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MORTALITY-RELATED PREDICTORS AND ASSOCIATED RISK FACTORS OF COVID-19- A RETROSPECTIVE OBSERVATIONAL STUDY

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Abstract

Background: Few resources discuss the relationship between COVID-19 comorbidities and ICU admission. Nevertheless, our review outlines the full range of comorbidities in COVID-19 patients and creates a scoring system for quicker care in patients admitted to tertiary hospitals. The primary aim was to establish a risk model to predict mortality in patients with COVID-19. **Materials and Methods:** This study examined data from COVID-19-infected individuals from the medical record department who had been admitted to the COVID ICU for six months. Only hospitalized patients who had tested positive for SARS-CoV-2 were considered in this investigation. Patients who were under the age of 18 or those who had been moved to other medical facilities were excluded. **Results:** Among 51 patients affected with COVID-19 infection, SpO2 was significantly positively correlated with COVID-19 illness severity by about 16 odd times (p 0.05), pO2 by two odd times, and HCO3 by four odd times. So, it was determined that spo2, hco3, and po2 had a statistically significant relationship with the mortality of COVID-19-affected people. **Conclusions:** The main benefit of this study was that it identified the top 5 clinical and laboratory factors that predict in-hospital death.

INTRODUCTION

Coronavirus disease (COVID-19) is an infectious illness brought on by the SARS-CoV-2 coronavirus, which causes severe acute respiratory syndrome.[1] Clinical traits of COVID-19 critical illness and severe illness patients have been reported in several investigations. 2,3 The clinical characteristics and risk variables aim to identify risk factors linked to fatal outcomes. 4,5 In patients older than 18 with ongoing COVID-19 infection and requiring ICU admission, this study will look at comorbid conditions, pinpoint specific symptoms, the course of the disease, and mortality rates.[6,7,8]

Besides, the study sought to establish a risk model to predict mortality and identify risk factors for mortality in ill patients so that clinicians could weigh the medical needs of patients with various risks and reduce mortality.

The study aims to establish a risk model to predict the mortality of patients affected with COVID-19 infection and to identify risk factors associated with the mortality of severe COVID-19 patients.

MATERIALS AND METHODS

Study Design

This retrospective observational study included COVID-19 patients admitted to an intensive care unit (ICU) at a tertiary care hospital in Tamil Nadu between April 2020 and September 2020.

The study included all SARS-CoV-2 infected patients aged 18 years or older who had positive results from a real-time polymerase chain reaction (RT-PCR) assay or a cartridge-based nucleic acid amplification test (CB-NAAT) on nasopharyngeal swab samples collected during admission. Patients under 18 and those who moved to different healthcare facilities were excluded. The clinical trial registry of India (CTRI) [CTRI NO: CTRI/2021/05/033327] accepted the study after the institutional Scientific and ethical committee review board had reviewed it.

Clinical and biological data

The Medical Records department gathered each patient's medical history, demographic details, comorbidities, ABG analysis, clinical observations, and laboratory data at admission for this study.

Socio-demographic factors include age, gender, pre-existing conditions (including respiratory disease, cardiac disease, hypertension, hyperlipidemia, diabetes, kidney disease, liver disease, post-operative, and more than two kinds of diseases), presenting symptoms like fever, cough, expectoration, vomit, and diarrhoea. Clinical features include blood oxygen saturation (SpO2) and mode of oxygen.

Arterial blood gas (ABG) analysis has pH, partial pressures of carbon dioxide (PCO2), oxygen (PO2), and bicarbonate (Hco3). Quick Sepsis-related Organ Failure Assessment (q-SOFA) scores at admission and the COVID-19 severity class were considered. Laboratory parameters and interventions include white blood cell count (WBC), haemoglobin (Hb), platelet count (PLT), lymphocyte percentage (LYM%), neutrophil percentage (NEU%), neutrophil to lymphocyte ratio (NLR), prothrombin time (PT), prothrombin activity (PTA), procalcitonin (PCT) and the ground-glass opacity assessed using computerized tomography (CT) imaging (GGO)". The initial hospital course and baseline characteristics were evaluated. The main result was the patient's survival. These patients' final prognoses were classified as either survivors or non-survivors.

Data collection tools/technique: The data was collected from the Medical Records department during hospital admission, including demographic data, chronic comorbidities, vital signs, symptoms, laboratory tests, and results. The tool for data collection was a structured questionnaire filled by the investigator from the pre-recorded medical records.

Data processing and analysis: The data was coded and imported into Excel. After that, it was moved and put through SPSS version 26 analysis. Categorical data as 31 indicators were identified using a straightforward frequency distribution. Pearson's chi-square examined the relationship between the dependent variable and the independent factors. Bivariate logistic regression analysis with a 95% confidence interval and a p-value of 0.05 was used to find parameters associated with the morality of COVID-19.

