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Clinical and laboratory characteristics of patients associated with severe COVID-19 infection and death at a tertiary care hospital in Sri Lanka

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Abstract

Introduction: COVID-19 caused a massive burden to the health sector in Sri Lanka. This study aims to describe the clinical and laboratory characteristics associated with severe COVID infection and death in patients with moderate or severe COVID-19.

Methods: This descriptive cross-sectional study was carried out from November 2021-June 2022 at a Teaching Hospital in Colombo. Consecutive sampling of adults admitted to hospital with moderate or severe COVID-19 was done. Data was collected from patient interviews and medical records.

Results: The study population consisted of 388 patients. Mean age (SD) was 61.1 (±14.7) years and 56.4% were men. In-hospital deaths were 39%. Shortness of breath was the commonest presenting complaint (89.4%). Death was more common among those with the following symptoms as opposed to those without; fever (49.3% vs 27.7%, p< .001), cough (64.2% vs 23.2%, p< .001) and chest pain (70.5% vs 34.9%, p < .001). Other factors associated with death were male gender (44.2% vs 32.1 %, p= .016), age >60years (66.5 vs 10.1, p< .001), diabetes (47.2% vs 23.7%, p< .001), hypertension (61% vs 23.5, p< .001), ischemic heart disease (78.6% vs 30.1%, p< .001), COPD (90.0% vs 35.8%, p< .001) and smoking (60.3% vs 34%, p< .001). Symptoms, demographics and comorbidities associated with severe disease compared to moderate disease were similar to those associated with in-hospital deaths. High white cell count, high CRP, low pH and low SpO2 on admission were significantly associated with death as well as severe disease.

Conclusions Clinical and laboratory characteristics associated with death in patients with COVID-19 were similar to those with severe COVID. These parameters help to detect patients who need close monitoring and more intensive management.

Key words: COVID- 19, clinical and laboratory characteristics, severe COVID-19 Infection, COVID-19 death

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Introduction

Coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a global pandemic that initially started in Wuhan, China, and spread rapidly across the world. The worldwide mortality among people infected with SARS-CoV-2 reached a peak of 101 600 deaths per week in January 2021. By March 2023 deaths reported per week were 6500.(1) As the novel coronavirus continues to evolve, there are still many unanswered questions as to which patients would be critically affected by this virus. Older adults and people of any age who have underlying medical conditions, such as hypertension and diabetes, have shown worse prognosis.(2) Patients with diabetes have increased morbidity and mortality rates and diabetes has been linked to more hospitalisation and intensive care unit (ICU) admissions.(2) People with chronic obstructive pulmonary disease (COPD) or any respiratory illness are also at high risk for severe illness from COVID-19.(3) The risk of contracting COVID-19 in patients with COPD is found to be 4-fold higher than patients without COPD.(3) A retrospective study of middle-aged and elderly patients with COVID-19 in China, found that the elderly population is more susceptible to this illness and is more likely to be admitted to the ICU with a higher mortality rate.(4)

In the USA, the Centers for Disease Control and Prevention (CDC) uses COVID-NET in 14 states to monitor the demographics of COVID-19 patients who are being hospitalised. From March 1 through 30, 2020, there were a total of 180 patients on COVID-NET, of which 89.3% had an underlying comorbidity. Of the 180 patients, 94.4% who were aged 65 years and older had at least one comorbidity. The most common comorbidities found were obesity, hypertension, and diabetes mellitus.(5)

While studies show that COVID-19 is common in patients with diabetes, hypertension, and cardiovascular disease (CVD), the prevalence rate of comorbidities varied in different countries. In the pooled data from the 10 Chinese studies (n = 2209) on characteristics of comorbidities in patients with COVID-19, Singh et al. have reported a prevalence of hypertension, diabetes and CVD in 21%, 11%, and 7% of patients, respectively.(6) In contrast, an Italian study by Onder et al. found diabetes in nearly 36%, while CVD was associated in nearly 43% of 355 patients admitted with COVID-19.(7)

A systematic review describing clinical presentation of COVID-19, in nearly 5000 patients globally has reported fever, cough, fatigue and dyspnoea as the most common presentations.(8) A meta-analysis of 86 studies has found that severe disease was strongly associated with fever, cough, dyspnoea, pneumonia, any computed tomography findings, any ground glass opacity, lymphocytopenia, elevated c-reactive protein, elevated alanine aminotransferase, elevated aspartate aminotransferase, older age and male gender.(9) Prior to the conception of this study, 306,662 cases of COVID– 19 were reported in Sri Lanka by 1st September 2022 and 4380 deaths due to COVID-19 had occurred.(10)

There is a scarcity of data from Sri Lanka regarding the association between clinical and laboratory characteristics and the outcome of COVID -19. We aimed to describe the clinical and laboratory characteristics, outcome and factors associated with death and severe disease in patients with moderate or severe COVID-19 admitted to a tertiary care hospital in Sri Lanka. This information is hoped to be useful for planning future activities related to prevention and management of COVID-19 in the public health and curative sectors.

