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Clinical Presentation and Outcome of Sars Cov2 Patients Admitted In Intensive Care Unit

Dr. G. Nikhil Swarup[1*], Dr. Payal Jain[2], Ms. Mahima Singh[3]

[1*]DNB General Medicine, GIMS (Government Institute of Medical Sciences).
[2]MD, General Medicine, GIMS (Government Institute of medical Sciences).
[3]M.Sc, Obstetrics and Gynecology in Nursing.

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ABSTRACT:

Introduction: Coronavirus disease 2019 (COVID-19) caused by Severe acute Respiratory Syndrome corona virus-2(SARS-CoV-2) infection has spread rapidly across the world and it is an international public health emergency. COVID-19 is an emerging disease all over the world and spreading at an unpredicted rate. The literature has been limited and the study was undertaken to assess the characteristics, clinical presentation, and outcomes of patients admitted in ICU with COVID 19 infection. **Aims and objectives:** Aim of the study is to determine the clinical characteristics and outcome of the SARS CoV2 patients admitted in intensive care unit. To assess the clinical features of COVID 19 infected patients and their correlation with ICU stay significance of laboratory parameters with the severity of disease and correlate with the outcome. **Material and Methods:** It is an Observational prospective study. After approval from the Institutional Scientific Research Committee and Ethical committee. After written informed consent all patients who are RT-PCR positive and above the age of >18 years satisfying inclusion and exclusion criteria who are admitted in intensive care unit are included in the study statistical analysis was performed by statistical software SPSS version 21.0. **Results:** Majority of the study population belonged to 60-70 years (30.8%) of which 87 (72.5%) males and 33 (27.5%) females. Mortality was reported among 30.8% subjects. The mean Days in ICU were significantly more among Discharge and referred group compared to Mortality group. **Conclusion:** Critical illness among patients admitted to hospital with COVID-19 is common and associated with a high frequency of invasive mechanical ventilation, and substantial in hospital mortality. Outcome and clinical presentations in of SARS-CoV-2 positive ICU patients are still not well defined and there is a need for further multicentre studies to add to the literature to the clinical impact of SARS-CoV-2 associations of various parameters.

1. Introduction

SARS-CoV2 is transmitted through close-up droplets and contact. It can also be transmitted through aerosols in the enclosed spaces. It can also spread by touching the surfaces contaminated and then touching nose, mouth and eyes. The clinical spectrum of COVID-19 disease appears to be wide spectrum. The symptoms mostly include fever, cough, sore throat, generalised body ache, fatigue. Other symptoms include loss of smell, loss of taste, diarrhoea, rashes. Although, most of the patients are asymptomatic. The case fatality ratio is around 2-3%.[3]

The patients clinically are categorised based on various parameters as mild, moderate and severe acute respiratory distress syndrome (ARDS) based on saturation and P:F ratio. And the treatment is given accordingly. Majority of the confirmed SARS-CoV-2 cases are mild disease with symptoms of fever, dry cough, sore throat, malaise with absence of dyspnoea. Management of the cases concentrated mostly who are symptomatic and need oxygen therapy. Secondary bacterial infections are treated by antimicrobials which are to be given early in the course of disease. Critically ill patients require high flow oxygen, glucocorticoids. Patients with respiratory failure may require intubation and mechanical ventilation. The treatment of septic shock includes vasopressor support. In most of the patients who are on mechanical ventilation there is more chance of mortality and morbidity.

Need For the Study

Estimating the case-fatality rate at the level of the total population is useful for understanding the average severity of a pandemic, but it is also crucial to identify patients who are at risk of dying within a population during the pandemic. Information on risk relative to different patient characteristics, especially co-morbidities, allows health care providers to focus on the most vulnerable and improve the allocation of health resources to those who need them most and have a real chance of survival.

Aim of the Study

To determine the clinical characteristics and outcome of the SARS CoV2 patients admitted in intensive care unit and to assess the clinical features of COVID 19 infected patients and their correlation with ICU stay significance of laboratory parameters with the severity of disease and correlate with the outcome.

