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The short-term outcome and risk factors associated with the outcome of severe Covid-19 disease – Retrospective evaluation of single-centre experiences from the second Covid-19 wave in Sri Lanka

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Abstract

Background: Prognostic data related to the Covid-19 is lacking for Sri Lankans, and for high-risk cohorts worldwide.

Objectives: To describe the short-term outcomes and risk factors related to severe and fatal Covid-19 disease in a high-risk symptomatic cohort with coexisting disease conditions.

Methods: The single-center retrospective study assessed 300 symptomatic Covid-19 infected adults admitted to Base-Hospital Homagama, Sri Lanka, from December 2020 to February 2021.

Results: The patients mean age (SD) was 58 (15) years, with 47% of them being men. At least one comorbidity was present in 84.3%, hypertension in 57.1% and diabetes in 53.8%. Overall, 24.3% had severe disease, 18.3% succumbed and 14.3% were managed in an ICU. Severe disease was more common among males (60.3%) than females (39.7%). Case severity (diabetes: $\chi2 = 4.838$; $p = 0.028$; CKD: $\chi2 = 9.459$; $p = 0.002$) and case fatality (diabetes: $\chi2 = 4.838$; $p = 0.028$); CKD: $\chi2 = 9.459$; $p = 0.002$) had a significant association with co-existing diabetes or chronic kidney disease (CKD). Predictors for severe disease include male gender (OR:2.292; 95%CI:1.228–4.279), low oxygen saturation (OR:2.436; 95%CI:1.304–4.552), and presence of comorbidity (OR:4.886; 95%CI:1.352–17.652). Predictors of the fatal disease include low oxygen saturation (OR:4.182; 95%CI:1.971–8.872) and the presence of comorbidity (OR:9.352; 95%CI:1.160–75.371).

Conclusion: Covid-19 infected adults who are having coexisting non-communicable diseases are more vulnerable to getting severe and fatal infections. And knowledge of vulnerable groups will help in developing new strategies to mitigate the effects of this pandemic.

Keywords: *Covid-19; risk factors; severe infection; mortality; comorbidity*

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INTRODUCTION

Covid-19 pandemic is the most critical global health challenge of the 21st century. Within a few months from the first infections noticed in December 2019 in Wuhan – China, a rapid global spread had led to the declaration of the Covid-19 pandemic on 11th March 2020 [1,2]. Within a year, 65,536,045 patients were reported from all over the world [3]. A Chinese tourist diagnosed on 27th January 2020 was the first confirmed Covid-19 case in Sri Lanka. After detecting the first local case on 11th March 2020, there were two infective outbreaks in Sri Lanka within 2020. As of early January 2021, 46,248 confirmed cases had been reported in Sri Lanka, with 219 deaths [4].

High infectivity, morbidity, and mortality rates have created pioneering medical concerns in Covid-19 disease [2,5]. Though the initial case fatality rate of SARS-CoV-2 viral infection was as high as 0.7 to 12.7% (with an average of 3.4%), a rapid change in the virulence has been observed with subsequent viral mutations [4].

Though the majority detected in the first wave in Sri Lanka were asymptomatic, higher death rates and a mixture of severe and non-severe infections were detected in the second wave [4,6,7]. Compared to the first wave, the widely spread second wave infected more high-risk individuals drifting the morbidity and mortality patterns. However, mutant lineages were not reported from Sri Lanka during the second wave [6]. Even for the same viral lineage, the virulence of this novel coronavirus may show geographical/ethnic variations and variations related to patient characteristics such as risk factors [7]. Therefore, it is empirical to pool data from many geographical regions to widen the understanding of this disease entity.

The disease spectrum of SARS-CoV-2 varies from asymptomatic infection or mild prodromal symptoms to severe illness that necessitates intense medical care. The predominant risk factors recognized for severe infection include male gender, smoking, and associated co-morbidities such as hypertension, diabetes, or chronic kidney disease [8,9,10,11]. Still, these risk factors may act differently under geographical or genetic influence. Thus, identifying risk factors associated with severe Covid-19 infection from Sri Lankans is an urgent need.

