO in February 2020. On March 11, 2020, WHO officially announced that COVID-19 can be characterized as a pandemic owing to rapid increase in the number of cases and growing number of countries affected. Ever since, the pandemic has been threatening the lives and livelihoods of people in nearly every country of the world and has become an unprecedented global challenge with continued increment of confirmed cases [4,5].

Baseline Characteristics and Presenting Symptoms

The earliest study done in Wuhan China which is conducted between late December 2019, and Jan 26, 2020; a retrospective, observational study, that enrolled 52 critically ill adult patients with SARS-CoV-2 pneumonia, who admitted to ICU of Wuhan Jin Yin-tan hospital found the mean age of patients was 59·7 (SD 13·3) years, of which 35 (67%) were men, 21 (40%) had chronic illness, 51 (98%) had fever [18]. In other study done in China, A multicenter, retrospective, observational study, a total of 45 COVID-19 patients who require ICU admissions from January 14, 2020, to April 20, 2020, to seven ICUs found in Guangdong Province were included. The mean age of the patients were 56.7 ± 15.4 years of them 29 were males (64.4%)]. The most common symptoms at onset were fever and cough [9].

Italy was one of the worst affected European countries especially in the first wave of the pandemic. More than 50% off the cases in Italy occurred in the northern region of Lombardy, causing saturation of health services [2,24]. In one retrospective case series of 1591 consecutive patients with laboratory-confirmed COVID-19 referred for ICU admission to the coordinator center of the COVID-19 Lombardy ICU Network and treated at one of the ICUs of the 72 hospitals in this network between February 20 and March 18, Of the 1591 patients included in the study, the median (IQR) age was 63 (56-70) years and 1304 (82%) were male and 709 (68%) had at least 1 comorbidity of those 48% were hypertensive [12].

In a retrospective analysis of 32 adult critically ill patients admitted to a community hospital in upstate New York; the mean (±SD) age was 62.2 ± 11.2 years, and 62.5% were men. 27 (84.4%) of patients had one or more medical co-morbidities. The mean (±SD) duration of symptoms was 6.6 (±4.4) days before presentation, with cough (81.3%), dyspnea (68.7%), and fever (65.6%) being the most common [25].

In a study done in Mexico that included 164 patients, the mean age was 57.3 years (SD 13.7), and 114 patients (69.5%) were men, with mean BMI of 30.7 kg/m2. A total of 38.4% of patients had hypertension, and 32.3% had diabetes. Patients presented to the hospital a median of 7 days (IQR 4.5-9) after symptom onset. The most common presenting symptoms were shortness of breath, fever, dry cough, and myalgias [26].

Outcomes and Associated Factors

In study done Wuhan, China that include 45 critically ill patients; Most patients presented with lymphopenia and elevated lactate dehydrogenase. Thirty-six patients (80%) developed acute respiratory distress syndrome at ICU admission, and 15 (33.3%) septic shock even though all patients were on antiviral drugs. Of them twenty patients (44.4%) were intubated, and 10 (22.2%) received extracorporeal membrane oxygenation (ECMO). The 60-day mortality was 4.4% (2 of 45)[9]. In other study done in similar City that included 52 critically ill covid-19 patients, there was a considerable 28-day mortality rate, where 32 (61·5%) patients had died. The median duration from admission to the ICU to death was 7 (IQR 3–11) days for non-survivors. Compared with survivors, non-survivors were older (64·6 years [11·2] vs 51·9 years [12·9]), more likely to develop ARDS (26 [81%] patients vs 9 [45%] patients), and more likely to receive mechanical ventilation (30 [94%] patients vs 7 [35%] patients), either invasively or non-invasively. Most patients had organ function damage, including 35 (67%) with ARDS, 15 (29%) with acute kidney injury, 12 (23%) with cardiac injury, 15 (29%) with liver dysfunction, and one (2%) with pneumothorax. 37 (71%) patients required mechanical ventilation. Hospital-acquired infection occurred in seven (13·5%) patients. Older patients (>65 years) with comorbidities and ARDS are at increased risk of death [18].

In a retrospective case series of 1591 patients with laboratory-confirmed COVID-19 referred for ICU admission to the coordinator center of the COVID-19 Lombardy ICU Network; 1300 patients with available respiratory support data, 1287 (99% [95% CI, 98%-99%]) needed respiratory support, including 1150 (88% [95% CI, 87%-90%]) who received mechanical ventilation and 137 (11% [95% CI, 9%-12%]) who received noninvasive ventilation [11]. In another study done in Italy, of 1023 COVID-19 positive patients admitted to the Inova Health System during March 5, 2020, and April 26, 2020. 164 (16.0%) were managed with invasive mechanical ventilation 70 patients (42.7%) had died and 94(57.3%) were still alive. Deceased patients were older (median age of 66 vs. 55, p <0.0001) just like the previous 2 Chinese studies and had a higher initial d-dimer (2.22 vs. 1.31, p = 0.005) and peak ferritin levels (2998 vs. 2077, p = 0.016) compared to survivors. 84.3% of patients over 70 years old died in the hospital. Conversely, 67.4% of patients aged 70 or younger survived and discharged. Younger age, non-Caucasian race and treatment at a tertiary care center were all associated with survivor status [27].

