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Predictors of critical illness and mortality based on symptoms and initial physical examination for patients with SARS-CoV-2: A retrospective cohort study

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ABSTRACT

Introduction: An unidentified cluster of pneumonia was identified in Wuhan city of China in the last week of December 2019, named Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-COV-2). The current study explored the predictors associated with critical illness and mortality based on symptoms at the time of admission and initial physical examination findings in patients with SARS-CoV-2.
Material and methods: A total of 249 records of laboratory-confirmed SARS-COV-2 patients were analyzed. Demographic profile and findings of initial physical examination were collected and analyzed. Bivariate logistic and multivariable stepwise forward regression analysis was used to identify the predictors of critical illness and mortality.
Results: A total of 249 records of SARS-COV-2 patients were retrospectively studied, of whom 66 (26.5%) developed a critical illness, and 58 (23.29%) died. The mean age of patients was 45.15 (16.34) years; 171 (68.71%) were men. From 27 potential predictors for developing a critical illness, 15 were reported independent predictors for critical illness, and 13 were for increased risk of mortality. Stepwise forward regression reported dyspnea as a single strongest predictor (OR, 5.800, 95% CI-2.724–12.346; p = 0.001, R^2 = 0.272) to develop critical illness. Likewise, the respiratory rate was alone reported as a strong predictor (OR, 1.381, 95% CI- 1.251–1.525; p = 0.000, R^2 = 0.329) for mortality.
Conclusions: Coronavirus disease is a new challenge to the medical fraternity, leading to significant morbidity and mortality. Knowledge of potential risk factors could help clinicians assess patients' risk with unfavourable outcomes and improve hospitalization decisions in the early stage.

Introduction

A cluster of unknown pneumonia cases was detected in the Wuhan city, Hubei province in China, in the last week of December 2019 [1]. After a month of the first coronavirus disease (COVID-19) case, it was renamed as Acute Respiratory Syndrome Coronavirus -2 (SARS-Cov-2) [2]. The virus has rapidly spread worldwide and was declared an emergency of public health concern by the World Health Organisation on January 30, 2020 [3].

The outbreak was reported from an enormous seafood market in China that also traded in live wild animals, and soon it became evident that person to person transmission is also possible [4]. The virus is highly infectious and is presumed to be transmitted through direct contact or droplet infection [5], though some differences of opinion do exist [6]. The clinical manifestation of coronavirus disease appears to be vague, including asymptomatic infection to mild upper respiratory tract infection symptoms, acute viral pneumonia with severe respiratory symptoms to respiratory failure, and even death in many cases [7,8]. However, clinical characteristics and outcomes among hospitalized patients with SARS-COV-2 have been variables across the globe [7,9–11].

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Earlier scientific work in a similar population reported increasing age [1,8], male sex [12,13], admission with coronary artery disease [1,8], pre-existing diabetes mellitus, hypertension, kidney disease, cerebral infarction, chronic obstructive pulmonary disease, cancer, and pancreatic problems shows a direct relation with poor outcomes and higher mortality in patients with COVID-19 [11,14,15]. Likewise, patients with multiple symptoms, more comorbidities, and advanced age had a higher risk than those without [12,16]. The patients with advanced age have more number comorbidities, compromised lung capacity, deteriorated organ functions, and an impaired immune system, which is a well-known reason for developing critical illness; therefore, the clinicians should manage them with more attention considering high risk [12,17].

The determination of risk factors for critical illness development and possible mortality can play a vital role in decision making for clinicians. Further, it is vital to understand the clinical behavior of the disease in the progression and recovery phase in the local population. Here, we summarize the characteristics, associated risk factors, and outcomes of patients hospitalized to a tertiary care hospital, North India-with laboratory-confirmed SARS-COV-2, and their outcomes, either discharged or dead from April 14, 2020 to August 15, 2020.

