Clinical Characteristics of Deceased with COVID-19 Infection: Data from the Largest COVID-19 Dedicated Hospital in Bangladesh

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Abstract

The death t*oll of the coronavirus disease 2019 (COVID-19) has been considerable. Several risk factors have been linked to mortality due to COVID-19 in hospitals. This study aimed to describe the clinical characteristics of patients who either died from COVID-19 at Dhaka Medical College Hospital in Bangladesh. In this retrospective study, we reviewed the hospital records of patients who died or recovered and tested positive for COVID-19 from May 3 to August 31, 2020. All patients who died during the study period were included in the analysis. A comparison group of patients who survived COVID-19 at the same hospital during the same period was systematically sampled. All available information was retrieved from the records, including demographic, clinical, and laboratory variables. Of the 3115 patients with confirmed COVID-19 during the study period, 282 died. The mean age of patients who died was higher than that of those who survived (56.7 vs 52.6 years). Approximately three-fourths of deceased patients were male. History of smoking (risk ratio 2.3; 95% confidence interval: 1.6–3.4), comorbidities (risk ratio: 1.5; 95% confidence interal:1.1–2.1), chronic kidney disease (risk ratio: 3.2; 95% confidence interval: 1.7–6.25), and ischemic heart disease (risk ratio:1.8; 95% confidence interval: 1.1–2.9) were higher among the deceased than among those who survived. Mean C-reactive protein and D-dimer levels [mean (interquartile range), 34 (21–56) vs. 24 (12–48); and D-dimer [1.43 (1–2.4) vs. 0.8 (0.44–1.55)] were higher among those who died than among those who recovered.* ***Older*** *age, male sex, rural residence, history of smoking, and chronic kidney disease were found to be important predictors of mortality. Early hospitalization should be considered for patients with COVID-19 who are older, male, and have chronic kidney disease. Rapid referral to tertiary care facilities is necessary for high-risk patients in rural settings.*

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Introduction:

The novel coronavirus, SARS-Cov-2, spread rapidly worldwide and the disease, termed coronavirus disease 2019 (COVID-19), was declared a pandemic by the World Health Organization (WHO) on March 11, 2020.[1,2] COVID-19 may manifest as an asymptomatic infection, influenza-like illness, pneumonia, or a critical illness such as acute respiratory distress syndrome, and can lead to death.[3] The pandemic has had an extraordinary impact on the global healthcare system and the death toll has been considerable. Through January 2022, more than 370 million people were affected globally, including approximately 5.7 million deaths.[4]

,In Bangladesh, the first confirmed case was detected on March 8, 2020, followed by a rapid increase in the number of cases due to the dense population. In addition, inadequate testing facilities made it difficult to identify and isolate cases, resulting in inadequate measures being taken for containment and mitigation processes in the region.[5] As of 13 February 2023, nearly 2 million confirmed cases have been reported and more than 29,000 deaths from confirmed COVID-19 have

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been recorded.[6] It is thought that the actual number of deaths and burden of infection is much higher than the reported numbers due to a lack of testing facilities and inadequate contact tracing, among other reasons.

Internationally, large COVID-19-related cohort studies revealed that older age, male sex, and comorbidities are strong non-modifiable risk factors that are associated with higher mortality rates.[7-9] Higher COVID-19-related in-hospital mortality in Black and Asian populations was also identified by several studies.[10,11] As most healthcare provisions were severely affected by COVID-19, there is no single repository available regarding this information in Bangladesh. Moreover, efforts to collect information directly from the hospital were hampered by inconsistent reporting and recording patterns, inadequate manpower, and an overflow of patients, which was more evident in a hospital setting such as ours.

,Dhaka Medical College Hospital, Dhaka, has been dedicated to COVID-19 management since May 2, 2020, and has become the largest referral center for the management of these patients. Patients with severe COVID-19 have been referred to our hospital from all over the country. In Bangladesh, there is limited information regarding the clinical characteristics of hospitalized COVID-19 patients who die or survive.[12,13] It is necessary to identify factors that are predictive of mortality in this setting. Therefore, this study was conducted at Dhaka Medical College Hospital to determine the demographic profile, clinical presentation, and laboratory parameters of COVID-19 patients admitted to this center who died or were discharged alive to determine the predictors of mortality.