In retrospective study done in Mexico, all of the patients admitted to ICU (a total of 164) received mechanical ventilation for a median of 11 days (IQR 6-14). Of them 89.4% patients received vasopressors, and 14.6% received renal replacement therapy during hospitalization. Of the 164 patients, 4.2% patients received high-flow nasal cannula oxygen therapy or noninvasive ventilation, and subsequently required mechanical ventilation. Infections were microbiologically confirmed in 15.9% patients. Antibiotics were administered empirically to 98.7% patients and 52.4% of patients received antiviral agents. The median length of ICU stay among survivors was 13 days (IQR 10 to 16), and the median length of hospital stay among survivors was 15 days (IQR 12 to 19). 51.8% patients died at or before 30 days, with a median survival of 25 days. Non-survivors were older and more likely to have comorbid conditions such as diabetes and hypertension. The study found age (OR, 1.05; 95% CI, 1.02-1.08, p<0.001) and C-reactive protein levels upon ICU admission (OR, 1.008; 95% CI, 1.003-1.012, p<0.001) were associated with an increased risk for in-hospital death and ICU length of stay was associated with reduced in-hospital mortality risk (OR, 0.89; 95% CI, 0.84-0.94, p<0.001) [26].

In a retrospective analysis of 32 critically ill patients admitted to community hospital in upstate New York, 71.9% patients received invasive mechanical ventilation and the remaining 9 were managed with noninvasive ventilatory support of which 4 received supplemental oxygen through high flow nasal cannula. Of them 15.6% died, 34.4% were discharged home, and 50% remained hospitalized, 8 (25%) of which were still in ICU. A greater percentage of patients aged 60 years or above died compared to patients under 60 years (21% vs. 7.7%). The lengths of ICU stay and hospital stay were significantly higher in those who received IMV than those managed by NIV (12.8 vs. 3.4 days and 16.9 vs. 9.2 days) respectively [28].

In study done in Kenya, data from 787 COVID -19 patients, 79 (11%) of patients required ICU admission and 90(7%) needed invasive ventilation, 107 died. The study concluded risk of death increased with age with patients over 60 years of having more than 1.5X risk of death when compared to those below 60 plus men, those who have at least one co morbidity and the presence of clinical symptoms had higher risk of mortality [29].

In a multicenter prospective observational study conducted in Libya, from 456 critically ill patients, at admission to ICU, qSOFA median (IQR) score was 1 [1,2], whereas total SOFA score was 6 [4,5,6,7]. At 60 days of follow-up, 184 (39.6%) were discharged alive, while 281 (60.4%) died in the ICU. The median (IQR) ICU length of stay was 7 days [4,5,6,7,8,9,10] and non-survivors had significantly shorter stay, 6 [3,4,5,6,7,8,9,10] days. The study showed, increased age, BMI, white cell count, neutrophils, procalcitonin, cardiac troponin, C-reactive protein, ferritin, fibrinogen, prothrombin, and d-dimer levels were associated with higher risk of mortality. Decreased lymphocytes and platelet count were associated with higher risk of mortality. Quick SOFA and total SOFA scores increase, emergency intubation, inotrope use, stress myocardiopathy, AKI, arrhythmia, and seizure were associated with higher mortality. The study reported the highest mortality rate (60.4%) among critically ill patients with COVID-19 60 day's post-ICU admission [30].

DM2 and obesity have been linked to higher morbidity and mortality in the setting of COVID-19 infection. In the study conducted in inner-city community hospital in Brooklyn, New York that included 521 patients with laboratory-confirmed Covid-19 infection it was found that; after adjustment for age, gender, race, BMI and creatinine obese patients, compared with normal-weight patients had significantly higher mortality rate (BMI > 30 kg/m2 [OR: 2.29, CI: 95%, P-value: <0.002] however this association was not observed for DM2 ([OR: 1.25, CI: 95%, P-value: <0.002]) [31].

A systematic review of 32 articles, that include a total of 69,093 patients, found most patients admitted to the ICU were male and the mean patient age was 56 (95% CI 48.5-59.8) years old. From the 32 articles, 15 of them had high ICU mortality (21,145/65,383; 32.3%). The median length of ICU stay was 9.0 (95% CI 6.5-11.2) days. More than half of patients required mechanical ventilation (31,213/53,465; 58%; 23 studies) and among them mortality was very high (27,972/47,632, 59%, 6 studies). The duration of mechanical ventilation was 8.4 (95% CI 1.6 – 13.7) days[32]. In another systematic review that is done in Ethiopia, the prevalence of mortality among hospitalized patients with COVID-19 in ICU was 15% (95% CI: 13 to 18, 12 studies, 1025 participants). The review found that mortality of patients among male increased the risk by thirty-seven percent when compared to the female counterparts, RR=1.63(95% CI: 1.33 to 1.99 and patients with any kind of co-morbidities had two times more likely to die than those who didn't have co-morbidities, RR= 2.20(95% CI:1.75 to 2.77). Patients with ARDS were eight times more likely to die as compared to those who didn't have, RR=7.99(95% CI: 4.9 to 13) and patients who had history of smoking were two times more likely to die as compared to those who dint have history of smoking, RR=2.19(95% CI: 1.48 to 3.22) [3].

