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Original Article

Anaesthesia Section

Clinical Characteristics and Outcome of Critically Ill SARS-CoV-2 Patients Admitted to Intensive Care Unit of a Tertiary Care Hospital in North India: A Retrospective Study

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ABSTRACT

Introduction: World Health Organisation (WHO) declared the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) outbreak a pandemic on 11 March 2020, due to the constantly increasing number of cases outside China. Previously, India had global record of highest single day spike of Corona Virus Disease-19 (COVID-19) cases, with 97,894 cases on 17th September 2020.

Aim: To find out the demographic and clinical characteristics of critically ill patients of SARS-CoV-2 and comparing the outcomes of patients admitted in COVID dedicated Intensive Care Unit (ICU) with and without co-morbidities and also in different age groups and sex.

Material and Methods: This retrospective study from July 2020 to December 2020 was a single centre observational experience of management of COVID-19 patients at COVID dedicated ICU in Firozabad, India. The following data were recorded: age, sex, comorbidities and mode of oxygen delivery (invasive mechanical ventilation, non-invasive mechanical ventilation, high flow nasal canula). Chi-square test was used to compare the outcomes of patients admitted in COVID dedicated ICU with and without co-morbidities and also in different age groups and sex.

Results: In this study, the data of 120 severely ill COVID-19 patients were reviewed. The mean age of patients were (58±15.29) years and male to female ratio was 3:1. At least one comorbid condition was reported in 53.3% of patients-most common being Hypertension (36.6%) followed by Diabetes mellitus 2 (20%), COPD (15%). Then Cardiovascular Diseases, Renal, Liver diseases and ailments followed. All patients admitted to COVID ICU had moderate to severe Acute Respiratory Distress Syndrome (ARDS). Older age (61 years and above, mortality 17%), male sex (16.7% deaths among 90 critically ill male COVID patients) and presence of comorbid conditions appear to have higher mortality in this study. However apart from comorbid conditions (p=0.001) none was statistically significant. The overall mortality in this study of 120 critically ill COVID patients was 14.16%.

Conclusion: From this study, it can be suggested that survival of critically ill COVID patients can further be improved by better management of their comorbid conditions and avoiding complications of invasive ventilation. However, further multicentric studies with large sample size are needed to confirm these findings.

Keywords: Severe acute respiratory syndrome-coronavirus-2, Coronavirus disease-2019, High flow nasal canula, Mechanical ventilation, Remdesivir

INTRODUCTION

World Health Organisation (WHO) declared the SARS-CoV-2 outbreak a pandemic on 11 March 2020, due to the constantly increasing number of cases outside China [1]. Patients infected with SARS-CoV-2 can develop Corona Virus Disease-19 (COVID-19) which has resulted in high rate of hospitalisation and ICU admissions [2]. In China, among hospitalised COVID-19 patients, rate of ICU admissions varies from 5%-32% [3,4]. The first case of COVID-19 in India was reported on 30th January 2020 [5]. Previously, India had global record of highest single day spike of COVID-19 cases, with 97,894 cases on 17th September 2020 [6]. The new grim record was set by US who reported 225,201 new COVID-19 cases in 24 hours on 5th December 2020. According to WHO website, case fatality rate of COVID-19 in India is 1.43% as on 5th February 2021, which is much less than global average of 2.17% and is further declining. According to previous studies, the outcome of COVID-19 is adversely affected by presence of comorbidity (hypertension, cardiac disease, diabetes mellitus, asthma, Chronic Obstructive Pulmonary Disease (COPD), tuberculosis, pneumonia, ARDS, renal disease and hepatic disease) history of smoking, and history of substance use, male gender and age greater than 60 years were more likely to die or develop undesirable outcomes [7,8]. The age related multiple co-morbid conditions and physiological changes facilitate atypical clinical presentation [9,10]. Immunosenescence is term used for several age related changes in immune system of older individual, it involves several cellular and molecular elements of both innate and adaptive immune systems making older individuals more vulnerable to infectious diseases [11]. In addition to this, high prevalence of cardiovascular diseases, malignancy and other chronic diseases are responsible for poor outcome in older individuals [12].

