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Original Article**Analysis of the clinical and laboratory characteristics of 45 COVID 19 deaths in TMSS Medical College and Rafatullah Community Hospital, Bogura, Bangladesh**Rahman AKMM¹, Ansary MAM³, Ahmed S⁴, Nibir NA⁵, Sahin MRR⁶

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Abstract

Introduction: COVID-19 pandemic or also known as corona virus pandemic is an ongoing pandemic of corona virus disease 2019 caused by SARS-CoV-2 is now a major concern for the world. It became a pandemic all over the world in only 3 months and now a cause of many deaths and disabilities. This study was conducted to better understand the clinical and laboratory characteristics of the dead patients due to COVID-19. **Materials and Methods:** Total 45 patients with confirmed SARS coV-2 have been chosen all of whom had died during admission to COVID-19 ward or COVID-19 ICU of TMSS Medical College and Rafatullah Community Hospital, Bogura for this retrospective study. Their socio-demographic data, clinical characteristics, morbidities, laboratory as well as CT scan results were analyzed & compared. **Results:** Among 45 deaths most were male. Most of them had at least one comorbidity, among them DM and HTN were most common. All the patients had increased levels of CRP and D-dimer on biochemical investigations. Of those who's CT scan of chest could be done, most had bilateral lung involvement with ground glass opacities most commonly affecting lower lobes. Acute respiratory failure was the most common cause of death followed by cardiovascular events. **Conclusion:** The common risk factors for COVID-19 deaths were male gender, presence of comorbidities like DM, HTN, CKD etc. Most of the dead patients had very severe symptoms on admission and died due to respiratory failure. These findings are consistent with other studies and more studies should be done to better understand the disease.

Key words: Clinical and laboratory characteristics, COVID-19, Death patients, TMC & RCH.

Introduction

The COVID-19 pandemic, also known as the corona virus pandemic, is an ongoing pandemic of corona virus disease 2019 (COVID-19) caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2), first identified in December 2019 in Wuhan, China. The World Health Organization declared the outbreak a Public Health Emergency of International Concern in January 2020 and a pandemic in March 2020.¹ The outbreak spread from the Chinese city of Wuhan to more than 180 countries and territories—affecting every continent except Antarctica.² Globally, the deaths-to-infections ratio stood at about 6.9 percent by April 22, with 175,694

deaths and over 2.54 million confirmed cases worldwide, according to WHO data. That means about 6.9 percent of people known to be infected with the corona virus have died worldwide.³ As of 18 November 2020, more than 55.6 million cases have been confirmed, with more than 1.34 million deaths attributed to COVID-19.⁴ Different virus epidemics take place throughout the world every year, but only a few rises to the level of public concern.⁵ Severe acute respiratory syndrome (SARS), swine influenza A H1N1 virus (H1N1), and Zaire Ebola virus (Ebola) brought on the public's attention because they caused many severe infections and thousands of deaths.⁵

Similarly, the disease COVID-19 caused by a corona virus (2019-nCoV) brought world-wide attention and caused public panic because many deaths had been reported without being put in the context of the many mild infections and its potentially low case fatality rate.^{6, 7} The effect of the outbreak of COVID-19 pneumonia and ultimate scope is unclear so far as the situation is rapidly evolving.^{8,9} As a matter of fact, the fear of ongoing COVID-19 epidemic was and is playing a major role in the economic and social consequences. The clinical spectrum of SARS-CoV-2 infection encompasses asymptomatic infection, mild upper respiratory tract infection, and severe viral pneumonia with respiratory failure and even death. A number of published case studies made summaries of all patients infected with SARS-CoV-2^{10, 11} and some death cases were included¹². However, very few clear descriptions or analyses of the clinical characteristics of patients who died of COVID-19 and the causes of death are available.

Objectives

General objective: The aim of this study is to identify incidence of death rate and factors associated with the death of patients with COVID-19.