As practised in many other countries, Sri Lanka also identified asymptomatic covid-19 patients by testing and contact tracing; patients were isolated in intermediate management centers to prevent the spread. The mildly symptomatic patients were admitted to hospital or intermediate care settings, while the severe disease was managed in high dependency or intensive care settings. Among the factors affecting the outcome of Covid-19 infection, restricted access to overcrowded treatment centers was significant in increasing high mortality rates even in affluent countries [12,13]. Thus, a triaging system is mandatory to recognize patients who need specialized care. For that defining risk factors of severe infection is a priority.

Though there is enough data on the clinical/epidemiological characteristics and outcome of Covid-19 in the healthy adult population, such knowledge is lacking for high-risk patients (Eg: patients with associated co-morbidities). The study center has been functioning as a multidisciplinary Covid-19 treatment center for symptomatic patients with co-morbidities. Thus, this center provided an opportunity to study risk factors related to severe Covid-19 infection in a cohort of symptomatic patients. This study aimed to describe the risk factors for severe and fatal Covid-19 disease in symptomatic patients and to describe the short-term outcome for patients with coexisting disease conditions.

METERIAL AND METHODS

All symptomatic Covid-19 infected adults (age >18 years) who underwent a chest radiograph at Base Hospital Homagama from 01st of December 2020 to 01st of March 2021 were retrospectively studied. In the second wave, the study center was the dedicated multidisciplinary Covid-19 treatment center for the entire country that provided care for high-risk patients. The infection was diagnosed either by a positive Covid-19 Reverse Transcriptase polymerase chain reaction (RT PCR) test or a rapid immunoassay test for SARS COV 2 antigen (rapid antigen test). The

symptomatic patients were selected by screening those who underwent a chest X-ray and confirmed by evaluating the records. This screening methodology was effective since a radiograph was requested only for symptomatic patients. Genomic sequencing done during the second wave detected only one Covid-19 viral strain, with B1.411 lineage [6]. Hence this data describes data related to this lineage. As a recommended vaccine was not available during this time, the study describes the features of an unvaccinated cohort.

Ethical clearance was granted by the Ethical review committee of the Sri Lanka Medical Association - ERC protocol No: ERC/21-001- by which obtaining informed written consent was waivered considering the retrospective nature. The sample size was determined using Lwanga and Lemeshow formula [14]. The study was reported according to the STROBE statement, and JBI critical appraisal tool [15,16].

The socio-demographic and clinical details, risk factors such as coexisting disease conditions (co-morbidities), smoking, days from test positivity; details of outcome and intensive care unit (ICU) admissions were extracted retrospectively.

Fatal disease was defined if the patient was died due to a complication of Covid-19 disease. The severe illness was defined in case of death or ICU admission. Oxygen saturation less than 96% was considered as low oxygen saturation.

STATISTICAL ANALYSIS

After preliminary analysis confirmed the normalcy of data, parametric analysis was done. Continuous variables were expressed as means and standard deviations, and categorical variables as percentages. Groups were compared using the T-test, and the relationship between groups was evaluated using Chi-square analysis and binary logistic analysis. Binary regression analysis was performed to define risk factors of severe and fatal infection. A $P < 0.05$ was considered significant.

RESULTS

The total admissions to the study center in this period were 966, and 31.1% (n = 301) of them required a CXR during the hospital stay. After excluding patients aged less than 18 years, the study included three hundred (n = 300) confirmed symptomatic Covid-19 cases in the 18 to 87-year age range, with the mean age (SD) of 58 (15) years. Of them, 141 (47%) were men (Figure 01). Table 01 describes the basic demographic information, the symptoms and co-existing conditions of the study group. The most common symptom was shortness of breath (154 [51.2%]), followed by cough (140 [46.5 %]), and fever (112 [37.2%]). Similar symptoms were observed in the patients with severe disease (shortness of breath: 24 [55.8%], cough: 15 [34.9%], & fever: 13 [30.2%]), and fatal disease as well (shortness of breath: 29 [52.7%], cough: [22 [40%], & fever: 15 [27.3%]).

