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Survival analysis of hospitalized COVID-19 patients in New Yangon General Hospital by prognostic indicators

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ABSTRACT

Background: Coronavirus disease (COVID-19) is an infectious disease of the SARS-CoV-2 virus and it can infect anyone resulting in serious illness and death.

Methods: A retrospective cohort study was conducted in New Yangon General Hospital (NYGH), Yangon between September and November, 2022. Previous records of COVID-19 in-patients admitted to NYGH from 1st June to 31st October, 2021, were reviewed. COVID-19 in-patients who tested positive by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) or rapid diagnostic test (RDT) were included in this study. Multivariate analysis by Cox proportional-hazards (CPH) model was used to identify the prognostic indicators associated with the survival of COVID-19 inpatients.

Results: Of (460) COVID-19 positive patients, there were 133 (28.9%) deaths with mortality rate of 16.9 per 1000 person-days. Then, 97 (72.9%) deaths occurred within 21 days of symptom onset, with median survival time of 28 (95% CI: 25-36) days. The results of the CPH model showed that the abnormal chest X-ray (CXR) [aHR=3.8, 95% CI: (1.1, 12.6), p=0.032], SpO₂ level below 92% [aHR=3.7, 95% CI: 2.3, 5.9, p<0.001)], serum creatinine level more than 133 μ mol/L [aHR=1.9, 95% CI: 1.1, 3.2, p=0.025] and C-reactive protein level (CRP) more than 10 mg/L [aHR=3.9, 95% CI: 1.2, 12.9, p=0.027] were the prognostic indicators of COVID-19 death among inpatients in NYGH.

Conclusions: Patients with abnormal CXR result, low SpO2 level, high serum creatinine level, and high CRP level may have increased risks of death among COVID-19 inpatients in NYGH. Thus, close monitoring of the hospitalized COVID-19 inpatients by using these prognostic indicators should be emphasized.

Keywords: Hospitalized COVID-19 patients, New Yangon General Hospital, Prognostic indicators

INTRODUCTION

Coronavirus disease (COVID-19) is a respiratory tract infection caused by the SARS-CoV-2 virus and it can infect anyone at any age resulting in serious illness and death.¹ COVID-19 outbreak was declared on 30 Jan 2020 and characterized as a pandemic on 11 March 2020 according to WHO.² As of date (9.8.22), there were 590 million total cases and 6.43 million deaths due to COVID-19 in the world, and in Myanmar, 614,240 labconfirmed cases among 8,588,979 tests and 19,434 deaths were reported and 593,036 cases recovered.^{3,4} Then, 30.2 million people of Myanmar were vaccinated according to the data of ministry of health, Myanmar (6.8.22).⁵ Delta variants of SARS-CoV-2 causes more severe COVID-19 than other variants such as Alpha, Beta, and resulted in rapid rise of COVID-19 cases, hospitalizations, and deaths across the U.S. and the rest of the world.⁶ In Myanmar, Delta variant was found in most of the COVID-19 cases in the third wave of pandemic.

Globally, the mortality rate of hospitalized COVID-19 patients varies between 4 and 70%.7 According to a systematic review, the mortality rate of the COVID-19 was 11.5% for general patients admitted to the hospital and 40.5% for those with critical illness.8 A recent study also highlighted that the mortality risks substantially elevated when the number of comorbidities increased from one to five or more.9 In New Yangon General Hospital (NYGH), all admitted COVID-19 patients were treated according to the national treatment guidelines of ministry of health (MOH).¹⁰ The in-patients admitted to NYGH on the first day of admission underwent the clinical and laboratory assessment, and all the findings and treatments given to the patients were noted in the patients' medical records, and all records were properly maintained in the medical record department of hospital.