Methods

Study setting and participants

This was a descriptive cross-sectional study carried out from November 2021-June 2022 at Colombo South Teaching Hospital in Sri Lanka. The Study population consisted of patients aged 18 years or more, who have been admitted to Colombo South Teaching Hospital and confirmed to have COVID-19 and diagnosed as having moderate or severe disease based on Revised Clinical Practice Guidelines on Institutional Management of COVID-19 patients in Sri Lanka issued by the Ministry of Health, Sri Lanka in May 2021 (issue date: 25.05.2021; My No: EPID/400/2019/n-CoV) (table 1).

The patients were confirmed to have COVID- 19 by a positive result on polymerase chain reaction or rapid antigen testing of a nasopharyngeal sample. At the time of the study, all patients presenting to the hospital underwent a mandatory COVID Rapid Antigen Test and if positive were transferred to 2 wards (80 beds in total) allocated solely to manage patients with COVID- 19. Here they were triaged and patients with severe illness were transferred to the COVID-19 HDU or ICU based on the need for respiratory support.

Sampling

Consecutive sampling was done until the required sample size of 385 participants was reached.

Table 1 - Classification of severity of COVID-19

Disease Category	Presentation
Asymptomatic individuals	Positive COVID-19 diagnostic test
Symptomatic, mild disease	Has signs and symptoms of COVID-19 but do not have shortness of breath, is not dyspnoeic and no abnormal chest imaging
Moderate disease	Has symptoms and signs of COVID-19 pneumonia (fever, cough, dyspnoea, respiratory rate up to 30/min, crepitations, etc), with low SpO2 ≤94% on room air*.BUT does not have features of severe pneumonia (See below). Chest imaging will show evidence of COVID related changes. *Lower SpO2 needs to be considered in patients with chronic respiratory diseases.
Severe Disease	Has features of severe COVID-19 pneumonia suggested by; 1) SpO2 <90 % with maximum oxygen supplement as standalone criteria **OR** 2) SpO2 ≤ 94 % on room air **AND** Evidence of severity assessed by the following criteria a)Respiratory rate > 30/min , excessive use of accessory muscles, and thoraco-abdominal dis-synchrony b) Radiographic infiltrates – > 50% multilobar infiltrations c) P/F ratio < 300 (Partial pressure of Oxygen/ Fraction of O2) d) S/F ratio < 235 (Saturation/Fraction of O2) e) Haemodynamic instability; - Heart rate > 120/ min; - SBP < 90 mmHg - Lactate > 2 mmol/L

Study measurements and data collection:
The study instrument was an interviewer administered data collection form. Eligible participants were recruited after obtaining informed written consent. Two investigators and two data collectors qualified with MBBS collected the data by patient interviews and from the bed head ticket using the data collection forms. The data collection form was used to collect demographic data, medical history of the participant and clinical and laboratory characteristics related to COVID-19. Participants were followed up till discharge from hospital or death to determine the disease severity (moderate/severe) and outcome. Maximum severity observed during the hospital stay determined each individual participant's disease severity category.

Data Analysis:
The collected data was analysed using the SPSS software package. Numerical values were summarised using the mean and standard deviation and categorical data was summarised using frequencies and percentages. The Chi squared test and the two-sample t-test were used to assess the statistical significance of associations. P values less than .05 ($p < .05$) were considered to be statistically significant.

Ethical Considerations:
The Ethics Review Committee of Colombo South Teaching Hospital, Sri Lanka approved the study. Study participants provided informed consent prior to recruitment.

Results

The mean age (SD) of the study population was 61.1 (±14.6) years, (range 18-95 years) and 56.4% of the patients were men. In-hospital deaths amounted to 39.0% while 61.0% recovered and were discharged. Out of the participants that passed away in hospital, 64.0% were men. Moderate disease was diagnosed in 55.8% while the rest were diagnosed to have severe disease. Majority (70.4%) were managed in the ward setup while 22.1% and 7.5 % were managed in the COVID high dependency unit (HDU) and intensive care unit (ICU), respectively.