SARS-CoV-2 Organ Involvement

Kidney involvement and renal replacement therapy is common in critically ill patients presenting with COVID-19. It is associated with increased severity of illness on admission to ICU, increased mortality and prolonged ICU and hospital length of stay. Recovery of renal function was complete in all survived patients [33]. A multi-centered, retrospective, observational study of 193 adult patients that were conducted in 2 hospitals in Wuhan, found that 59% had proteinuria, 44% had hematuria and 10% had elevated serum creatinine concentrations on admission. The prevalence of elevated blood urea nitrogen was 14%. The study concludes AKI is common in COVID-19 patients and patients that developed AKI had a ~5.3-times mortality risk compared with those without AKI, much higher than that of those with comorbid chronic illnesses (~1.5 times risk of those without comorbid chronic illnesses) [4,34]. There is some evidence that SARS-CoV-2 infects the kidney directly, including AKI and contributing to viral spread in the body [4,35].

SARS-CoV-2 poses significant challenges for patients with pre-existing cardiovascular conditions. Such patients have an increased risk of severe diseases and death. The infection also appears to cause cardiovascular- related complications, including acute myocardial injury and myocarditis due to direct viral myocardial damage, hypoxia, venous thromboembolism and arrhythmias [4,36,37]. Furthermore, over and above systemic and respiratory symptoms, SARS-CoV-2 appears to cause severe damage to the nervous system [38].

2. Method and Material

Institution based descriptive; hospital based cross sectional study was conducted among all patients who were admitted to COVID-ICU of SPHMMC from January 1, 2021, to May 30, 2021. SPHMMC is in Gulele Sub-City, Addis Ababa, Ethiopia. It is one of the largest referral hospitals in the country which provides health services in many specialty departments. The College sees an average of 1200 emergency and outpatient clients daily. After the occurrence COVID-19 infection in our country, previously functioning ICU beds were converted into COVID-19-dedicated ICU beds. In the following days, operating rooms and several hospital wards were repurposed to accommodate COVID-19 patients. Currently the hospital dedicated 280 beds, 14 of them for ICU, 12 for semi-ICU, 50 for HDU and the rest for wards. It also has an isolation center with 18 beds which started functioning in the mid of March 2020. The ICU is equipped with 14 mechanical ventilators and 1 dialysis machine.

3. Sample Size Determination

Sample Size

$n = \frac{z^2 P(1-P)}{w^2}$ was used to estimate the sample size

Where **n** is the desired sample size, **z** is the confidence level at a certain value of significance which is 1.96 at 95% confidence interval, **P** is the proportion of the interest variable (86% of ICU mortality rate), and **w** is margin of error which is 5% $n = \frac{1.96^2 0.86(1-0.86)}{0.05^2}$, giving a sample size of 185.

4. Operational Definition

- **Clinical Characteristics**: The manifestation of the disease, which include fever, myalgia, cough, shortness of breath, sore throat, runny nose, headache etc.
- **Outcome**: Patient status after critical care in the ICU which include survived, or died
- **Died on arrival**: If the patient died or is dead during admission
- **Comorbidities**: A known diagnosed underlying illness the patient have like diabetes and hypertension
- **Hypotension**: Systolic blood pressure (SBP) < 90 mmHg, > 40 mmHg drops from usual SBP, mean arterial pressure < 65 mmHg
- **Leukopenia**: White blood cell < 4.0×10^9/L
- **Leukocytosis**: White blood cell > 10×10^9/L
- **Lymphopenia**: Lymphocytes <1.0×10^9/L or below 20%
- **Thrombocytopenia**: Platelet count below 150×10^9/L
- **Adult**: A person with age greater than >18

5. Statistical Analysis

The data was analyzed using SPSS version 26. Continuous variables are presented as either mean ± standard deviation (SD) or median with interquartile range (IQR), in accordance with either normal or non-normal distributions. For categorical variables, the frequency and percentage of patients in each category were calculated. Differences between survivors and deceased patients were assessed with two-sample t-test or Wilcoxon rank-sum test, depending on parametric or non-parametric data for continuous variables and $\chi 2$ test for categorical variables. A multivariate logistic regression was done for variables with a p value ≤ 0.2. A p value < 0.05 was considered statistically significant

6. Result

Sociodemographic and Baseline Characteristics of Patients

In this study 185 critically ill patients were included. Out of these more than half, 119 (64.3%) of the patients were males. The mean age of the patients was 60.59 ± 14.53 years. Majority 95 (51.4%) of participants were in the age group of 50 and 69 years old. A total of 126 patients (68.1%) had at least one preexisting condition, hypertension being the leading one in 85 (45.9%) of the patients, followed by DM in 74 (40%) of patients and 37(20%) of patients having cardiac disease. 16 (8.6%) of patients were smokers, with a mean cigarette smoking year of 9.44 ± 3.78.

Clinical Characteristics and Laboratory Findings

Clinical Characteristics of Patients

The most common symptoms were cough (74.1%), shortness of breath (71.4%) and fever (48.1%). The median time from onset of symptoms to ICU admission was 6 days (IQR, 3-7 days). The median quick sequential organ failure (qSOFA) assessment scores of all patients at ICU admission were 1, with the minimum and maximum score of 0 and 3. The mean systolic and diastolic blood pressure at admission to ICU was 126.85 ± 23.10 and 72.06 ± 15.64 mmHg respectively. The median respiratory rate during admission was 28 breaths per minute (IQR, 23-35). During presentation to ICU 41 (22.2%) were intubated, 25 (13.5%) were on NIPPV, the majority 118 (63.8%) were on face mask oxygen support, while 1 patient didn't require any kind of oxygen support.

