CLINICAL PROFILE AND OUTCOMES OF CRITICALLY ILL COVID-19 PATIENTS ADMITTED IN A TERTIARY CARE HOSPITAL

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ABSTRACT:

BACKGROUND: Ever since the COVID -19 pandemic took hold in India, its clinical characteristics, course of illness and outcome of critically ill patients requiring ICU care has not been studied in detail, especially in South India which bares almost one third of COVID-19 cases in India. Hence this study is carried out to fill the gaps in identifying the population that are risk of severe illness and in management strategies. AIM: To analyze the clinical profile and outcome of critically ill COVID -19 patients. METHODOLOGY: This retrospective study was conducted in a tertiary care hospital based on medical records of those patients diagnosed with COVID -19 by RT-PCR of nasopharyngeal and throat swabs or typical patterns on HRCT chest suggestive of COVID- 19 who required intensive care treatment. RESULTS: Among study population (n=50), males were more commonly affected than females (82% versus 18%). The mean age of study population 55.96 ± 14.52 years. Dyspnea was the most common presenting symptom. Diabetes Mellitus was the most common comorbidity. The most common complication

observed was ARDS(94%). History of smoking, hypertensives and those treated with tocilizumab had significantly higher mortality (p<0.05). Patients treated with antivirals has significantly better outcome. The mean duration of ICU stay was 9.2±3.7 days mortality rate was 38%.

CONCLUSION: This study highlights the clinical characteristics, response to treatment and outcome among critically ill COVID-19 patients. Delay in presentation, comorbidities and smoking history had higher chances of severe illness. Early initiation of effective treatment can reduce the mortality rates.

Key words: COVID-19, SARS CoV2, South India, critically ill, ARDS


Introduction

SARS CoV2, the novel coronavirus emerged as a cause of COVID 19 infection in Wuhan city of China in late 2019. It was a rapidly disseminating virus, spreading across several countries within few months and then was declared as a global pandemic by WHO in the month of March 2020. This is the third established coronavirus as a cause of severe acute respiratory syndrome after the severe acute respiratory syndrome coronavirus (SARS-CoV) outbreak in 2002 and the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak in 2012 [1]. The index case in India was late in January and gradually the disease took a foothold by the month of May. As on mid-October, India has emerged as the second most infected country in the world after USA with the total of 7.3 million cases with mortality rate of 1.7%. Though it was initially recognized as a zoonotic infection, human-human transmission was also occurring via droplet and through contact with fomites. SARS-CoV2 portrays its pathogenicity by penetrating epithelial cells of the human respiratory tract by communication between viral S protein and angiotensin-converting enzyme 2 (ACE 2) on the surface of epithelial cells [2]. It has a wide variety of clinical presentation ranging from completely asymptomatic course to severe life threatening illnesses especially in elderly and persons with comorbidities [3-5]. The incubation period of COVID 19 is approximately 14 days and chiefly presents as fever, fatigue, myalgia, anosmia, loss of taste and cough [1,6]. As the disease progresses, almost 5% of symptomatic individuals start experiencing complications such as ARDS, AKI, MODS, myocarditis, respiratory failure, shock and death [1,7,8]. In India which is second most populated country, the infection is widely
prevalent among its population, with predominant asymptomatic individuals. Ignorance and lack of adequate resources has caused delay in presentation to the hospital where complications have already set in, thus saturating the ICU beds. South India accounts for about 35% of total cases in the country, 28.7% of the India’s total deaths. Yet the clinical characteristics, course and progression of the illness and outcome of critically ill patients has not been studied till date\cite{9}. The current mortality rate in India is 1.7%. Hence this study is aimed at analyzing the clinical course in patients requiring ICU care and their response to treatment and outcome with the available knowledge about the infection and treatment protocols, and to our knowledge this is the first of its kind in this region.

**Materials and Methodology:**

**Study Design:**

The study was designed to be retrospective observational study and was carried out in the COVID ICU and medical records section in a tertiary care center, who were admitted from March 2020 to August 2020.

**Selection of Participants – Inclusion and Exclusion Criterion:**

Patients of age ≥18yrs, with COVID RT-PCR positive (oropharyngeal or nasopharyngeal swab) or HRCT-CHEST suggestive of COVID included in this study. All the patients admitted in intensive care unit due to rapid deterioration of health who are critically ill defined as respiratory rate>30cycles/min, resting tachycardia>120/min, hypotension BP<90/60mmHg ,SpO2<92%despite oxygen support, evidence of myocarditis, sepsis or MODS.