Table 2 - Presenting complaints among patients with confirmed COVID -19

Presenting Complaint	n (%)
Shortness Of Breath	344 (89.4)
Fever	201 (52.0)
Cough	148 (38.4)
Sore Throat	64 (16.6)
Chest Pain	22 (11.4)
Anosmia	42 (10.9)
Reduced level of Consciousness	5 (1.3)
Prior to Surgery	3 (0.7)
Fits	2 (0.5)
Cardiac Arrest	1 (0.2)

Shortness of breath was the most common presenting complaint (89.4 %). While the other common presenting complaints were fever and cough (table 2). However, shortness of breath was not associated with a higher death rate. Presenting complaints associated with a higher death rate were fever (49.3% vs 27.7%, p< .001), cough (64.2% vs 23.2%, p< .001) and chest pain (70.5% vs 34.9%, p < .001) (table 3).

The presenting complaints associated with severe disease were also fever (58.7% vs 28.3%, p< .001), cough (79.7% vs 21.9%, p< .001) and chest pain (77.3% vs 39.9%, p < .001) (table 4).

The most prevalent comorbidities in the study population were diabetes (65.0 %), hypertension (41.4%) and ischemic heart disease (18.5%).

All risk factors except allergic rhinitis were associated with death and severe disease were significant (table 3 and 4).

The investigation findings significantly associated with death were high WBC count, high neutrophil percentage, high CRP and low SPO2 on admission. The same investigation findings were associated with severe COVID illness. Blood gas analysis results significantly associated with death were low pH, high PCO2, low HCO3- and high lactate. The same results were associated with severe illness (table 5).

Discussion

Our study describes the clinical and laboratory characteristics, outcome and factors associated with severe disease and death in patients with COVID-19 admitted to a tertiary care hospital in Sri Lanka. This hospital caters to a diverse population which includes the urban, suburban and rural socio demographic sectors of the country. Vast majority of the study population were from the western province of Sri Lanka which had the highest confirmed COVID-19 cases and deaths related to COVID -19. The study was conducted during the peak of the COVID pandemic.

Fever, cough, fatigue and dyspnoea had been reported as the most common presentations.(8) Similarly, Shortness of breath (89.4 %), fever (52.2 %) and cough (38.6%) were the most common presentations in our study population. Our study showed that fever, cough and chest pain were significantly associated with death as well as severe illness which is in keeping with previous studies that showed that severe illness was associated with fever and cough(9), although some studies showed that fever was not significantly associated with mortality. (10,11) However, shortness of breath, which was the most common presenting complaint, was not associated with death nor severe disease. This was in contrast to previous studies that showed that dyspnoea was associated with a higher risk of severe disease.(11) Shi L et al. suggested that since dyspnoea was positively associated with the risk of

Table 3 - Clinical characteristics associated with death

Presenting complaint		Outcome		p value
		Discharge n(%)	Death n(%)	
Shortness of breath	Yes	212(61.6)	132(38.4)	.52
	No	23(56.1)	18(43.9)	
Fever	Yes	102(50.7)	99(49.3)	< .001
	No	133(72.3)	51(27.7)	
Cough	Yes	53(35.8)	95(64.2)	< .001
	No	188(76.8)	55(23.2)	
Chest pain	Yes	13(29.5)	31(70.5)	< .001
	No	222(65.1)	119(34.9)	
Risk factors				
Age	<=60 years	169(89.9)	19(10.1)	.016
	>60 years	66(33.5)	131(66.5)	
Gender	Male	121(55.8)	96(44.2)	< .001
	Female	114(67.9)	54(42.1)	
Diabetes Mellitus	Yes	132(52.8)	118(47.2)	< .001
	No	103(76.3)	32(23.7)	
Hypertension	Yes	62(39.0)	97(61.0)	< .001
	No	173(76.5)	53(23.5)	
Ischaemic heart disease	Yes	18(21.4)	55(78.6)	< .001
	No	217(68.9)	95(30.1)	
Chronic obstructive pulmonary disease	Yes	2(9.1)	20(90.9)	< .001
	No	233(64.2)	130(35.8)	
Smoking	Yes	29(39.7)	44(60.3)	< .001
	No	206(66.0)	106(34.0)	
Allergic rhinitis	Yes	10(83.3)	2(16.7)	.11
	No	225(60.5)	148(39.5)	

mortality in patients with COVID-19, it, rather than fever, should be recommended as an indicator of poor outcome.(11)

Singh, et al. demonstrated that hypertension and diabetes were associated with a worse prognosis in patients with COVID-19.(2) Another study showed that patients with COPD or any respiratory illnesses were also at higher risk for severe illness from COVID-19.(3) Similarly, our study showed that diabetes, hypertension, ischemic heart disease, COPD and smoking were significantly associated with death as well as severe illness.