Table 1. Sociodemographic Characteristics of patients admitted to SPHMMC COVID-ICU

Variables	Improved (n=42)	Died (n=143)	All Patients (n=185)
Age, Years	49.55 ± 12.91	63.91 ± 13.33	60.59 ± 14.53
Sex			
Female	23 (54.8%)	43 (30.1%)	66 (35.7%)
Male	19 (45.2%)	100 (69.9%)	119 (64.3%)
Chronic Medical Illness	12 (28.6%)	114 (79.7%)	126 (68.1%)
Asthma	1 (2.4%)	8 (5.6%)	9 (4.9%)
Cardiac Disease	3 (7.1%)	34 (23.8%)	37 (20%)
Cerebrovascular Disease	0	7 (4.9%)	7 (3.8%)
COPD	1 (2.4%)	3 (2.1%)	4 (2.2%)
Chronic Renal Disease	2 (4.8%)	27 (18.9%)	29 (15.7%)
Diabetes	5 (11.9%)	69 (48.3%)	74 (40%)
Hypertension	5 (11.9%)	80 (55.9%)	85 (45.9%)
HIV	0	4 (2.8%)	4 (2.2%)
Peripheral Arterial Disease	0	2 (1.4%)	2 (1.1%)
Epilepsy	0	2 (1.4%)	2 (1.1%)
Psychiatric Disease	1 (2.4%)	3 (2.1%)	4 (2.2)
Malignancy	0	2 (1.4%)	2 (1.1%)
Gout Arthritis	1 (2.4%)	0	1 (0.5%)
Smoking (+ ex-smoker)	1 (2.4%)	15 (10.5%)	16 (8.6%)

All reports are either in mean ± SD, or N (%)

Table 2. Clinical presentation, Vital Signs and Mode of Ventilation of Patients Admitted to SPHMMC COVID-ICU

Variables	Improved (n=42)	Died(n=143)	All patients(n=185)
Duration of symptoms, days	5.9 ± 3.27	6.28 ± 3.85	6.19 ± 3.72
Symptoms			
Fever	21(50%)	68 (47.6%)	89 (48.1%)
Cough	27 (64.3%)	110 (76.9%)	137 (74.1%)
Shortness of breath	29 (69%)	103 (72%)	132 (71.4 %)
Sore throat	0	6 (4.2%)	6 (3.2%)
Myalgia	13 (31%)	35 (24.5%)	48 (25.9%)
Arthralgia	0	16 (11.2%)	16 (8.6%)
Anosmia	1 (2.4%)	4 (2.8%)	5 (2.7%)
Abdominal pain	4 (9.5%)	3 (2.1%)	7 (3.8%)
Chest pain	3 (7.1%)	9 (6.3%)	12 (6.5%)
Easily fatiguability	15 (35.7%)	73 (51%)	88 (47.6%)
Loss of appetite	10 (23.8%)	53 (37.1%)	63 (34.1%)
Headache	5 (11.9%)	18 (12.6%)	23 (12.4%)
Nausea and Vomiting	3 (7.1%)	12 (8.4%)	15 (8.1%)
Vital signs at admission			
Systolic blood pressure, mmHg	125.90 ± 22.30	127.13 ± 23.40	126.85 ± 23.10
Diastolic blood pressure, mmHg	72.69 ± 17.56	71.87 ± 15.09	72.06 ± 15.64
Respiratory rate, breath per min	31.74 ± 12.34	30.36 ± 14.29	30.68 ± 13.85
Pulse rate, beat per min	92.69 ± 21.58	99.29 ± 22.47	97.79 ± 22.38
Mode of Ventilation at admission			
Mechanical ventilation	7 (16.7%)	34 (23.8%)	41 (22.2%)
NIPPV	9 (21.4%)	16 (11.2%)	25 (13.5%)
Face Mask	26 (61.9%)	92 (64.3%)	118 (63.8%)
No Oxygen requirement	0	1 (0.7%)	1 (0.5%)

All reports are either in mean ± SD, or N (%), vital signs are recorded during admission

Table 3. Laboratory Values of Critically Ill Patients admitted to SPHMMC COVID-ICU

Variables	Improved (n=42)	Died (n=143)	All patients (n=185)	P value
White blood cell count ($\times 10^9$/L)	12. 20 ± 6.58	13.89 ± 9.57	13.50 ± 8.99	0.195
Neutrophil (%)	86.47 ± 6.98	89.78 ± 7.25	89.03 ± 7.30	0.010
Lymphocyte (%)	7.29 ± 5.27	5.10 ± 4.75	5.60 ± 4.94	0.019
Hemoglobin (g/dl)	13.83 ± 4.20	12.54 ± 3.96	12.84 ± 4.05	0.071
Platelet count ($\times 10^9$/L)	231.43 ± 126.53	226.87 ± 103.85	227.90 ± 109.06	0.812
Prothrombin time (s)	16.62 ± 3.16	15.87 ± 3.75	16.03 ± 3.63	0.351
Activated partial thromboplastin time (s)	29.32 ± 9.58	30.40 ± 11.81	30.20 ± 11.38	0.645
INR	1.22 ± 0.27	1.23 ± 0.37	1.23 ± 0.35	0.941
Serum creatinine (mg/dl)	0.77 (0.6 – 1.28)	1.16 (0.88 - 4)	1.07 (0.74 -3.59)	<0.001
Aspartate aminotransferase (U/L)	34.8 (23.6 – 50.8)	43.5 (30.4 – 62.5)	41 (27.33 – 61.30)	0.014
Alanine aminotransferase (U/L)	21.8 (13.4 - 29)	34.3 (20.1- 51)	28.35 (17.2 – 48.8)	0.002
Potassium (mEq/L)	4.22 ± 0.82	4.85 ± 0.97	4.70 ± 0.97	<0.001
Sodium (mEq/L)	137. 36 ± 4.81	136.98 ± 8.17	137.07 ± 7.50	0.775