Due to complexity of its transmissions and the lack of a proven treatment, COVID-19 is posing a very high challenge globally [13,14]. In the developing countries, this disease may be more catastrophic due to poor healthcare system, lack of skilled health personnel, high illiteracy and low awareness of the disease and its preventions, scarce ICU and a limited number of mechanical ventilators and prevalence of co-morbidities/infections along with malnutrition [14].

The outcomes of COVID-19 in different studies vary widely. Rate of ICU admissions of COVID-19 patients was higher which ranged from 3%-100% of confirmed cases [15-17]. The mortality of critically ill COVID-19 patients in different studies was very high which ranged from 6%-86% of admitted patients [15-17]. The aim of this study was to find out the demographic and clinical characteristics of critically ill patients of SARS-CoV-2 and comparing the outcomes of patients from COVID dedicated ICU in different age, sex and in those with and without comorbid conditions.

MATERIALS AND METHODS

This retrospective observational study was carried out from July 2020 to December 2020 is a single centre, COVID dedicated ICU of state-run tertiary care hospital in Firozabad, India. After approval from Institutional Ethics Committee (Ref. No-ASMC/IEC/2020-21/05) deidentified data of critically ill patients, who were laboratory Confirmed for SARS-CoV-2 infection, and admitted to COVID dedicated ICU was reviewed.

Inclusion criteria: Data of all patients who were admitted to COVID dedicated ICU during the mentioned study period were included in this study.

Exclusion criteria: Data of those patients who were referred to other centres during study period.

According to the WHO guidance, [18] laboratory confirmation for SARS-CoV-2 was defined as a positive result of Real-Time Reverse Transcriptase–Polymerase Chain Reaction (RT-PCR) assay of nasal and pharyngeal swabs. This guideline was implemented locally.

Only those COVID-19 patients who had severe disease, were admitted to COVID dedicated ICU. Severe COVID-19 disease is defined by Ministry of Health and Family Welfare, India as clinical sign of pneumonia plus one of the following; respiratory rate > 30 breaths/min, severe respiratory distress, Spo_2 <90% on room air [19]. Patients were discharged from ICU after clinical recovery and negative: RT-PCR report (after resolution of symptom).

Data collection: In this study, clinical data were collected from indoor files of COVID ICU admissions. A total of 128 severe COVID-19 patients were admitted to COVID dedicated ICU from July 2020 to December 2020. Among these 128 severe COVID patients, eight patients were referred to other centres. All referrals were due to the patients or their family's willingness to sought treatment at top corporate hospitals in metropolitan cities. So, sample size of this study was 120. Data of these admissions were collected and recorded- age, sex, comorbidities and mode of oxygen delivery (invasive mechanical ventilation, non-invasive mechanical ventilation, high flow nasal canula). The number of patients who were discharged successfully and died during the treatment were recorded. Different age groups were defined as follows: up to 40 years; 41 through 60 years; 61 years and above.

STATISTICAL ANALYSIS

Chi-square test was used to compare the outcomes of critically ill COVID patients with and without co-morbidity, in different age groups and in both sexes. The statistical significance is defined as p-value<0.05. Analyses is performed using SAS 9.4 (previously "Statistical Analysis System").

RESULTS

In this study, the data of 120 severely ill COVID-19 patients were reviewed who were admitted to COVID dedicated ICU between July 2020 to December 2020. By the 25th of January 2021, all these 120 COVID ICU admissions have been disposed. Among these 120 admissions there were 90 male patients and 30 female patients with male to female ratio of 3:1. The age of patients varies from 17-88 years with a mean age of (58±15.29) years [Table/Fig-1].

Age group	Male	Female	Total
Under 40 years	12	3	15
41 to 60 years	41	11	52
61 years and above	37	16	53
Total	90	30	120

[Table/Fig-1]: Age & sex distribution of critically ill COVID patients.