Materials and methods

Study design, setting, and sample size

This retrospective cross-sectional study was conducted at Dhaka Medical College Hospital, Dhaka, Bangladesh, from May 2, 2020, to August 31, 2020. We reviewed the hospital records of patients with confirmed cases of COVID-19 who died or were discharged alive. Prior calculation for sample size was not perfomed, as all consecutive patients who died during the study period were included. Every tenth patient was sampled from all discharged patients according to the hospital registry until we reached the required sample size. .The paper files of patients were retrieved from the records section of the hospital, as only paper-based recordings were maintained in the hospital. A preformed case record form (CRF) was used to collect all available information from the files. .A nasal swab was taken from patients, and a real-time reverse transcription-polymerase chain reaction (RT-PCR) assay was performed in the virology department of Dhaka Medical College to detect SARS-Cov-2 RNA. Biochemical and hematological investigations were performed in the clinical pathology department of the hospital, and paper reports were sent to the respective patients' files. Laboratory measurements were collected for analyses, which were available in the files of all patients.

Participants

Patients who tested positive for SARS-CoV-2 by RT-PCR were defined as confirmed cases according to the National Guidelines on Clinical Management of Coronavirus Disease 2019 (Covid-19) Version 4.0, March 30, 2020 [14]. Patients with suspected COVID-19 were excluded from the study if they tested negative by RT-PCR for SARS-CoV-2.

Issue of interest (exposure)

Demographic data, clinical presentation during admission, and initial measurements during the hospital stay were all defined as variables. COVID-19 disease classification was based on national guidelines [14]. Mild disease was defined as COVID-19 without dyspnea or radiological abnormalities. Moderate disease was defined as having abnormal chest imaging with an oxygen saturation level more than or equal to 90%. Severe disease was defined as an oxygen saturation level less than 90%. The metropolitan area was considered an urban setting, district towns other than the metropolitan area were considered semi-urban residential settings, and the remaining areas were considered rural. The pulse, systolic blood pressure (SBP), diastolic blood pressure, and oxygen saturation (SPO_2) reported in this study were measured at presentation. The duration of a patient's hospital stay was measured from the day of admission to the day of death or discharge; if a patient died or was discharged on the same day, it was counted as one day. Days suffering from fever or dyspnea were counted from the day before presentation.

Comparison

Two groups were considered in the study, where the variables of deceased patients were compared with those of discharged patients.

Ethics and endpoint

Ethical clearance was obtained from the Ethical Review Committee of the Dhaka Medical College (Ref: ERC-DMC/ECC/2020/142). The committee waived the requirement for informed consent from patients, as the study maintained anonymity because it was a review of hospital records. Files of deceased and discharged patients collected from the records section of the hospital were examined independently

by two investigators. Every file indicating death was confirmed by checking the death certificate, and RT-PCR for SARS-CoV-2 was performed for both dead and discharged patients. Files were discarded if any confusion existed for any investigator, and the principal investigator was responsible for the overall data collection.

Statistical analysis

Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) version 26. Categorical variables are presented as n (%), normally distributed continuous variables as mean (standard deviation [SD]), and skewed continuous variables as median (interquartile range [IQR]). Categorical variables were compared using the chi-square test and continuous variables were compared using an independent sample Student's t-test. Relative risk (RR) with a 95% confidence interval (CI) was calculated using crosstab analysis. The Mann–Whitney U test was used to compare skewed continuous variables. A binary logistic regression model was developed to determine predictors of mortality. The independent variables included in the model were sex, age group, smoking, residence, diabetes, hypertension, CKD, and chronic lung disease. A forward conditional method was used and step 5 was considered. Statistical significance was set at $P < 0.05$.

Results

A total of 9037 patients were admitted to the dedicated COVID-19 unit of Dhaka Medical College Hospital during the study period after triage at the emergency department. A total of 3115 patients tested positive for SARS-CoV2 by RT-PCR and were shifted to a ward dedicated to confirmed cases. Cases without an RT-PCR report or with a negative test report were forwarded to the suspected COVID-19 ward from triage. Among the RT-PCR-positive COVID-19 cases, 282 patients died and were included in the study. The remaining 2833 patients were discharged alive among whom every tenth patients upto a total number of 282 patients were included for comparison in the final analysis (Fig 1).