The following patients were excluded from the study Age <18 years , patient who are negative for COVID 19 with RT-PCR (oropharyngeal and nasopharyngeal swab) and CT-CHEST, Covid19 positive patients who did not require intensive care, patients with incomplete records due to referral to higher centre.

**Data Collection:**

After obtaining the institutional ethical committee clearance, patient details, history and duration of illness, symptoms on presentation, vitals on presentation, comorbidities, substance abuse, investigations, mode of ventilation required, treatment given, complications, procedures, duration of hospital stay and duration of ICU stay and outcomes noted for 50 patients were noted who met inclusion criteria and exclusion criteria. Baseline ECG,
COVID RT-PCR, HRCT-Chest and CT severity, ABG analysis were done in all the cases. The diagnosis of COVID was based on COVID RT-PCR and HRCT-CHEST suggestive of COVID. The complications such as ARDS, AKI, MODS, Myocarditis were defined as per standard reference book[13]

Statistical Analysis:
All collected data were processed and analyzed by using IBM SPSS version 21.0. Sample statistics i.e., mean, median and standard deviation were calculated for quantitative data. Categorical variables were expressed as frequencies and percentages. The comparison of normally distributed continuous variables between the groups was performed using Student’s t-test. Test results were deemed significant at 95% confidence intervals P<0.05.

Results
A total of 50 cases that were positive for COVID 19 RT-PCR and critically ill requiring intensive care on admission were studied during the study period of March 2020 to August 2020. The mean age of study population 55.96 ± 14.52 years. 26% (n=13) of them belonged to the age group of 45-54 years, followed by 24% (n=12) aged 55-64 years. Our study had predominant males (82%) being affected than females (18%). Table 1

The most common presenting symptom is dyspnea (84%) respiratory symptoms (cough, breathlessness, etc.,) followed by fever (70%). Diabetes was the most common co-morbidity among our subjects (64%) followed by hypertension (44%). Smokers constituted 26% (n=13) and alcoholics 12% (n=6) of the study subjects. Frequency distribution is shown in table 2.

The room air saturation ranged from 65% to 92% with mean saturation of 84%. Respiratory rate of our subjects varied from 16 breaths per minute to 39 breaths per minute. Out of the patients presented with dyspnea, 14% had grade 1, 48% had grade 2, 28% had grade 3, and 10% had grade 4 dyspnea as per MRC grading.

The CT severity score of lung infiltrates were grouped into mild (CTSS 1-8) moderate (CTSS9-15), and severe (CTSS >15). 8% of patients had mild, 48% of patients had moderate and 44% had severe infiltration. New onset ECG abnormalities were noted in 12 patients in the form of sinus bradycardia (n=2), AVNRT (n=2), ST-T changes (n= 4) and PR prolongation (n=4).

Regarding modes of ventilation 54% of patients required high flow nasal oxygen supplementation (HFNO), 50% of them were kept on NIV-CPAP and 40% of the patients ultimately required invasive mechanical ventilation including...
tracheostomy. 74% of patients required NRBM and 70% of the patients were maintained on facemask during their stay in ICU. The initial ABG done for all the patients showed mean PaO2 of 67.5±14.89mmHg. Duration of illness before admission to the hospital ranged from 3-11 days with mean of 6 days. The mean duration of ICU stay was 9.22±3.75 days.

All the patients were started on antibiotics in the form of Azithromycin 500mg once daily (82%) and/or Doxycycline 100mg twice daily (24%) for 5 days. Based on nature of secondary infection antibiotics were escalated to intravenous antibiotics appropriately. As per the treatment protocol 25 patients were started on hydroxychloroquine (HCQ) and 41 patients were started on Ivermectin due to contraindication to HCQ. Steroids were meticulously added using either dexamethasone (42%) or methylprednisolone (56%). 12 patients required insulin infusion in view of poor glycemic control. Anticoagulants were required in 96% of subjects. Antivirals were given in the form of either favipravir or remdesivir. 24 patients were tried on Remdesivir and 8 patients on favipravir and rest of patients did not receive any antivirals. Based on Interleukin-6 levels, 11 patients required Tocilizumab. Bradycardia was observed in 6 patients and deranged liver function tests were noted in 5 patients after starting injection Remdesivir, however it was not treatment limiting factor in our study, hence all our patient continued to receive the drug for 5 days. Heart rates and LFTs normalized after discontinuation of the drug. There were no obvious side effects noted following administration of any of the other drugs. Convalescent plasma therapy was tried in 4 patients shown in table 3.