Specific objectives

- To see the socio demographic information of the dead patients due to COVID-19;
- To see the radiological and laboratory findings of the patients; and
- To assess the cause of death of the patients.

Materials and Methods

Study design and participants

This is a retrospective, single-center study from 1st June, 2020 to 31st August, 2020, at Department of Medicine, TMSS Medical College and Rafatullah Community Hospital, Bogura, Bangladesh. A total 654 COVID-19 positive patients were admitted in this hospital in that period and 45 patients were dead. This being a retrospective study informed consent was not taken. The study was not involved in any additional investigative procedures and significant risk as well as economic burden to the patient. Ethical review committee of TMSS Medical College and Rafatullah

Community Hospital reviewed and approved of this study and all research procedures are performed according to the criteria of the Declaration of Helsinki.

Data Collection

All the data including demographic, clinical, laboratory, radiological characteristics, treatments and hospital outcomes were obtained from patients' electronic medical records and treatment files. All the patients were confirmed cases of COVID-19 and all the COVID-19 negative and suspected cases were excluded from this study. Purposive sampling method was done as per these inclusion and exclusion criteria. Inclusion criteria are all the dead patients who were confirmed COVID 19 positive. Exclusion criteria are COVID 19 negative cases. Evaluation of patient was based on history, physical examination and investigations and treatment given at inpatient department.

Laboratory test process

Real-time rt-PCR assays have been used to detect SARS-CoV-2 in respiratory specimens of patients. Patients with positive results and pulmonary infection detected by chest CT were confirmed to have COVID-19 and admitted to Rafatullah Community Hospital. Laboratory tests such as ECG and arterial blood gas analysis and determination of routine complete blood count (CBC), coagulation function, serum biochemical indexes (incl. liver and kidney functions and lactate dehydrogenase), myocardial enzymes, brain natriuretic peptide, CRP and procalcitonin (PCT) were carried out. The examination frequency was determined by their doctors.

Definitions

An axillary temperature above 37.6 °C (99.7°F) is considered a fever. The diagnosis of sepsis and septic shock is based on the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) issued in 2016¹³. Acute myocardial infarction (AMI) is diagnosed by an increase in the serum level of cardiac biomarkers (cardiac troponin I) or new abnormalities found in ECG and echocardiography.

Statistical Analysis

Descriptive statistics included frequency analysis (percentages) for categorical variables and mean $\pm$ SD

or median and inter-quartile range for continuous variables. Comparisons will be determined by one sample t-test or Mann–Whitney U-test for continuous variables, as appropriate, and by the use of the Chi-squared test or Fisher exact test for categorical variables. The interested variables were processed, edited and analyzed by SPSS windows version 25. *P* value <0.05 was considered as statistically significant with the 95% confidence interval. The results were presented in tables.

Results

Analysis of clinical characteristics

From 1st June, 2020 to 31st August, 2020, a total of 654 COVID-19 patients were admitted to the Rafatullah Community Hospital and 45 (including 36 males and 9 females) of those patients died. The mean age of the patient at death was 61.87(SD 12.9) years old, the number of COVID-19 deaths in males was higher than that in females (80% vs. 20%), and the mean age at death for males was lower than that in females (61±10.8 vs. 65±19.5). Most patients had symptoms like fever, cough and dyspnoea. A total of 40 patients (88.9%) had underlying diseases. Among them, 80% had diabetes mellitus(36), 73.3% had hypertension (33), 35.6% had chronic kidney disease (16), and 28.9% had heart disease (13) and 64.4% patients (29) had a history of smoking (Table-I).

Laboratory tests

The results of laboratory tests, including complete blood count, D-dimer levels and biochemical and inflammatory marker levels within 24 hours of admission, are summarized in Table - II. Due to sudden death very shortly after hospital admission all relevant investigations could not be done to each patient. Among those who were tested, 100% had increased serum C-reactive protein (CRP) (mean 86 ± 50) and D-dimer (mean 3.3 ± 3.4, median 2.0; 0.6-16.2) levels, 89.5% had increased Neutrophil Lymphocyte ratio (mean 5.5 ± 2.1), 73.3% had increased serum creatinine (median 1.9; 1.0-14.8) and 53.8% had increased serum alanine transaminase (ALT) (mean 44 ± 19.7).