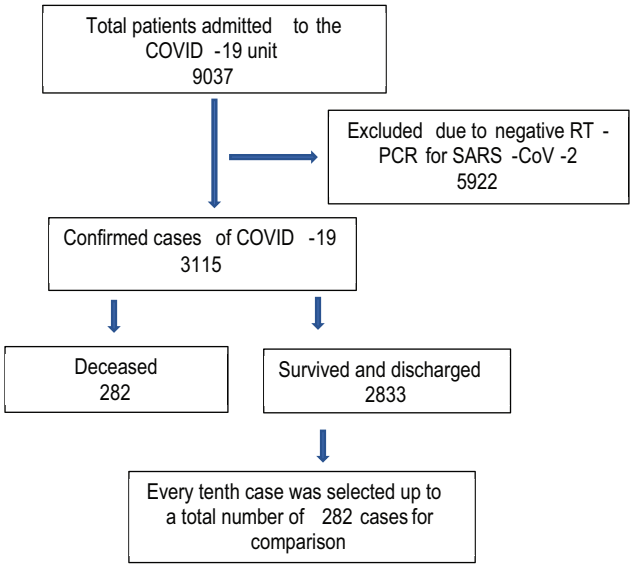

Figure 1. *Selection of study samples*

All patients who tested positive for SARS-CoV-2 by RT-PCR and died were included in the analysis. Surviving patients were selected from among confirmed COVID-19 patients who survived and were discharged based on systematic sampling.

Sociodemographic characteristics

The mean age of all patients was 54.7 years (SD±16.1), and the mean age of patients that died and were discharged alive was 56.7 years and 52.6 years, respectively (Table 1). A significant proportion of patients were young in both groups, with approximately 21.8% (n=123) of deceased patients and 62.6% (n=77) of recovered patients being less than 40 years old. About 61% of all patients were older than 60 years, and 55% and 45% of deceased and discharged patients were older than 60 years, respectively. There was male predominance among the patients, and male sex was determined to be a significant risk factor for a fatal outcome, as 75.2% (n=212) of deceased patients and 51.8% of discharged patients were male. Patients who resided in urban areas were more prevalent in both groups (47.7% of deceased vs. 52.4% of survived), but the proportion of patients from rural settings was higher among the deceased than among those who survived (76.9% vs. 23.1%, respectively). A large proportion of patients (27.5%) were smokers, although the prevalence was higher in the deceased group than that in the discharged group (65% vs. 35%, respectively). Table 1.

Comorbidity

Among the comorbidities, diabetes mellitus (41.5% of all patients) was the most common in both deceased and discharged groups (55.6% vs. 44.4%, respectively), followed by hypertension (38% of all patients). Other comorbidities that were more common in deceased than discharged patients included chronic kidney disease (7.8%), cardiovascular disease (13.1%), and chronic lung disease (9%) in all patients. More than one-quarter of the patients in both groups had both hypertension and diabetes.

Table 1. *Demographic characteristics and co-morbidities of the study population*

Trait	Total	Deceased	Discharged alive	P-value	RR (95% CI)
Age (years), mean (SD)	54.7(16.1)	56.7(14.9)	52.6(16.8)	0.003	
Age group, n (%)				0.005	
Less than 40 years	123(21.8)	46(37.4)	77(62.6)		
40 – 60 years	190(33.7)	98(51.6)	92(48.4)		
More than 60 years	251(44.5)	138(55.0)	113(45)		
Sex, Male n (%)	346(61.3)	212(61.3)	134(38.1)	<0.001	3.3(2.3-4.8)
Residence[1], n (%)				<0.001	
Urban	312(55.3)	149(47.8)	163(52.2)		
Peri-urban	174(30.9)	73(42)	101(58)		
Rural	78(13.8)	60(76.9)	18(23.1)		
Smoking[2] n (%)	155(27.5)	101(65.2)	54(34.8)	<0.001	2.3(1.6-3.4)
Comorbidities, n (%)					
Diabetes mellitus[3]	234(41.5)	130(55.6)	104(44.4)	0.03	1.5(1.1-2.1)
Hypertension[4]	215(38.1)	111(51.6)	104(48.4)	0.6	1.1(0.83-1.7)
Chronic lung disease[5]	44(7.8)	21(47.7)	23(52.3)	0.8	0.9(0.49-1.7)
Chronic kidney disease[6]	51(9)	38(74.5)	13(25.5)	<0.001	3.2(1.7-6.25)
Ischemic heart disease[7]	74(13.1)	46(62.2)	28(37.8)	0.03	1.8(1.1-2.9)

[1]Patients' current residence or dwelling; the metropolitan area was considered an urban setting, district towns other than the metropolitan area were considered semi-urban, and the remaining areas were considered rural [2]Current smoking status just before hospitalization [3]Known case of diabetes based on medical history, documentation, or treatment [4]Known case of hypertension based on medical history, documentation, or treatment [5]Bronchial asthma or chronic obstructive lung disease based on medical history [6]Known case of CKD based on medical history or documentation [7]Known case of IHD based on medical history or documentation. Note:Post hoc analysis with Bonferroni methods revealed- age groups 40–60, and > 60 years were significantly higher among the deceased group- residence in rural and peri-urban areas was significantly higher among the deceased group. Table 1.