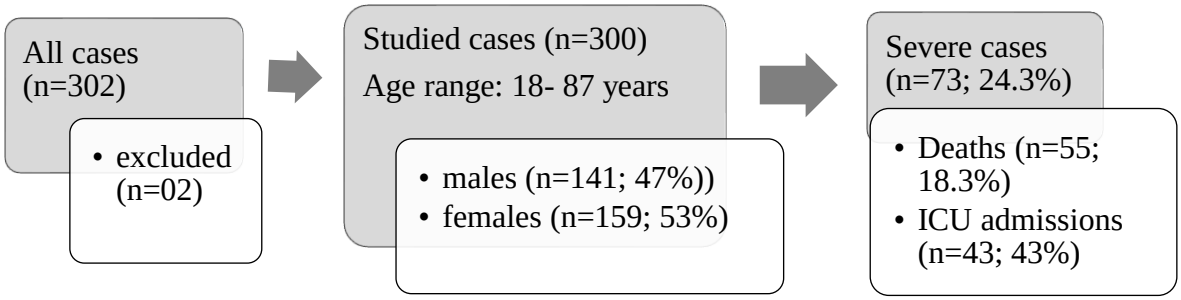

Figure 1: Flow chart describing the study cohort

Table 01: Socio-demographic details, symptoms and associated comorbidities of the study sample

	All cases (n=300)	Severe cases (n=73)	Fatal cases (n=55)
Demographic details			
Age: mean (SD)	58 (15) years	59 (13) years	58 (14) years
Age groups			
18 - 39 years	31 (10.3 %)	4 (5.5 %)	1 (1.8 %)
40 – 49 years	52 (17.3 %)	12 (16.4 %)	7 (12.7 %)
50 – 59 years	63 (20.9 %)	16 (21.9 %)	13 (23.6 %)
60 – 69 years	77 (25.6 %)	20 (27.4 %)	18 (32.7 %)
70 – 79 years	55 (18.3 %)	17 (23.3 %)	12 (21.8 %)
>80 years	21 (7.0 %)	3 (4.1 %)	3 (5.4 %)
Gender distribution			
Male	141 (47%)	44 (60.3 %)	30 (58.8 %)
Female	159 (53%)	29 (39.7%)	21 (41.2 %)
Symptoms present			
Shortness of breath	154 (51.2 %)	24 (55.8 %)	29 (52.7 %)
Cough	140 (46.5 %)	15 (34.9 %)	22 (40 %)
Fever	112 (37.2%)	13 (30.2 %)	15 (27.3 %)
Body aches	59 (19.6%)	3 (3 %)	6 (10.9 %)
Headache	58 (19.3 %)	4 (9.3 %)	7(12.7 %)
Sore throat	44 (14.6 %)	0 (0 %)	1 (1.8 %)
Diarrhoea	32 (10.6 %)	5 (11.6 %)	6 (10.9 %)
Vomiting	26 (8.6 %)	4 (9.3 %)	5 (9.1 %)
Anosmia	24 (8 %)	0 (0 %)	0 (0 %)
Cold	10 (3.3 %)	0 (0 %)	0 (0 %)
Abdominal pain	9 (3 %)	0 (0 %)	1 (1.8 %)
Coexisting conditions			
Any condition	257 (84.3%)	67 (91.8 %)	52 (94.5 %)
Diabetes	162 (53.8%)	47 (65.2 %)*	38 (69.1 %)*
Hypertension	172 (57.1%)	46 (63 %)	17 (30.9 %)
Ischemic heart disease	93 (30.9%)	20 (27.4 %)	15 (38.5 %)
Asthma/COPD	60 (19.9%),	14 (19.2 %)	11 (20 %)
Other pulmonary disease	6 (2%)	2 (2.7 %)	2 (3.6 %)
Chronic kidney disease	93 (30.9%)	33 (45.2 %)*	27 (49.1 %)*
Active malignancy	16 (5.3%)	4 (5.5 %)	3 (5.5 %)
Hypothyroidism	12 (4%)	2 (2.8 %)	1 (1.8 %)
Chronic liver disease	8 (2.6%)	1 (1.4 %)	0 (0%)
Smoking	18 (6 %)	4 (5.5 %)	4 (7.3 %)

(* $p<0.05$)

Out of all symptomatic Covid-19 patients (n = 300), 73 (24.3%) had severe disease, and either succumbed (n = 55; 18.3%) or managed in an ICU (n = 43; 14.3%) during the course of illness. The mean age of the demised patients was 58 years (median 63 years; percentiles: P10 = 46 years; P25 = 51 years; P75 = 70 years; P90 = 76 years) and the age ranged from 39 to 83 years (Table 01). The mean age of patients who required an ICU admission was 58 years (median 63 years; percentiles: P10 = 40 years; P25 = 46 years; P75 = 70 years; P90 = 73 years) and the age ranged from 21 years to 77 years. On average, death occurred 14 days after PCR/ RAT positive date (median 14 days; percentiles: P10 = 5 days; P25 = 9 days; P75 = 19 days; P90 = 24 days; ranged from 3 to 32 days). There was no significant correlation between the

age of the patient and the disease severity (R = 0.38, p = 0.511) or case fatality (R = 0.98, p = 0.89).