Data is written in mean ± SD or median (IQR), all results were recorded during admission

Laboratory Values

White blood cell count was elevated in 92 (49.7%) of patients with predominant neutrophils and 5 patients (2.7%) had leukopenia during admission. One hundred and sixty-six patients (89.7%) presented with lymphopenia. Thrombocytopenia was observed in 36 patients (19.5%) and hemoglobin was low in 66 (35.7%) of the patients. Twenty-five had liver enzyme derangement at admission, while 80 patients (43.2%) had elevated levels of creatinine and BUN at admission. 92 (49.7%) had electrolyte disturbance during admission, where 54 (29.2%) and 8 (4.3%) had serum potassium and serum sodium level elevation respectively; and 25.9% (48) and 5.9% [11] of the patients had shown a decrease in serum sodium and potassium level, whereas 8 (4.3%) patients had coagulation profile derangement at admission.

Treatment and Clinical Outcome

Treatment

All patients receive antibacterial therapy. Antifungal agents were given to 46 (24.9%) patients while five patients (2.70%) received antiviral therapy. A total of 159 (85.9%) of patients were given steroids, while 69 (37.3%) patients received vasopressors, and 139 (75.1 %) took antithrombotic therapy mainly heparin [94.24% patients (131/139)]. Among the patients who take heparin, 81 of them (61.83%) received therapeutic dose. Hemodialysis was given for 36 critically ill patients (19.5%).

During admission 41 (22.2%) were on mechanical ventilation, 25 (13.5%) on NIPPV, 118 (63.8%) on different liters of face mask oxygen and 1 patient maintaining saturation without oxygen support. Including patients who were already on mechanical ventilation, a

total of 132 patients (71.35%) required mechanical ventilation during their stay.

Among 118 patients who were on face mask oxygen support, 22 failed and were intubated; among the 22 who needed mechanical ventilation, 11 patients were intubated at the day of admission. For 91 patients, support was changed to NIPPV and 51 of them failed again and were intubated ultimately. A total of 73 patients (61.86%) who were on face mask required mechanical ventilation during their stay.

From twenty-five patients who were on NIPPV during admission, 16 of them failed and were intubated. Five of them got intubated at the day of admission. The patient who wasn't on oxygen support during admission was put on face mask during his course and ultimately, he failed and required mechanical ventilation.

Twenty patients (10.81%) arrested on the same day as they were intubated but we couldn't find further information whether the patients arrested during intubation, if it was crush intubation or they expired after a successful intubation.

Clinical Outcomes

Our ICU mortality was 77.3% (143 patients), 7 out of 10 patients who were admitted to ICU died during our study period. Among them 16 patients were younger than 50 years. Sixteen (8.65%) patients died at the day of admission, 4 of them were intubated when they were admitted to the ICU and 6 of the patients were intubated immediately after they got admitted to ICU.

ICU mortality in patients requiring mechanical ventilation was 86.4% (114/132), with most ventilated patients being older than 60 years (Figure 2). The average time from admission to intubation was 4.95 ± 4.20 days (Range: 0-18 days), however 17 (9.19%) were intubated on the day of admission. There was a statistically significant difference in the meantime to intubation between the deceased patients and survivors (5.20 vs 3.09, p=0.043) The mean ventilation days were 4.93 ± 3.60 days (Range: 1-16 days). The mean ICU length of stay were 8.24 ± 5.23 days (Range: 1-36 days). The Ventilator and ICU length of stay for deceased patients were, 4.91 ± 3.77 days, and 7.62 ± 5.07 days respectively. For those who died, the probable cause of death was hypoxemic cardiorespiratory failure in the majority of patients (n= 65, 35.1%), followed by multiorgan failure secondary to refractory septic shock (n= 58, 31.4%). Other causes of death include cardiogenic shock in 3 patients (1.6%), respiratory failure secondary to massive alveolar hemorrhage in 4 (2.2%) patients, sudden cardiac arrest in 9 (4.9%), respiratory failure secondary to massive aspiration in one (0.5%) and brain herination in another patient (0.5%).

Out of 132 patients who got intubated, eighteen patients (13.64%) were successfully weaned from invasive ventilation. A total of 42 patients (22.7%) had been discharged from ICU after improvement.

Most patients had developed organ function damage during ICU stay, including 72 (38.9%) with acute kidney injury manifested by an increase in serum creatinine level, 29 (15.7%) patients with liver injury manifested by raised liver enzymes and 2 patients (1.8%) with cardiac injury as they developed acute coronary syndrome after admission to ICU, which is confirmed by elevated troponin and ECG findings. The most common complication was acute kidney injury and serum electrolyte disturbance.

Factors Affecting Outcomes

In a bivariate analysis, qSOFA score at admission was associated with mortality of the patient, deceased patients had a high qSOFA score when compared with those who survived p=0.028. The same is true for cigarette smoking where 93.75% of the patients (15/16) died, white blood cell count, where patients who survived had a lower count when compared with those who are deceased; hemoglobin levels at admission, where survived patients had a higher levels hemoglobin, Aspartate transaminase level at admission, which was increased in deceased patients; and serum creatinine levels which was statistically significantly higher in deceased patients when compared to those who survived, at p values less than or equal to 0.2.

