



Epidemiological & clinical characteristics & early outcome of COVID-19 patients in a tertiary care teaching hospital in India: A preliminary analysis

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Received July 4, 2020

Background & objectives: In this study we describe the epidemiological data, comorbidities, clinical symptoms, severity of illness and early outcome of patients with coronavirus disease 2019 (COVID-19) from a tertiary care teaching hospital in New Delhi, India.

Methods: In this preliminary analysis of a prospective observational study, all adult patients admitted to the screening intensive care unit (ICU) of the institute who fulfilled the WHO case definition of COVID-19 and confirmed to have SARS-CoV-2 infection by reverse transcription-polymerase chain reaction were included. Demographics, clinical data and 24 h outcome were assessed.

Results: The preliminary analysis of 235 patients revealed that the mean age was 50.7±15.1 yr and 68.1 per cent were male. Fever (68.1%), cough (59.6%) and shortness of breath (71.9%) were the most common presenting symptoms. Hypertension (28.1%) and diabetes mellitus (23.3%) were the most common associated comorbid illnesses. Patients with mild, moderate, severe and critical illness were 18.3, 32.3, 31.1 and 18.3 per cent, respectively, at the time of ICU admission. The proportions (95% confidence interval) of patients requiring any form of oxygen therapy, oxygen therapy by high-flow nasal cannula and invasive mechanical ventilation were 77, 21.7 and 25.5 per cent, respectively, within 24 h of hospital admission. The 24 h ICU mortality was 8.5 per cent, and non-survivors had higher respiratory rate ($P<0.01$, $n=198$) and lower baseline oxyhaemoglobin saturation ($P<0.001$, $n=198$) at presentation and higher baseline serum lactate ($P<0.01$, $n=122$), total leucocyte count ($P<0.001$, $n=186$), absolute neutrophil count ($P<0.001$, $n=132$), prothrombin time ($P<0.05$, $n=54$) and INR ($P<0.05$, $n=54$) compared to survivors.

Interpretation & conclusions: Nearly half of the patients presented with severe and critical disease and required high-flow nasal oxygen or invasive mechanical ventilation at admission. Severity of the presenting respiratory illness, haematological parameters and lactate rather than age or presence of comorbidity predicted early death within 24 h.

Key words COVID-19 - epidemiology - high-flow nasal cannula - intensive care unit - lactate - mechanical ventilation - mortality

Early reports of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-associated coronavirus disease 2019 (COVID-19) suggested that it was a SARS-like atypical pneumonia in which 26 to 33 per cent of patients required intensive care with a mortality of 4 to 15 per cent¹⁻³. A large series of 72,314 infected individuals has since refined these initial estimates in China to severe disease in 14 per cent and a case fatality rate of 2.3 per cent⁴. Subsequently, large series from China⁵, Lombardy, Italy⁶ and New York, USA⁷ described the clinical presentation and early outcome characteristics of COVID-19 patients.

The first case of COVID-19 was reported in India on January 31, 2020⁸ and by July 31, 2020, more than 1.6 million patients were diagnosed as COVID-19 and more than 36,000 patients died⁹. We describe here the epidemiological data, comorbidities, clinical symptoms and severity of illness and early outcome of patients with COVID-19 from a tertiary care teaching hospital in New Delhi, India.

Material & Methods

In this prospective observational study, all adult patients who fulfilled the WHO case definition of SARS-CoV-2 infection¹⁰, were included within 24 h of admission. A confirmed case of COVID-19 was diagnosed by a real-time reverse transcription-polymerase chain reaction (RT-PCR) of the nasopharyngeal and oropharyngeal swabs. All such patients diagnosed between May 11 and June 28, 2020 and admitted in the screening intensive care unit (ICU) of All India Institute of Medical Sciences (AIIMS), New Delhi, were included in this study. The institute's Ethics Committee approval (IEC: 321/27.04.2020, RP-09/2020) was obtained before data collection. Written informed consent was obtained from each participant or his/her legally acceptable representative.