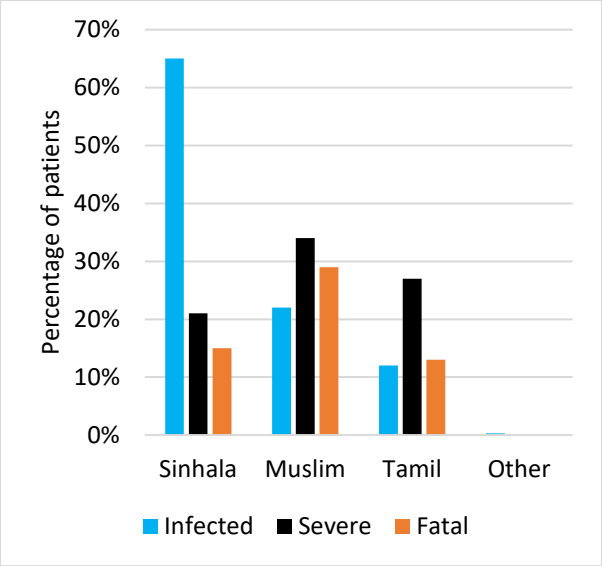

Figure 2: Distribution of disease severity/ fatality among the ethnic groups

Figure 2 describes the ethnic distribution of the study cohort. Severe (n=22, 34%) and fatal cases (n = 19, 29.2%%) were proportionately higher among the Muslim (Moor) ethnic group with a significant association between ethnic difference and severe/ fatal disease (χ2 = 7.633; p=0.045).

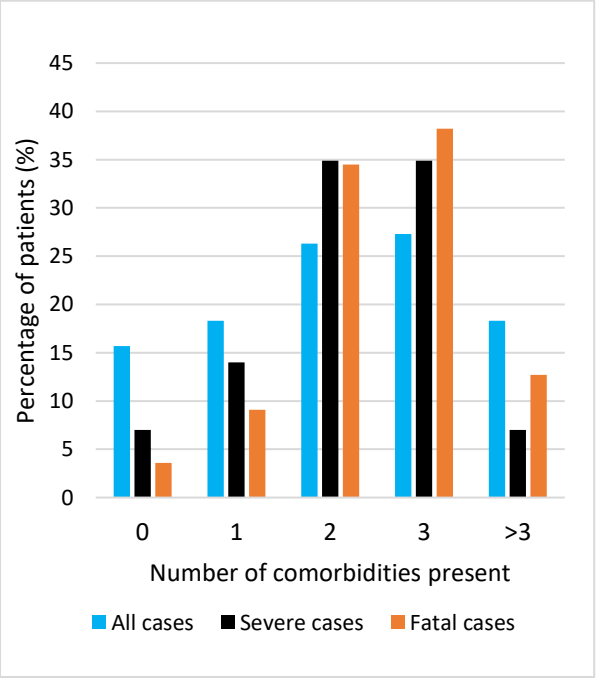

Figure 3: Distribution of associated comorbidities according to the disease severity

Severe disease was more common among males (n = 44; 60.3%) than females (n = 29; 39.7%; Table 01), with a statistically significant gender influence on disease severity (χ2 = 7.0; p = 0.01). Thirty (n = 30; 58.8%) men succumbed due to Coivd-19 disease, while twenty-five (n = 25; 58.1%) need an ICU admission. Out of all deaths (n = 55), 58.8% were men. The mean age (SD) of demised men was 59 (11) years, and women were 64 (11) years. Out of all ICU admissions (n = 43), 58.1% were men. The males (54 ± 15 years) who needed an ICU admission were younger than the females (62 ± 11 years; T = 1.857, P = 0.07). However, the age difference among demised males (59 ± 11 years) and females (64 ± 11 years) was statistically not significant (T = 1.4, P = 0.17).