RESULTS

A total of 51 patients were included in the study. Based on the clinical parameters such as SpO2, HCO3, LDH and PO2, the patients were grouped into two outcome variables (mild/moderate and severe/critical). Age was categorized into 50th percentile (i.e. 60 years). During admission,35 patients were recorded with SpO2 levels less than 92% who were categorized as mild/moderate outcome and 7 of the subjects had SpO2 levels more than 92% who were categorised as severe/critical and this difference was found highly significant with p-value <0.001 [Table 1].

Table 1: Baseline demographic, clinical characteristics and outcome variables

Parameters		**Outcome**		**P-value**
		Survivors (N =39)	**Non-Survivors (N =12)**	
Age	<60 years	19	7	0.560
	>60 years	20	5	
Gender	Male	26	11	0.087
	female	13	1	
Comorbidities	Absent	18	8	0.214
	Present	21	4	
SpO2	<92%	35	5	0.001*
	>92%	4	7	
O2 mode	NP, FM	34	12	0.245
	NRBM, HFNO, intubation	5	0	

[Table 2] uses the chi-square test to describe the association between ABG parameters and outcome variables. pO2 and HCO3 were statistically significant with outcome variables ($p<0.05$).

Table: 2 Arterial Blood Gas (ABG) analysis and its association with outcome variables

Parameters		**Outcome**		**P-value**
		Survivors (N =39)	**Non-Survivors (N =12)**	
pH	7.35-7.45	26	8	0.643
	<7.35/>7.45	13	4	
pCO2	35-45	14	4	0.579
	<35/>45	25	8	
pO2	75-100	21	2	0.024*
	<75/>100	18	10	
HCO3	22-26	16	1	0.034*
	<22/>26	23	11	
Q-SOFA	>3	14	2	0.186
	<3	25	10	

Survivors had significantly higher mean levels of haemoglobin (>10 g/dl) and normal level of LDH levels (105-333 IU/L). There is no significantly elevated parameter among the severe/critical group of survivors [Table 3].

Table 3. Baseline laboratory parameters and interventions in the patients

Parameters		Outcome		P-value
		Survivors (N =39)	Non-Survivors (N =12)	
Platelet	< 1 lakh	31	10	0.567
	>1 lakh	8	2	
N/L ratio	<0.7/>3	19	3	0.147
	1-2	20	9	
Haemoglobin (g/dl)	<10g/dl	17	10	0.016*
	>10g/dl	22	2	
WBC (cells/microlitre)	4500-11000	25	7	0.486
	<4500/>11000	14	5	
Urea (mg/dl)	6-24	25	8	0.579
	<6/>24	14	4	
Creatinine (mg/dl)	0.7-1.3	28	11	0.151
	<0.7/>1.3	11	1	
Sodium (mEq/L)	135-145	26	7	0.421
	<135/>145	13	5	
Potassium (mEq/L)	3.5-4.5	29	9	0.642
	<3.5/>4.5	10	3	
Chloride (mEq/L)	96-106	26	9	0.435
	<96/>106	13	3	
Bicarbonate (mEq/L)	22-29	20	6	0.938
	<22/>29	19	6	
Total bilirubin (mg/dl)	1-2	33	9	0.354
	<1/>2	6	3	
AST (U/L)	8-48	21	5	0.460
	<8/>48	18	7	
ALT (U/L)	7-55	18	3	0.167
	<7/>55	21	9	
Albumin (g/dl)	3.4- 5.4	18	5	0.730
	<3.4/>5.4	20	7	
D Dimer	<0.5	15	4	0.514
	>0.5	24	8	
Serum ferritin (mcg/L)	24-336	22	4	0.177
	<24/>336	15	7	
IL-6 (pg/ml)	0-7	32	12	0.174
	<0/>7	6	0	
LDH (IU/L)	105-333	26	4	0.044*
	<105/>333	13	8	

[Table 4] depicts the linear logistic regression between several physical parameters and outcome variables. It shows that SpO2 is about 16 odd times significantly positively associated with the severity of COVID-19 illness ($p<0.05$). pO2 of COVID-19 patients are about two times more statistically associated with the mortality of the patients ($p<0.05$). The level of HCO3 in COVID-19 patients is about four times more statistically associated with the mortality of the patients ($p<0.05$). Thus SpO2, HCO3, and pO2 are statistically significant in the mortality of the COVID-19-affected individuals.

Table 4. Logistic regression between physical parameters and outcome variables

Variables	Coefficient	Adjusted odds ratio	Standard error	P-value
SpO2	2.829	16.92	1.27	0.026*
Hb	-1.870	0.15	1.15	0.104
LDH	.607	1.84	1.025	0.554
pO2	2.652	14.18	1.28	0.038*
HCO3	4.024	55.90	1.67	0.016*

The equation for the risk model is framed as follows: Outcome = -6.76 + 16.92 (SpO2) + 14.18 (pO2) + 55.899 (HCO3).
In this study, a risk equation model was framed to predict the mortality using SpO2, Po2 and HCO3 variables of COVID-19 cases after checking for the co-linearity of independent variables.