New Yangon general hospital was purposively selected as the study area because it was one of the tertiary and referral hospitals of COVID-19 patients in Yangon, where patients' clinical information and data were properly recorded. Although all COVID-19 patients are treated with the standardized treatment guidelines of ministry of health, the outcomes of patients can differ depending on the prognostic indicators of COVID-19 infection. On the other hand, being a newly emerging disease, limited medical approaches and treatments are available for severe COVID-19 globally and therefore, it is important to determine effective prognostic predictors for timely intervention.¹¹ In addition, researches regarding the clinical progress of COVID-19 and survival outcomes are scarce in Myanmar. Therefore, the study was conducted to identify prognostic indicators of mortality of COVID-19 patients admitted to NYGH during the third wave of COVID-19 in Myanmar. Moreover, laboratory-confirmed cases and deaths distinctly increased within 9 weeks of the onset of the third wave in Myanmar, and COVID-19 epidemic began with a surge of confirmed cases in the last week of May 2021.12 By exploring the prognostic indicators of COVID-19 among the in-patients, better decision making in disease management can be achieved to reduce the mortality of patients with COVID-19 in the future. COVID-19 death was defined as a death resulting from a clinically compatible illness, in a probable or confirmed COVID-19 case, unless there is a clear alternative cause of death that cannot be related to COVID disease and there should be no period of complete recovery from COVID-19 between illness and death.¹³ The outcome of the study was time to death since COVID-19 symptom onset. The survival time was defined as days and that was discrete type of variable. Therefore, survival was 100% at time zero and the end point of study was death.

METHODS

Study setting and participants

A retrospective cohort study was conducted between September and November, 2022 in New Yangon General Hospital (NYGH) located in Yangon region of Myanmar. Previous admission records of COVID-19 in-patients admitted to hospital, from June to October, 2021 were reviewed. Among 876 total COVID-19 patients' records, 460 patients were selected randomly. COVID-19 inpatients who resulted positive by real time reverse transcriptase-polymerase chain reaction (RT-PCR) or rapid diagnostic test (RDT) test were included in this study.

Data collection method and tools

Advocacy meeting with the authorized people in NYGH was carried out before the data collection and the permission to conduct the research was obtained. Before data collection, principal investigator trained and discussed with the research assistance team for the data collection procedure to avoid inter-observer variation between data collectors. Pro-forma was developed including the following information: clinical symptoms of COVID-19 infection, time to admission and duration of hospital stay, presence of comorbidities, laboratory findings, clinical parameters, and COVID-19 vaccination status.

Statistical analysis

Data entry, checking and cleaning was carried out using Microsoft excel 2016, and data analysis was conducted using STATA 14.2 version. The main outcome variable was survivor (discharged) and non-survivor (dead). To identify the prognostic indicators associated with survival of COVID-19 patients and analyze whether the included variables were predictive of inpatient mortality, a multivariable analysis by Cox proportional hazards model was applied. The covariates with a p-value of less than 0.2 in the bivariate analysis were used as a potential for multivariate Cox-regression analysis. Kaplan-Meier survival analysis was used to compare the variation trend of survival rates and Log-rank test was used to compare the differences in survival functions between levels of comorbidities. P value less than 0.05 was considered statistically significant.

RESULTS

Total 460 COVID-19 patients' medical records were involved in this study. Mean (SD) age of the patients was 60 (15.7) years with minimum age being 17 and maximum age being 95. Male to female proportion was not significantly different in both survivor and dead groups. There were 133 (28.9%) deaths with mortality rate of 16.87 cases per 1000 person-days (95% CI: 14.23, 19.99). Median survival time was 28 (95% CI: 25-36) days. According to the results, among the patients who died, 105 (38.9%) of patients had the symptom of dyspnea with a death rate of 21.9 cases per 1000 persondays (95% CI: 18.1, 26.5) (Table 1). Patients with diabetes, had higher death rates of 22.1 cases per 1000 person-days than non-diabetic patients (Table 2). Moreover, the patients who had low SpO₂ level, abnormal CXR findings, high WBC count, neutrophil count, CRP, D-Dimer, ALP, ALT, urea, creatinine and high serum sodium level had higher death rates of, 33.9, 20.0, 27.6, 26.8, 19.6, 28.3, 26.7, 19.8, 24.1, 31.4 and 40.3 cases per 1000 person-days respectively (Table 3). Table 4 showed the death rate and survival probability of COVID-19 patients admitted to NYGH, and based on the life table estimate, among the 133 COVID-19 deaths, 97

(72.9%) deaths occurred within 21 days of symptom onset. Multivariate Cox-regression analysis results showed that patients with the abnormal chest X-ray (CXR) [aHR=3.8, 95% CI: (1.1, 12.6), p=0.032], low SpO₂ level [aHR=3.7, 95% CI: 2.3, 5.9, p<0.001)], high serum creatinine level [aHR=1.9, 95% CI: 1.1, 3.2, p=0.025] and high C-reactive protein level (CRP) [aHR=3.9, 95% CI: 1.2, 12.9, p=0.027] had an increased risk of death in this study (Table 5).

