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Probability-based Equation for Predicting Mortality in COVID-19 Patients

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Abstract

Background The global mortality rate for coronavirus disease-2019 (COVID-19) continues to climb. The study goal is to provide a proper equation to predict mortality in COVID-19 patients based on medical history, and laboratory examination

Methods This was a case-control study. Patients with COVID-19 confirmed case was taken for medical history, physical, and laboratory examination. CBC and D-Dimer were checked when patients were admitted to the hospital. Statistical analysis that was use include Chi-Square or Fisher's test as comparative study, risk estimate for odds ratio, and logistic regression to formulated the equation.

Results Ninety-six patients were gathered at the end of study. The study grouped patients based on survival at end of care which is life and death as dependent variable. We also grouped patients based on several parameter like geriatric age, comorbidities, symptoms (fever, cough, anosmia, cold, dysphagia, and shortness of breath), anemia, leukocytosis/leukopenia, thrombocytopenia, elevated D-Dimer, and pneumonia, as independent variables. Geriatric, comorbidities, fever, cough, shortness of breath, anemia, leukocytosis/ leucopenia, lymphopenia, and elevated D-Dimer had significant differences with $p < 0.05$. Odds ratio and 95% CI for these parameters were 3.02 (1.11-8.20), 4.07 (1.35-12.27), 3.57 (0.96-13.23), 5.04 (1.08-23.34), 4.75 (1.02-22.02), 3.26 (1.15-9.25), 6.40 (2.19-18.63), 3.16 (0.97-10.30), and 0.70 (0.61-0.81), respectively. Multivariate analysis using logistic regression based on this result was calculated and we were able to make this probability equation, $p = 1/(1+e-y)$, with $e = 2.7$, and $y = - 24.99 + 1.621$(comorbidities) + 1.944(cough) + 1.643(leukocytosis/leukopenia) + 1.397(anemia) + 20.625(elevated D-Dimer). ROC was use to confirm this predicted probability with AUC 0.88

Conclusion This equation was simple enough to be used as tool for clinician to predict mortality in COVID-19 patients. If we were to assume that for example patient with COVID-19 with comorbidities had cough as symptoms, and also had leukocytosis/leukopenia, anemia, and elevated D-Dimer level based on laboratory result, then that patient had 90.25% probability of death as outcome. The study was able to predict death in COVID-19 patients with up to 90.25% probability using our equation with excellent discrimination between these patients

Keywords: equation; mortality; COVID-19.

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Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of coronavirus disease 2019 (COVID-19). The World Health Organization (WHO) declared a global pandemic after SARS-CoV-2 was initially discovered in December 2019. Worldwide public health and economic consequences have resulted from the current worldwide epidemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As of May 2023, the World Health Organization (WHO) estimated that 6.9 million people have died from COVID-19, out of over 760 million instances of the virus.

The SARS-CoV-2, a single-strand positive-strand RNA virus that is a member of the beta coronavirus genus, resembles the Middle East respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome-related coronavirus (SARS-CoV) despite appearing to be unrelated to them[1-3]. According to recent research, SARS-CoV-2 shares approximately 89% of its sequence with bat SARS-like-CoVZXC21 and 82% with human SARS-CoV [4]. SARS-CoV-2 has presented challenges to populations and global health care systems during the past 20 years, similar to those faced by the MERS and SARS epidemics [5]. The extremely contagious COVID-19 virus can cause severe pneumonia, multiple organ dysfunction syndrome (MODS), acute respiratory distress syndrome (ARDS), and even

Method

This was a case-control study. Patients with COVID-19 confirmed case was taken for medical history, physical, and laboratory examination. The cell blood count and D-Dimer were checked when patients were admitted to the hospital. Statistical analysis that was use include Chi-Square or Fisher's test as comparative study, risk estimate for odds ratio, and logistic regression to formulated the equation.

Result and Discussion

Table 1. Baseline characteristic of COVID-19 patients

	Total (n: 96)
Age (years old)	59 (23-91)
Sex	
Male	51 (53.2%)
Female	45 (46.8%)
Comorbidities	49 (51%)
Symptoms	
Fever	65 (67.7%)
Cough	68 (70.8%)
Anosmia	12 (12.5%)
Cold	13 (13.5)
Dysphagia	8 (8.3%)
Shortness of breath	69 (71.9%)
Lab result	
Hemoglobin (g/dL)	13.19 + 1.85
Leucocyte (x10^3/mL)	8.61 + 4.97
Neutrophil (x10^3/mL)	7.67 + 9.34
Lymphocyte (x10^3/mL)	1.44 + 1.18
Platelet (x10^3/mL)	270.07 + 112.57
D-Dimer (ng/mL)	1169.69 + 1970.80
Chest X-ray	
Normal	17 (17.7%)
Pneumonia	79 (82.3%)
Outcome	
Life	75 (78.12%)
Death	21 (21.87%)