In this study, 64 (53.3%) COVID ICU admissions have at least one comorbid condition. Hypertension was the most common comorbid condition reported in 44 (36.6%) admissions, followed by type 2 diabetes mellitus which was found in 24 (20%) patients. Eighteen (15%) patients had Chronic Obstructive Pulmonary Disease (COPD) [Table/Fig-2].

Comorbid condition	Number of patients
Hypertension	44 (36.6%)
Diabetes mellitus	24 (20%)
Chronic obstructive pulmonary disease (COPD)	18 (15%)
Cardiovascular diseases	16 (13.3%)
Chronic kidney disease	10 (8.3%)
Chronic liver disease	08(6.6%)
Active Pulmonary Tuberculosis	06(5%)

[Table/Fig-2]: Different comorbid condition among critically ill COVID patients.
*As patients could report more than one comorbid condition so, summation of percentage exceeds category's percentage and may exceed 100% (n=64)

All COVID-19 patients admitted to COVID dedicated ICU had moderate to severe ARDS (as per Berlin definition) [20]. The median baseline Pao_2/Fio_2 ratio was 124 (range 72 to 184). Chest radiograph was taken in all patients at the time of admission and daily thereafter. Bilateral infiltrates were found in radiographs of 86 (71.7%) patients and unilateral infiltrate in radiograph of 34 (28.3%) patients. Pleural effusion was not evident in any chest radiograph. Baseline laboratory investigations were done at the time of ICU admissions, which shows normal median total leucocyte count 7.6 (5.2-11.3)×10^3/cmm, elevated median serum ferritin 614 (240-964) ng/mL and elevated median C-Reactive Protein (CRP) 108 (44-152) mg/L.

All COVID ICU patients were monitored continuously by pulse oximetry. The highest mode of oxygen support in these patients was documented and it was determined by Spo_2, respiratory rate and breathing pattern of the patient and Arterial Blood Gas Analysis (ABG). The oxygen support was escalated and de-escalated according to the clinical condition of patients, and for this reason all deaths were reported in patients who were on invasive ventilation. The Extracorporeal Membrane Oxygenation (ECMO) facility is not available at the centre. Among these 120 patients, 40 (33.3%) patients were put on invasive ventilation whereas, 48 (40%) patients were managed with non-invasive ventilation. High-Flow Nasal Cannula (HFNC) was used initially in 48 patients (40%), but HFNC failure was reported in 13 cases and 3 patients complained of severe headache and lacrimation due to high flow of HFNC. All these 16 patients (13+3) were shifted to non-invasive ventilation, the use of high flow nasal canula was sufficient to manage 32 (26.7%) patients [Table/Fig-3].

Highest mode of oxygen support	Number of patients
Invasive ventilation	40 (33.3%)
Non-invasive ventilation	48 (40%)
High flow nasal canula	32 (26.7%)

[Table/Fig-3]: Highest mode of oxygen support in critically ill COVID patients.

Apart from oxygen support, severe COVID patients were treated with parenteral antibiotics guided by total leucocyte counts and in few cases by blood culture, parenteral methyl prednisolone, parenteral remdesivir, subcutaneous Low Molecular Weight Heparin (LMWH) and other supportive medications (vitamin C, zinc, paracetamol, IV fluids, vasopressors etc.,). Treatment of comorbid conditions was done accordingly.

Among these 120 COVID ICU admissions, 1 patient who was on invasive ventilation developed bilateral pneumothorax and was managed with bilateral intercostal drains but unfortunately died. One patient suddenly developed massive haematemesis and succumbed. Two patients developed urethral bleeding and one epistaxis, all were successfully managed by administrating IV tranexamic acid 500mg 12 hourly till bleeding subsides and withholding LMWH, which was given 0.4 mg subcutaneously twice daily.