Methods

The study was approved by the institutional ethics committee of All India Institute of Medical Sciences (AIIMS) Rishikesh (AIIMS/IEC/20/442); the need for written informed consent was deferred considering the use of anonymous record analysis. The probable and confirmed cases of SARS-COV-2 was established by using case definition as per WHO interim guidelines [18]. The records of laboratory-confirmed SARS-COV-2 patients hospitalized in a tertiary care public hospital, North India, were accessed from the medical record department (MRD). SARS-COV-2 diagnosis was confirmed by positive real-time reverse-transcription polymerase-chain reactions (RT-PCR) method using nasal and pharyngeal swab specimens. A team of experienced physicians in medicine studied, reviewed, and extracted the data using a pre-standardized validated checklist. A nursing expert has cross-checked each record independently for its accuracy and validation of the findings. A detailed checklist helped extract all relevant information of an individual patient on the following aspects; socio-demographic variables, clinical, and laboratory findings, including their symptomatology, discharge, or death status. Records of laboratory-confirmed SARS-COV-2 patients admitted during 4 months from April 15, 2020, to August 15, 2020, were studied in the present work.

Outcomes

We define the critical SARS-COV-2 (critical vs. non-critical) in line with the management guidelines issued by Govt. of India, Ministry of Health & Family Welfare (MoHFW), Directorate General of Health Services (DGHS) for clinicians taking care of hospitalized patients with COVID-19 [19]. These guidelines stated critical illness like fever or suspected respiratory infection, plus one of the three criteria; respiratory rate <30 breath/min, critical respiratory distress, and SpO2 < 90% at room air. Further, it stated that the cases with worsening respiratory symptoms within one week, those with bilateral opacities, not fully explained by effusions, lobar or lung collapse, or nodules in chest imagining (radiograph, CT scan, or lung ultrasound) are to be included in acute respiratory distress syndrome (ARDS) [19]. However, the present study excluded the findings of imaging modalities and other laboratory investigations. Critical illness in the present work refers to a hospitalization composite to the intensive care unit (ICU), need of a ventilator, or mortality. These outcomes are very well explained as indicators of critical illness of SARS-COV-2 in earlier published work [20–22].

Potential predictive variables

Potential predictive variables included patient characteristics at hospitalization, socio-demographic variables, medical history, initial clinical signs and symptoms, imaging studies, and laboratory investigations. Demographic variables included age, gender, travel history, and smoking status. Details on medical history included comorbidity statuses such as hypertension, diabetes, chronic obstructive pulmonary disease (COPD), coronary artery disease (CAD), chronic kidney disease (CKD), and immunodeficiency diseases. Clinical symptoms included information on temperature, fever, heart rate, respiratory rate, systolic and diastolic blood pressure, abnormal cardiac rhythm, headache, nasal congestion, sore throat, expectoration, cough, fatigue, haemoptysis, dyspnoea, diarrhoea, nausea and vomiting, myalgia and arthralgia, and unconsciousness.

Data analysis

Records of all patients admitted with COVID-19 were reviewed retrospectively for information on socio-demographic variables, clinical findings, laboratory investigations, and possible outcomes. Two researchers independently reviewed the data and double-checked the data extraction form to ensure the accuracy of information. The data collected was entered in to excel sheet and analyzed using SPSS Version 23 statistical software.

Statistical evaluation was done using descriptive statistics that included frequency and percentage for categorical variables and mean and standard deviation for continuous variables. The comparison was estimated using independent sample t-test and Chi-square or Fisher exact test as appropriate for continuous and categorical variables.

The univariate logistic regression method was used to explore the association of symptoms and initial physical examination findings with the development of critical illness and mortality in COVID-19 patients. Forward stepwise regression is applied to explore the predictors of critical illness and mortality in patients. P-value <0.05 (two-tailed) was considered significant for study.

Results

Characteristics of the study cohort

Details on socio-demographic data, clinical presentation, and laboratory findings are summarized in Table 1. In this study, each variable that displayed a significant difference at $p < 0.05$ between critical and non-critical patients were processed using bivariate analysis. In the cohort, we retrieved information from records of 249 patients admitted at a tertiary care hospital between April 15, 2020, to August 15, 2020. In the cohort, 26.5% of patients developed critical illness, and the rest were considered non-critical as per guidelines issued by Govt. of India, Ministry of Health & Family Welfare (MoHFW), Directorate General of Health Services (DGHS) [19]. Out of 58 patients, 34 (58.6%) died during hospitalization. The mean age of patients in the cohort was 45.15 (16.35) years; amongst these, 68.67% were males, and 31.33% were females. History of smoking either in the past or present was found in 18.18%; 34.54% had at least 1 existing comorbidity, including diabetes mellitus (19.68%), hypertension (9.68%), chronic obstructive pulmonary disease (12.45%), and coronary artery disease (7.23%). Fever (38.55%), dyspnea (32.1%), sore throat (7.23%), and productive cough (7.23%)

Table 1
Demographic and Clinical Characteristics of SARS-COV-2 Patients (N = 249).