Clinical presentation at admission

Fever was the most common symptom at admission, which was observed in approximately 80% of patients. Fever was less common in the deceased than in discharged patients. The duration of fever before admission was higher in deceased patients than that in discharged patients [mean (IQR 7): 7 (4-9.5) vs. 5 (4-8)]. Cough and dyspnea were both common features at presentation, but dyspnea was more prevalent than cough in the deceased, and cough was more prevalent in discharged patients. The duration of dyspnea before admission was significantly longer in deceased patients than that in discharged patients. Chest pain (4.6%), body ache (26.6%), anosmia (27.3%), diarrhea (19.7%), and altered levels of consciousness (3.9%) were present at presentation in a considerable number of patients.

Most patients had severe COVID-19 (49.8%, n=281) at admission to the hospital, followed by moderate disease. In patients who were discharged alive, mild disease was the most common form of presentation, followed by moderate disease. Patients who died had a high pulse (mean pulse, 97±17.26) and respiratory rate (mean respiratory rate, 27.71±5.97); mean systolic and diastolic blood pressures in this group were 119 (±25.1) and 70.34 (±15.51), respectively.

Table 2. *Presentation of patients at admission to the hospital*

Trait	Total	Deceased	Discharged alive	P-value	RR (95% CI)
Fever[1], n (%)	449(79.6)	198(44.1)	251(55.9)	<0.001	0.32(0.20-0.50)
Number of days suffering from fever at presentation, median (IQR)	5(4-8)	7(4-9.5)	5(4-8)	0.001	
Cough, n (%)	358(63.5)	150(41.9)	208(58.1)	<0.001	0.4(0.28-0.58)
Dyspnea at presentation, n (%)	404(71.6)	249(61.6)	155(38.4)	<0.001	6.1(4.0-9.5)
Number of days suffered from dyspnea at presentation	2(1-3)	2(2-4)	2(1-2)	<0.001	
Chest pain	26(4.6)	21(80)	5(19.2)	0.002	4.4(1.7-12)
Body ache	150(26.6)	82(54.7)	68(45.3)	0.21	1.2(0.9-1.9)
Anosmia[2]	154(27.3)	80(57.9)	74(48.1)	0.6	1.1(0.8-1.6)
Diarrhea[3]	111(19.7)	59(53.2)	52(46.8)	0.5	1.2(0.8-1.8)
Altered consciousness[4]	22(3.9)	20(90.9)	2(9.1)	<0.001	10.6(2.4-46.1)
Disease severity[5]					
Mild	137	9(3.2)	128(45.4)		
Moderate	146	65(23)	81(28.7)		
Severe	281	208(73.8)	73(25.9)		
Duration (number of days) of hospitalization[6], mean (IQR)		4(1-8) days	7(5-10) days		

[1]Temperature more than 99° F [2]Anosmia – loss or alteration of sensation of smell [3]Passing of loose stool [4]Glasgow Coma Scale less or equal to 14 [5]Mild disease was COVID-19 without dyspnea and radiological abnormalities, moderate disease was abnormal chest imaging with oxygen saturation more than or equal to 90%, and severe disease was oxygen saturation less than 90% [a]Mann–Whitney U tests and chi-square tests were performed for the remaining categorical variables. Table 2

Examination and investigation

The mean systolic blood pressure was 120 mmHg among all participants, and there was no significant difference between deceased and discharged groups. The pulse rate was high among all participants and modestly higher among the deceased. Full blood counts were performed in most patients, and the mean hemoglobin concentration was 11.6 mg/dl, which was similar between the deceased and discharged patients. The mean total white blood cell count in the population was high, indicating neutrophilia. There was a significant difference in the total WBC count, which was markedly higher in deceased patients than that in discharged patients. The differential neutrophil count was also significantly higher in deceased patients than that in discharged patients (81% vs. 78%). Although the mean platelet count was lower in deceased than in discharged patients (157 vs. 206 x 10^9/L), the count was within the normal reference range. The mean C-reactive protein (CRP) level was higher in fatal cases than that in recovered cases (34 mg/dL vs. 24 mg/dL) and serum ferritin levels were markedly higher in the deceased (856 ng/mL vs. 436 ng/mL). A low mean sodium concentration was observed in the study population, and hyponatremia was observed to a greater extent in the deceased (133 mmol/L vs. 136 mmol/L). The mean D-dimer level was higher in the deceased than that in discharged patients (1.43 mcg/ml vs. 0.44 mcg/ml). Table 3.