The following data were retrieved from the case history and available clinical investigation of the patients by manual as well as electronic data record-keeping system: (i) demographic parameters (age, sex and body weight) of the patients; (ii) presenting symptoms and duration of symptoms; (iii) presence of any comorbid illness [hypertension, diabetes, coronary artery disease, malignancy, neurologic diseases, chronic obstructive pulmonary disease, bronchial asthma, chronic kidney diseases (CKDs), chronic liver disease (CLD) *etc.*]; (iv) any available investigations (complete blood count, liver and kidney function tests, electrolytes, chest X-ray *etc.*); (v) mode of respiratory

support [oxygen by facemask, high-flow nasal cannula (HFNC), non-invasive or invasive ventilation]; and (vi) death within 24 h of admission.

Statistical analysis: The data were entered in a Microsoft Excel spreadsheet, and statistical analysis was performed in STATA version 13 for Mac OS X (StataCorp LP, TX, USA). All the continuous data were presented as median (interquartile range, IQR) and categorical data were presented as absolute number and percentages. Non-parametric tests were used for all analyses, and clinical characteristics were compared between survivors and non-survivors.

Results & Discussion

Data from 235 adult patients were analyzed in this study who had a mean age of 50.7±15.1 yr, of whom 68.1 per cent were male (160 of the 235 patients). The median (IQR) duration of symptom was four (2-5) days before admission in the hospital. Fever (68.1%), cough (59.6%) and shortness of breath (71.9%) were the most common presenting symptoms. Twenty nine of the 235 patients (12.3%) also had some degree of gastrointestinal symptoms at the time of admission. Two patients presented with non-ST elevation myocardial infarction and five patients presented with acute ischaemic stroke. As per the WHO classification, number (%) of patients with mild, moderate, severe and critical illness were 43 (18.3%), 76 (32.3%), 73 (31.1%) and 43 (18.3%), respectively, at the time of presentation. Twenty patients (8.5%) died within 24 h. The number and proportion [95% confidence interval (CI)] of severe and critically ill patients who died within 24 h of ICU admission was 7 [9.6 (4.7-18.5)%] and 12 [27.9 (16.8-42.7)%], respectively. No patient died in the moderate category, and one patient from the mild category died from acute myocardial infarction with cardiogenic shock. All other deaths were due to refractory hypoxia.

Oxyhaemoglobin saturation (SpO₂) in room air and respiratory rate (RR) at the time of ICU admission were recorded in 198 patients. The median (IQR) SpO₂ and RR at the time of ICU admission were 90 (80-96) per cent and 26 (22-30) breaths/min, respectively. Hypertension (n=65, 28.1%) and diabetes mellitus (n=54, 23.3%) were the most common associated comorbid illness. CKD was present in 22 (9.5%) of the patients, 10 (4.3%) patients had CLD and 26 (11%) had associated underlying malignancy. All the CKD patients were in various stages between stages 3 and 5. None of the malignancy patients were in stage 4. The mean

haemoglobin level was 11.3 ± 2.6 mg/dl, and the median (IQR) total leucocyte count and platelet count were 9000(6200-12,400)/and $1.7(1.2-2.5) \times 10^5/\mu\text{l}$, respectively, at the time of admission. All the comorbidities and laboratory investigations are summarized in the Table.

Chest X-ray was available at the time of diagnosis with 159 patients, and the number and proportion (95% CI) of patients who had bilateral involvement was 128 [80.5 (73.7-85.9)%] and 14 [8.8 (5.3-14.2)%] had unilateral involvement. Normal chest X-ray was present in 17 [10.7 (6.8-16.5)%] patients at the time of diagnosis.