Characteristics	Total, Mean (SD), [Range]
No	249
Age (mean SD) years	45.15 (16.35) [7–85]
<40	118(47.39)
≥40	117(46.99)
Gender	
Male	171(68.67)
Female	78(31.33)
Admission criteria	
Temperature	
Febrile	112(44.98)
Afebrile	137(55.02)
Respiratory rate, (/mints)	21.81(4.01)[14–38]
Heart rate, b/mints	97.76(19.82)[50–169]
Blood pressure (mmHg)	
Systolic (SBP)	126.9 (21.24) [60–260]
Diastolic (DBP)	78.68/ (14.49)[40–140]
Smoking status	47/249 (18.88)
Former/Current	
History of travel	66/249 (26.51)
Comorbidity[a]	86/249 (34.54)
CKD	12/249 (4.82)
CAD	18/249 (7.23)
HTN	49/249 (19.68)
DM	49/249 (19.68)
COPD	31/249 (12.45)
Immunodeficiency	14/249 (5.62)
Signs-symptoms	
Fever	96/249 (38.55)
Cough	62/249(24.9)
Abnormal cardiac rhythm	07/249 (2.8)
Dyspnea	80/249 (32.1)
Sore throat	18/249 (7.2)
Myalgia	10/249 (4.5)
Headache	07/249 (2.8)
Productive cough	18/249 (7.2)
Nausea & vomiting	8/249 (3.21)
Diarrhea	18/249 (7.23)
Unconsciousness	66/249 (26.51)

COPD- Chronic obstructive pulmonary disease; LAP- Lymphadenopathy; HTN-Hypertension; DM- Diabetes mellitus.
[a] Comorbidity (yes); CKD-Chronic kidney disease; CAD-Coronary artery disease.

were the common self-reported symptoms in patients at the time of presentation for physical examination. 44.98% of patients were febrile, and 26.51 % had a travel history to other parts of the country—a summary of the findings presented in Table 1.

Tables 2 and 3 depicts the association of initial symptoms and physical examination with developing critical illness and mortality among patients with SARS-COV-2. These findings depict that in the mortality cohort, patients were more advanced in age (difference, 3.07 years), had higher respiratory rate (difference, 1.28 breath/mints), higher heart rate (difference, 7.21), and reported slightly higher systolic and diastolic blood pressure.

Predictor selection

27 variables were analyzed, including symptoms and initial physical examination of the patients to explore the predictors of critical illness and mortality. Chi-square and/or Fisher exact test and independent-sample t-test were used as appropriate for continuous and categorical variables to find the association of variables to the critical illness and death among SARS-COV-2 patients. Age, body temperature, heart rate, respiratory rate, current or former smoking status, presence of comorbidity, fever, cough, abnormal cardiac rhythm, dyspnea, sore throat, chronic kidney disease (CKD), coronary artery disease (CAD), hypertension (HTN), diabetes mellitus (DM), and chronic obstructive pulmonary disease (COPD), found a significant association (all p < 0.05) with development of critical illness in SARS-COV-2 patients (Table 2).

Table 2
Symptoms and Initial Physical Examination Findings for Patients with SARS-CoV-2 in association with Critical Illness (N = 249).

