Clinical and Laboratory Predictors for ICU Admission among COVID-19 Infected Egyptian Patients, A multi-Center Study

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Background and study aim: The incremental global spread of the SARS-CoV-2 virus imposes an enormous burden on medical health systems. We focused on determining the predictors for the COVID-19 patient's course of illness and what level of care will be actually needed at hospital admission.

Patients and Methods: 170 symptomatic COVID-19 Egyptian patients were gleaned from August 2020 to January 2021, were categorized into a group that managed at home or ward admitted and a group that necessitated ICU hospitalization at Tanta University or Kafr El-sheikh University isolation hospitals. Each patient's demographics, clinical, laboratory, and radiological data were gathered and several classification strategies were applied. The variables that predicted the severity of disease and ICU admission were established via logistic regression. The area under the receiver operating characteristic curve was used to assess performance.

Results: The top risk variables predicting ICU admission were blood oxygen saturation ($P<0.001$), serum ferritin ($P= 0.023$), WHO assessment scale ($P= 0.001$) and presence of fatigue ($P= 0.001$) or myalgia ($P= 0.028$) and with the best accuracy for WHO assessment scale >4 and oxygen saturation ≤90 with an AUC of 0.850 (95% CI [0.795 – 0.905]) and 0.800 (95% CI [0.735 – 0.865]), respectively.

Conclusion: Fatigue, myalgia, oxygen saturation, pulse, respiratory rates, ferritin, and C- reactive protein may prove useful for physicians to distinguish which COVID-19 patients will be required to be managed critically at hospital admission.

INTRODUCTION

SARS-CoV-2 pandemic around the world, with fatality rates ranging from 0.4% to 7%, has killed hundreds of thousands of people **[1]**. While the majority of COVID-19 patients have no symptoms or very modest respiratory symptoms, not demanding hospitalization, and only a minuscule proportion of patients are hospitalized owing to systemic or severe respiratory symptoms **[2, 3]**, the virus's rapid spread is putting undue strain on public health systems **[4]**. So, increased medical supplies are being sought to alleviate this burden **[5]**.

The biggest concern in the assessment of patients infected with COVID-19 in a pandemic situation is to identify patients who are already at high risk of mortality early in the disease and to give proper medical care **[6]**. The condition of high-risk patients, in particular, might quickly deteriorate. According to certain studies, COVID-19 patients who ended up dead had minor symptoms at first but speedily escalated to a critical stage, leading to death **[7, 8]**.

Governments and hospitals have battled to allocate limited supplies, such as diagnostics, treatment in critical care units (ICUs), and ventilators, throughout this pandemic **[9, 10]**. Furthermore, ICU capacity varies by country, with lesser availability in lower-middle-income parts of the world **[11]**.

Specific evidence on the patient risk factors linked to COVID-19 mortality is scarce, and approaches to reliably predict disease severity at the time of hospital admission are inadequate **[12-14]**. As a result, there is a pressing need to assist field doctors in optimally triaging COVID-19 patients **[15]**.

To preserve healthcare system capacity in Egypt, the goal of this study is to investigate the prognostic usefulness of combined clinical, laboratory, and imaging results in predicting critical disease among Egyptian COVID-19 patients.

PATIENTS AND METHODS

Study design and settings

Enrollment of patients in this prospective observational study was done after Tanta University Ethical committee of scientific research approval (approval code: 33988/8/20) complying with the declaration of Helsinki. A total of 200 patients who were either home isolated or admitted to Tanta University and Kafr El-sheikh university isolation hospitals, in the period from August 2020 to January 2021, were screened for participation in this study.

Inclusion criteria

Adult (≥ 18 years) patients who have diagnosed with COVID-19 infection with positive PCR test (if the first PCR test of highly suspicious critical cases was negative, it was repeated within 48 hours) and the presence of typical computed tomography (CT) features were included in this study. All patients received treatment according to the Egyptian protocol for the management of COVID-19 **[16]**.

Exclusion criteria

Patients aged < 18 years and patients with a history of any of the following; cancer, severe kidney and liver diseases, presence of other known infection, pregnancy, taking medications before the initial visit, uncontrolled diabetes mellitus (DM) (HbA1c >9), chronic pulmonary disease, alcoholism, organ transplant, refusing to be included in this study were excluded.

Method

All of the following data were collected on admission: history taking for co-morbidities and clinical presentation, clinical examination (including vital signs assessment), laboratory investigations including; liver enzymes; alanine aminotransferase (ALT), aspartate aminotransferase (AST), AST/ALT ratio and ALT/AST ratio were calculated, renal function tests (blood creatinine), serum ferritin, C-reactive protein (CRP), complete blood count; to detect total leucocytic count (TLC), neutrophil %, lymphocytes %, hemoglobin, platelet count, to calculate: Neutrophil-to-Lymphocyte ratio (NLR), Platelet–to–Lymphocyte ratio (PLR), pregnancy test for females in the child-bearing period. Also, the high resolution CT chest was interpreted by severity scoring. Follow-up of all included patients was done to detect the fate of every patient (either cured or died).