Among these 120 COVID ICU admissions, 103 patients were successfully treated and discharged from the ICU rest 17 patients

died during the course of treatment. In this study, only one patient who had no comorbid condition died due to development of bilateral pneumothorax and remaining 16 death were among patients who had at least one comorbid condition. In this study, it was observed that presence of comorbid condition is a poor prognostic factor and it is found to be statistically significant (p=0.001) [Table/Fig-4].

Groups	Total number of patients	Number of patients discharge successfully	Number of patients died	p-value
With co-morbid condition	64	48 (75%)	16 (25%)	0.001
Without co-morbid condition	56	55 (98.2%)	01 (1.8%)	

[Table/Fig-4]: Outcome of critically ill COVID patients in co-morbid and non-co-morbid groups.
*Chi-square test was used to compare the outcomes of groups

Male sex has also appeared to be poor prognostic factor in critically ill COVID patients. Fifteen deaths were among 90 critically ill male COVID patients (16.7%) whereas, only 2 deaths were reported in 30 critically ill female COVID patients (6.7%). However, it was not found to be statistically significant (p>0.05) [Table/Fig-5].

Groups	Total number of patients	Number of patients discharge successfully	Number of patients died	p-value
Male	90	75 (83.3%)	15 (16.7%)	>0.05
Female	30	28 (93.3%)	02 (6.7%)	

[Table/Fig-5]: Outcome of critically ill COVID patients in both sex groups ; * Chi-square test was used to compare the outcomes of groups

There was only one death under 40 years of age (mortality 6.7%). In age group of 41-60 years, 7 patients died (mortality 13.5%) and 45 were discharged successfully. In age groups 61 years and above 9 patients died (mortality 17%) and rest 44 patients were discharged successfully. However, difference in mortality of different age groups was not statistically significant (p>0.05) [Table/Fig-6]. The overall mortality in this COVID ICU study is found to be 14.16%.

Age group	Total number of patients	Number of patients discharge successfully	Number of patients died	p-value
Under 40 years	15	14 (93.3%)	1 (6.7%)	>0.05
41 to 60 years	52	45 (86.5%)	7 (13.5%)	
61 years and above	53	44 (83%)	9 (17%)	
Total	120	103(85.8%)	17 (14.16%)	

[Table/Fig-6]: Outcome of critically ill COVID patients in different age groups.
*Chi-square test was used to compare the outcomes of groups.

DISCUSSION

In this study, critically ill COVID patients were predominantly male with a mean age of (58±15.29) years. An 87.5% of COVID ICU Patients were above 40 years of age. In comparison to this, study conducted in Italy by Grasselli G et al., shows 82% of critically ill patients were male and median age was 63 [21].

In the present study, 53.3% of critically ill patients had at least 1 comorbid condition, which is less as compared to 68% reported by Grasselli G et al., and Wang D et al., (72.2%) [21,22]. We reported higher percentage of chronic obstructive pulmonary disease (COPD) 15% in our patients as compared to 4% of study conducted by Grasselli G et al., [21]. The higher prevalence of COPD in current study is due to predominant habit of bidi smoking in local area and local population is mainly comprises of factory workers.

In this study, bilateral infiltrates in chest radiograph were found in 71.7% patients and unilateral in 28.3% patients, this percentage was 87.5% and 12.5%, respectively in another study conducted in western India [23].

Baseline normal median leucocyte count 7.6 (5.2-11.3)×10^3/cmm and elevated median serum ferritin 614 (240-964) ng/mL and C-Reactive Protein (CRP) 108(44-152) mg/L was also in accordance with study conducted in western India [23].

The majority of patients were admitted to COVID ICU in need of respiratory support due to acute hypoxemic respiratory failure. In this study, 33.3% patients were intubated and put on invasive ventilation, this percentage of invasively ventilated patients is less as compared to other recently reported COVID ICU studies: 42% (Wuhan, China) [8], 47% (Wuhan, China) [22], 71% (Washington State, US) [7]. The need of invasive ventilation in our ICU was slightly higher than data reported by two Chinese studies from Wuhan with rates of 14.5% and 17%, respectively [3,24].