Characteristics	Critical Illness		p-value
	Yes (f, %), Mean (SD)	No (f, %), Mean (SD)	
No	66 (26.5)	183(73.5)	
Age (mean SD) years	49.33(16.57)	40.97(16.11)	0.001*
Gender			0.303
Male	42 (63.6)	129(70.5)	
Female	24(36.4)	54(29.5)	
Admission criteria			
Temperature			
Febrile	22(33.3)	90(49.2)	0.027*
Afebrile	44(66.7)	93(50.2)	
Respiratory rate, (/mints)*	23.50(4.35)	20.11(3.66)	0.001*
Heart rate, b/mints	101.08(24.24)	94.44(15.39)	0.012*
Blood pressure (mmHg)			
Systolic (SBP)	129.80(24.12)	124(19.56)	0.097
Diastolic (DBP)	79.31(15.84)	78.05(13.13)	0.531
Smoking status	18(27.3)	29(15.8)	0.042*
Former/Current			
History of travel	18(27.3)	35(19.1)	0.166
Comorbidity^	41 (62.1)	45 (24.6)	0.001*
CKD[#]	4(2.2)	8(12.1)	0.003*
CAD[#]	9(4.9)	9(13.6)	0.027*
HTN	22(12)	27(40.9)	0.001*
DM	25(13.7)	24(36.4)	0.001*
COPD	16(8.7)	15(22.7)	0.003*
Immunodeficiency[#]	8(4.4)	6(9.1)	0.209
Signs-symptoms			
Fever	36(54.5)	60(32.8)	0.002*
Cough	25(37.9	37(20.2)	0.004*
Abnormal cardiac rhythm[#]	5(7.6)	2(1.1)	0.015*
Dyspnea	45(68.2)	35(19.1)	0.001*
Sore throat	6(9.1)	12(6.6)	0.044*
Myalgia[#]	1(1.5)	9(4.9)	0.299
Headache[#]	2(3)	5(2.7)	1.000
Productive cough[#]	6(9.1)	12(6.6)	0.579
Nausea & vomiting[#]	3(4.5)	5(2.7)	0.440
Diarrhoea[#]	5(7.6)	13(7.1)	1.000
Unconsciousness[#]	05(7.6)	61(92.4)	0.015*

^Comorbidity (yes); CKD-Chronic kidney disease; CAD-Coronary artery disease, COPD- Chronic obstructive pulmonary disease; LAP- Lymphadenopathy; HTN-Hypertension; DM- Diabetes mellitus; Independent t-test for continuous data and Chi-square and/or (#) Fisher exact test for categorical variables; SD- standard deviation; * - Significant @ P < 0.05.

All 17 variables showing significant association with developing critical illness among SARS-COV-2 patients were included in the bivariate logistic regression model. Of these 17 variables, 15 variables were reported as independent predictors for developing critical illness among hospitalised patients. These variables were, age >40 years (OR, 2.222; 95% CI, 1.207–4.090; *P* = 0.010), temperature (OR, 0.517; 95% CI, 0.287–0.930; *P* = 0.028), RR (OR, 1.225; 95% CI, 1.134–1.324; *P* = 0.013), HR (OR, 1.020; 95% CI, 1.004–1.036; *P* = 0.013), fever (OR, 2.460; 95% CI, 1.385–4.369; *P* = 0.002), cough (OR, 2.406; 95% CI, 1.302–4.448; *P* = 0.005), dyspnea (OR, 9.061; 95% CI, 4.799–17.109; *P* = 0.001), unconsciousness (OR, 7.418; 95% CI, 1.403–39.221; *P* = 0.018), comorbidity (OR, 5.029; 95% CI, 2.759–9.168; *P* = 0.001), hypertension (OR, 5.066; 95% CI, 2.611–9.830; *P* = 0.001), CAD (OR, 3.053; 95% CI, 1.156–8.062; *P* = 0.024), DM (OR, 3.611; 95% CI, 1.875–6.955; P=0.001), COPD (OR, 3.070; 95% CI, 1.420–6.637; *P* = 0.004), CKD (OR, 6.172; 95% CI, 1.793–21.249; *P* = 0.004) and smoking (OR, 1.991; 95% CI, 1.018–3.897; *P* = 0.044) (Table 4).

The stepwise forward regression analysis was performed, entering all significant independent variables on bivariate analysis in a stepwise manner to analyze the prediction of the critical illness. Dyspnea was the single strongest predictor (OR, 5.800, 95% CI-2.724–12.346; P < 0.001) with a variance of 27.5% attributed to the critical illness (Nagelkerke r square = 0.272). Entering the uncon-

Table 3
Symptoms and Initial Physical Examination Findings for Patients with SARS-CoV-2 in association with Mortality (N = 249).