In a multivariate logistic regression, age, male gender, pulse rate at admission, history of co-existing illness, mechanical ventilation, serum potassium and ALT, as well as lymphocyte levels and length of the stay, have been found to be significantly associated with the outcome of Covid-19 patients.

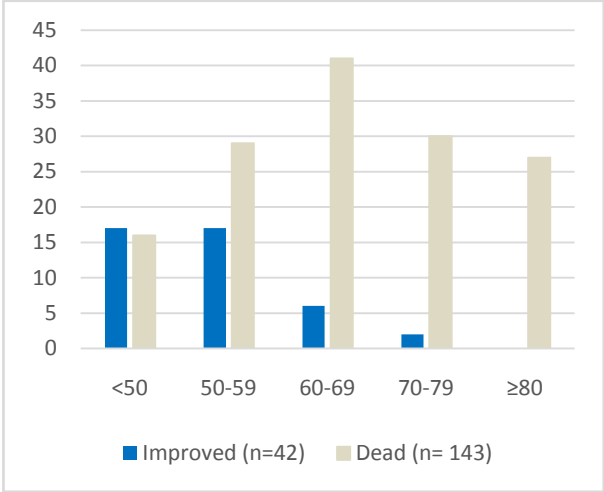

Figure 1. Disposition of 185 patients admitted to SPHMMC COVID-ICU, by age

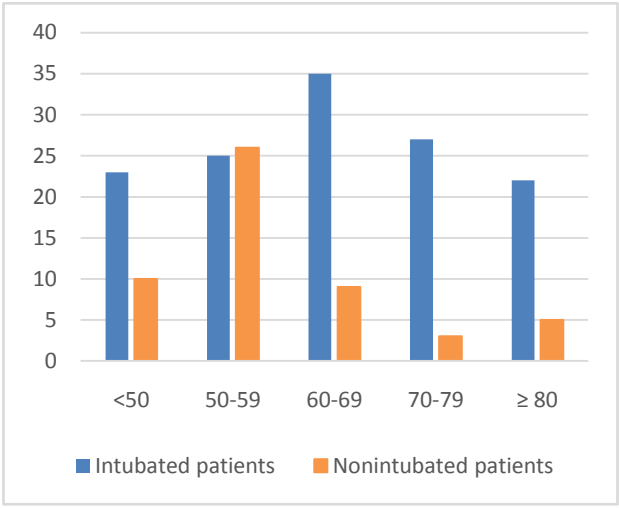

Figure 2. Intubation status of 185 patients admitted to SPHMMC COVID-ICU, by age

Figure 1 displays the age distribution for deceased patients and survivors. Patients over 60 years accounted for approximately two third of deaths in our study. In fact, no one above age 80 survived. In a multivariate analysis, younger age was significantly associated with the survival of a patient with p=0.001 (AOR= 0.88, 95% CI= 0.82-0.95) meaning as age is increased by one unit the odd of survival decreases by 12%.

In our study male gender had a significantly higher rate of death when compared with female p=0.044 (OR=0.173, 95% CI=0.33-0.93). The same was true for having co-existing illness and mechanical ventilation, where patients who had co-existing illness had a higher probability of death when compare with patients without comorbidities with p<0.001(AOR= 22.05, 95% CI= 4.17- 116.68); and more patients who require mechanical ventilation died when compared with those who were not intubated p<0.001(AOR=11.48, 95% CI= 3.91- 33.71). Neutrophil counts were significantly higher in deceased patients when compared to those who survived [p= 0.022, AOR=0.701, 95% CI=0.52-0.95]. Similarly, compared with patients who improved and got discharged from the ICU, those who don't survived showed significant decrease in lymphocyte count [7.29 ± 5.27 vs. 5.10 ± 4.75, p = 0.023, AOR=0.64, 95% CI= 0.44-0.94]. A higher levels of serum potassium at admission, was observed in deceased patients when compared to survived ones [4.85 ± 0.97 vs. 4.22 ± 0.82, p<0.033, OR=0.242, 95% CI=0.07- 0.89]. Similar to serum potassium, deceased patients had a significantly higher levels of alanine transaminase (ALT) when compared to patients who got discharged after improvement [34.3 (20.1- 51) vs. 21.8 (13.4 - 29), p= 0.017, OR=0.98, 95% CI=0.96-0.99].