In this study, 40% of critically ill COVID patients were managed with non-invasive ventilation which is similar to the data collected from Wuhan, china (42%) [22]. In different studies use of noninvasive ventilation varied widely from 56% in another study of Wuhan China [8] to 19% in Washington State US [7].

In a retrospective review of COVID patients in two hospitals of Chongqing, China 27 patients experienced severe acute respiratory failure out of which 17 patients (63%) were treated with HFNC for first time. The HFNC failure was reported in 7 cases (41%) [25]. In this study, we initially put 48 patients (40%) on HFNC. A 32 COVID ICU patients (66.6% of initial HFNC trial) were successfully treated with HFNC, whereas 16 patients who were initially on HFNC shifted to non-invasive ventilation. Among these16 patients, 13 (27% of initial HFNC trial) were shifted to non-invasive ventilation because of HFNC failure and 3 patients (6.3% of initial HFNC trial) who were otherwise maintaining spo_2 and Pao_2 complained severe headache and lacrimation due to high flow of HFNC, hence shifted to non-invasive ventilation.

In this study, one patient (0.83%) developed bilateral pneumothorax, which is in accordance with other retrospective COVID studies where reported incidence of pneumothorax is 1 to 2 % [8,13]. One patient was succumbed to massive haematemesis in this study reported incidence of upper GI bleed in COVID patients is 0.47% in a study conducted by Mauro A et al., [26]. In this study, two patients developed urethral bleeding and one epistaxis all were treated successfully by intravenous tranexamic acid and withholding LMWH. Bathula SSR et al., reported a case series of four COVID positive epistaxis patients, all were on LMWH [27].

Presence of comorbid condition adversely affect outcome, as out of 17 COVID patient deaths, 16 patients had at least one comorbidity and only one non-comorbid patient died due to development of bilateral pneumothorax. In this study, we observed that presence of comorbid condition is a poor prognostic factor and it is found to be statistically significant (p=0.001). In a study conducted by Sanyaolu A et al., it was reported that COVID-19 patients with comorbidities were more likely to develop a more severe course and progression of the disease [28].

Male sex is also appeared to be poor prognostic factor in critically ill COVID patients. Only two death were reported in 30 critically ill female COVID patients (6.7%), whereas rest 15 death were among 90 critically ill male COVID patients (16.7%). However, it was not found to be statistically significant (p>0.05). Yanez ND et al., found that man had a higher risk of COVID 19 death than women [29].

There was only one death in under 40 years of age (mortality 6.7%), in 41 to 60 years of age mortality was 13.5% and in 61 years and above age group mortality was 17%. According to the study conducted by Yanez ND et al., the mortality rate of COVID-19 was strikingly higher in persons aged 65 years or older [29].

Compared to study conducted by Grasselli G et al., who reported 26% ICU mortality of critically ill COVID patients, mortality at the COVID dedicated ICU is 14.16% [21]. The lesser mortality in comparison to Italy is partially because we have younger population and partially because COVID outbreak was later in our locality so we had some knowledge regarding the nature and management of disease. At the centre mortality of critically ill COVID patients is decreasing with time.

Limitation(s)

Firstly, the patients comprised of small local population so data derived from this study is difficult to compare with other studies. Secondly, follow-up time is very less and the difficulties faced by the discharged patients some of which may have breathing problems are not known.

CONCLUSION(S)

Among 17 COVID patient deaths, 16 patients had some comorbidity and only one non-comorbid patient died due to bilateral pneumothorax as a complication of invasive ventilation. Males were predominant among critically ill patients, mortality of male patients (16.7%) was higher than female patients (6.7%). Age specific mortality was highest (17%) in older patients, 61 years and above. Overall mortality of critically ill COVID patients at the ICU was 14.16%. From this study, it can be suggested that survival of critically ill COVID patients can further be improved by better management of their comorbid conditions and avoiding complications of invasive ventilation. However, further multicentric studies with large sample size are needed to confirm these findings.

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