RESEARCH ON PROGNOSTIC FACTORS FOR MORTALITY IN MODERATE TO SEVERE COVID-19 PATIENTS AT THE COVID-19 RESEARCH AND TREATMENT CENTER, HUE CENTRAL HOSPITAL

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Objectives: To investigate the clinical and paraclinical characteristics of moderate to severe COVID-19 patients at the COVID-19 Research and Treatment Center, Hue Central Hospital. To evaluate certain prognostic factors for mortality in moderate to severe COVID-19 patients.

Methods: Patients aged 18 years or older diagnosed with moderate to severe COVID-19 (according to Decision No. 250 of the Ministry of Health, dated January 28, 2022), at the COVID-19 Research and Treatment Center, Hue Central Hospital, from December 2021 to September 2023. This research employed a prospective approach.

Results: A total of 300 patients were enrolled in this study. The average age was 64,57 ± 18,45 years. The most common comorbidity was hypertension (50.2%). Patients who have been vaccinated (75.3%). The most common clinical signs and symptoms included cough (72%), shortness of breath (56.9%), and fatigue (87.5%). Abnormal paraclinical findings were WBC > 10.109/L (35.7%), LYM < 1.109/L (52.5%), D-dimer > 1000 ng/mL (52.9%), CRP > 10 mg/L (75.5%), Ferritin > 500 ng/mL (52.7%), LDH > 300 U/L (33.2%), positive cytokine storm (23.3%), and TSS 3-6 points (51.9%). The mortality rate was 18%. There was a significant association between underlying conditions, vaccination, LYM, LDH, D-dimer, Ferritin, chest X-rays, cytokine storm, and mortality prognosis in moderate to severe COVID-19 patients ($p < 0.05$). Non-vaccination was an independent prognostic factor for mortality in moderate to severe COVID-19 patients (OR 2.741; 95%CI: 1.168-6.431; $p < 0.005$). LDH > 300 U/L was an independent prognostic factor for mortality in moderate to severe COVID-19 patients (OR 6.696; 95%CI: 2.335-19.199; $p < 0.001$).

Conclusions: Cough, shortness of breath, and fatigue are common symptoms in moderate to severe COVID-19 patients. LYM < 1 x 109/L, D-dimer > 1000 ng/mL, Ferritin > 500 ng/mL, and CRP > 10 mg/L were mainly found in lab tests. The patient mortality rate was 18%. Non-vaccination and LDH > 300 U/L are independent predictors of mortality in moderate to severe COVID-19 patients.

Keywords: COVID-19, mortality prognosis.

INTRODUCTION

COVID-19 is an emerging infectious disease caused by SARS-CoV-215. The disease first appeared in late December 2019 at the Huanan Seafood Market in Wuhan, Hubei Province, China, and then spread worldwide, causing a global pandemic. The WHO declared a global emergency on January 30, 2020[12]. Since then, the SARS-CoV-2 virus has developed various variants such as Alpha, Beta, Delta, and Omicron. As of July 22, 2023, there have been over 750 million cases worldwide, with 6.5 million deaths, while in Vietnam, there have been over 11.5 million cases and 43,206 deaths[13]. SARS-CoV-2 is transmitted directly from person to person via

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respiratory droplets (mainly through droplet spread) and contaminated objects. In addition, the disease can spread through aerosols in enclosed spaces with poor ventilation, crowded places, or during aerosol-generating procedures in treatment facilities. These factors have led to a rapid increase in cases. When infected, patients may present with symptoms or be asymptomatic.

A meta-analysis by Rodrigues-Morales A. et al. on the clinical characteristics of COVID-19 noted that common symptoms include fever, cough, and shortness of breath. The study by Chen Nanshan et al. in China, published in The Lancet, showed that 75% of patients had bilateral lung lesions on chest X-rays and CT scans, 35% had reduced lymphocytes, 36% had elevated D-dimer, 52% had elevated IL-6, 63% had elevated Ferritin, and 86% had elevated CRP. The study also pointed out that the cytokine storm in the body triggers immune responses that cause widespread reactions in various organs, worsening the condition. Other studies indicated that about 20% of hospitalized patients develop severe disease, with 5% requiring ICU care, and the ICU mortality rate reaches 50%[1]. However, this rate can vary depending on many risk factors.

Early diagnosis of COVID-19 based on clinical and paraclinical symptoms to initiate timely treatment, as well as evaluating prognostic factors for mortality to apply effective treatment measures, is crucial and highly practical. Therefore, we conducted this study with two objectives: (1) To investigate some clinical and paraclinical characteristics of moderate to severe COVID-19 patients at the COVID-19 Research and Treatment Center, Hue Central Hospital; (2) To evaluate some prognostic factors for mortality in moderate to severe COVID-19 patients. The results of this study promise to provide valuable information not only to improve the diagnosis and treatment of COVID-19 patients but also to open new research directions in the medical field.