Characteristics	Mortality		p-value
	Yes (f, %), Mean (SD)	No (f, %), Mean (SD)	
No	66 (26.5)	183(73.5)	
Age (mean SD) years	52.40(18.51)	40.39(14.97)	0.001*
Gender			
Male	42 (63.6)	129(70.5)	0.303
Female	24(36.4)	54(29.5)	
Admission criteria			
Temperature			
Febrile	22(33.3)	90(49.2)	0.003*
Afebrile	44(66.7)	93(50.2)	
Respiratory rate, (/mints)	24.78(4.99)	19.87(3.01)	0.001*
Heart rate, b/mints	108.29(21.90)	92.53(15.40)	0.001*
Blood pressure (mmHg)			
Systolic (SBP)	131.07(32.18	124.62(15.94)	0.041*
Diastolic (DBP)	) 81.39(20.84)	77.48(10.89)	0.062
Smoking status			
Former/Current	17(29.3)	41(70.7)	0.020*
History of travel	16(27.6)	42(72.4)	0.181
Comorbidity^	39(76.2)	19(32.8)	0.001*
CKD	08(13.8)	50(86.2)	0.001*
CAD	06(10.3)	52(89.7)	0.295
HTN	22(37.9)	36(62.1)	0.001*
DM	22(37.9)	36(62.1)	0.001*
COPD	15(25.9)	43(74.1)	0.001*
Immunodeficiency#	06(10.3)	52(89.7)	0.291
Signs-symptoms			
Fever	32(55.2)	26(44.8)	0.002*
Cough	22(37.9)	36(62.1)	0.009*
Abnormal cardiac rhythm #	02(3.4)	56(96.6)	0.666
Dyspnea	43(74.1)	15(25.9)	0.001*
Sore throat	01((1.7)	57(98.3)	0.009*
Myalgia#	02(3.4)	56(96.6)	1.000
Headache#	01((1.7)	57(98.3)	1.000
Productive cough#	07(12.1)	51(87.9)	0.095
Nausea & vomiting#	02(3.4)	56(96.6)	0.592
Diarrhoea#	02(3.4)	56(96.6)	0.259
Unconsciousness#	06(10.3)	52(89.7)	0.001*
SpO2	89.21(9.08)	95.38(4.66)	0.001*

^Comorbidity (yes); CKD-Chronic kidney disease; CAD-Coronary artery disease, COPD- Chronic obstructive pulmonary disease; LAP- Lymphadenopathy; HTN-Hypertension; DM- Diabetes mellitus; Independent t-test for continuous data and Chi-square and/or (#) Fisher exact test for categorical variables; SD- Standard deviation; *- Significant @ P < 0.05.

Table 4
Bivariate Logistic Regression for Predictors of Critical Illness in Patients. (N = 249).

Variables	OR (95% CI)	p-value
Age (>40 years)	2.222 (1.207–4.090)	0.010*
Temperature (Yes vs No)	0.517 (0.287–0.930)	0.028*
RR (breaths/Min)	1.225 (1.134–1.324)	0.013*
HR (beats/Min)	1.020 (1.004–1.036)	0.013*
Fever (Yes vs No)	2.460 (1.385–4.369)	0.002*
Cough (present vs absent)	2.406 (1.302–4.448)	0.005*
Dyspnea (Yes vs No)	9.061 (4.799–17.109)	0.001*
Unconsciousness (Yes vs No)	7.418 (1.403–39.221)	0.018*
Comorbidity (Yes vs No)	5.029 (2.759–9.168)	0.001*
HTN (present vs absent)	5.066 (2.611–9.830)	0.001*
CAD (Yes vs No)	3.053 (1.156–8.062)	0.024*
DM (Yes vs No)	3.611 (1.875–6.955)	0.001*
COPD (Yes vs No)	3.070 (1.420–6.637)	0.004*
CKD (Yes vs No)	6.172 (1.793–21.249)	0.004*
Smoking (Yes vs No)	1.991 (1.018–3.897)	0.044*

* P-value <0.05; HTN-Hypertension; DM- Diabetes Mellitus; CAD- Coronary artery disease; HR-Heart rate/mints; RR-Respiratory rate/mints; CKD- Chronic kidney diseases; COPD- Chronic obstructive pulmonary disease.