Age (years)	N (%)	N (%)	Death rate (95% CI) per 1000 person-days	P value ^a
			× v	
	162 (77.1)	48 (22.9)	14.1 (10.6, 18.7)	0.000
>60 1	165 (66.0)	85 (34.0)	19.2 (15.5, 23.7)	0.230
Sex	· · · · · ·	. ,		
Male 1	150 (64.1)	84 (35.9)	20.1 (16.3, 24.9)	0.051
Female 1	177 (78.3)	49 (21.7)	13.3 (10.1, 17.7)	0.051
Fever				
Yes 2	265 (70.5)	111 (29.5)	17.0 (14.1, 20.4)	0.062
No 6	52 (73.8)	22 (26.2)	16.8 (11.0, 25.4)	0.962
Cough		. ,		
Yes 1	195 (69.2)	87 (30.8)	17.6 (14.2, 21.7)	0.701
No 1	132 (74.2)	46 (25.8)	15.9 (11.9, 21.2)	0.791
Dyspnea				
	165 (61.1)	105 (38.9)	21.9 (18.1, 26.5)	-0.001
No 1	162 (85.3)	28 (14.7)	9.2 (6.4, 13.3)	< 0.001
Sore throat				
Yes 3	32 (76.2)	10 (23.8)	15.2 (8.2, 28.2)	0.907
No 2	295 (70.6)	123 (29.4)	17 (14.3, 20.3)	0.897
Loss of smell				
Yes 5	52 (75.4)	17 (24.6)	15.6 (9.7, 25.1)	0.092
No 2	275 (70.3)	116 (29.7)	17.2 (14.3, 20.6)	0.983
Loose motions				
Yes 4	40 (74.1)	14 (25.9)	16.4 (9.7, 27.6)	0.886
No 2	287 (70.7)	119 (29.3)	17 (14.2, 20.4)	0.000

^aLog-rank test

Table 2: Comorbidities and treatment outcome of hospitalized COVID-19 patients, (n=460).

Variables	Survived/ discharged, (n=327) N (%)	Death, (n=133) N (%)	Death rate (95% CI) per 1000 person-days	P value ^a	
Mortality rate			16.9 (14.3, 20.1)		
Comorbidities					
Yes	210 (69.5)	92 (30.5)	17.9 (14.6, 21.9)	0.482	
No	117 (74.1)	41 (25.9)	15.2 (11.2, 20.7)	0.462	
Coronary artery dis	ease				
Yes	57 (64.0)	32 (35.9)	22.3 (15.7, 31.5)	0.065	
No	270 (72.8)	101 (27.2)	15.8 (12.9, 19.2)	0.065	
Hypertension					
Yes	141 (69.8)	61(30.2)	17.5 (13.7, 22.5)	0.915	
No	186 (72.1)	72 (27.9)	16.5 (13.1, 20.8)	0.915	
Diabetes mellitus					
Yes	85 (62.0)	52 (37.9)	22.1 (16.8, 29.0)	0.021	
No	242 (74.9)	81 (25.1)	14.8 (11.9, 18.3)		
Chronic pulmonary	diseases				
Yes	35 (79.6)	9 (20.5)	11.8 (6.1, 22.7)	0.166	
No	292 (70.2)	124 (29.8)	17.5 (14.7, 20.9)	0.100	

Continued.

Variables	Survived/ discharged, (n=327) N (%)	Death, (n=133) N (%)	Death rate (95% CI) per 1000 person-days	P value ^a			
Chronic kidney dise	ease						
Yes	17 (62.9)	10 (37.0)	20.4 (10.9, 37.9)	0.724			
No	310 (71.6)	123 (28.4)	16.7 (14.0, 19.9)	0.724			
Malignancy							
Yes	12 (70.6)	5 (29.4)	15.8 (7.4, 42.7)	0.974			
No	315 (71.1)	128 (28.9)	16.9 (14.2, 20.1)				
History of COVID-19 vaccination							
Yes	24 (82.8)	5 (17.2)	9.9 (4.14, 23.9)	0.102			
No	303 (70.3)	128 (29.7)	17.3 (14.6, 20.7)	0.192			
Time between	Mean (SD) (Days)	Mean (SD) (Days)					
symptom onset and admission	6.9 (7.3)	9 (6.0)		0.002 ^b			
Duration of hospital stay	10.5 (6.2)	7.5 (6.5)		<0.001 ^b			

^aLog-rank test, ^bMann-Whitney U test.