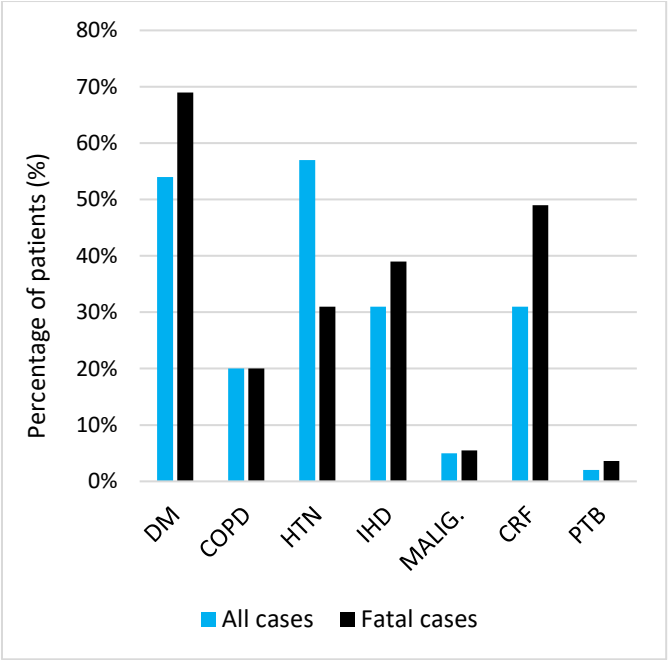

Figure 4: Distribution of associated comorbidities with case fatality in Covid 19 disease

(DM: diabetes; COPD: chronic obstructive pulmonary disease or bronchial asthma; HTN: hypertension; IHD: ischemic heart disease; MALIG.: malignancy; CRF: chronic kidney disease; PTB: past tuberculosis)

A total of 252 (84.3%) patients had at least one coexisting disease condition; hypertension (n = 172, 57.1%) and diabetes (n = 162, 53.8%) being the most common (Table 01). Figure 03 describes the distribution of associated comorbidities in the study cohort and among severe and fatal cases.

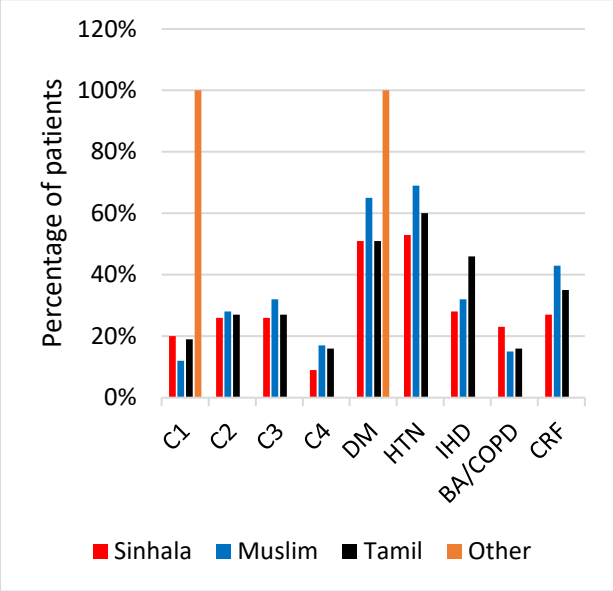

Figure 05. Distribution of comorbidities in the ethnic groups

(C1: number of comorbidities =1; C2: number of comorbidities =2; C3: number of comorbidities =3; C4: number of comorbidities =4; DM: diabetes; HTN: hypertension; IHD: ischemic heart disease; BA/COPD: bronchial asthma or chronic obstructive pulmonary disease; CKD: chronic kidney disease)

The prevalence of having two or three co-existing disease conditions was 53.6%. In severe and fatal infections, the prevalence of two or three disease conditions raised respectively up to 69.8% and 72.7%. Figure 04 describes the distribution of associated co-morbidities among fatal Covid-19 cases. Compared to non-fatal cases, diabetes (69%) and chronic kidney disease (49%) were more prevalent among fatal cases (Figure 04; Table 01). There was a significant association between case fatality and diabetes ($\chi 2$ = 6.958; p = 0.008) or chronic kidney disease ($\chi 2$ =10.981; p=0.001). A similar statistically significant association was found between case severity and diabetes ($\chi 2$ = 4.838; p = 0.028) or chronic kidney disease ($\chi 2$ = 9.459; p = 0.002).