2. Materials and Method

Study population was all the patients admitted in intensive care unit above the age of 18 years. Study design was prospective Observational Study. All the patients admitted in intensive care unit during the study were the samples. Pregnant females were excluded from the study. After approval from the Institutional Scientific Research Committee and Ethical committee, all patients were selected as per inclusion and exclusion criteria. A detailed history, complete physical examination and routine & appropriate investigations were done for all patients. Informed written consent from the patient or the attendant of the patients fulfilling the inclusion and exclusion criteria was enrolled. The epidemiological, demographic data was recorded in case record form.

3. Results and Discussion

Majority of the study population belonged to 60-70 years (30.8%) followed by 40-50 years (22.5%), 50-60 years (20.8%), Above 70 years (12.5%), 20-30 years (7.5%) and 30-40 years

(5.8%). The mean age of the study population was 55.18±14.42 (20-85) years. There were 87 (72.5%) males and 33 (27.5%) females among study population. The symptoms reported were Shortness of Breath (89.2%), Cough (63.3%), Fever (52.5%), Sore throat (12.5%) and others (6.7%). The co-morbidities reported were Diabetes Mellitus (41.7%), Hypertension (39.2%), COPD (6.7%) and Coronary Artery Disease (5.0%). Smoking was reported among 25 (20.8%), Alcohol use among 8 (6.7%) and Tobacco use among 3 (2.5%) subjects.

SpO2 at admission (ICU) was reported to be < 90% among 69.2%, 90-95% among 15.0% and >95% among 15.8%.

The comparison of mean Days in ICU using the one-way ANOVA test with inter-group comparison using the post-hoc bonferroni test showed that mean Days in ICU was significantly more among Discharge and referred group compared to Mortality group.

The comparison of mean Days on ventilator using the one-way ANOVA test with inter-group comparison using the post-hoc bonferroni test showed that mean Days on ventilator was significantly more among Mortality group compared to Discharge and referred group. The comparison of mean TLC at admission and at discharge using the one-way ANOVA test with inter-group comparison using the post-hoc bonferroni test showed that mean TLC at admission and at discharge was significantly more among mortality group compared to discharge and referred groups. The comparison of mean Platelet count at admission and at discharge using the one-way ANOVA test with inter-group comparison using the post-hoc bonferroni test showed that mean Platelet count was significantly more among discharge and referred groups compared to mortality group. Low platelet count is seen more in mortality group when compared to discharge group. The comparison of mean D-dimer at admission and at discharge using the one-way ANOVA test with inter-group comparison using the post-hoc bonferroni test showed that mean D-dimer at admission and at discharge was significantly more among mortality group compared to discharge and referred groups. The comparison of mean Sr. Ferritin at admission and at discharge using the one-way ANOVA test with inter-group comparison using the post-hoc bonferroni test showed that mean Sr. Ferritin at admission and at discharge was significantly more among mortality group compared to discharge and referred group. The comparison of mean IL-6 using the one-way ANOVA test with inter-group comparison using the post-hoc bonferroni test showed that mean IL-6 was significantly more among mortality group compared to discharge and referred groups. The comparison of mean N/L ratio at admission and at discharge using the one-way ANOVA test with inter-group comparison using the post-hoc bon ferroni test showed that mean N/L ratio at admission and at discharge was significantly more among mortality group compared to discharge and referred groups. There were B/L alveolar & reticular opacities-ARDS among 12 (10.0%), B/L lower zone haziness among 59 (49.2%) and B/L Lower zone patchy opacities among 49 (40.8%).

Age

In our study, majority of the study population belonged to 60-70 years (30.8%) followed by 40-50 years (22.5%), 50-60 years (20.8%), Above 70 years (12.5%), 20-30 years (7.5%) and 30-40 years (5.8%) with a mean age of 55.18±14.42 (20-85) years. Ahmad et al.[52] found that the mean age of the study population was 48.6±16.8 years with the highest rate of admission in age group of 51-60 years. This finding of higher rate of admission in middle and advancing age group is in line with previous studies where mean age group ranged from 43.5-48.9 years.[67,68] Cummings et al.[55] found that the median age of patients was 62 years (IQR 51-72). Ismail et al. [40] found that mean age was 53±13 years. Shayganfar et al. [2] stated that the sample had a mean age of 57.5 ± 16.1 years. Participants with poor outcomes had significantly higher means of age than the discharge group (67±13.2 years vs. 54.9±15.9 years). ICU admissions and death due to COVID-19 have been shown to occur more often with increasing age. [12,69] Shayganfar et al. [2] found that age more than 60 years was the strongest independent predictor of ICU admission and in-hospital mortality. These findings are in concordance with other studies from China, Europe, and the USA. [69-73] Older patients are particularly vulnerable to worse outcomes from COVID-19 disease and should be targeted for aggressive preventive measures. [74] The higher rates of admissions in mid and higher age groups could be due to occurrence of various comorbidities like diabetes and hypertension among them which increased risk of complications in this age group. In our study we included all the cases admitted to the hospital including the ICU patients. Another reason for higher rates of admission in mid and advancing age group in our study could be due to the fact our hospital also provided intensive critical care with facilities of non-invasive and invasive mechanical ventilation which are more often required in advancing age groups. [52]