Table 4. Factors Associated with Outcome of Critically Ill Coivd-19 Patients

Variables	Category	Outcome of the patient		P value	AOR	95% CI for AOR	P value
		Improved	Died				
Age in years		49.55 ± 12.91	63.91 ± 13.33	<0.001	0.881	0.82-0.95	0.001
Gender	Male	19 (45.2%)	100 (69.9%)	0.003	0.173	0.33-0.93	0.044
	Female	23 (54.8%)	43 (30.1%)		1		
Pulse rate at admission		92.69 ± 21.58	99.29 ± 22.47	0.093	0.941	0.904-0.980	0.003
qSOFA at admission, median (IQR)		1 (1-1.25)	1(1-2)	0.028	0.473	0.116 - 1.93	0.297
History of comorbidities	Yes	12 (28.6%)	114 (79.7%)	<0.001	1		
	No	30 (71.4%)	29 (20.3%)		22.05	4.17- 116.68	< 0.001
Cigarette smoking	Yes	1 (2.4%)	15 (10.5%)	0.10	1		
	No	41 (97.6%)	128 (89.5%)		1.7	0.11-26.18	0.704
Mechanical Ventilation	Intubated	18 (13.6%)	114 (86.4%)	<0.001	1		
	Not Intubated	24 (45.3%)	29(54.7%)		11.48	3.91- 33.71	< 0.001
White blood cell count (×109/L)		12. 20 ± 6.58	13.89 ± 9.57	0.195	1.03	0.87-1.22	0.709
Hemoglobin (g/dl)		13.83 ± 4.20	12.54 ± 3.96	0.071	1.14	0.97-1.34	0.123
Neutrophil (%)		86.47 ± 6.98	89.78 ± 7.25	0.010	.701	0.52-0.95	0.022
Lymphocyte (%)		7.29 ± 5.27	5.10 ± 4.75	0.019	0.64	0.44-0.94	0.023
Alanine aminotransferase (U/L)		21.8 (13.4 - 29)	34.3 (20.1- 51)	0.002	0.98	0.96-0.99	0.017
Aspartate aminotransferase (U/L)		34.8 (23.6-50.8)	43.5 (30.4 – 62.5)	0.014	0.98	0.95-1.00	0.05
Serum creatinine (mg/dl)		0.77 (0.6 -1.28)	1.16 (0.88 - 4)	<0.001	0.68	0.38- 1.23	0.201
Potassium (mEq/L)		4.22 ± 0.82	4.85 ± 0.97	<0.001	0.242	0.07- 0.89	0.033
Length of ICU stay, days		10.36 ± 5.27	7.62 ± 5.07	0.003	1.13	1.02-1.26	0.019

Data is reported in mean ± SD, median (IQR) or n (%)

7. Disscusion

This study presents a cross-sectional study of 185 critically ill patients with confirmed SARS-COV-2 infection, admitted to St. Paul covid ICU. 143 (77%) of critically ill patients had died. 132 (71%) required mechanical ventilation and 36 (19.5%) required hemodialysis.

Our study population had many of the clinical characteristics of patients with COVID-19. The mean age of the patients was 60.59 ± 14.53 years which is comparable to the study done in Jin Yin-tan hospital, Wuhan, China which reported a mean age of 59.7 ± 13.3 years [9] and our population was younger than the study done in New York; where the mean age was 62.2 ± 11.2 years. Similar to other studies males were predominate in our study [25]. A total of 126 patients (68.1%) had at least one preexisting condition, hypertension being the leading one in 85 (45.9%) of the patients, followed by DM in 74 (40%) of patients and 37(20%) of patients having cardiac disease. This result was similar to the one done in Lombardy, Italy where 68% of the study population had at least 1 comorbidity where the majority of them were hypertensive (48%). A study done in a community hospital in upstate New York, 62.5% were men. 27 (84.4%) of patients had one or more medical co-morbidities[25] which is a comparable finding to our study. Like other studies we reported the most common symptoms being shortness of breath and cough. Fever though it was the third common symptom, it wasn't as common as it is in other studies [9,18,25,26]. Our patients reported fever in only 48% of cases and most of it wasn't objective, as the mean temperature of patients during admission was 36.7 ± 0.64˚C.

Lymphocytopenia occurred in more than 90% of Covid-19 patients admitted to ICU, which is like the studies done in Wuhan and Guangdong province, China. we also found that patients who survived had a significantly lower lymphocyte counts than patients who died. This was similar to the study done in Guangdong

province, China. Though that study showed lymphocyte difference between intubated and non-intubated patients, our deceased population consist of many intubated patients. Lymphocytopenia is common in viral pneumonia, particularly in SARS-COV, it is a prominent feature of critically ill patients, because targeted invasion by SARS-COV viral particles damages the cytoplasmic component of the lymphocyte and causes its destruction. Additionally, lymphocytopenia is also common in the critically ill patients with MERS infection, which is the result of apoptosis of lymphocytes. It was postulated that necrosis or apoptosis of lymphocytes also induces lymphocytopenia in critically ill patients with SARS-CoV-2 infection. It was reported that lymphocyte count $<0.8 \times 10^9$/L was an independent risk factor for 90- day mortality in viral pneumonia, the case in our study [9,18].

The primary finding of our analysis is that mortality in critically ill COVID-19 patients that are admitted in our ICU was high, particularly in patients of advanced age. Despite the high mortality, the outcomes of critically ill patients in our ICU were comparable to those reported elsewhere. For instance, in the report done by Muhammed, et. Al in 13 hospitals found in Libya, a highest morality rate of 60.4% was reported in Covid -19 patients admitted to the ICU [39]. Similarly, in the report by Zhou, et. al. on Jinyintan Hospital and Wuhan Pulmonary Hospital, 39/50 (78%) patients died in ICU [40]. Data from Washington state, USA reported by Arentz, and colleagues found that 11 out of 13 patients (85%) died in ICU. Case series of patients with Covid-19 admitted to 12 hospitals in New York City, Long Island, and Westchester County, New York, within the Northwell Health system, reported that 291 patients out of 371 (78%) who got admitted to ICU died[41]. Another study done in Lombardy region, Italy, out of 1581 patients whose ICU disposition data is available, 405(26% [95% CI, 23%-28%]) had died in ICU, though during the time of reporting 920 (58%) of patients were still in the ICU and it is reported only 16% of the patients were discharged from the ICU [12]. Even though there are similar studies that has comparable mortality with our finding, we can't deny the fact that our study had a very high mortality rate compared to study done by Mitra et al, on Jewish General Hospital, Montreal Canada, which reported a 17% ICU mortality rate [42], or a study conducted in Indianapolis, USA, by Maatman and colleagues, which reported 27 patients died from 106 patients that were admitted to ICU, reporting a 26% mortality rate [43]. The set-up difference might play a significant role here, but aside from than infection rate was high in our set up where, septic shock was the major cause of death for 31.4% of patients and more than 80% of our patients were diagnosed with infection, where only 20% of patients in Montreal Canada developed an ICU acquired infection. Though our management practices evolved as we gained clinical experience and new data emerged in the literature, some treatment options, like prone positioning which was proved to reduce mortality especially in ARDS patients were not practiced in our setup.