Table 5
Multivariable Stepwise Regression to find the Predictors of Critical Illness (N = 249).

Step	Predicators	B	OR (95% CI)	Sig.
Step 1[a]	Dyspnea	2.204	9.061(4.799–17.109)	0.001*
R^2 = 0.272	Constant	−1.953	0.142	0.001
Step 2[b]	Dyspnea	2.247	9.464 (4.935–18.150)	0.001*
	Unconsciousness	2.286	9.834 (1.572–61.523)	0.015*
R^2 = 0.303	Constant	−2.053	0.128	0.001
	RR/Min	.099	1.104 (1.013–1.203)	0.025*
Step 3[c]	Dyspnea	1.878	6.542 (3.205–13.353)	0.001*
	Unconsciousness	2.048	7.756 (1.155–52.094)	0.035*
R^2 = 0.326	Constant	−4.025	0.018	0.001

[a] variable(s) entered on step 1: Dyspnea.
[b] variable(s) entered on step 2: Unconsciousness.
[c] variable(s) entered on step 3: RR/Min (Respiratory rate/minute).
* P value < 0.05; HR-Heart rate/mints; RR-Respiratory rate/mints.

Table 6
Bivariate Logistic Regression for Predictors of Mortality in SARS-COV-2 Patients. (N = 249).

Variables	OR (95% CI)	p-value
Age (higher vs. lower)	1.046 (1.026–1.066)	0.001*
Temperature (Yes vs. No)	0.377(0.198–0.716)	0.003*
Fever (Yes vs. No)	2.442(1.343–4.443)	0.003*
Cough (present vs. absent)	2.307(1.223–4.352)	0.010*
Dyspnea (Yes vs. No)	11.932(5.993–23.755)	0.001*
Sore throat	0.107(0.014–0.802)	0.030*
Unconsciousness (Yes vs. No)	21.923(2.582–186.168)	0.005*
Comorbidity (Yes vs. No)	6.289(3.317–11.922)	0.001*
HTN (present vs absent)	3.712(1.902–7.244)	0.001*
DM (Yes vs. No)	3.712(1.902–7.244)	0.001*
COPD (Yes vs. No)	3.815(1.750–8.318)	0.001*
CKD (Yes vs. No)	7.480(2.164–25.851)	0.001*
Smoking (Yes vs. No)	2.225(1.120–4.422)	0.022*

* P-value < 0.05; HTN-Hypertension; DM- Diabetes Mellitus; CAD- Coronary artery disease; HR-Heart rate/mints; RR-Respiratory rate/mints; CKD- Chronic kidney diseases; COPD- Chronic obstructive pulmonary disease.

sciousness at the second step and dyspnea increases the chance to predict critical illness in 30.3% cases with a slight increase of 2.8% (Nagelkerke r square = 0.303) in variance. Further, combining the respiratory rate with dyspnea and unconsciousness at the third model would able to predict critical illness in 32.6% cases with a slight increase of prediction of 5.1 % chances from baseline (Nagelkerke r square = 0.326) (Table 5).

Further, findings show that age, body temperature, respiratory rate, heart rate, smoking status, presence of comorbidities, like chronic kidney disease, hypertension, and symptoms such as fever, cough, dyspnea, sore throat, and unconscious status, and partial pressure of oxygen (SpO2) in patients at the time of physical examination and screening were found to be significantly associated (all p < 0.05) with mortality (Table 3).