SUBJECTS AND METHODS

Subjects: Adult COVID-19 patients treate at the COVID-19 Research and Treatment Center, Hue Central Hospital, from December 2021 to September 2023.

Inclusion criteria: Patients aged 18 or older who met the diagnostic criteria according to the guidelines for diagnosing and treating moderate to severe COVID-19 (Decision No. 250/QD-BYT dated January 28, 2022).

Exclusion criteria: Patients who refused to participate in the study or voluntarily left treatment.

Methods

Study design: Prospective study.

Sample size: 300 patients diagnosed moderate to severe COVID-19 with medical records meeting the criteria from December 2021 to September 2023.

Data collection and processing: Clinical and paraclinical data were collected from medical records onto data collection forms. Data were entered and analyzed using SPSS software version 20.0.

RESULTS

During the period from December 2021 to September 2023, we collected data from 300 patients treated at the COVID-19 Research and Treatment Center, Hue Central Hospital, who met the study criteria. Our findings are as follows:

General Characteristics of patients with moderate to severe COVID-19

Table 1. Patient distribution by gender and age group

Gender	n	Percentage (%)
Male	156	52.0
Female	144	48.0

Gender	n	Percentage (%)
Age group	n	Percentage (%)
18 - 40	38	12.6
41 - 60	74	24.7
> 60	188	62.7
Total	300	100.0
Average age	64.57 ± 18.45 (18 - 101)	

Remarks: The proportion of male patients was slightly higher than 50%, and the average age was 64.57 ± 18.45 years.

Table 2. Comorbidities in COVID-19 patients

Characteristics		n	Percentage (%)
Comorbidities (n = 300)	Yes	249	83.0
	No	51	17.0
Underlying medical conditions	Hypertension	125	50.2
	Diabetes	66	26.5
	Overweight, obesity	60	24.1
	Cardiovascular disease, Cerebrovascular, hematology	77	30.9
	Neurologic diseases	39	15.7

Remarks: Most COVID-19 patients had ≥ 2 comorbidities, with hypertension being the most common (50.2%).

Table 3. COVID-19 vaccination status of patients

Characteristics		n	Percentage (%)
Vaccinated (n = 300)	Yes	226	75.3
	No	74	24.7
Number of doses received	1 Dose	24	10.6
	2 Dose	80	35.4
	3 Dose	104	46.0
	4 Dose	18	8.0

Remarks: A majority of COVID-19 patients were vaccinated, with most receiving three doses.

Table 4. Treatment outcomes

Outcome	n	Percentage (%)
Mortality	54	18.0
Survival	246	82.0

Remarks: The mortality rate was 18%.

Clinical and laboratory characteristics of patients with moderate to severe COVID-19

Table 5. Clinical symptom characteristics

Characteristics		n	Percentage (%)
Presence of symptoms	Yes	297	99.0
	No	3	1.0
Specific symptoms	Fever	97	32.6
	Cough	214	72.0
	Dyspnea	169	56.9
	Fatigue	260	87.5
	Sore Throat	103	34.6
		67	22.5

Remarks: Over 95% of patients displayed symptoms, with cough, dyspnea, and fatigue being the most common.

Table 6. Hematologic, biochemical, and cytokine laboratory characteristics

Characteristics		n	Percentage (%)
WBC (n = 300) (x 10^9/L)	< 4	28	9.3
	4 - 10	165	55.0
	> 10	107	35.7
LYM (n = 299) (x 10^9/L)	< 1	157	52.5
	≥ 1	142	47.5
D-dimer (n = 289) (ng/mL)	> 1000	153	52.9
	≤ 1000	136	47.1
CRP (n = 274) (mg/L)	> 10	207	75.5
	≤ 10	67	24.5
Ferritin (n = 258) (ng/mL)	≤ 500	122	47.3
	> 500	136	52.7

Characteristics		n	Percentage (%)
LDH (n = 292) (U/L)	> 300	97	33.2
	≤ 300	195	66.8
Cytokine Storm (n = 300)	Yes	70	23.3
	No	210	70.0
	Undetermined	20	6.7

Remarks: Laboratory tests showed that LYM < 1 x 10^9/L, D-dimer > 1000 ng/mL, and CRP > 10 mg/L were common findings, each observed in more than 50% of cases.

Table 7. Chest X-ray lung damage severity based on TSS score

TSS score	1 - 2 points	3 - 6 points	7 - 8 points	Normal	Indeterminate
n	58	122	55	**42**	**23**
Percentage (%)	24.6	51.9	23.5	**14.0**	**8.0**

Observations: A TSS score of 3-6 points accounted for more than 51% of cases.