Since there was a significant association between ethnicity and case fatality, co-morbidity distribution among the ethnic groups was evaluated (Figure 05). Compared to other ethnic groups (35%–43%), multiple co-existing diseases were more prevalent in the Muslim ethnic group (49%). Diabetes (65%), hypertension (69%), chronic kidney disease (43%) was most prevalent among the Muslims when ischemic heart disease (46%) was most prevalent in the Tamils and bronchial asthma or chronic obstructive pulmonary disease (23%) in the Sinhalese.

The possible risk predictors of severe disease were assessed with binary logistic regression; which revealed male gender (OR: 2.292; 95% CI: 1.228–4.279), low oxygen saturation (< 96 %) at the time of chest radiograph (OR: 2.436; 95% CI: 1.304–4.552) and having an associated co-morbidity (OR: 4.886; 95% CI: 1.352–17.652) were independently associated with severe Covid-19 disease (Table 02).

Table 02: Possible risk predictors for severe disease in Covid-19 infection

Risk factor	B	S.E.	Wald	df	Odds	95% CI		
						Lower	Upper	P value
Age	–0.106	0.325	0.106	1	0.900	0.476	1.702	0.745
Gender (1)	0.829	0.318	6.782	1	2.292	1.228	4.279	0.009*
Smoking	0.127	0.634	0.040	1	0.881	0.254	3.052	0.842
SPO2	0.890	0.319	7.789	1	2.436	1.304	4.455	0.005*
Comorbidity (1)	1.586	0.655	5.859	1	4.889	1.352	17.652	0.015*

(Gender (1): male; SPO2: oxygen saturation less than 96%; Comorbidity (1): comorbidity present)

Low oxygen saturation (< 96%) at the time of chest radiograph (OR: 4.182; 95% CI: 1.971–8.872), and presence of associated co-morbidity (OR: 9.352; 95% CI: 1.160–75.371) were found as the possible risk predictors of fatal disease (Table 03). Unlike severe illness, the male gender was not a high-risk factor for subsequent progression into a fatal disease.

Table 03: Possible risk factors for fatal disease in Covid-19 infection

Risk factor	B	S.E.	Wald	df	ODDs	95% CI		P value
						Lower	Upper	
Advanced age	–0.189	0.370	0.261	1	0.828	0.401	1.709	0.610
Gender (1)	–0.489	0.360	1.842	1	1.632	0.805	3.301	0.175
Smoking	0.494	0.658	0.563	1	1.639	0.451	5.955	0.453
SPO2	1.431	0.384	13.903	1	4.182	1.971	8.872	<0.001**
Comorbidity (1)	2.236	1.065	4.408	1	9.352	1.160	75.371	0.036*

(Gender (1): male; SPO2: oxygen saturation less than 96%; Comorbidity (1): comorbidity present)

DISCUSSION

This study of 300 symptomatic Covid-19 infected high-risk adults treated at Base Hospital Homagama Sri Lanka demonstrates an 18.3% case fatality rate. The risk factors associated with the fatal outcome include the presence of associated comorbidity and low oxygen saturation (SPO2 < 96%) at the time of chest X-ray. In this cohort, severe infection was reported in 24.3%, and male gender, associated comorbidity, and hypoxemia (SPO2 < 96%) were the recognized risk factors for severe infection. Among the comorbidities, diabetes and chronic kidney disease have shown a significant positive association with severe or fatal Covid-19 disease.

The mortality rate (18.3%) reported in this study was higher than in previous studies where the mortality ranged from 4.3% to 16.7%. [8,17]. A parallel Chinese study has reported a fatality of 14% (95% CI 3.9–32%) among hospitalized patients [18]. The case fatality rate reported in Sri Lanka as of January 2020 was as low as 0.047% [19]. The high fatality rates reported in this study are multifactorial. The study cohort included symptomatic patients suspected to have Covid-19 pneumonia; the majority (84.7%) had one or more associated co-morbidities. We studied a high-risk cohort as the study centre was the national multi-disciplinary centre dedicated to managing patients with severe disease or who were liable for severe disease. Collectively, this study reports the mortality rates of high-risk Covid-19 patients, which is an overestimate of the mortality rates of the general Sri Lankan population. Since previous studies described the presence of associated co-morbidity as a risk factor for death and severe Covid-19 disease [8,9,11], this study describes the Sri Lankan perspective of the impact of non-communicable disease burden on the short-term outcome of Covid-19 disease.