The variables were entered in to the bivariate logistic regression model and analysed out of these, 14 variables could independently predict mortality in SARS-COV-2 patients. These variables were, age (OR, 1.046; 95% CI, 1.026–1.066; P = 0.001), temperature (OR, 0.377; 95% CI, 0.198–0.716; P = 0.003), fever (OR, 2.442; 95% CI, 1.343–4.443; P = 0.003), cough (OR, 2.307; 95% CI, 1.223–4.352; P = 0.010), dyspnea (OR, 11.932; 95% CI, 5.993–23.755; P = 0.001), sore throat (OR, 0.107; 95% CI, 0.014–0.802; P = 0.030), unconsciousness (OR, 21.923; 95% CI, 2.582–186.168; P = 0.005), comorbidity (OR, 9.289; 95% CI, 3.317–11.922; P = 0.001), HTN (OR, 3.712; 95% CI, 1.902–7.244; P = 0.001), DM (OR, 3.712; 95% CI, 1.902–7.244; P = 0.001), COPD (OR, 3.815; 95% CI, 1.750–8.318; P = 0.001), CKD (OR, 7.480; 95% CI, 2.164–25.851; P = 0.001) and smoking (OR, 2.225; 95% CI, 1.120–4.422; P = 0.022) (Table 6).

The stepwise forward regression analysis was used to enter all significant variables to analyze the predictors of the risk of mortality in SARS-COV-2 patients. Respiratory rate alone was inserted

Table 7
Multivariable stepwise regression to find the Predictors of Mortality (N = 249).

Steps	Predictors	B	OR (95 % CI)	Sig.
Step 1[a]	RR/Min	0.323	1.381(1.251–1.525)	0.001*
R^2 = 0.329	Constant	−8.295	0.001	0.001
Step 2[b]	RR/Min	0.247	1.280 (1.152–1.423)	0.001*
R^2 = 0.429	Dyspnea	1.758	5.800 (2.724–12.346)	0.001*
	Constant	−7.458	0.001	0.001
Step 3[c]	RR/Min	0.235	1.265 (1.137–1.408)	0.001*
R^2 = 0.474	Spo2	−0.083	0.921 (0.874–0970)	0.002*
	Dyspnea	1.427	4.166 (1.881–9.227)	0.001*
	Constant	0.661	1.937	0.813
Step 4[d]	RR/Min	0.222	1.249 (1.123–1.369)	0.001*
R^2 = 0.509	Spo2	−0.077	0.926 (0.879–0.976)	0.004*
	Dyspnea	1.630	5.102 (2.213–11.762)	0.001*
	Unconsciousness	3.409	30.237 (2.175–420.294)	0.011*
	Constant	0.211	1.235	0.940
Step 5[e]	RR/Min	0.173	1.189 (1.065–1.328)	0.002*
R^2 = 0.539	HR/Min	0.033	1.033 (1.009–1.058)	0.007*
	Spo2	0–.073	0.930 (0.879–0.984)	0.011*
	Dyspnea	1.697	5.458 (2.290–13.004)	0.001*
	Unconsciousness	4.062	58.071 (2.666–1265.010)	0.010*
	Constant	−2.413	0.090	0.440

[a] variable(s) entered on step 1: RR/Min (Respiratory rate/minute).
[b] variable(s) entered on step 2: Dyspnea.
[c] variable(s) entered on step 3: Spo2.
[d] variable(s) entered on step 4: Unconsciousness.
[e] variable(s) entered on step 5: HR/Min (Heart rate/minute).
* *P* value < 0.05.

in the first step of the model (OR, 1.381, 1.251–1.525) reported a variance of 32.9% to predict death (Nagelkerke r square = 0.329). In the second model, dyspnea was adjusted along with respiratory rate would increase the prediction of death to 42.9% cases (Nagelkerke r square = 0.429 %) with a change of 10 % in variance. Further, in the third model, the partial pressure of oxygen (SpO2) was adjusted with dyspnea, and respiratory rate increased the probability of death in 47.4% cases (Nagelkerke r square = 0.474%). Model 4 adjusted unconsciousness along with the other three variables entered in model 3. Model 4 could predict death in 50.9%, adding merely another 3.5% to model 3. Model 5 included heart rate and other existing 4 variables used in model 4, and an adjusted effect was measured to predict death in SARS-COV-2. The final model predicted death in 53.9% cases with a slight increase of 3% (Nagelkerke r square = 0.539) to existing model 4 (Table 7).

Discussion

In this study, we explored the predictors of critical illness and mortality based on the symptoms at the time of admission and initial physical examination of SARS-COV-2 patients hospitalized at a tertiary care public hospital.