Table 3: Clinical parameters and treatment outcome of hospitalized COVID-19 patients, (n=460).

Variables	Survived/discharged, (n=327)	Death, (n=133)	_ Death rate (95% CI)	P value ^a	
variables	N (%)	N (%)	per 1000 person-days		
SpO ₂					
Normal SpO ₂	74 (42.1)	102 (57.9)	6.4 (4.5, 9.1)	-0.001	
Low SpO ₂ (<92%)	253 (89.1)	31 (10.9)	33.9 (27.9, 41.2)	< 0.001	
Temperature					
Normal	269 (71.9)	105 (28.1)	16.5 (13.6, 19.9)	0.527	
High temperature	58 (67.4)	28 (32.6)	19 (13.2, 27.6)	0.327	
Heart rate					
Normal	234 (73.8)	83 (26.2)	15.5 (12.5, 19.2)		
Bradycardia	7 (77.8)	2 (22.2)	13.2 (3.3, 52.6)	0.290	
Tachycardia	86 (64.2)	48 (35.8)	20.5 (15.4, 27.2)		
Blood pressure					
Normal BP	79 (66.9)	39 (33.1)	15.9 (13.0, 19.5)	0.253	
Increased BP	248 (72.5)	94 (27.5)	19.9 (14.6, 27.3)	0.233	
ECG					
Normal	251 (74.0) 88 (25.9) 15.2 (12.3, 18.7)		15.2 (12.3, 18.7)	0.070	
Abnormal	76 (62.8)	45 (37.2)	21.9 (16.3, 29.3)	0.069	
CXR					
Normal	95 (96.9)	3 (3.1)	2.2 (0.72, 6.9)	< 0.001	
Abnormal	232 (64.1)	130 (35.9)	20 (16.8, 23.8)	<0.001	
WBC					
Normal	219 (92.3)	45 (17.1)	10.4 (7.8, 13.9)		
Low	24 (92.3)	2 (7.7)	4.8 (1.2, 19.3)	< 0.001	
High	84 (49.4)	86 (50.6)	27.6 (22.4, 34.1)		
Neutrophil					
Normal	206 (86.9)	31 (13.1)	8.2 (5.7, 11.6)		
Low	15 (93.8)	1 (6.3)	3.6 (0.5, 25.4)	< 0.001	
High	106 (51.2)	101 (48.8)	26.8 (22.1, 32.6)		
Lymphocyte					
Normal	200 (75.5)	65 (24.5)	14.6 (11.5, 18.7)		
Low	114 (63.3)	66 (36.7)	20.9 (16.4, 26.6)	0.096	
High	13 (86.7)	2 (13.3)	14.6 (11.5, 18.7)		
Platelet					
Normal	262 (71.8)	103 (28.2)	16.6 (13.7,20.2)	0.000	
Low	44 (70.9)	18 (29.0)	17.9 (11.3, 28.4)	0.890	

Continued.

Variables	Survived/discharged, (n=327)	Death, (n=133)	Death rate (95% CI)	P value ^a	
High	21 (63.6)	12 (36.4)	18.7 (10.6, 32.9)		
Hemoglobin					
Normal	211 (70.3)	89 (29.7)	17.6 (14.3,21.6)	0.461	
Anemia	116 (75.5)	44 (27.5)	15.8 (11.8,21.3)		
MCV	× /	,			
Normal	193 (70.9)	79 (29.0)	16.8 (13.4,20.9)		
Low	133 (71.5)	53 (28.5)	17.2 (13.2,22.6)	0.793	
High	1 (50)	1 (50.0)	18.5 (2.6,131.5)	0.775	
C-reactive prot					
Normal	69 (95.8)	3 (4.2)	2.6 (0.8, 8.1)	< 0.001	
High	222 (65.1)	119 (34.9)	19.6 (16.4, 23.5)		
D-Dimer (n=442		· · /			
Normal	231 (84.0)	44 (16.0)	9.8 (7.3, 13.2)	< 0.001	
High	78 (46.7)	89 (53.3)	28.3 (22.9, 34.8)		
ALP		· /			
Normal	278 (74.9)	93 (25.1)	14.7 (12.0, 18.1)	0.012	
Low	4 (80.0)	1 (20.0)	12.3 (1.7, 87.6)		
High	45 (53.6)	39 (46.4)	26.7 (19.5, 36.6)	-	
AST					
Normal	117 (77.5)	133 (28.9)	13.3 (9.5, 18.6)	0.065	
High	210 (67.9)	99 (32.0)	18.8 (15.4, 22.8)		
ALT					
Normal	162 (77.9)	46 (22.1)	13.3 (9.9, 17.8)	0.044	
High	165 (65.5)	87 (34.5)	19.8 (16.0, 24.4)		
Urea					
Normal	153 (83.2)	31 (16.9)	10.2 (7.2, 14.6)	< 0.001	
Low	44 (83.0)	9 (16.9)	9.5 (4.9, 18.2)		
High	130 (58.3)	93 (41.7)	24.1 (19.6, 29.5)		
Serum creatinin					
Normal	300 (73.7)	107 (26.3)	15.3 (12.6,18.4)	< 0.001	
High	27 (50.9)	26 (49.1)	31.4 (21.4,46.1)		
Serum sodium					
Normal	139 (70.1)	58 (29.4)	17.1 (13.2,22.2)	0.021	
Low	184 (72.4)	70 (27.6)	16.2 (12.8,20.4)		
High	4 (44.4)	5 (55.6)	40.3 (16.8,96.9)		
Serum potassiu					
Normal	251 (71.1)	102 (28.9)	17.0 (14.0,20.7)	0.290	
Low	65 (77.4)	19 (22.6)	13.4 (8.5,20.9)		
High	11 (47.8)	12 (52,2)	27.6 (15.7,48.6)		