The proportion (95% CI) of patients requiring any form of oxygen therapy, oxygen therapy by HFNC and invasive mechanical ventilation was 77 (71.2-81.9), 21.7 (16.9-27.4) and 25.5 (20.4-31.5) per cent, respectively, within 24 h of hospital admission. All the patients except the ones with mild disease received

hydroxychloroquine and steroid as per the institute's protocol. Twenty four hour ICU mortality (95% CI) was 8.5 (5.6-12.8) per cent, and non-survivors had higher baseline serum lactate ($P < 0.001$, $n=122$), total leucocyte count ($P < 0.001$, $n=186$), absolute neutrophil count ($P < 0.001$, $n=132$), prothrombin time ($P < 0.05$, $n=54$) and INR (international normalized ratio) ($P < 0.05$, $n=54$). Non-survivors also had higher RR ($P < 0.01$, $n=198$) and lower baseline SpO_2 ($P < 0.001$, $n=198$) at presentation. However, age, baseline haemoglobin, platelet count, creatinine, bilirubin and absolute lymphocyte count were similar between survivors and non-survivors. There was no difference in age or comorbidities between survivors and non-survivors (Table).

Epidemiology and baseline parameters of this representative Indian population were similar to those of previously observed data from other countries such as China, USA and Italy⁵⁻⁷. The median incubation period

Table. Demographic characteristics, comorbidities and laboratory parameters in survivors and non-survivors at the time of presentation

Parameters	All patients (n=235)	Survivors (n=215)	Non-survivors (n=20)	P
Age (yr)	50 (40-60)	50 (40-60)	51 (40.5-60)	0.92
Sex (M/F)	160/85	146/79	14/6	>0.99
Duration of symptoms (days)	4 (2-5)	4 (3-5)	3 (2-5)	0.18
Comorbid illness				
Hypertension (yes/no)	65/170	62/153	3/17	0.30
Diabetes mellitus (yes/no)	54/181	51/164	3/17	0.57
CAD (yes/no)	13/222	13/202	0/20	0.61
CKD (yes/no)	22/213	19/196	3/17	0.41
CLD (yes/no)	10/225	8/207	2/18	0.21
COPD (yes/no)	5/230	5/210	0/20	>0.99
Malignancy (yes/no)	26/209	24/191	2/18	>0.99
Laboratory investigations				
Haemoglobin (g/dl) (n=184)	11.5 (9.8-13.3)	11.5 (9.8-13.2)	12 (8.3-13.4)	0.87
Total leucocyte count unit (cells/ μl) (n=186)	9000 (6,200-12,400)	8600 (5,890-12,000)	13,500 (10,500-15,800)	<0.001
Absolute neutrophil count (cells/ μl) (n=132)	7042 (4,020-10,400)	6300 (3,745-9,856)	11,334 (8,837-13,462)	<0.001
Absolute lymphocyte count (cells/ μl) (n=134)	1388 (1,020-1,866)	1380 (951-1,833)	1760 (1,326-2,043)	0.17
Platelet count ($10^3/\mu\text{l}$) (n=181)	169 (112-242)	166 (111-241)	184 (150-320)	0.16
Prothrombin time (sec) (n=54)	13.8 (12.7-15.6)	13.5 (12.7-15.3)	15.6 (14.8-19.7)	<0.05
INR (n=54)	1.17 (1.09-1.32)	1.13 (1.07-1.3)	1.3 (1.3-1.73)	<0.05
Serum creatinine (mg/dl) (n=189)	1 (0.8-1.5)	1 (0.8-1.5)	1.2 (0.9-1.5)	0.28
Serum bilirubin (mg/dl) (n=123)	0.8 (0.5-1.35)	0.85 (0.5-1.35)	0.6 (0.5-0.9)	0.32
Arterial lactate (mmol/l) (n=122)	1.9 (1.3-3.2)	1.8 (1.25-2.75)	4.1 (2.4-6.4)	0.002

Data expressed as proportion or median (IQR); Mann-Whitney U-test or Fisher's exact test applied as applicable. IQR, interquartile range; CAD, coronary artery disease; CKD, chronic kidney disease; CLD, chronic liver disease; COPD, chronic obstructive pulmonary disease; INR, international normalized ratio

was four days, similar to the data from China⁵. Fever, cough and difficulty in breathing were the predominant presenting symptoms and desaturation and tachypnoea were the common signs. Gastrointestinal symptoms were uncommon, similar to other published studies⁶. In line with previous studies^{5,6} hypertension was the most common comorbidity followed by diabetes and other disorders.