Gender

In present study, there were 87 (72.5%) males and 33 (27.5%) females among study population. Cummings et al. [55] reported that 67.0% were men. Ismail et al. [40] found that the majority were male (84.6%). Shayganfar et al. [2] stated that 61.0% were male patients. Elhadi et al. [45] stated that 51.6% were male and 48.4% were female.

Symptoms

In present study, the symptoms reported were Shortness of Breath (89.2%), Cough (63.3%), Fever (52.5%), Sore throat (12.5%) and others (6.7%). Ismail et al. [40] found that the symptoms most commonly reported prior to hospital admission were cough (79.8%), fever (77.6%), dyspnea (77.4%), malaise (49.6%), and headache (32.1%). The most common symptoms were reported as fever, cough, shortness of breath and fatigue in hospitalised patients in previous studies. [75,76] Kocayiğit et al. [43] observed that fatigue, shortness of breath, cough and fever were most common symptoms. Sore throat, anosmia, and diarrhoea were less frequently observed as initial symptoms in our study. According to the initial symptoms, there was no significant difference between the patients who were discharged and died.

Comorbidities

Covid-19 is a relatively mild condition in most of the affected cases but it can be severe and deadly in older individuals with comorbidities. [9] These patients require intensive care and have higher mortality rates, similar to published data from China. [43] In current study, the co-morbidities reported were Diabetes Mellitus (41.7%), Hypertension (39.2%), COPD (6.7%) and Coronary Artery Disease (5.0%). Shayganfar et al. [2] found that the most prevalent comorbidities were HTN (30.7%), DM (22.2%), and CVD (19.3%), respectively. Cummings et al. [55] found that 82% patients had at least one chronic illness, the most common of which were hypertension (63%) and diabetes (36%) and 46% patients had obesity. Ismail et al. [40] demonstrated that the most common comorbid conditions were diabetes mellitus (44.2%), systemic hypertension (43.1%), and cardiovascular disease (17.0%). Grasselli et al. [5] found that hypertension was the most frequent comorbidity, and patients with hypertension had significantly decreased survival. Despite this, in the multivariable analysis, hypertension was not an independent factor associated with mortality. Conversely, a history of chronic obstructive pulmonary disease, hypercholesterolemia, and diabetes, although affecting a smaller percentage of patients, were independently associated with mortality. Consistent with data from China,77 and Italy,5 hypertensions was associated with poor in-hospital survival. Given the globally high burden of hypertension and emerging [43] understanding of interactions between SARS-CoV-2 and angiotensin-converting-enzyme-[2,78] further investigations are needed to better define a relation—if any—between hypertension, exposure to renin angiotensin aldosterone system antagonists, and severe COVID-19. Kerai et al. [36] stated that among the comorbid conditions in patients admitted to ICUs, hypertension was found to be significantly more prevalent among non-survivors. Previousmstudies have demonstrated that after adjusting for age and sex, hypertension showed a significant correlation with increased disease severity and mortality. The exact mechanism for association of hypertension with severity of COVID-19 infectionis not clear. One of the plausible explanations is interaction of both hypertension and SARS-CoV-2 withangiotensin converting enzyme 2 (ACE2) receptors. There is a high affinity of SARS-CoV-2 for binding toACE2 receptors to gain entry to host cells. ACE2 is a modulator of renin–angiotensin–aldosterone system, which regulates blood pressure and fluid balance and has a role in pathogenesis of hypertension. [36]

