

Clinicoepidemiological Features and Mortality Analysis of Deceased Patients with COVID-19 in a Tertiary Care Center

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ABSTRACT

Background and objective: A large number of studies describing the clinicoepidemiological features of coronavirus disease-2019 (COVID-19) patients are available but very few studies have documented similar features of the deceased. This study was aimed to describe the clinicoepidemiological features and the causes of mortality of COVID-19 deceased patients admitted in a dedicated COVID center in India.

Methodology: This was a retrospective study done in adult deceased patients admitted in COVID ICU from April 4 to July 24, 2020. The clinical features, comorbidities, complications, and causes of mortality in these patients were analyzed. Pediatric deceased were analyzed separately.

Results: A total of 654 adult patients were admitted in the ICU during the study period and ICU mortality was 37.7% (247/654). Among the adult deceased, 65.9% were males with a median age of 56 years [interquartile range (IQR), 41.5–65] and 94.74% had one or more comorbidities, most common being hypertension (43.3%), diabetes mellitus (34.8%), and chronic kidney disease (20.6%). The most common presenting features in these deceased were fever (75.7%), cough (68.8%), and shortness of breath (67.6%). The mean initial sequential organ failure assessment score was 9.3 ± 4.7 and 24.2% were already intubated at the time of admission. The median duration of hospital stay was 6 days (IQR, 3–11). The most common cause of death was sepsis with multi-organ failure (55.1%) followed by severe acute respiratory distress syndrome (ARDS) (25.5%). All pediatric deceased had comorbid conditions and the most common cause of death in this group was severe ARDS.

Conclusion: In this cohort of adult deceased, most were young males with age less than 65 years with one or more comorbidities, hypertension being the most common. Only 5% of the deceased had no comorbidities. Sepsis with multi-organ dysfunction syndrome was the most common cause of death.

Keywords: Clinicoepidemiological features, Comorbidities, COVID-19 deceased, ICU, Mortality analysis, Multi-organ dysfunction syndrome.

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INTRODUCTION

Coronavirus disease-2019 (COVID-19) emerged in China in December 2019 and engulfed the whole world in a very short period of time. Worldwide till now around 95 million patients have been infected and there have been more than 2 million deaths. India is also severely affected. It has infected more than 10 million people in India and has led to more than 1.5 lakh deaths till now.¹

The clinical spectrum of COVID-19 is varied, ranging from asymptomatic carriers to severe pneumonia, acute respiratory distress syndrome (ARDS) profiles, multi-organ involvement, and death.² Nearly 14–15% of patients develop severe disease and 5% become critically ill.³ Earlier thought to be primarily affecting the pulmonary system, a number of symptoms related to other organ systems have been widely recognized as initial presenting features of COVID-19 infection.^{4,5} These extrapulmonary manifestations can lead to complications and increase morbidity. The prevalence of mortality among hospitalized patients with COVID-19 disease varies from 6.3 to 26.85% in different parts of the world.⁶ Various studies have looked into and analyzed the risk factors for severe disease and predictors of mortality.^{7,8} However, studies regarding the clinicoepidemiological features of the deceased and causes of mortality are sparse. Some studies of COVID-19 related mortalities from US, China, Italy, and Spain are available;^{9–17} however, such

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descriptive study has not been done from Indian subcontinent so far. This study was aimed to describe the clinicoepidemiological features and the causes of mortality of COVID-19 deceased patients

admitted in our hospital during the initial period of the pandemic spread in the country from April to July.

MATERIALS AND METHODS

This was a retrospective study conducted in the COVID center of AIIMS, New Delhi, after approval from the institutional ethics committee. This study analyzed data of patients who died in the course of treatment in the ICU of COVID-19 center during the study period between April 4 and July 24, 2020. All the patients admitted to the center were moderate to severe confirmed COVID-19 patients whose real-time reverse-transcription polymerase chain reaction assay findings for nasal or pharyngeal swab specimens were positive. Mild cases were admitted in different centers. Criteria for ICU admission were patients with severe disease i.e., tachypnea with respiratory rate greater than 30/minute or SpO₂ less than 90% on room air, patient with hemodynamic instability, encephalopathy or patients with moderate disease who had risk factors for severe disease.