Prognostic factors for mortality in the study population

Table 8. Age group and treatment outcome in COVID-19 patients

Age group	Treatment outcome			
	Mortality		Survival	
	n	%	n	%
18 - 40	4	10.5	34	**89.5**
41 - 60	13	17.6	61	**82.4**
> 60	37	19.7	151	**80.3**
Total	54	18.0	246	**82.0**
p-value	0.405			

Observations: There was no statistically significant association between age and treatment outcome (p > 0.05).

Table 9. Comorbidity and treatment outcome in COVID-19 patients

Comorbidity	Treatment outcome			
	Mortality		Survival	
	n	%	n	%
Yes	52	20.9	197	**79.1**
No	2	3.9	49	**96.1**
Total	54	18	246	**82**
p-value	0.004			

Observations: There was a statistically significant difference between comorbidities and treatment outcomes (p < 0.05).

Table 10. Vaccination status and treatment outcome in COVID-19 patients

Comorbidity	Treatment outcome				p-value
	Mortality		Survival		
	n	%	n	%	
Yes	23	10.2	203	89.8	< 0.001
No	31	41.9	43	58.1	
Total	54	18.0	246	82.0	

Observations: There is a statistically significant difference between vaccination status and treatment outcome ($p < 0.05$).

Table 11. Relationship between lymphocytes, CRP, LDH, D-dimer, ferritin, cytokine storm, chest X-ray findings, and treatment outcome in COVID-19 patients

Laboratory tests		Treatment Outcome				p-value
		Mortality		Survival		
		n	%	n	%	
LYM (x 10^9/L)	< 1	36	22.9	121	77.1	0.021
	≥ 1	18	12.7	124	87.3	
CRP (mg/L)	≥ 10	34	16.4	173	83.6	0.376
	< 10	8	11.9	59	88.1	
LDH (U/L)	> 300	43	44.3	54	55.7	< 0.001
	≤ 300	10	5.1	185	94.9	
D-Dimer (ng/mL)	> 1000	36	23.5	117	76.5	0.002
	≤ 1000	13	9.6	123	90.4	
Ferritin (ng/mL)	≤ 500	10	8.2	112	91.8	< 0.001
	> 500	39	28.7	97	71.3	
Cytokine storm	Yes	29	42.3	41	57.7	< 0.001
	No	21	9.6	189	90.4	
Chest X-ray	Abnormalities present	48	20.4	187	79.6	0.005
		1	2.4	41	97.6	

Observations: Significant differences were observed between laboratory test results (e.g., lymphocyte count, LDH, D-dimer, Ferritin, cytokine storm, and chest X-ray abnormalities) and treatment outcomes ($p < 0.05$).

Table 12. Multivariate logistic regression analysis of factors related to severe prognosis in moderate to severe COVID-19 patients

Risk factor		OR	95%CI		p-value
			Lower	Upper	
Comorbidity	Yes	3.025	0.578	15.827	0.190
	No	1	-	-	-
Vaccination status	Yes	1	-	-	-
	No	2.741	1.168	6.431	0.021
LYM (x 109/L)	< 1	0.527	0.053	5.217	0.584
	≥ 1	1	-	-	-
LDH(U/L)	> 300	6.696	2.335	19.199	<0.001
	≤ 300	1	-	-	-
D-Dimer (ng/mL)	> 1000	2.109	0.811	5.484	0.126
	≤ 1000	1	-	-	-
Ferritin (ng/mL)	≤ 500	1	-	-	-
	> 500	1.514	0.511	4.486	0.454
Chest x-ray	Abnormalities present	2.388	0.252	22.631	0.448
	Normal	1	-	-	-
Cytokine sorm	Yes	4.033	0.378	43.009	0.248
	No	1	-	-	-

Observations: Non-vaccination and LDH > 300 U/L were independent predictors of mortality in patients with moderate to severe COVID-19, with odds ratios of 2.741 and 6.696, respectively ($p < 0.05$).

DISCUSSIONS

General characteristics of patients with moderate to severe COVID-19

The average age of the patients was 64.57 ± 18.45 years, with the youngest being 18 years old and the oldest 101 years old, predominantly in the > 60 age group, which accounted for 62.7%. This result is similar to the study by Parag et al., which reported an average age of 62.2 years[6]. It is higher than the studies by W Guan et al. (47 years)[7] and the COVID-19 surveillance report in the U.S. by Stokes EK et al. (48 years)[10]. This difference could be explained by varying hospitalization criteria across countries.

Regarding gender, our study aligns with other studies in that the proportion of males is consistently higher than females. This may be due to females having a more robust immune system, with higher CD4+ T-cell counts, stronger CD8+ T-cell cytotoxic activity, and increased B-cell immunoglobulin production compared to males. Moreover, B-cells in females produce more antigen-specific IgG and INF, making them less likely to develop severe COVID-19.