The most common complication observed was ARDS (94%) followed by AKI (52%) and MODS (52%) and secondary bacterial infection (52%). The other complications observed were hepatitis and myocarditis. Of the 26 patients who had acute kidney injury 3 patients required hemodialysis. The case fatality rate in our study was 38% (n=19). Table 4.

On comparing various parameters among survivors and non survivors, mortality was observed more in age groups 45-54 years than the elderly population. Smokers and hypertensives constituted significantly higher proportions in non survivors. Clinically, systolic blood pressure and PCO2 were significantly more in non survivors where PO2 and duration of hospital was significantly lower (p value<0.05). Patients treated with Tocilizumab had significantly higher mortality (p=0.04), whereas patients treated with Favipravir and Remdesivir had lower mortality which was
Discussion

COVID 19 is one of the worst hit pandemic of the 21st century, and has greatly affected Indian country in terms of breakdown of economy and burden on our health sector \[11\]. Though different researches are being conducted on the overall epidemiological characteristics \[9, 10\], clinical presentations \[10\] and preventive measures \[12\], the studies on critically ill patients and their outcome is very limited. Hence this study was conducted to focus on the clinical parameters, response to treatment, outcome and predictors of mortality in acutely ill patients requiring intensive care.

The mean age of patients in our study was 55.96 ± 14.52 years which is similar to the study conducted by Chavali et al., in Maharashtra.\[13\]. Male preponderance was observed in our study as it was in other similar studies, probably due to high mobility and socialization among male gender when compared to females \[10,13,14\]. The mean duration symptoms before hospital admission was nearly 6 days in our study which was comparable to studies conducted by Bhatraju et al., (7 days) and Xie et al., (6 days) and few other studies thus indicating that delay in presentation more than 5 days of onset of symptom has high chances of severe illness and need for intensive care \[7,15,16\]. Though hypertension was significantly more prevalent among non survivors, we observed that the most common underlying co morbidity in all our patients was Diabetes Mellitus which was against several international studies that reported hypertension to be the predominant underlying comorbidity \[5,8,14,17\]. However, a meta-analysis by Awdhesh Kumar Singh and Anoop Misra have concluded that Diabetes Mellitus was more prevalent among Indian COVID 19 patients.\[18\]. Likewise, history of smoking significantly correlated with mortality as it was also found with a report by Liu et al., and Polverino\[21,22\]. Yet there is also a hypothesis that an inverse relationship exists between the two. This needs to be studied further for future references. The ECG changes noted were secondary to viral myocarditis, drug effect or arrhythmias and RBBB due to severe pulmonary involvement, and it did not significantly affect the mortality \[15\]. The duration of ICU stay is varying among different studies in different parts of the world. Respiratory failure with severe ARDS was the most common complication in our study as well as reports by Wang et al., Guan et al., and Xie et al., as pulmonary epithelium serves as receptor to the viral protein, hence being commonly
This leads to several patients requiring oxygen supplementation in the form of NIV, HFNO or invasive ventilation. We did not observe any statistical significance between mode of ventilation required and mortality. Among the treatment modalities, there was a significant improvement among those treated with antivirals (Favipravir and Remdesivir) which act by inhibiting viral RNA polymerase and has been widely accepted choice of treatment for patients requiring oxygen support in addition to steroids\cite{23,24}. On the other side, mortality was significantly higher in the patients who were given Tocilizumab, as is also being withdrawn from several guidelines with inputs from various studies as it did not show any survival benefit\cite{25}. We did not observe any significant difference between survivors and non survivors among those who were treated with steroids or antibiotics, though there have been several evidences on survival benefits of systemic corticosteroids in critical patients\cite{7,26}. The mortality rate in our study is 38% which was similar to another study by Wang et al., conducted on intensive care patients\cite{19}.

The limitation of this study is that it’s a single center retrospective study. Furthermore, we enrolled only those subjects within period of March 2020 to August 2020, hence interpretation of the results might be limited by the sample size. Third, it also included patients who were admitted early during the emergence of this pandemic in our locality, when there were not enough evidences to support the treatment options available, which might have led to increase in complication, ICU stay and even mortality.

To conclude, this series showed that middle aged men with comorbidities and history of smoking are at higher risk of severe COVID illness and have poor outcome. Also delay in presentation and treatment initiation has led to burden on health care resources, saturating the available ICU beds. Hence, a larger study group with multicenter involvement is required in each state to tackle the regional and ethnic differences in public awareness and individual treatment response, more trials are to be conducted to commit to a standard treatment protocol and with active contribution ofevery individual in the society, these hardships can be overcome to sustain the human race.

References