Nine of the 10 patients had chest X-ray abnormality, and bilateral disease was most common (80.5%). However, 10.7 per cent (n=17) patients did not have any abnormality on chest X-ray. Data from Wuhan, China, also revealed that as many as 17.5 per cent of the patients did not have any abnormality on chest X-ray or CT scan⁵.

Requirement of endotracheal intubation and invasive mechanical ventilation was much lower (25.5%) in the present study as compared to other initial series from Italy⁶ and USA⁷, which reported intubation rates as high as 88 and 71 per cent, respectively, among severe COVID-19 cases admitted to the hospital. However, two studies from China reported less intubation rate (15 and 17%) in patients admitted with severe disease^{5,11}. This may be due to the differences in intubation criteria adopted in various centres. In the current study, invasive mechanical ventilation was initiated if SpO₂ was <90 per cent and RR >40/min for more than 10-30 min in a patient already on HFNC or non-invasive ventilation or in a patient who had already developed haemodynamic instability or deterioration of neurologic status.

HFNC was required in one-fifth of the patients at ICU admission in our study. If patients had RR >24/min and/or SpO₂ <94 per cent in spite of oxygen by facemask at 10 l/min flow for 30 min, it was considered failure of oxygen therapy by facemask and HFNC was initiated as per our management protocol. Based on our initial experience (unpublished data), HFNC can be considered to potentially delay or avoid intubation as observed by other investigators¹². However, this needs further exploration in the setting of severe COVID-19 pneumonia.

In the present study, higher total leucocyte count, absolute neutrophil count and prothrombin time were observed among non-survivors compared to survivors. Higher neutrophil count and prolonged prothrombin time have been reported as poor prognostic markers by previous investigators¹³. Although lymphopenia is the

most consistent haematological observation in these patients, nadir of lymphocytes may develop over a few days during hospitalization and it may be missed in the data at presentation¹³.

In this preliminary analysis, early outcome was reported as 24 h ICU mortality. This was done as many of the patients were at various stages of their hospital admission and it was not possible to report hospital mortality or discharge data for all the patients. Presentation with severe disease (tachypnoea and desaturation) and presence of elevated lactate, elevated total leucocyte and neutrophil count and deranged coagulation parameters were identified as risk factors for early death. Therefore, the severity of illness rather than demographics was an important determinant of early death in ICU. However, in the analysis of overall hospital mortality, whether age and comorbidity become important risk factors remains to be seen.

The study had certain limitations. Complete follow up data were not presented as many patients were at various stages of hospitalization. Rate of co-infections with other bacterial/viral disease and baseline medication use (such as type of antihypertensive/antidiabetic *etc.*) were not recorded. Due to the low event rate of outcome (8.5% early death), a multivariate analysis to identify risk factors could not be performed.

To conclude, nearly half of the patients with COVID-19 presented to the hospital with severe or critical disease and required either high-flow nasal oxygenation or invasive mechanical ventilation at presentation to the ICU. The 24 h ICU mortality was 8.5 per cent, and the severity of presenting respiratory illness, haematological parameters and lactate rather than age or presence of comorbidity predicted early death within 24 h.

Acknowledgment: Authors acknowledge the contribution of all the faculty and residents of all the relevant departments (e.g., Medicine and all other allied clinical departments, Microbiology, Community Medicine, Laboratory Medicine, Biochemistry and Hospital Administration), the COVID Task Force, Hospital Infection Control Committee and all the healthcare providers of the institute.

Financial support & sponsorship: None.

Conflicts of Interest: None.

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