Imaging examination

Some patients died hours after admission and some patient's condition was too critical to move to CT scan room. So a total of 21 (46.7%) patient's CT scan of the chest could be done. Among them, 20 (95.2%) had bilateral lesion, 17 (81%) had lesions in all five lobes of the lungs, 17 (81%) patient's lesion pattern was ground glass opacities with crazy paving patterns, 10 (47.6%) had consolidations, 2 (9.5%) had pleural effusion. (Table -III)

Treatment plans and causes of death

After admission, 40 patients (88.9%) received antiviral treatment with remdisivir, 5 patients (11.1%) received favipiravir and 43 patients (95.6%) received steroid and antibiotic treatment. Regarding respiratory support, 22 patients (48.9%) received high flow nasal cannula and 6 patients received mechanical ventilation. Acute respiratory failure (34, 75.6%) was the main cause of death, followed by heart disease (7, 15.6%), neurological diseases (3, 6.7%) and sepsis (1, 2.2%). The mean survival time (from disease onset to death) was 13.4±4.7 days. (Table-IV)

Intergroup analysis

In this study, intergroup analysis was carried out based on a series of baseline characteristics, including gender, age and survival time and the results were showed in table 4 and the most significant findings were as follows:

Among the initial symptoms of patients who died, females were more prone to dyspnoea (*P*-value 0.0178) and more likely to have heart disease (*P*-value 0.048), while the incidence of cerebro-vascular disease was observed in 3 male male patients in comparison to 0 female patient. In addition, anemia was more common in females, while elevated levels of total count of WBC was more common in males (*P*-value 0.021). Mean Survival time (from disease onset to death) was less for elderly patients (≥ 65) in comparison to young and middle aged group (<65 years) (*P*-value 0.019). Mean survival time was also less in people who initially had dyspnoea (*P*-value 0.044) and increased serum ferritin level (*P*-value 0.0299).

Table-I: Clinical characteristics of COVID-19 deaths and cause of death (SD= Standard deviation)

Clinical Characteristics		All cases (N=45), mean ($\pm$SD)	Percentage (n%)
Gender	Male	36	80.0
	Female	9	20.0
Age (years)	Total (Mean $\pm$ SD)	61.87 ($\pm$ 12.9)	
	Male (Mean $\pm$ SD)	61.03 ($\pm$ 10.8)	
	Female (Mean $\pm$ SD)	65.22 ($\pm$ 19.5)	
	30-39	1	2.2
	40-49	4	8.9
	50-59	15	33.3
	60+	25	55.6
Symptoms	Fever	43	95.6
	Cough	40	88.9
	Shortness of breath	40	88.9
	Fatigue	11	24.4
	Sore throat	14	31.1
	Headache	10	22.2
	Chest pain/tightness	8	17.8
	Diarrhoea	10	22.2
	Myalgia	13	28.9
	Nausea/vomiting	14	31.1
Smoker		29	64.4
Co-morbidities	No Comorbidity	5	11.1
	DM	36	80.0
	HTN	33	73.3
	Heart disease	13	28.9
	Bronchial asthma	7	15.6
	CKD	16	35.6
	CVD	3	6.7
	COPD	4	8.9
Cause of death	Respiratory failure	34	75.6
	Heart disease	7	15.6
	Cerebro vascular disease	3	6.7
	Sepsis	1	2.2

Table-II: Initial laboratory analysis of COVID-19 deaths (SD= Standard Deviation ↓= below normal and ↑= above normal)