DISCUSSION

This study examined COVID-19-infected individuals who had been admitted to the COVID ICU of a tertiary hospital for six months, from April 2020 to September 2020. Among 51 patients affected by COVID-19 infection, the association between physical parameters with outcome variables was assessed. Spo2, haemoglobin, LDH, pO2, and HCO3 were significant with outcome variables. The study indicated a higher association for oxygen saturation, haemoglobin, LDH, partial pressure of oxygen, and bicarbonate level towards overall mortality.

The risk model was equated with 16 times SpO2, 14 times SpO2 and 55 times bicarbonate. While evaluating target oxygen saturation in COVID-19 patients in both inpatient and outpatient settings by Shenoy et al.[11], a phenomenon known as "silent hypoxemia" occurs when certain patients report to the hospital with severe hypoxia out of proportion to their symptoms. This occurrence harms outpatient monitoring and the prompt initiation of oxygen supplementation in many regions of the world. Similarly, Sada et al.[12] found clinical worsening among 54% of high bicarbonate levels (>27mEq/L). Thus, monitoring oxygen saturation and bicarbonate levels may help predict the outcome in COVID-19 patients.

There was no association between age, gender, or comorbidities with outcome variables in this study. But this was inconsistent with other study findings such as Chen et al.[9], Zhou et al.[13], and Higgins et al.[14], which showed that the risk of death from coronavirus has risen with age. According to Van Gerwen et al.[15] male patients had a higher risk of COVID-19 mortality. Compared to non-smokers, smokers had a significantly higher risk of dying from a coronavirus, as mentioned in some studies like Xu et al. 16 and Wang et al.[17] (pOR= 1.42; 95% CI = 1.01-1.83). A strong correlation between obesity and coronavirus mortality was found by combining the effect sizes from several investigations.

Alizadehsani et al.[18] discovered a link between specific blood types and COVID-19-related mortality, with O- playing a protective function. Anorexia, anosmia, ageusia, fever, dyspnea, weakness, shivering, tiredness, dry cough, and disorientation strongly correlated with COVID-19. A higher mean age and an elevated CRP were associated in COVID-19 patients.

Dessie et al.[19] examined mortality-related risk variables for COVID-19 in 42 papers through a systematic review and meta-analysis. The main risk factors for COVID-19 mortality were diabetes, CVDs, COPD, hypertension, and acute renal injury. These factors have been identified as coronavirus risk factors by the CDC and WHO. According to various other studies, COPD patients with COVID-19 had higher hospitalisation and mortality rates, showing a connection between patients' COPD status and COVID-19 mortality.[8,20] Viral infections in COPD patients, which promote systemic inflammation, may be to blame for the protracted recovery of reported symptoms.[21] COPD patients deal with various comorbidities, some of which are linked to a higher risk of hospitalization.

Jain et al.[22] stated that mortality is significantly influenced by old age and comorbid conditions like diabetes, hypertension, and coronary artery disease. The model did not statistically distinguish between blood pressure, GCS (almost all patients were conscious at admission), PaO2, FiO2, platelet counts, or laboratory variables like bilirubin or creatinine. This shows the need for distinct models with predictors with stronger connections with variables to forecast COVID-19 admissions outcomes.

High D-dimer levels have been linked to significantly higher mortality risks. A high amount of D-dimer increases the risk of fatal and severe infection, according to a prior study.[23] Moreover, a study conducted in China revealed that the poorest long-term results are linked to increased D-dimer levels during hospitalization.[13] Therefore, using D-dimer levels as a stand-in marker for illness severity may be advantageous, particularly in coronavirus patients who cannot receive specialized imaging.

Strengths: This research is among the first to look at the effect of specific risk variables on COVID-19 mortality, clinical outcomes, and prediction. Our results reveal that laboratory and clinical parameters are the most significant predictors of patient mortality. This study might help with early death prediction and mortality risk reduction in COVID-19-infected patients. Additional study, including long-term follow-ups, is needed to support our findings.

Limitations

The paper does have certain constraints. It only offers the initial instances admitted at our tertiary centre due to volume considerations, and we recognize the necessity to proceed with a large sample size. Second, all the admitted patients in the study had not received all testing, such as the expensive pro-inflammatory tests, at the preliminary stage. Thus their impact on the total predicted model for death may have been overestimated. The COVID-19 mortality in the community or a tertiary care setting does not accurately reflect the in-hospital mortality at our facility, which is the third and most important point.

CONCLUSION

The main benefit of this study is that it has identified the top 5 clinical and laboratory factors that predict in-hospital death and is currently working to create an incremental model that can reliably forecast a patient's risk at an early stage. It enables the healthcare professional to identify the crucial factors for prompt and immediate management. Before being widely used, these predictors need additional research and comprehensive validation using additional internal and out-of-sample data from other centres.

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