The typical clinical manifestations at the time of admission were fever, dry cough, dyspnea, sore throat, myalgia, headache, productive cough, and abnormal cardiac rate. However, a significant number of patients reported atypical symptoms initially, including nausea, vomiting, and diarrhea, which is closely similar to the earlier published work on characteristics of SARS-COV-2 patients [7,23,24].

Risk factors related to critical illness and progression from critical illness to death included older age and comorbidity conditions, including hypertension, diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease, smoking status, raised body temperature, and unconscious status at the time of initial physical examination.

Also, we observed that several factors (e.g., comorbidities, hypertension, diabetes mellitus, febrile temperature, fever, cough, and dyspnea) associated with critical illness were more closely associated with death, which is consistent with the previous work that reported critical illness or higher death in patients with comorbidities, hypertension and or diabetes [21,24–26]. The effect of advanced age and comorbidities had been studied to the critical illness and addressed consistent findings in a similar cohort of patients with SARS-COV-2 [3,27–29].

Likewise, the impact of kidney disease and other respiratory problems on the critical illness and unfavorable outcomes in SARS-COV-2 patients agrees with the results noted in earlier studies in the same cohort population [7,21,23,24,30]. Data are scanty on the role of body temperature, fever, cough, and dyspnea on progression to critical illness and mortality and need further research in this direction to generalize the findings.

Considering comorbid conditions, fewer patients who died had comorbid conditions than those who developed a critical illness. Interestingly, the findings highlighted that advanced age might be at a higher risk of death, which is in line with the study's findings by Wang et al. [7]. These findings are further strengthened by evidence published in earlier work from China, which suggested that advanced age and existing comorbidities were associated with disease severity or higher mortality of SARS-COV-2 patients [7,21,23,24,26,31].

Current data suggests that several signs-symptoms were associated with developing critical illness in SARS-COV-2 patients (unconsciousness, fever, cough, abnormal cardiac rhythm, dyspnea, and sore throat). Interestingly, these factors were found to be associated with higher severity and worst outcome. However, abnormal cardiac rhythm pathogenesis could not be understood well concerning developing critical illness in the cohort. Risk factors studied matched with the earlier scientific work on SARS-COV-2, which suggested that fever, dyspnea, and unconsciousness were associated with increased illness severity [4,30]. However, the findings on fever were negatively related to mortality in earlier work, which remains inconclusive and suggests the need for more research to reach an agreement [32]. However, the author advises interpreting these findings with caution due to potential bias and limitation of small sample size and need to be validated using double-blind, randomized controlled trials.

The presence of comorbidities, especially diabetes mellitus and hypertension, respiratory disease, and kidney diseases, was a decisive contribution to our patients' outcomes. The effect of comorbidities including diabetes mellitus, heart disease, and other

comorbid conditions (hypertension, lung disease, and cerebrovascular disease) was independently associated with unfavorable outcomes (ICU admission, mechanical ventilation, and death) in SARS-COV-2 patients [3,33]. However, this is not surprising; the role of heart diseases and /or diabetes mellitus is well studied and found to increase the poor or unfavorable outcomes, including death in a patient with community-acquired pneumonia in current and previous work as well [3,8,21,26,28].

Limitations

This record analysis should be appraised under many limitations. First, owing to only tertiary care public facilities in the region, only patients with critical illness were admitted during the coronavirus outbreak. Second, the study is limited to a single center with a small sample size. The study only considers findings on symptoms and clinical examination and excluded all laboratory and imaging work, which plays a critical role in decision making in the clinical setting and hence, may be considered preliminary in the area. A more extensive cohort study of patients with SARS-COV-2 from other regions or multicentre of the country would help reach a concrete conclusion on the predictors of critical illness and mortality in SARS-COV-2 patients.

Conclusion

In conclusion, we identified many risk factors for developing critical illness and mortality among SARS-COV-2 patients. This single-center retrospective analysis gives a new insight describing the impact of epidemiological and initial physical examination findings on developing critical illness and fatal outcomes in patients with COVID-19. Considering the unpredictable nature of the novel coronavirus and predicting frequent waves and long duration of the pandemic, it is urged to clinicians consider the symptoms and initial physical examination findings of SARS-COV-2 patients in clinical decision making. These determinants may find helpful for clinicians to identify the patients with fatal outcomes at an early stage.

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Competing interests

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