Initial laboratory analysis	Normal range	No. of test done	Mean (±SD)	Abnormal Percentage
Hemoglobin percentage	>13.0 g/dL	25	10.88 (±2.07)	28.0%
Total count of white blood cells	4000-11000 mm ³ of blood	19	13325 (±5071)	68.4%
Percentage of Neutrophil	40-60%	19	77 (±10.01)	
Percentage of Lymphocyte	20-40%	19	16 (±7.20)	
Neutrophil lymphocyte ratio	1-3	19	5.54 (±2.19)	89.5%
Random blood glucose	4.4-7.8 mmol/L	14	16 (±5.51)	92.8%
C- reactive protein	<10 mg/L	23	86.8 (±50.94)	100%
Serum ferritin	male 24-336 µg/L, female 11-307 µg/L	22	703.0 (±514.17)	72.7%
Serum creatinine	0.84 to 1.21 mg/dL	30	3.81 (±3.68)	73.3%
Serum ALT	<40 IU/L	26	79 (±19.73)	53.8%
D-dimer	<0.50 mg/L	39	3.26 (±3.45)	100%

Table-III: HRCT scan of chest analysis of 21 patients

Variables	Frequency	Percent
Number of lobes involved		
One (1)	1	4.8
Two (2)	2	9.5
Three (3)	1	4.8
Five (5)	17	81.0
Pattern of lesion		
Ground glass opacities	17	81.0
Crazy paving pattern	17	81.0
Consolidation	10	47.6
Pleural effusion	2	9.5

Table-IV: Comparison of clinical characteristics among different subgroups. NA = not applicable. *Chi-square test is used (a Pearson Chi-Square, b Likelihood Ratio or c Fisher's Exact Test was done where applicable). P-value < 0.05 was considered significant.

Cause of death	Sex of the patient		P-value	Age group		P-value
	Male	Female		<65 years (N = 36)	≥ 65 (N = 9)	
Respiratory failure	29	5	0.069 ^a	20	14	0.772 ^a
Heart disease	3	4		4	3	
Neurological disease	3	0		2	1	
Sepsis	1	0		1	0	

Discussion

This study includes a group of 45 COVID-19 deaths who were admitted to Rafatullah Community Hospital, Bogura, Bangladesh. According to Worldometers.info, cases which had an outcome, the death is about 3% of all COVID-19 patients all over the world and 1.76% in Asia. Among hospitalized patients, it is much higher.¹³⁻¹⁴ Up to 22 November, 2020 a total of 77652 men died and 59591 women died,¹⁵ ratio is about 1.3. In this study 36 men and 9 women died. More men are dying than women and this is consistent with most other studies.¹⁵⁻¹⁸ Men are more at risk for worse outcomes and death, independent of age, with COVID-19.¹⁶

COVID-19 mortality risk is many times higher for the old than the young, and the vast majority of COVID-19 deaths are of older people. About 70% of all US COVID-19 deaths are to age 70 years or above, somewhat above the 64% for normal mortality.¹⁷

While COVID-19, the disease caused by the new coronavirus has caused the most severe health issues for adults over the age of 60 with particularly fatal results for those 80 years and older.¹⁸⁻¹⁹ In this study among 45 COVID-19 deaths 25 (55.6%) were above 60 years old, 15 (33.3%) were aged between 50 and 60 years and only 5 (11.1%) were aged below 40 years (Table 1). These findings are consistent with other studies.¹⁷⁻²¹

In one study, 78% had fever, 64.6% had cough and 63.4% had shortness of breath. Diarrhea was present in 12.2% of patients.²⁰ In another study, initial symptoms were shortness of breath (98.8%), fever (94%), myalgia or fatigue (90.4%), anorexia (82%), cough (60.2%), hemoptysis (6%), pharyngalgia (6%), headache (3.6%), nausea or vomiting (2.4%) and diarrhea (4.8%).²¹ In this study, most patients had fever (95.6%), cough (88.9%) and shortness of breath (88.9%) followed by fatigue and myalgia (40%), sore throat (31.1%), diarrhea (22.2%), headache (22.2%) and chest pain/ tightness (17.8%). Fever, cough and shortness of breath are the most frequent findings and are consistent with most other studies.¹⁸⁻²¹