Data Collection

Data related to demography and clinical course of all the patients who died in the ICU during the study period was collected from their electronic medical records, patients' daily progress charts, and nursing notes. Patients' age, sex, comorbidities, complaints at the time of presentation, complications during treatment, duration of hospital stay, and cause of death were noted and analyzed. Data regarding adult and pediatric deceased were analyzed separately. Adult patients were further divided into age-groups of 18 to 50, 51 to 65, and more than 65 years and their clinical characteristics and outcomes were compared.

Statistical Analysis

The data were summarized and analyzed using STATA (Version 14.0) software and expressed as mean \pm SD/Median (min, max) and numbers and percentages as appropriate to describe the patient's demographic and clinical characteristics. Wilcoxon–Ranksum test was used to compare the non-normal quantitative values while chi-square/Fisher's exact test was applied for association between categorical variables and for comparison between stratified age-groups. Kruskal–Wallis was used to see the difference in age-groups for the days of stay followed by multiple comparison tests between the groups. A value of *p* less than 0.05 was considered as statistically significant in the study.

RESULTS

During the study period, a total of 1,420 patients (adult and pediatric) were admitted in the center. The deaths of adults and pediatric age-groups were analyzed separately.

Adult Fatalities

There were 654 adult admissions in the ICU during the study period out of which 247 died. The ICU mortality for adults was 37.7% (247/654).

Among the adult patients who did not survive, the youngest was 18 years old and the eldest was 97 years old. The median age was 56 years [interquartile range (IQR), 41.5–65] and most of them were males (65.9%). Age distribution of adults in various age-groups is given in Table 1.

Most of the adult patients who died (94.74%) had 1 or more comorbidities. Preexisting hypertension was the most frequently

seen comorbidity in 107 (43.32%) patients followed by diabetes mellitus in 86 (34.82%) patients and chronic kidney disease in 51 (20.6%) patients. Other comorbidities are tabulated in Table 1. Among the patients with comorbidities, 39% of patients had one comorbidity, 27.5% had two comorbidities, 21% had three, and 6% had more than three comorbidities. The frequency of patients with different numbers of comorbidities is depicted in Figure 1.

Twenty-nine patients had some kind of malignancy, out of which 14 suffered from hematological malignancies and remaining 15 had solid organ tumors. Besides these, other infrequently encountered comorbidities were postrenal transplant, cardiomyopathy, cholelithiasis, complete heart block with pacemaker *in situ*, HIV,

Table 1: Clinical characteristics of study patients

Characteristics	Patients
Age median (IQR) (years)	56 (41.5–65)
Age distribution (years)	No. (%)
18–50	104/247 (42.1)
51–65	86/247 (34.8)
More than 65	57/247 (23.1)
Male sex (%)	163/247 (65.9)
Comorbidities	No. of patients (%)
Hypertension	107 (43.3)
Diabetes mellitus	86 (34.8)
Chronic kidney disease	51 (20.6)
Coronary artery disease	40 (16.2)
Malignancy	29 (11.7)
Cerebrovascular event	29 (11.7)
Tuberculosis	21 (8.5)
Chronic liver disease	19 (7.7)
Hypothyroidism	13 (5.3)
Chronic obstructive airway disease	11 (4.5)
Trauma	7 (2.8)
Rheumatic heart disease	5 (2.0)
Others	55 (22.3)

IQR, interquartile range

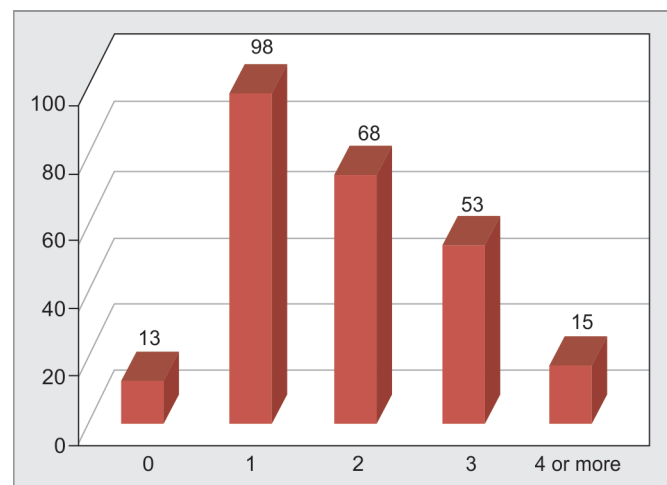


Fig. 1: Frequency of patients with different number of comorbidities

ulcerative colitis, sarcoidosis, interstitial lung disease, liver abscess, aspergilloma, shoulder abscess, peripheral vascular disease, parkinsonism, corrosive ingestion, mesenteric ischemia, dementia, depression, aplastic anemia, cervical spondylosis, systemic sclerosis, ulnar, and subclavian artery thrombosis.