Diabetes is a key risk factor for several reasons. Firstly, individuals with diabetes are more likely to

Table 4 - Clinical characteristics associated with severe disease

Presenting complaint		Outcome		p value
		Moderate n(%)	Severe n(%)	
Shortness of breath	Yes	190(55.2)	154(44.8)	.48
	No	25(61.0)	16(39.0)	
Fever	Yes	83(41.3)	118(58.7)	< .001
	No	132(71.7)	52(28.3)	
Cough	Yes	30(29.3)	118(79.7)	< .001
	No	185(78.1)	52(21.9)	
Chest pain	Yes	10(22.7)	34(77.3)	< .001
	No	205(60.1)	136(39.9)	
Risk factors				
Age	<=60 years	152(80.9)	36(19.1)	< .001
	>60 years	63(32.0)	134(68.0)	
Gender	Male	108(49.8)	109(50.2)	.016
	Female	107(63.7)	61(36.3)	
Diabetes Mellitus	Yes	113(45.3)	137(54.8)	< .001
	No	102(76.0)	33(24.0)	
Hypertension	Yes	43(27.0)	116(73.0)	< .001
	No	172(76.4)	54(24.6)	
Ischaemic heart disease	Yes	15(20.4)	58(79.5)	< .001
	No	200(64.1)	112(35.9)	
Chronic obstructive pulmonary disease	Yes	3(13.6)	19(86.4)	< .001
	No	212(58.4)	151(41.6)	
Smoking	Yes	24(32.9)	49(67.1)	< .001
	No	191(61.2)	121(38.8)	
Allergic rhinitis	Yes	10(83.3)	2(16.7)	.11
	No	205(54.9)	168(45.1)	

have other comorbidities such as obesity, cardiovascular disease, and kidney disease which in turn are associated with a risk of severe illness. Secondly, the treatment of severe COVID-19 infection involved treatment with intravenous dexamethasone which led to poor control of blood glucose in patients with diabetes.

Age >60 years was associated with death, and it was statistically significant. This was compatible with the previous studies that showed the elderly population with COVID- 19 were more likely to be admitted to the ICU with a higher mortality rate.(4) This was probably due to a weaker immune system which is less efficient in fighting off the COVID infection leading to a higher viral load and presence of other

Table 5 - Laboratory characteristics associated with death, moderate and severe disease

Investigation	Death		Discharge		p value
	n	Mean(SD)	n	Mean(SD)	
WBC (x109/L)	150	13.7(4.1)	235	10.5(3.6)	< .001
Neutrophils (%)	150	80.4(18.4)	235	72.3(17.8)	< .001
Platelets (x109/L)	150	305.0(131.6)	235	291.0(98.0)	.236
Haemoglobin(g/dL)	150	11.0(1.8)	235	12.0(1.5)	< .001
CRP (U/L)	150	135.7(70.1)	235	51.2(67.9)	< .001
LDH (U/L)	69	711.0(658.0)	30	552(253.0)	.2
Saturation on pulse oximeter at room air (%)	139	83.0(7.6)	98	90.0(7.7)	.01
pH	112	7.3(0.1)	116	7.4(0.1)	< .001
PCO2 (mmHg)	100	37.5(12.5)	41	29.6(10.2)	< .001
HCO3- (mmol/L)	113	16.1(3.9)	117	20.0(4.2)	< .001
Lactate (mmol/L)	109	3.8(2.1)	117	2.5(2.4)	< .001
Investigation	**Moderate**		**Severe**		**p value**
	n	**Mean(SD)**	**n**	**Mean(SD)**	
WBC (x109/L)	215	9.9(3.0)	170	13.9(4.1)	< .001
Neutrophils (%)	215	72.7(13.3)	170	78.9(22.9)	< .001
Platelets (x109/L)	215	281.0(97.4)	170	314.0(126.7)	.23
Haemoglobin(g/dL)	215	12.2(1.6)	170	11.0(1.8)	< .001
CRP (U/L)	215	39.4(55.5)	170	140.0(70.2)	< .001
LDH (U/L)	13	467.0(211.0)	86	692.0(611.0)	.18
pH	98	7.4(0.1)	130	7.3(0.1)	< .001
PCO2 (mmHg)	25	29.3(11.7)	116	36.5(12.2)	.009
HCO3- (mmol/L)	99	20.7(3.6)	131	16.0(4.2)	< .001
Lactate (mmol/L)	99	2.1(1.7)	127	3.9(2.4)	< .001