Non-communicable diseases have a direct impact on the outcome of Covid-19 disease; having one or more co-morbidity was associated with high fatality with high ODDs (Cao et al. OR: 4.88, CI [1.47–16.21], p < 0.05); Chen T et al. OR: 2.70, CI [1.64–4.43], p < 0.05; Benelli et al. OR: 4.10, CI [2.08–8.06], p < 0.05) [9,14,20]. Our findings agree with that of other geographical regions by reporting a fivefold risk for severe infection (OR: 4.89, CI [1.35–17.6], p = 0.015) and a nearly nine-fold risk (OR: 9.352, CI [1.16–75.37], p = 0.036) for the fatal disease for those who with co-morbidity.

Additionally, this study has identified co-existing diabetes and chronic kidney disease as high-risk factors for Covid-19 disease severity and fatality. The presence of diabetes has shown an increased need for hospitalized Covid-19 management (OR: 2.24; 95% CI: 1.84–2.73) and high risk for critical Covid-19 illness (OR:1.24; 95% CI: 1.03–1.50) [8,19,20]. Interestingly, newly diagnosed diabetics have reported higher mortality than long-standing

diabetics [10]. According to the literature, high blood glucose levels and other diabetes-associated conditions such as ketoacidosis, nephropathy, and ischemic heart disease have led to severe disease outcomes among diabetic Covid-19 patients [11]. A limited number of studies have described chronic kidney disease as a risk factor for poor Covid-19 outcomes. The high incidence of hypertension, diabetes and cardiovascular diseases among chronic kidney disease patients probably contributes to the high case fatality [13,22,23].

Similar to the present study, previous studies have also reported a relatively minor association between fatality and the presence of cardiovascular disease, COPD or malignancy [9]. Reciprocally, Ejaz et al. have found a significant contribution from COPD to severe Covid-19 disease by describing structural lung damage, low immunity and increased mucus production in COPD as possible contributors [8].

We have not recognized hypertension as a risk factor for either disease severity or fatality. A significant inhomogeneity has been observed among the studies that describe the association between hypertension and Covid-19 severity [10]. Some studies described hypertension as an independent risk factor (OR: 2.01 to 1.562) for severe Covid-19 disease [8,24], and others described uncontrolled hypertension as a risk factor. The negligible impact of mild controlled hypertension on disease severity has also been highlighted [8]. High average systolic blood pressure and variability in systolic or diastolic blood pressure were associated with severe and fatal Covid-19 disease [10]. Therefore, controlling hypertension and maintaining stable blood pressure appear to be the cornerstones in achieving a good outcome in Covid-19 infection among patients with hypertension.

We recognized ~~the~~ male gender as a risk factor for severe disease; males were at two-fold risk than females (OR: 2.292, CI [1.13–4.28], p = 0.009). Even before the Covid-19 era, non-communicable disease-related mortality among Sri Lankan males was higher than females; this may explain the risk of male gender in adverse Covid-19 outcomes [25]. Even for other populations, the male gender was a recognized risk factor for severe Covid-19 disease, principally explained by lifestyle differences such as smoking and hormonal differences affecting the inflammatory process in Covid-19 disease pathogenesis [10].

Silent hypoxemia is a feature of Covid-19 pneumonia which can present as a respiratory failure without warning signs such as dyspnea [26]. The significant lung involvement in silent hypoxemia has been described as a high CT (computed tomographic) severity score [26,27]. The pathophysiology of hypoxia in Covid-19 disease is related to deficient oxygen-exchanging capacity in the presence of diffuse pulmonary infiltrates [28]. Patients with silent or symptomatic hypoxemia were found to have poor outcomes [26,27]. We also confirmed a high mortality risk (OR: 4.182; 95% CI: 1.971–8.872) and need for ICU management (OR: 2.436; 95% CI: 1.304–4.552) among patients with low peripheral oxygen saturation. Identification of silent hypoxia is reliable using a pulse oximeter with high sensitivity (75%), specificity (99.29%), and positive predictive values (99.94%) [28]. Therefore, triaging into risk categories is possible using the pulse oximeter values.