The most common presenting symptom among deceased was fever (75.7%) followed by cough (68.8%), shortness of breath (67.6%), and altered sensorium (19.8%) as shown in Table 2. Besides these, other patients presented with chest pain, abdominal pain or distension, generalized weakness, diarrhea, and headache. Approximately 20% of patients presented with nonspecific complaints including myalgia, decreased urine output, jaundice, upper limb pain, generalized edema, epistaxis, and joint pain.

The patients had varying degrees of severity of illness. The initial sequential organ failure assessment (SOFA) score was calculated for 232 deceased, the data were missing for 15 patients. The mean SOFA score was 9.3 with a standard deviation of 4.07. The initial SOFA score was significantly higher in males as compared to females ($p = 0.03$). Out of 247 deceased, 60 patients were received intubated in our center from the screening area. Patients were given treatment according to the institutional protocol. The patients were initially managed on oxygen by facemask and then as the oxygen requirement increased, they were managed on high flow nasal cannula (HFNC) and noninvasive ventilation (NIV) before invasive ventilation as per SCCM guidelines. Seventy-five patients were intubated in the first 24 hours of admission. The number of patients who received HFNC and NIV are mentioned in Table 3. As the disease advanced, many patients developed multisystem involvement. However, the predominant system involved due to COVID was the respiratory system in 66% of the patients followed by the neurological system and cardiovascular system. One twenty one patients developed acute kidney injury (AKI) and 39 received RRT (Table 3). Repeat SOFA score was calculated on day 4 of admission after 72 hours. Repeat SOFA was available for 133 patients as 99 patients died within 3 days of admission to ICU.

Duration of Stay and Cause of Death

Among the deceased adults, the median duration of hospital stay was 6 days (IQR, 3–11) with maximum stay of 37 days and minimum of 1 day.

The cause of death was analyzed in all the deceased (Table 4). Sepsis with multi-organ dysfunction remained the leading cause of death (55.1%) followed by severe ARDS (25.5%), cardiogenic shock, intracranial hypertension, and suspected pulmonary embolism.

There were 41 patients who died within 24 hours of admission. Among these, 90.24% of them reported a history of one or more

comorbidities and majority had respiratory distress at presentation. Most of them were shifted intubated to our center. Four patients received cardiopulmonary resuscitation in the emergency room and were postarrest patients. The cause of death of these patients is depicted in Figure 2.

Table 3: SOFA scoring, modes of oxygen therapy given, and renal complications in deceased

ICU parameters	Mean (SD) or No. of Patients (%)
Initial SOFA (232 patients)	9.3 (4.07)
SOFA at 72 hrs (133 patients)	10.2 (3.9)
Patients received intubated	60 (24.2)
Patients intubated within first 24 hrs	75 (30.3)
Patients received HFNC	112 (45.3)
Patients received NIV	45 (18.2)
Patients developed AKI	121 (48.9)
Patients received RRT	39 (15.8)

SOFA, sequential organ failure assessment; HFNC, high-flow nasal cannula; NIV, noninvasive ventilation; AKI, acute kidney injury; RRT, renal replacement therapy

Table 4: Cause of death

Sl. No.	Cause of death	Frequency (% of patients)
1	Sepsis with multi organ dysfunction	136 (55.1)
2	Severe ARDS	63 (25.5)
3	Cardiogenic shock	23 (9.3)
4	Stroke/cerebral bleed	17 (6.9)
5	Pulmonary embolism	7 (2.8)
6	Hemorrhage	1 (0.40)

MODS, multi-organ dysfunction syndrome; ARDS, acute respiratory distress syndrome

Table 2: Distribution of presenting complaints

Presenting complaints	No. (%)
Fever	187 (75.7)
Cough	170 (68.8)
Shortness of breath	167 (67.6)
Altered sensorium	49 (19.8)
Chest pain	13 (5.3)
Abdominal pain/distension	12 (4.9)
Weakness	6 (2.4)
Diarrhea	6 (2.4)
Headache	4 (1.6)
Others	50 (20.2)