Most moderate to severe COVID-19 patients had underlying comorbidities, with hypertension being the most common. A study by Jianfeng et al. in China found a 74.4% comorbidity rate[14]. A meta-analysis by Rodriguez-Moralesa et al. reported hypertension (18.6%) as the most prevalent.

Regarding vaccination, 75.3% of patients had been vaccinated, which is higher than in the study by Duc P. Dang et al[4]. This difference could be due to unequal vaccine distribution across regions and varying levels of public awareness.

Clinical and laboratory characteristics of patients with moderate to severe COVID-19

In our study, most patients presented with clinical symptoms, with cough (72%), shortness of breath (56.9%), and fatigue (87.5%) being the most common. These results are consistent with the study by Li X et al., which found cough (75.5%) and shortness of breath (56.6%) as common symptoms[9], and the study by Huang C et al., which reported cough (76%) and shortness of breath (55%)[8]. The study by Tuan M. Pham et al. yielded similar results, with cough (61.7%) and shortness of breath (56.0%)[11]. The study by Chi V. Le et al. also showed a similar result for cough (70.54%)[2].

Paraclinical tests revealed significant abnormalities, with LYM < 1 x 109/L (52.5%), D-dimer > 1000 ng/mL (52.9%), ferritin > 500 ng/mL (52.7%), and CRP > 10 mg/L (75.5%) being the most prevalent. Additionally, WBC > 10 x 109/L accounted for 35.7%, LDH > 300 U/L for 33.2%, and positive cytokine storm for 23.3%. These results are similar to those in the study by Huang C et al., which found WBC > 10 x 109/L (30%) and LYM < 1 x 109/L (63%)[8]. It was higher than the study by Tran Van Giang et al., where CRP ≥ 10 mg/L predominated (57%)[5]. It was also higher than the study by Fei et al. in China, which reported D-dimer > 1000 ng/mL (42%)[16]. It was lower than the study by Nguyen Hai Cong et al., which reported a 54.3% cytokine storm rate[3].

Regarding lung damage on chest X-ray assessed by the TSS score, most patients had lung damage, with moderate severity (TSS 3-6 points) accounting for 51.9%. This result is consistent with the study by Dang Phuc Duc et al[4].

Prognostic factors for mortality in the study population

The mortality rate in our study was 18%, higher than the study by Huang C et al. in China[8]. This discrepancy could be influenced by factors such as vaccines, medications, and different intervention therapies between countries during the pandemic.

In our study, the relationship between age and treatment outcomes showed no statistically significant difference ($p > 0.05$). This result differs from the study by Fei et al. in China, where the difference was statistically significant, with OR 1.10, 95% CI: 1.03 - 1.17, $p < 0.001$[16]. This could be due to differences in patient selection criteria between the two studies. We also found a statistically significant difference between underlying conditions, vaccination, and treatment outcomes ($p < 0.05$).

In Table 13, we found a significant relationship between LYM, LDH, D-dimer, Ferritin, cytokine storm, and lung damage on chest X-ray, and the outcome of death or survival in patients, with $p < 0.05$. The study by Pham Minh Tuan et al. also showed that LDH and D-dimer were related to disease prognosis[11]. This emphasizes the importance of regularly ordering tests, chest X-rays, and evaluating the cytokine storm score and TSS score to monitor and better predict patient outcomes.

Multivariate logistic regression analysis showed a significant association between independent variables such as non-vaccination, LDH > 300 U/L, and the dependent variable of patient treatment outcomes, with OR of 2.741 and 6.696, respectively, $p < 0.05$. This means that patients who were unvaccinated and had LDH levels > 300 U/L were independent factors associated with severe prognosis in moderate to severe COVID-19 patients. Our study found that patients with LDH > 300 U/L had a 6.696 times higher risk of death than patients with LDH ≤ 300 U/L, with 95% confidence. Our study aligns with the study by Li X et al., which found that LDH > 445 U/L (adjusted HR, 2.0; 95% CI, 1.2 - 3.3) upon admission was a significant risk factor for mortality in severe COVID-19 cases[9]. Additionally, our study indicated that unvaccinated individuals had a 2.741 times higher risk of death than vaccinated individuals, with 95% confidence. Therefore, vaccination is essential in the prevention and treatment of COVID-19.

CONCLUSIONS

Cough, shortness of breath, and fatigue are common symptoms in moderate to severe COVID-19 patients. LYM < 1 x 10^9/L, D-dimer > 1000 ng/mL, Ferritin > 500 ng/mL, and CRP > 10 mg/L were primarily found in lab tests. The mortality rate of the patients was 18%.

Non-vaccination and LDH > 300 U/L are independent predictors of mortality in moderate to severe COVID-19 patients.

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