The elderly, a vulnerable population, with chronic health conditions such as diabetes and cardiovascular or lung disease are not only at a higher risk of

developing severe illness but are also at an increased risk of death if they become ill.²² In one study, the most common co-morbidities were chronic lung disease and diabetes mellitus.²³ In another study, several co-morbidities, such as hypertension, ischemic heart disease, and obesity were present in most patients who died from COVID-19.²⁴ In another study, hypertension, type 2 diabetes mellitus, heart disease, renal failure, dementia, COPD, cancer etc were most common co-morbidity respectively.²⁵ In this study, out of 45 COVID-19 death, a total of 40 patients (88.9%) had known underlying diseases, and diabetes mellitus (80%) was the most common, followed by hypertension (73.3%), chronic kidney disease (16, 35.6%), heart disease (28.9%), chronic pulmonary disease (24.4%) and neurological disease (6.7%).

In one study, all patients had bilateral involvement on chest radiographs. On admission, lymphopenia (89.2%), neutrophilia (74.3%), and thrombocytopenia (24.3%) were usually observed. All the patients had increased C-reactive protein levels (100%), and most patients had a high NLR of >5.0 (94.5%) high D-dimer (97.1%) levels.²⁰ In another study, many patients had an abnormal liver function and renal function. Aspartate aminotransferase in 57% patients, gamma-glutamyl transpeptidase in 49% patients, serum creatinine in 47% patients and blood urea nitrogen in 53% patients were above the normal range. Most patients have abnormal coagulation function, which showed the elevation of D-dimer in 94% patients. Moreover, procalcitonin (83%) and C-reactive protein (95%) increased above the normal range in most patients.²¹ In another study, 77% of patients have increased D-dimer levels and are considered to be in a hypercoagulable state.²⁶ In another study pneumonia was confirmed in all 83 patients and 71 patients were involved in the bilateral lung. Radiographic features from chest CT scans mainly included ground glass opacity, consolidation, air bronchogram, bronchial dilatation and pleural effusion or thickening. Multiple patchy ground-glass shadows were the main feature in the chest CT of most patients, followed by consolidation.²⁷ In this study, among those who were tested, 100% had increased serum C-reactive protein (CRP) and D-dimer levels, 89.5% had increased Neutrophil Lymphocyte ratio

(mean 5.5 ± 2.1), 73.3% had increased serum creatinine and 53.8% had increased serum alanine transaminase (ALT). 21 patient's CT scan of the chest could be done and among them, 20 (95.2%) had bilateral lesion, 17 (81%) had lesions in all five lobes of the lungs, 17 (81%) patient's lesion pattern was ground glass opacities with crazy paving patterns, 10 (47.6%) had consolidations, 2 (9.5%) had pleural effusion. All these findings were consistent with the above-mentioned studies.^{20-21, 26-27}

Recent studies showed that, main causes of death due to COVID-19 are respiratory failure, sepsis renal failure, cardiac failure, hemorrhage etc.^{20, 26-27} In this study, acute respiratory failure (75.6%) was the main cause of death, followed by heart disease (15.6%), neurological diseases (6.7%) and sepsis (2.2%).

Conclusions

The majority of COVID-19 deaths are male, especially elderly patients with underlying diseases. Among the dead patients, COVID-19 often starts with fever, cough and dyspnoea and DM, HTN and chronic kidney disease are most common co-morbidities. Common investigation abnormalities are increased serum C-reactive protein, D-dimer levels, Neutrophil Lymphocyte ratio, serum creatinine and serum alanine transaminase (ALT). Most patients had bilateral ground glass opacities with crazy paving pattern in all five lobes of the lungs, followed by consolidation and pleural effusion. The majority of patients in the short-term survival group are male and the main cause of death is acute respiratory failure.

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