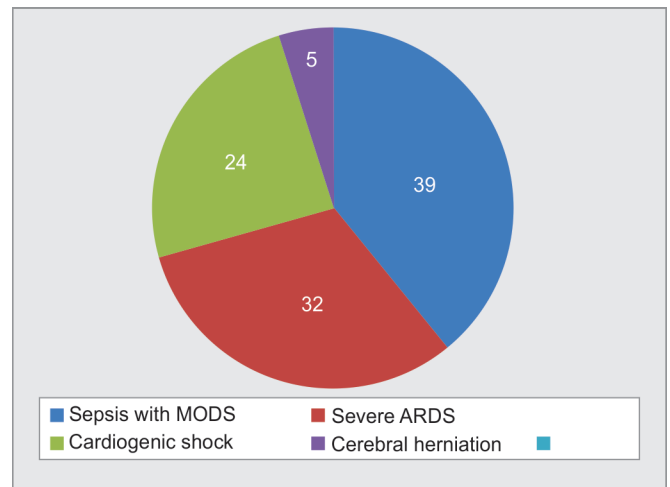


Fig. 2: Cause of death in patients who died within 24 hours of admission to COVID-19 center. MODS, multi-organ dysfunction; ARDS, acute respiratory distress syndrome



Age-related Analysis

The study patients were stratified into three age-groups (18–50, 51–65, and >65 years) to find out age-related differences in the number of comorbidities, presenting symptoms, duration of illness, and cause of death (Table 5).

In the study cohort, 42.1% of the deceased were in age-group between 18 years and 50 years, 34.8% in age-group 51–65 years, and 23.1% in the group above the age of 65 years. There was no difference in the male-to-female ratio between the three groups. The percentage of deceased having multiple comorbidities (two or more) was significantly higher in the age-group above 65 years as compared to younger age-groups. Multiple comorbidities were seen in 68.4% of patients above the age of 65 years, as compared to 59.3% in age-group 51–65 years and 44.2% in patients in 18–50 years of age.

The most frequent presenting complaints were similar in deceased of all age-groups with no significant difference. Initial SOFA score and percentage of patients given HFNC and NIV,

and patients developing AKI were also similar in all the three groups. However, the duration of stay in the hospital was higher in the elderly deceased population. The percentage mortality was significantly higher in the age-group of more than 65 years as compared to other groups. The percentage mortality in different age-groups was 30.2% in age-group between 18 and 50 years, 43.2% in age-group between 51 years and 65 years, and 51.3% in age-group more than 65 years.

Pediatric Fatalities

There were 46 pediatric admissions during the study period and six COVID-19 related deaths, the ICU mortality among the pediatric age-group being 13% (6/46). The age-group of the deceased varied from 6 months to 16 years as depicted in Table 6. All of these patients had comorbidities including congenital heart disease, tubercular meningitis, endocrine disorders, and hematologic malignancies. Mean hospital duration of stay was 4.33 days. Most common cause of death was ARDS followed by sepsis with multi-organ dysfunction.

Table 5: Characteristics of the patients according to different age-groups

Total admissions in COVID-19 center	Age-group (years)			p value
	18–50 n (%)	51–65 n (%)	>65 n (%)	
ICU admissions (% of total ICU admissions)	344 (48.6)	199 (28.1)	111 (15.7)	<0.001
ICU mortality (%)	104 (30.2)	86 (43.2)	57 (51.3)	<0.001
Sex (male:female)	65:39	57:29	41:16	0.48
Number of comorbidities (% of patients)				
0	9 (8.6)	3 (3.5)	1 (1.7)	
1	49 (47.1)	32 (37.2)	17 (29.8)	
≥ 2	46 (44.2)	51 (59.3)	39 (68.4)	0.024
Presenting complaints (% of patients)				
Fever	77 (74.0)	65 (75.6)	45 (78.9)	0.78
Cough	71 (68.3)	56 (65.1)	43 (75.4)	0.42
Breathlessness	67 (64.4)	58 (67.4)	42 (73.7)	0.48
Altered sensorium	21 (20.2)	15 (17.4)	13 (22.8)	0.72
Abdominal pain/distension	6 (5.8)	6 (6.9)	0 (0)	0.11
Chest pain	3 (2.9)	8 (9.3)	2 (3.5)	0.14
Nonspecific symptoms	28 (26.9)	16 (18.6)	6 (10.5)	0.04
Initial SOFA mean (SD)	9.8 (3.9)	9.2 (4.1)	8.4(3.9)	0.86
Patients ventilated within first 24 hrs including patients received intubated	57 (54.8)	51(59.3)	27 (47.3)	0.37
Patients given HFNC	47 (45.1)	35 (40.7)	30 (52.6)	0.37
Patients given NIV	21(20.1)	11 (12.7)	13 (22.8)	0.24
Patients developing AKI	51 (49.0)	45 (52.3)	25 (43.8)	0.61
Patients received RRT	20 (19.2)	12 (13.9)	7 (12.2)	0.43
Median days of illness (IQR)	5 (2–8)	5 (3–11)	9 (5–13)	0.001
Cause of death				
Sepsis with MODS	50 (48.1)	49 (56.9)	37 (64.9)	
ARDS	28 (26.9)	22 (25.6)	13 (22.8)	
Cardiogenic shock	8 (7.7)	9 (10.5)	6 (10.5)	
Stroke, CNS bleed	13 (12.5)	4 (4.6)	0 (0)	
Pulmonary embolism	4 (3.8)	2 (2.3)	1 (1.7)	
Hemorrhage	1 (0.9)	0 (0)	0 (0)	0.115