We also reported a higher mortality rate of 86.4% among intubated patients. This result is comparable to the report by Richardson, et. al. on the Northwell Health System in New York, where 1151 patients required IMV. At the time of their report, 24.5% of the patients had died, while only 3.3% were discharged alive, and 72% remained in the hospital. If only those with a confirmed endpoint (death or discharge) from this cohort are analyzed, the reported mortality rate for patients requiring IMV is 88.1% [44]. Data from Wuhan, China reported by Zhou and colleagues found that 96.8% treated with IMV died [40] and finally, a report from Seattle, Washington, USA included data on 24 critically ill COVID-19 patients, 18 of whom required IMV. At the time of data censoring, 50% of the patients died and 27.7% were still on mechanical ventilation. We feel the higher death rate among intubated patients was because of avoiding intubation unless patients were truly unable to maintain their oxygenation or ventilation, which can be shown in our delayed average time from admission to intubation, which was 4.95 ± 4.20 days. This result when compared to other studies which had favorable outcomes like the study done by Christopher S. King in Italy which had an average time from admission to intubation of 2.5 ± 3.0 days and reported a mortality rate of 42.7% among intubated patients[45] and ICNARC, the Intensive Care National Audit and Research Centre from the United Kingdom, reported that 58.3% of patients received invasive ventilation in the first 24 hours of admission which reported a mortality rate of 28.3% [46]. The patients managed with invasive mechanical ventilation in our study was likely sicker than those reported in some of series and could be expected to have less favorable outcomes plus mechanical ventilation should be considered early in the course of illness and should not be delayed until the need becomes emergent.

In our study, older age, male gender, tachycardia at admission, history of co-existing illness, requirement mechanical ventilation, elevate serum potassium and ALT at admission, as well as low lymphocyte levels have been found to be significantly associated with a higher risk of mortality. The result was comparable to the study done by Muhammed and his colleagues, which showed, increased age, BMI, decreased lymphocytes and platelet count, white cell count, neutrophils, procalcitonin, cardiac troponin, C-reactive protein, ferritin, fibrinogen, prothrombin, and d-dimer levels were associated with higher risk of mortality [39].

The commonest complication was acute kidney injury and serum electrolyte disturbance in our study. This was similar to study done by Stephen Su Yang and his colleagues in Montreal, Canada, which reported acute kidney injury (20/106, 18.9%) and thromboembolic events occurred in 15.1% of the patients as the most common complication [42].

Limitation of the Study

- The data collected was a secondary data and there were some records with missed information
- Given the observational nature of our study, any causal link between our intervention and observed outcomes is speculative
- Thromboembolic events occurred during our study was not available, thereby limiting our interpretation
- Our study is a single center study, and the results obtained may not be generalizable to other centers

Abbreviations

AIDS: Acquired Immunodeficiency Syndrome
AKI: Acute Kidney Injury
ARDS: Severe Acute Respiratory Syndrome
BMI: Body Mass Index
CKD: Chronic Kidney Disease
COVID-19: Coronavirus Disease 2019
DM: Diabetes Miletus
ECMO: Extracorporeal Membrane Oxygenation
ICU: Intensive Care Unit
HIV: Human Immunodeficiency Virus
MERS: Middle East Respiratory Syndrome
qSOFA: Quick Sequential Organ Function Assessment
PCR: Polymerase Chain Reaction
SARS: Severe Acute Respiratory Syndrome
SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus Disease 2
SBP: Systolic Blood Pressure
SPHMMC: St. Paul's Hospital Millennium Medical College
WHO: World Health Organization

Declarations

Author Contributions: conceptualization, Methodology, Investigation, Analysis, and Writing of the manuscript- Rediet Assefa Gudeta, Muluken Alemayehu Workiye, Atiklet Zerihun Zewdie, Henok Bahru Wodajeneh

Methodology, Data curation, Drafting, Interpretation, and Supervision and edition of the manuscript- Eyosias Lemma Teshome, Beimnet Ayenew Tamene, Eyerusalem Yalew Talemma ,Ayanaw Guadie Mamo ,Ermias Fikru Yesuf, Asnake Abebe Kotu

All authors revised the manuscript and have approved the final version of the manuscript.

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Ethical Clearance

Institutional Review Board Statement: The study was conducted by the Declaration of Helsinki and approved by the Institutional Review Board of St Paul's hospital millennium medical college.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The authors confirm that the data supporting the findings of this study are available within the article.

Acknowledgments: Not applicable.

Conflicts of Interest: The authors declare no conflicts of interest

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