Ethnic influence on Covid-19 disease severity and fatality has been established. Black patients and South Asians were at a higher mortality risk compared to white ethnic groups. The need for hospitalized care and mortality rates have also been influenced by ethnicity [10]. However, a few studies have not recognized race as a risk factor for severe disease after adjusting for clinical and socio-demographic factors [10,29]. We also reported a significant association between ethnicity and fatal disease. As suggested for other geographical regions, the ethnic association for the fatal disease may represent the differences in socioeconomic and or co-morbidity status in different ethnic groups [29,30]. Further studies that include the adjustment for confounders are recommended to evaluate the ethnic influence on Covid-19 disease severity or fatality.

Moderate heterogeneity was observed among the studies focused on the influence of smoking on Covid-19 disease severity. Compared to ex-smokers and non-smokers, active smoking has been reported as a risk factor for severe and fatal diseases [31,32]. Reciprocally, when the major source of heterogeneity was removed, the effect of smoking on disease severity was said to be

insignificant [33]. The current study has also not established a positive relationship between smoking and disease severity. The rate of smoking in the study population (6%) was much lower than (14.4%) the national values [34]. The high disease transmissibility affecting the direct doctor-patient interviews and patient factors such as pandemic anxiety may have deteriorated the quality of data collected. Also, in a novel disease like Covid-19 where there is a lack of knowledge on the relevance of risk factors such as smoking, the interviewing doctors' focus on asking relevant questions to assess the risk factors would naturally be leading to low quality data. Therefore, the burden of smoking on Covid-19 disease severity may represent an underestimate of the actual values. As reported in the current study, falsely reporting low smoking rates may have influenced previous studies. Thus, more objective studies are recommended to evaluate the influence of smoking on the outcome of Covid-19 disease.

Though many cohort studies have recognized advanced age (> 60 years) as a significant risk factor for severe disease [9,10], we have not recognized advanced age as a risk factor for either severe or fatal infection. Age-related factors such as increased frequency of having associated co-morbidities and weaker immunity to combat the disease have been recognized as possible causes for high fatality [10]. Our biased cohort, with co-morbidities (84%) even at a younger age, has probably modified the risk. Therefore, advanced age has not acted as an independent risk factor.

In agreement with the previous studies, fever, cough, dyspnoea, body aches, and headache were the most prevalent symptoms [10,17]. In contrast to other studies, we could not establish a significant association between the presenting symptoms and subsequent severe disease [9,10].

Infectious disease prevention activities are categorized into three: primary, secondary and tertiary. Successful secondary prevention is based on host and disease features were identifying and treating high-risk groups is crucial. A population-based vaccination program is an effective primary prevention strategy that improves the host's immunity, controls disease transmission, and reduces mortality and morbidity in Covid-19 disease [36]. Though there are few newly recommended vaccines against the Covid-19 infection, the limited vaccine availability is the major obstacle to implementing a whole-population vaccination program. Therefore, vaccinating vulnerable groups is a practical, quick option to reduce mortality and morbidity.

Also, defining high-risk groups facilitates effective resource allocation. The prognosis of Covid-19 disease is multifactorial; hospital factors, particularly the hospital facilities, are crucial in determining a positive patient outcome [13]. In the climax of the pandemic, with growing patient numbers, even the health systems of affluent countries collapsed due to the high demand for resources [12,13]. Thus, allocating limited available resources for vulnerable patients would dampen the mortality rates. Therefore, defining high-risk groups for the Sri Lankan population would help make policy and resource allocation decisions in this country and countries in nearby geographical regions.

The predominant viral lineage present in Sri Lanka during the study period was B.1.411 [6]. Since virulence and viral factors may change with the viral lineage, the findings of this study would be more relevant to B.1.411 lineage.

CONCLUSION

This single-centre study of adult Covid-19 patients complicated with co-existing non-communicable diseases has reported high morbidity and mortality rates. The host-related risk factors associated with a severe/ fatal disease recognized in this study were compatible with other studies. Defining the vulnerable groups helps clinicians and policymakers to develop strategies to mitigate the effects of this disastrous pandemic. Since the knowledge of this novel virus is constantly changing, frequent updates may further strengthen the ability to combat the current pandemic.

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Author contribution
IK- Conceptualization, study design, data acquisition and management, analysis, interpretation, drafting and editing manuscript, approval of the final version
BAG - Conceptualization, data acquisition, critically analyzing manuscript, approval of the final version
HMASD - Data acquisition, critically analyzing manuscript, approval of the final version

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all authors declare no conflict of interest

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