SOFA, sequential organ failure assessment; HFNC, high flow nasal cannula; NIV, noninvasive ventilation; AKI, acute kidney injury; RRT, renal replacement therapy

Table 6: Pediatric patients

Sl. No.	Age (years)/sex	Presenting symptoms	Length of stay in hospital	Comorbidities	Cause of death
1	0.5/M	Fever	2	Cyanotic congenital heart disease	ARDS
2	3/M	Fever, shortness of breath	7	ALL with CNS metastasis	Sepsis
3	13/M	Fever, vomiting, hematemesis	1	Aplastic anemia	ARDS
4	12/M	Shortness of breath	7	DM, Hypothyroid, nephrotic syndrome	ARDS
5	15/M	Fever, altered sensorium	1	TB meningitis with hydrocephalus	Cerebral herniation
6	16/F	Fever, cough	8	AML with fungal pneumonia	Acute pulmonary hemorrhage

MODS, multi-organ dysfunction syndrome; ARDS, acute respiratory distress syndrome; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; CNS, central nervous system; DM, diabetes mellitus; TB, tuberculosis

DISCUSSION

This study retrospectively analyzed clinicoepidemiological characteristics, course of the disease, and cause of mortality of COVID-19 patients who died in the ICU. Total of 1,420 confirmed COVID-19 patients of all ages were admitted in the COVID center in the study period. Almost half (49.3%) of the hospitalized patients received ICU care during the course of illness. This figure varies from 5 to 46.8% of hospitalized patients in different studies⁹⁻¹¹ and is related to the availability of ICU resources in that region.

The ICU mortality of COVID-19 patients varies from 8.0 to 66.7% in different studies.¹⁸ In our center, the hospital mortality was 18.2% and ICU mortality was 36.1%. Similar mortality rates have been reported in other studies from US, Spain, Italy, and few studies from China.^{9,10,16} However, there are other studies from China² which depict lower overall mortality rates. As the pandemic is evolving and our understanding of the disease is increasing, there has been a steady decline in the mortality rate.¹⁹

Approximately 60% of all admitted patients were males in our center. An almost alike proportion of male patients has been documented in all other studies suggesting male predisposition for this disease across various ethnic and racial groups.^{9,10,15} Similarly, among the deceased adults, 66% were males and among pediatric fatalities, all were males except one.

In our study population of adult deceased, 42.1% were of age-group of 18–50 years, 35% in the age-group 51–64 years, and only about 23% were above 65 years age-group. This was a deviation from the studies from other parts of the world where most of the nonsurvivors were from a much older age-group^{10,15,20} and could be explained by the majority of the young population in India, the percentage of the elderly population (>60 years) being 6.8%.²¹ In our study, 95% of the adults deceased and all of the pediatric ones had at least one comorbid condition. Mortality studies from Spain and Italy^{10,15} have reported a similar incidence of comorbidities in nonsurvivors. However, few other studies^{11,16} report lesser incidence of comorbidities than ours. In our cohort, hypertension was the most common comorbidity seen followed by DM and CKD. Similarly, worldwide studies have shown hypertension followed by diabetes mellitus and cardiovascular comorbid conditions to be associated with the highest mortality.^{12,14,22} Role of ACE-2 receptor in entry of SARS-CoV-2 virus into a host cell is one of the proposed reasons for the highest incidence of COVID-19 in hypertensive patients.²³

In the present study, the elderly (>65 years old) deceased had more comorbidities than younger deceased suggesting that elderly population with higher number of comorbidities are more susceptible to adverse outcomes following COVID-19 infection, while factors other than number of comorbidities could be

a significant variable in younger population.¹⁵ Malignancy was seen in 11.74% of patients in our study which was higher than other reported incidences.^{12,13,16}

The most common presenting complaints in our deceased population were fever, cough, and breathlessness similar to the findings of earlier studies.^{3,24} Few patients initially presented for unrelated diagnoses and then later tested positive for COVID-19. Nonspecific symptoms were significantly more common in younger deceased.