^aLog-rank test

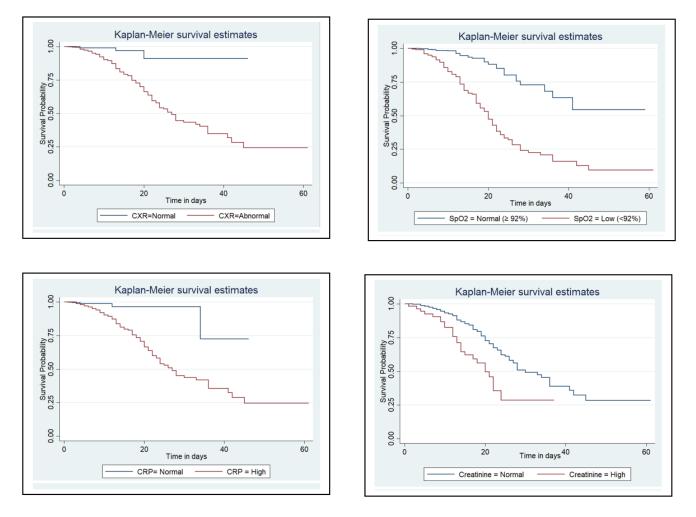
Table 4: Death rate and survival probability of hospitalized COVID-19 patients, (n=460).

Interval (days)	No. at risk	Death	%	Censored	Survival probability	Cumulative survival prob.
0-7	460	14	10.5	13	0.97	0.96
8-14	433	42	31.6	115	0.90	0.86
15-21	276	41	30.8	120	0.85	0.69
22-28	115	23	17.3	45	0.80	0.52
29-35	47	7	5.3	16	0.85	0.42
36-42	24	4	3.0	10	0.83	0.33
43-49	10	2	1.5	5	0.80	0.25
50-56	3	0	0	1	1	0.25
57-63	2	0	0	2	1	0.25

Table 5: Multivariate Cox-regression analysis of prognostic indicators of mortality among hospitalized COVID-19					
patients in NYGH.					

Prognostic indicator	Category	β Coefficient (95% CI)	aHR (95% CI)	P value
Chost V nov	Abnormal	1.3 (0.1, 2.5)	3.8 (1.1, 12.6)	0.032
Chest X-ray	Normal (Ref)	1.5 (0.1, 2.3)	1	0.032
SO	Low level	- 1.3 (0.8, 1.8)	3.7 (2.3, 5.9)	<0.001
SpO ₂	Normal (Ref)		1	< 0.001
Construction in a	High	0.6 (0.0, 1.2)	1.9 (1.1, 3.2)	0.025
Creatinine	Normal (Ref)		1	0.025
C-reactive protein	High	1.4 (0.2, 2.6)	3.9 (1.2, 12.9)	0.027
	Normal (Ref)		1	0.027

aHR = Adjusted hazard ratio.