comorbidities. Another reason that was noted in our study was that elderly patients presented later to hospital. This was probably due to lack of public transport, lack of knowledge on contacting the relevant resources in ministry of health which did arrange transport to hospital for the critically ill, time taken for the children to arrange transport and general reluctance to come to hospital due to the fear of contracting COVID-19 which was coupled with the reluctance to accept the possibility that they could have COVID-19.

Smilowitz NR et al showed that high CRP, is strongly associated with venous thromboembolism, acute kidney injury, critical illness, and mortality in COVID-19.(13) In this study of 2782 patients hospitalised with COVID-19, 2601 (93.5%) had a median CRP measurement of 108 mg/L [interquartile range (IQR)

53-169]. CRP concentrations above the median value were associated with venous thromboembolism, critical illness and mortality.(13) Another study showed that higher total leucocyte count, neutrophilia, lymphopenia, eosinopenia were associated with severe COVID-19.(14)

In a systematic review to identify prognostic factors , demographic factors: age, male sex, smoking; patient history factors: cerebrovascular disease, chronic obstructive pulmonary disease, chronic kidney disease, cardiovascular disease, dyspnea , tachypnea, fever; laboratory factors: high white blood cell count (WBC), high blood lactate, low blood platelet count, plasma creatinine increase, high blood lactate dehydrogenase (LDH), high blood c-reactive protein (CRP), decrease in lymphocyte count , high blood neutrophil count were found to be valuable prognostic factors with high to moderate certainty. (15)

Investigation findings associated with death and severe COVID in our study were a high WBC count, high neutrophil percentage, high CRP, low pH, high PCO2, low HCO3- and high lactate which are in keeping with previous studies.(13-15)

The high WBC and neutrophil count are probably a result of the cytokine storm triggered by the COVID-19 virus while the high lactate and low PH is evidence of lactic acidosis due to anaerobic respiration and widespread tissue inflammation which is an effect of the low oxygen saturation in majority of the patients on admission.

Though low platelets have been associated with severe COVID in previous studies(14,15), our study showed a tendency to have high platelet counts in those with severe disease and who died in the hospital. However, it was not statistically significant.
Our study also showed that a lower oxygen saturation on pulse oximetry on admission was associated with death similar to previous studies which showed that indices of respiratory compromise at initial presentation that are readily measurable at home (oxygen saturation <92% or a respiratory rate >22 breaths per minute) were each associated with elevated mortality in hospitalised COVID-19 patients. (16) The mean oxygen saturation (on admission) of 83.0% in patients who died of COVID-19 is an indication of the late presentation to hospital which is likely due to the phenomenon of happy hypoxia along with the other reasons mentioned above that resulted in the elderly patients presenting late to hospital.

The inability to measure the weight and therefore the BMI of critically ill patients was a limitation of the study. This was because the majority of patients were severely dyspnoeic and hypoxic on presentation and therefore unable to be mobilised.

Conclusion

In this descriptive cross sectional study, age > 60 years, male gender, diabetes, hypertension, ischemic heart disease, COPD, smoking , high white cell count, high CRP, low pH , high lactate were associated with death and severe illness. A lower SpO2 on admission was another factor associated with death. These findings provide valuable prognostic information and will help clinicians identify patients who need closer monitoring and more intensive treatment which would improve patient outcomes. Severe COVID-19 patients with diabetes in particular would warrant HDU/ICU care due to difficulties in controlling blood glucose with ongoing dexamethasone therapy.

Declarations

Author contributions
IW, SMS, CNW, SW, CS conceived and designed the study. IW, SMS, CNW,SW, AGHS, MIM contributed to the conduct of the study and acquisition of data. IW, CNW, and SMS contributed to data analysis and interpretation. IW prepared the first draft of the manuscript and CNW revised the manuscript critically. All authors approved the final manuscript. All authors have full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Conflicts of interest
Authors declare there's no conflict of interest

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Ethics approval
The Ethics Review Committee of Colombo South Teaching Hospital, Sri Lanka granted approval for this study (Application no. 995/ 2021). All participants provided informed consent prior to participation in the study.

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