Laboratory findings and Inflammatory markers

Novel findings in this study include establishing independent associations between biomarkers for inflammation (IL-6) and thrombosis (D-dimer) and in-hospital mortality, as well as identifying a high incidence of critical illness. It has been reported that elevated d-dimer levels, IL-6, hs-troponin, lactate dehydrogenase and lymphopenia levels were commonly seen in severe Covid-19 illness. The neutrophil to lymphocyte ratio (N/L) mean showed was significantly high among the mortality group when compared to discharged group. Kocayiğit et al. [43] found that procalcitonin, hs-troponin, d-dimer, and C-reactive protein levels were significantly higher at admission to ICU in patients who died compared to discharged patients. Admission platelet levels were significantly higher in discharged patients compared to the patients who died. Elhadi et al.[45] reported that increased blood laboratory values, such as white cell count and neutrophils, were significantly associated with higher mortality risk, which is in line with previous reports.[79] In contrast, a lower lymphocyte count was significantly associated with a higher risk of mortality, which has been reported previously.[80] In addition, a lower platelet count was significantly associated with mortality rate, which has also been reported in the literature as a risk factor.[81] Tan et al.[49] suggested that lymphopenia could be considered a useful indicator of severe COVID-19 disease. There was a significant association between poor in-hospital outcomes and lymphopenia. In a study by Xu et al., [28] ≥ 2 comorbidities, leukocytosis and lymphopenia were associated with increased odds of poor outcome. Regarding other laboratory findings, procalcitonin levels were significantly associated with a 7-fold higher risk of mortality in critically ill patients with COVID-19, which has also been reported in several previous studies as a predictor of mortality. [82] Elhadi et al. [45] found that biomarkers, such as cardiac troponin, C-reactive protein, ferritin, fibrinogen, prothrombin time, and D-dimer were shown to be associated with a higher risk of mortality among critically ill COVID-19 patients. These biomarkers have been reported in several studies and metaanalyses regarding their role as risk factors and factors predicting mortality and worsening of COVID-19 severity. [83-86] Ahmad et al. [52] found that abnormally high leukocyte count at the time of admission was found to be independent risk factor for higher mortality in our study (AOR = 1.147). Similar associations have been reported in a couple of studies. [87-89] However, in multivariable analysis the relationship was not found to be statistically significant. Abnormally high rate of total leukocyte count at the time of admission reflects severe inflammatory state which might be the reason for higher mortality. A prospective cohort study in Wuhan, China reported that serum creatinine (hazard ratio = 2.10) were independent risk factors in-hospital death.85 Another study calculated estimated Glomerular filtration rate and reported that baseline eGFR was independently associated with mortality (OR = 0.974).23 The lymphocyte count decreases progressively, whereas the neutrophil count increases in patients with severe COVID-19.[90,91] Indeed, a pooled analysis of 10 studies, including 2967 COVID-19 patients, found that an elevated NLR had both sensitivity and specificity of 0.83 for discriminating between survivors and non-survivors.[92] The elevation of NLR in ICU patients compared patients with milder disease forms may be explained by the time lag between the onset of the disease and ICU admission, enabling NLR to reach higher levels than those reported in patients hospitalized with mild disease progression. Elevated LDH levels were independently associated with a higher risk of in-hospital death in our study. LDH is an intracellular enzyme in the glycolytic pathway, which catalyzes the interconversion of pyruvate and lactate.[93] Since LDH is present in lung tissue, patients with severe COVID-19 infection can be expected to release greater amounts of LDH into the circulation.[94,95] Elevated LDH levels may also be associated with multiple organ dysfunction and subsequently poor outcome.[94] In a pooled analysis of 9 studies including 1532 COVID-19 patients, Henry et al.[94] found that elevated LDH levels, measured at the earliest possible time after hospital admission, were associated with a 6-fold increase in the odds of developing severe disease and a 16-fold increase in the odds of mortality in these patients. The presence of a high LDH value on admission to the ICU may, therefore, be a potential marker of poor prognosis in critically ill patients with COVID-19. Kukoč et al. [1] demonstrated that ferritin with HR of 1.03 per each 0.1 mg/L increase and IL-6 with HR 1.11 per each 0.1 mcg/L increase shortened ICU survival times, while increases in CRP showed a reduction of HR with 0.74 per each 100 mg/l increase (in contrast to having a univariate OR 1.28), which can be linked to increased survival times of patients with bacterial superinfections (where patients without had a HR of 2.31 compared to those with bacterial superinfections). These results are in partial agreement with previously published data, [96,97] where CRP levels at admission were a more significant factor in determining survival rates. In the studied population, the CRP cut-off value with highest ability to discriminate between survivors and non-survivors was similar to levels reported by Liu et al. (41.3 vs 41.8 mg/L) but area below the receiver operating curve was much lower (0.58 vs 0.86), limiting its usefulness.