Table 3. *Clinical examination and laboratory findings of patients*

Trait	Total	Number	Deceased Mean(IQR)	Number	Discharged alive Mean(IQR)	Number	P* value
Systolic blood pressure in mmHg	120(100-130)	277	120(100-132)	137	120(110-125)	140	0.45
Diastolic blood pressure in mm Hg	70(70-80)	277	70(60-80)	137	75(70-80)	140	0.1
Pulse (per second)	96(84-108)	291	100(86-109)	141	94(80-107)	150	0.01
Hb% (mg/dl)	11.6(10.3-12.9)	411	11.3(10.2-12.5)	163	11.8(10.4-13.1)	248	0.005
Total count($10^{9/}$/L)	10.0(7.1-13.5)	403	11.0(7.3-13.7)	161	9.4(6.5-13.1)	242	0.02
Neutrophil (%)	80(69-85)	402	81(73-86)	161	78(67-85)	241	0.01
Platelet count (x 10^9/L)	230(168-331)	363	211(161-303)	157	250(172-351)	206	0.01
C-reactive protein (mg/dl)	30(16-53)	361	34(21-56)	156	24(12-48)	205	<0.001
Sodium (mmol/L)	135(132-139)	195	133(130-139)	43	136(133-138)	152	0.9
Ferritin (ng/ml)	446(243-1029	195	856(243-1489)	27	436(242-994)	168	0.1
D-dimer (mcg/ml)	0.9(0.49-1.72)	249	1.43(1-2.4)	36	0.8(0.44-1.55)	213	<0.001

* Mann-Whitney U test

Predictors of Mortality

We determined the predictors of mortality in COVID-19 patients using a binary logistic regression analysis. Older age (OR, 95% CI, p-value: 0.8, 0.61–0.97, 0.02), male sex (3.3, 2.3–4.8, <0.001), residence in rural areas (0.6, 0.5–0.8, 0.001), positive smoking history (2.4, 1.6–3.7, <0.001), and chronic kidney disease (0.3, 0.1–0.6,0.001) were found to be predictors of mortality in this study. Table 4

Table 4. *Predictors of the mortality (binary logistic regression analysis)*

Trait	Reference	B	Wald	P-value	Odd ratio (OR)	95%CI
Age groups [b]	<40 years	-0.27	5.1	0.02	0.8	0.61-0.97
Sex	Male	1.2	38.6	<0.001	3.3	2.3-4.8
Residence [c]	Urban	-0.4	11.6	0.001	0.6	0.5-0.8
Smoking	Presence	0.9	18.2	<0.001	2.4	1.6-3.7
CKD	Absence	-1.2	10.9	0.001	0.3	0.1-0.6
Constant			0.9	0.35	0.5	

a-Independent variables - sex, age group, smoking, residency, Diabetes, hypertension, CKD, chronic lung disease as independent variables. Omnibus test of model coefficient 0.00, Hosmer and Lemeshow test 0.66, Nagelkarke score 0.20. Forward conditional method was used, step 5 was takenb-Age groups- <40 years, 40-6- years, >60 yearsc-Residence-Urban, Peri-urban, Rural

Discussion

In this study, we described the demographic profile, clinical features at admission, and initial measurements of hospitalized COVID-19 patients who either died or survived to be discharged. In this study, we found that deceased patients were older than those who were discharged, and that there was a significant male predominance among the deceased patients. Patients from rural areas and smokers were more prevalent in the deceased group. All comorbidities were more common among the deceased patients than those among discharged patients. Fever, dyspnea, and cough were the most common symptoms. Neutrophilic leukocytosis and high CRP, ferritin, and D-dimer levels were more marked among the deceased than among those discharged.