Table 2. Result of bivariate analysis

		Life		**Death**				**95% CI**	
		n	%	n	%	p	OR	Min	Max
Geriatric	Yes	20	26.6	11	52.3	0.02	3.02	1.11	8.20
	No	55	73.4	10	47.7		Ref		
Comorbidities	Yes	33	44	16	76.1	0.001	4.07	1.35	12.27
	No	42	56	5	23.9		Ref		
Symptoms									
Fever	Yes	47	62	18	85.7	0.046	3.57	0.96	13.23
	No	28	38	3	14.3		Ref		
Cough	Yes	49	65.3	19	90.4	0.025	5.04	1.08	23.34
	No	26	34.7	2	9.6		Ref		
Anosmia	Yes	11	14.6	1	4.7	0.45	0.29	0.03	2.39
	No	64	85.4	20	95.3		Ref		
Cold	Yes	11	14.6	2	9.5	0.72	0.61	0.12	3.00
	No	64	85.4	19	90.5		Ref		
Dysphagia	Yes	6	8	2	9.5	1	1.21	0.22	6.48
	No	69	92	19	90.5		Ref		
Shortness of breath	Yes	50	66.7	19	90.4	0.03	4.75	1.02	22.02
	No	25	33.3	2	9.6		Ref		
Anemia (<12 g/dL)	Yes	14	18.6	9	42.8	0.02	3.26	1.15	9.25
	No	61	81.4	12	57.2		Ref		
Leukocytosis/Leukopenia (>11/<3.5 x10^3/mL)	Yes	11	14.6	11	52.3	0.001	6.40	2.19	18.63
	No	10	85.4	10	47.7		Ref		
Lymphopenia (<1.5 x10^3/mL)	Yes	43	57.3	17	80.9	0.048	3.16	0.97	10.30
	No	32	42.7	4	19.1		Ref		
Thrombocytopenia (<150 x10^3/mL)	Yes	6	8	4	19	0.21	2.70	0.68	10.66
	No	69	92	17	81		Ref		
Elevated D-Dimer (>250 ng/mL)	Yes	53	70.6	21	100	0.003	0.70	0.61	0.81
	No	22	29.4	0	0		Ref		
Pneumonia	Yes	59	78.6	20	95.2	0.10	5.42	0.67	43.54
	No	16	21.4	1	4.8		Ref		
Total		75	100	21	100				

Ninety-six patients were gathered at the end of study. The study grouped patients based on survival at end of care which is life and death as dependent variable. We also grouped patients based on several parameter like geriatric age, comorbidities, symptoms (fever, cough, anosmia, cold, dysphagia, and shortness of breath), anemia, leukocytosis/leukopenia, thrombocytopenia, elevated D-Dimer, and pneumonia, as independent variables. Geriatric, comorbidities, fever, cough, shortness of breath, anemia, leukocytosis/ leucopenia, lymphopenia, and elevated D-Dimer had significant differences with $p < 0.05$. Odds ratio and 95%CI for these parameters were 3.02 (1.11-8.20), 4.07 (1.35-12.27), 3.57 (0.96-13.23), 5.04 (1.08-23.34), 4.75 (1.02-22.02), 3.26 (1.15-9.25), 6.40 (2.19-18.63), 3.16 (0.97-10.30), and 0.70 (0.61-0.81), respectively.

Multivariate analysis using logistic regression based on this result was calculated and we were able to make this probability equation, $p = 1/(1+e-y)$, with $e = 2.7$, and $y = - 24.99 + 1.621$ (comorbidities) + 1.944(cough) + 1.643 (leukocytosis/leukopenia) + 1.397(anemia) + 20.625(elevated D-Dimer). ROC was use to confirm this predicted probability with AUC 0.88.