The median initial SOFA score was 9.3 in our study. This was higher as compared to studies from US and China^{11,25,26} reflecting increased severity of COVID-19 at ICU admission in our cohort. High SOFA scores at ICU admission or their progression over 48 hours have been associated with poor outcome of COVID-19.^{25,27} Around 24% of our deceased were received intubated from the screening area and another 30% got intubated within the first 24 hours. HFNC was used in 45% of deceased in our study similar to studies from China where HFNC use among nonsurvivors was 21.1 to 41%.^{11,14} Only 18.2% of patients received NIV in our cohort and even in the published literature, proportion of nonsurvivors receiving noninvasive ventilatory support has been variable.^{11,14,17} Use of NIV was greater in elderly subgroup of nonsurvivors in other studies¹⁶ unlike our study.

The median duration of ICU stay among deceased was 6 days in our study. There was significant variation in median duration of ICU stay reported in other studies ranging from 6 days to 11.5 days.^{12,16} Elderly deceased (>65 years) had significantly longer average duration of hospital stay of 9 days while younger had average 5 days of stay. However, a study in China on deceased patients²⁸ reported a longer average duration of hospital stay in younger patients. The reason for shorter stay in the younger age-group could be either the patients presented to the hospital late in the disease process or had severe cytokine storm-related multi-organ failure. Ours being a tertiary care center, patients were shifted after deterioration from other hospitals. The incidence of AKI in our study was 48.9 and 15.8% received RRT similar to the study by Ahmed et al. in which AKI incidence was around 10 to 50% in critically ill nonsurvivors and around 10–18.5% received RRT.²⁹

Forty-one patients died within 24 hours of admission to ICU. These patients either had severe illness, coexisting decompensated comorbid illness, or were referred from other hospitals. Some were postarrest patients who collapsed in the emergency room, received CPR, and were revived. These patients were more likely to have a poor prognosis and shorter clinical course in the hospital.

Sepsis with multi-organ dysfunction syndrome (MODS) was the most common cause of death in our adult patients followed by severe ARDS and cardiogenic shock. Earlier studies^{11,24} have

also described multi-organ failure as the most common cause of death in the Chinese population while many other studies reported respiratory failure as the leading cause of death.^{12,13,30} The reduced incidence of respiratory failure among the deceased in our study can be explained on the basis that 95% of our study cohort had one or more comorbidities that already compromised other organs. Moreover, all our severely affected patients were given ICU admissions as there were enough ICU beds available and we were able to give rescue therapies like prone ventilation for severe ARDS patients. Our scenario was different from other studies where many patients were not able to get supportive treatment as the number of patients requiring ICU care overwhelmed their medical system. Other rare causes of death were raised intracranial pressure and suspected pulmonary embolism.

Of all the admitted patients, COVID-19 related mortality was much lower (5.6%) in pediatric age-group compared to adults (18.8%). This correlated with the acknowledged low pediatric mortality rates by other authors.³¹⁻³³ In pediatric patients, respiratory failure secondary to ARDS was the most common cause of death. Only a few cases of pediatric COVID-19 mortality have been reported in the literature, wherein comorbidities and multi-organ dysfunction are the most common cause.³³

Limitations

Ours was a retrospective study done in patients who died in ICU. As only data related to the deceased was studied, it is not possible for us to comment on risk factors for more severe infection or death due to COVID-19. Only deaths till July 24 were included in the study. Patients admitted to the hospital during the study duration could have died later during the illness, which has not been included.

CONCLUSION



In this single-center retrospective study of the deceased, 65.9% of the deceased were males. Most of them (76.8%) were of the age less than 65 years indicative of the majority of young population of India. Nearly all patients had single or multiple comorbidities, most common being hypertension followed by diabetes mellitus and chronic kidney disease. The most common cause was of death was sepsis with MODS followed by ARDS. There were a significant number of patients (16.6%) who presented late in the disease process and died within 24 hours.

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