DISCUSSION

The study result revealed that nearly one third (28.9%) of patients died among the hospitalized COVID-19 inpatients in NYGH, during the third wave of COVID-19 pandemic. The patients with abnormal CXR result, low SpO₂ level, high serum creatinine level, and high Creactive protein (CRP) level had an increased risk of death. All COVID-19 patients admitted to NYGH had at least one symptom. Dyspnea, fever and cough were the most common symptoms among the study population, and this is consistent with the findings from a study in Bhutan.¹⁴ Regarding the mortality rate, there was (29%) in the study from Congo, and similar to the current study result (28.9%).¹⁵ However, comparing with Ethiopia and Iran, where there were (11.14%) and (17.4%) deaths respectively, the mortality rate of the current study was higher than Ethiopia and Iran, probably owing to the difference in the predominant viral strains during the study periods.^{16,17} Most of COVID-19 deaths in Iran were associated with longer time-lag before hospital admission which was similar to the current study. Duration of

hospital stay was shorter among non-survivors than survivors in this study which was similar with the study result of Iran.¹⁷ It is reasonable that critical patients died earlier within a few days of hospital stay due to the severity of the disease itself. Besides, survivors have to complete 11 to 21 days of isolation period depending on the disease severity according to the national guideline of MOH Myanmar.¹⁰ Median survival time was 28 days in the current study, and 9 days in the study from Ethiopia.¹⁶ More than half of the COVID-19 deaths (72.9%) occurred within 21 days of symptom onset in this study, and however, the majority (87.2%) of deaths occurred within the first 14 days of admission in the Ethiopia study.¹⁶ Therefore, COVID-19 patients should be closely monitored within 21 days of illness to reduce mortality. Previous studies mentioned that old age was more likely to increase the mortality rate.7,15,16,18-20 However, there was no statistically significant association between age and mortality of COVID-19 patients in this study although death rate was higher in the older age group (>60 years old). The target range of oxygen saturation for COVID-19 patients as recommended by the national institutes of health (NIH) is 92-96%.²¹ The COVID-19 patients who had low SpO₂ level in the current study were found to have higher mortality, and this finding was similar to that of a study from Congo and Iran.^{15,22} Then, patients with abnormal chest X-ray (CXR) results had increased mortality rate in this study, and the common findings were moderate and severe chest infections. The cut-off point values of clinical parameters involved in this study were adopted from the laboratory reference values of Massachusetts general hospital.²³ Higher serum creatinine level was associated with increased mortality rate, and similarly, in the study conducted in Kinshasa medical center, level of creatinine was clearly elevated in non-survivors compared with survivors.⁷ In a retrospective cohort study conducted in 13 hospitals in metropolitan New York, it was also stated that acute kidney injury (AKI) in hospitalized COVID-19 patients was associated with a significant risk of death.24 Regarding body temperature, a patient is considered febrile or pyrexial if the oral temperature exceeds 37.5°C (99.5°F), and axillary temperature is about $0.55^{\circ}C$ (1.0°F) less than the oral temperature.²⁵ In the study, body temperature was not associated with the mortality of COVID-19; however, a study conducted in Wuhan stated that maximum body temperature on admission was the risk factor for disease progression.²⁰ Furthermore, CRP was strongly associated with mortality of COVID-19 in a study from New York and Iran which was consistent with the current study result.^{22,26} Similarly, study from Wuhan mentioned that CRP level was a risk factor for disease progression of COVID-19.20 Full vaccination against COVID-19 was associated with lower mortality among critically ill patients, however, there was no statistically significant association between COVID-19 vaccination and mortality in this study.²⁷ Owing to the healthcare workforce shortage and political crisis during 3rd wave of COVID-19, most of study population were unvaccinated at that time, and only 29 (6.3%) of COVID-19 patients

had history of COVID-19 vaccination, and among them, 18 (62.1%) patients completed two doses of vaccination.

Limitations

As a limitation, the study was conducted only in a single center, and COVID-19 patients in the community were not included in the study. Therefore, the study result can only be generalized to COVID-19 inpatient population.

CONCLUSION

The COVID-19 inpatients with abnormal CXR result, low SpO2 level, high serum creatinine level, and high CRP level may have increased risks of death among hospitalized patients. Therefore, screening and close monitoring of the hospitalized patients by using these prognostic indicators should be emphasized to prevent the death due to COVID-19 disease.

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Ethical approval: The study was approved by the Institutional Ethics Committee of the ministry of health, Myanmar with IRB approval number [IRB/2022-02] and the Institutional Review Board of the university of California, Davis.

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