Mortality

In current study, Mortality was reported among 30.8% subjects. Ahmad et al. [52] showed that in-hospital mortality among admitted COVID-19 patients was 11%. One study which was done in reported in-hospital mortality to be 20.3%.[98] However, an Indian study done at Jaipur among mild cases of young adult population reported that all patients recovered from the disease.[99] Another study done in Switzerland among 25% patients admitted in ICU reported about in-hospital mortality to be about 17%.[100] Another study which assessed in-hospital mortality of patients with COVID-19 across globe which combined findings from 43 studies from 12 countries reported that in-hospital mortality across America, Europe, and Asia to be 22%, 2%, and 12% respectively.[101] In a large multicenter prospective study in three European countries including Belgium, France, and Switzerland that included 4224 critically ill patients with COVID-19, the mortality rate was 31% on day 90 after ICU admission.[19] Another multicenter study in Spain and Andorra[102] reported a mortality rate of 31.0%. Another multicenter prospective study in France [103] of 335 critically ill patients reported a mortality rate of 7.76%. In a single-center study [104] in Sweden, the mortality was found in 60 of those admitted to the ICU. In Germany, a multicenter prospective study of 223 patients found a mortality rate of 35% among ICUpatients.[105] In a large multicenter prospective study among 639 patients admitted to ICUs, ICU mortality was 24%.[106] A retrospective multicenter study in Georgia in the United States found a mortality rate of 28.6% among critically ill patients with COVID-19.[107] Another retrospective single center in Ohio[108] found that 18.4% patients died in the ICU. A single registry report from Victoria State in Australia reports very low mortality of 10.6% whereas in the Middle East, the mortality was reported to be as high as 61.9%. Thesestudies are variable in terms of the country of origin (two from high-income countries,one upper middle,[113] and one low-income[114]), quality (two were at high risk of bias); and one is from a critical care unit in an area of humanitarian crisis – despite this, the studies showed similar mortality rates and considerable homogeneity (I2 = 30%). There are several potential explanations for this finding, including the fact that studies from the Middle East included patients early in the pandemic when mortality was higher and those included in Australia arose later in the pandemic when mortality was lower. It is possible that variations in healthcare resource, variation in admission criteria and clinical and statistical uncertainty associated with single-centre and small reports could have also contributed.

Oxygen saturation

In our study, SpO2 at admission (ICU) was reported to be < 90% among 69.2%, 90- 95% among 15.0% and > 95% among 15.8%. Shayganfar et al. stated that those who died or were admitted to ICU had more prevalence of lowered O2 saturation in comparison to discharged patients (85.21±8.6% vs. 90.29±5.9%). Ahmad et al. found that higher oxygen saturation at the time of admission has been found to protective against in-hospital mortality (AOR = 0.848). which reported decreased oxygen saturation at time of admission was associated with higher mortality (OR = 1.09). This signifies decreased oxygen saturation at the time of admission must be due to already involved lung parenchyma and disease being in advanced stage this study is among the oldest ones reported so far.

4. Conclusion

The mean Days in ICU was significantly more among Discharge and referred group compared to Mortality group. The mean Days on ventilator was significantly more among Mortality group compared to Discharge and referred group. The mean Days of Hospitalization was significantly more among Discharge group compared to Mortality group. Critical illness among patients admitted to hospital with COVID-19 is common and associated with a high frequency of invasive mechanical ventilation, and substantial in-hospital mortality. Several factors were found to be predictive of mortality, which should be considered by clinicians and healthcare policy makers in future planning and support for hospitals and healthcare workers. Multicenter studies of larger populations managed based on the current knowledge of COVID-19-related ARDS are needed to further compare associations between ventilator type and patient outcomes.

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