Patient age has been determined as an independent risk factor of death due to COVID-19 [15]. Although the mean age of the deceased was higher than that of the patients who survived, and older age was found to be a predictor of mortality, the mean age of the deceased was remarkably lower than that found in similar studies and meta-analyses.[16-19] Male predominance has been observed in deaths due to COVID-19[18]; in this study, male sex was more prevalent in the deceased group than in the discharged group, and it was determined to be a predictor of mortality. Smoking has been associated with severe COVID-19 and is a risk factor for death[20] and in this study, smoking was found to be a predictor of death. Urban and peri-urban populations were more greatly affected due to transmission being higher in urban and peri-urban areas during the study period. In addition, mortality was higher in those from rural and peri-urban areas. As Dhaka Medical College Hospital is a tertiary care hospital dedicated to COVID-19 management, critical patients were referred from different areas of the country, resulting in delays and treatment interruptions, which may have increased the risk of mortality from COVID-19 among these patients.

Diabetes was the most common comorbidity, followed by hypertension. The proportion of patients with hypertension was similar to the pooled data from a meta-analysis by Qiu et al. However, the proportion of patients with diabetes was markedly higher[18] in the deceased group than in those who were discharged in this study. Diabetes has been found to be independently associated with an increased in-hospital mortality and hypertension has been associated with a 2.5 fold increase in mortality in COVID-19 patients.[21,22] The proportion of patients with diabetes and hypertension was significantly higher in all hospitalized patients than in the general population of Bangladesh, where diabetes was five times and hypertension two times more prevalent in the deceased.[23,24] CKD was found to be one of the predictors of mortality in this study. During the study period, many patients with COVID-19 and CKD were undergoing dialysis in this hospital because of the lack of facilities for such patients in other centers.

More than 70% of patients presented to our hospital with fever, which is consistent with other studies; however, the mean duration of fever before admission to the hospital was lower in deceased patients.[17,25] Dyspnea was found to be more common in the deceased in this study than in patients described by Chen et al. Reappearance of fever after initial influenza-like symptoms has been associated with the development of cytokine release and ARDS, leading to dyspnea.[26] A remarkable number of patients presented with chest pain, body ache, abdominal pain, and diarrhea, indicating multisystem involvement of the disease. The clinical condition of most of the deceased patients was poor at admission, as more than three-fourths of these patients suffered from severe illness at that time. Dyspnea, tachycardia, and tachypnea were present, and the mean oxygen saturation was approximately 80% in those who died, indicating ARDS, which was found to be a major risk factor for death. Altered consciousness may have been due to multifactorial causes, including cerebral infarction, intracerebral hemorrhage, hypoxia, metabolic derangement, and possibly encephalitis.[27]

A limited investigation was performed in the present study because of the lack of resources at this public hospital. Not only was the investigation limited, but "point of care" testing of common biochemical and hematological parameters was also lacking. Leukocytosis with neutrophilia was observed in this study, similar to the 113 deceased patients described by Chen et. al.[17] Total leukocyte count and neutrophil counts were significantly higher, and lymphocyte and platelet counts were lower in deceased cases.[28,29] High neutrophil counts may have resulted from secondary sepsis and the use of glucocorticoids. Higher concentrations of CRP and ferritin were common findings in fatal cases of COVID-19, and CRP was determined to be an independent risk factor that predicts the severity of the disease.[17,30] The development of Acute Kidney Injury is associated with increased mortality. High mean serum creatinine levels in this study were reflected not only by the development of AKI in patients who eventually died, but also the presence of an increased number of patients with CKD (14%).[31] A modestly low mean level of serum Na^+ was observed, which is consistent the association of hyponatremia severe COVID-19 .[32]

The median time from admission to death was lower than that found in another study in which approximately one-fifth of patients died on the day of admission and one-third of the total patients died within 48 h of hospitalization.[17] Oxygen saturation at admission was associated with the duration of hospitalization from admission to death, and the mean saturation was significantly lower in patients who died less than 48 hours after admission than that in those who died 48 hours or more after admission. This indicates that most severely ill patients that were referred from other hospitals were admitted to our hospital in critical condition, which was reflected by the proportion of ill patients requiring oxygen at admission.

This was a retrospective, single-center study, and the data were obtained from paper-based documents, which is the current practice in this hospital. This resulted in a loss of information regarding the parameters needed for this study.

During the COVID-19 pandemic, both management and documentation were difficult due to a lack of manpower, trained personnel, and the existing record-keeping process in this setting. Therefore, the quality of the documentation did not reach the standard mark for many parameters, leading to a lack of information.

Conclusions

Older age, male sex, rural residence, history of smoking, and chronic kidney disease were found to be important predictors of mortality among patients who died from COVID-19. Early hospitalization should be considered for patients with COVID-19 who are older, male, and have chronic kidney disease. Rapid referral to tertiary care facilities is necessary for severe and high-risk patients in rural settings.

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