The COVID-19 pandemic is evolving very rapidly. The diverse clinical features and rapid spread present challenges for clinicians in classifying clinical conditions and determining the prognosis of the disease. This condition makes it difficult for doctors to predict the progression of the disease and the risk of death of patients with COVID-19 infection. Clinical manifestations of respiratory system infections such as fever, cough, and shortness of breath are common symptoms. In addition to these clinical manifestations, many other factors influence the severity of the disease and the prognosis of patients. Our study revealed that advanced age, presence of comorbidities, fever, cough, and shortness of breath before hospital admission were associated with an increased risk of death. These findings are consistent with several studies conducted previously. [17-19]

In addition to age, the presence of comorbidities and clinical symptoms at the time of infection, our study also identified abnormalities in laboratory parameters such as anemia, leukocytosis/leucopenia, lymphopenia, and elevated D-dimer to be associated with an increased risk of death. This result is consistent with the previous review conducted by C. Buttia et al. (2022), where from a total of 314 published studies from 40 countries, including 152 studies on mortality prognosis and 35 studies on mortality prognosis and intensive care. Factors found to have a significant impact on mortality risk were age, gender, hypoxemia, body temperature, pulse rate, underlying disease, impaired consciousness, C-reactive protein (CRP), urea, and D-dimer levels, neutrophil count, lymphocyte percentage, and platelet count. The area under the receiver operating characteristic (ROC) curve for mortality prognostic models ranged from 0.49 to 0.99, with sensitivity ranging from 15.4% to 100% and specificity ranging from 10.9% to 98.7% [20].

Since the beginning of the pandemic, many studies have focused on developing prognostic models to effectively stratify patients to reduce disease severity and mortality. This study aims to develop a clinical symptom-based prognostic model to assess the risk of death at hospital admission. We focused on selecting objective clinical factors and easily assessable laboratory results associated with mortality risk.

Until now, many prognostic models have been developed to predict the mortality of patients infected with COVID-19. This study found a simple equation to predict death from COVID-19. This equation is quite easy to use as a tool for doctors to predict the risk of death in COVID-19 patients. If we assume that for example a COVID-19 patient with comorbidities, presents with cough symptoms, and also has the conditions of leukocytosis/leukopenia, anemia, and elevated D-dimer levels based on laboratory results, then the patient has a 90.25% chance of death.

There have been many studies to determine the effectiveness of a prognostic model related to COVID 19 infection. A multivariate analysis approach to assess the prognostic ability of the CURB-65 scale, which consists of five variables (impaired consciousness, uremia, tachypnea, low blood pressure, and age≥65 years), for predicting in -hospital mortality with COVID-19 has previously been conducted. This study showed that the CURB-65 scale showed promising prognostic ability, with a CURB-65 score ≥2 points showing 82% sensitivity and 83% specificity in predicting mortality [21]. Another study also used the MH175 score which, showed good prognostic ability of mortality, as indicated by the area under the AUROC of 0.87. The optimal threshold value for predicting mortality using the MH175 score was≥3 points, resulting in a sensitivity of 96.1%, specificity of 63.4%, positive predictive value of 58%, and negative predictive value of 96.9%[22].

In a meta-analysis conducted to assess the predictive performance of four commonly used prognostic scores (ISARIC-4C, COVID-GRAM, qCSI, and NEWS) for in-hospital mortality of COVID-19 patients, there was good predictive value for assessing mortality risk. The ISARIC-4C score showed the highest AUROC at 0.799, followed by COVID-GRAM with 0.785, NEWS with 0.764, and qCSI with 0.749 [23].

Variations in healthcare systems dealing with COVID-19 in different countries may introduce bias in prognostic models, but the ISARIC-4C mortality prognostic model, developed based on a UK database, has shown a relatively low risk of bias. The 4C scale incorporates eight variables: age, gender, respiratory rate, oxygen saturation, comorbidities, state of consciousness, blood urea,

and C-reactive protein [17, 24]. The clinical variables included in the 4C scale have some similarities with the predictive equation in this study. However, this study also included several laboratory parameters such as anemia, leucocytosis/leukopenia, and elevated D-dimer, which are laboratory parameters that are easy and quick to assess when the patient is admitted to the hospital.

However, it is important to recognize the limitations of our study. Firstly, as a single-site study, the generalize of the findings is limited. Secondly, the sample size used in the study was relatively small, requiring further investigation with a larger sample size. In addition, regarding the prognostic ability of this equation, it was not stratified.

All prognostic models have limitations when applied in clinical practice. Diverse patient characteristics in various countries, variations in the management of COVID-19, make it difficult to apply one prognostic model that is mutually agreed upon for use. Therefore, ideally, the prognostic model that will be used as a common guideline must undergo rigorous evaluation across a wide variety of patient characteristics and health service variations. Such a model would help reduce errors in decision-making, patient classification, and treatment options [25].

Conclusion

This equation was simple enough to be used as tool for clinician to predict mortality in COVID-19 patients. If we were to assume that for example patient with COVID-19 with comorbidities had cough as symptoms, and also had leukocytosis/ leukopenia, anemia, and elevated D-Dimer level based on laboratory result, then that patient had 90.25% probability of death as outcome. The study was able to predict death in COVID-19 patients with up to 90.25% probability using our equation with excellent discrimination between these patients.

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