Patients were given scores according to severity of the disease; mild cases: patients with mild symptoms (either one or more of the following symptoms: fever, fatigue, cough, sore throat, headache, runny nose, body aches, diarrhea and or vomiting, the new loss of taste or smell) and normal imaging, moderate cases: patients with positive CT findings of COVID-19 and saturation of peripheral Oxygen $SpO_2 \geq 92\%$, sever cases: fulfilling any of the following criteria: respiratory rate >30 breaths/min, SpO2< 92%. PaO2/FiO2 ratio <300 or lung infiltrate >50%, critical case: patients with any of the following; respiratory failure, septic shock, and/or multi-organ dysfunction **[16]**, and World Health Organization (WHO) assessment score: 0 =no infection 1=no limitation of activities 2 =limitation of activities 3 =hospitalized, no oxygen therapy 4=oxygen by mask or nasal prong 5=non-invasive ventilation or high-flow oxygen 6 =intubation and mechanical ventilation 7 =ventilation + additional organ support 8 =death **[17]**.

Statistical analysis

IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) was administered for the analysis of the gathered data. The Kolmogorov- Smirnov was used to verify the normality of distribution of variables. Mean, standard deviation, median and range were used for describing quantitative variables while qualitative variables were illustrated as frequency and percentages. Chi-square test (Fisher or Monte Carl) was used for the comparison of the categorical variables between the two studied groups. Student t-test and Mann Whitney test were utilized to compare between the two groups as regard normally and not normally distributed quantitative variables respectively. Pearson coefficient was used to correlate between two normally distributed quantitative variables, while Spearman coefficient was done for abnormally quantitative variables. Univariate and multivariate regression analyses were done to detect the main independent factor for ICU admission. The area under the receiver operating characteristic (ROC) curve was calculated to measure the discriminatory power of factors predicting the need for ICU admission. p value was considered significant if < 0.05.

RESULTS

200 patients were evaluated for participation in this study. But only 170 patients were included and divided into two groups; Group I included 89 patients who were treated either at home or ward admitted; Group II included 81 patients who needed ICU admission. Group I patients has a median of age 49 years and male/female (m/f) ratio 50/39, while patients in group II has a median of age 52 years and m/f ratio 47/34 with no significant differences recorded between two studied groups as regard age, and sex (P= 0.119, 0.808 respectively) **(Table 1)**. Various predisposing factors were recorded in patients included in both groups with no significant difference detected **(Table 1)**.

Pulse rate, respiratory rate, and body temperature were significantly higher in ICU group (P=0.002, <0.001, 0.028 respectively), whereas SpO_2 was significantly lower (P=<0.001), while blood pressure either systolic or diastolic showed no difference (P=0.84, 0.091) (Table 1). Several clinical manifestations were recorded in this study from them; fever, fatigue, myalgia, malaise, body aches and cyanosis were presented in higher percentage in group II (P= 0.017, <0.001, 0.033, 0.021 and <0.001 respectively) **(Table1)**.

A higher percentage of group II patients had CT findings of severe infection including (ground glass/consolidation, crazy paving and vascular thickening), while ground glass/consolidation were predominant in group I (P <0.001) **(Table 2)**.

Patients in group II had higher scores of both: Severity score and WHO assessment scale (P <0.001) (Table 2). As regard death rate 11(13.6%) patients in group II died; 4 females and 7 males. Hypertension, diabetes mellitus, ischemic heart disease and history of thrombosis (deep venous thrombosis, pulmonary embolism or stroke) were the main co-morbidities in those patients. 2 patients had arrhythmia (acute atrial fibrillation and premature ventricular contractions (PVC)) **(Table 1)**.

Neutrophil %, serum ferritin and CRP were significantly elevated in group II (P = <0.001, 0.012, 0.001 respectively), while platelet count was significantly decreased (P= 0.045) (Table 2). ICU admitted patients had a higher median total hospital stay days than group I (12 vs 9) (P<0.001) **(Table 2)**.

A significant negative correlation was noticed between oxygen saturation level and age, pulse rate, RR, temperature, TLC, neutrophil %, N/L ratio, serum ferritin, CRP and total hospital stay (P= 0.002, 0.002, <0.001, 0.049, <0.001, <0.001, 0.023, <0.001, <0.001 and <0.001 respectively), while positively correlated with lymphocyte % (P= 0.002) **(Table 3)**. While WHO assessment scale was positively correlated with pulse rate, RR, temperature, TLC, neutrophil %, N/L ratio, serum ferritin, CRP and total hospital stay (P= <0.001, <0.001, 0.005, 0.022, <0.001, 0.001, <0.001, <0.001 and <0.001 respectively), and negatively correlated with lymphocyte % (P= 0.001) **(Table 3)**.

Disease severity was positively correlated to age, pulse rate, RR, temperature, TLC, neutrophil %, N/L ratio, serum ferritin, ALT, AST, CRP and total hospital stay (P= <0.001, <0.001, <0.001, <0.001, <0.001, 0.001, <0.001, <0.001, 0.013, 0.022, <0.001 and <0.001 respectively), while negatively correlated to hemoglobin and lymphocyte% (P= 0.029 and <0.001 respectively) **(Table 3)**.

A multivariate regression analysis demonstrated that, blood oxygen saturation (P<0.001), serum ferritin (P= 0.023), WHO assessment scale (P= 0.001) and presence of fatigue (P= 0.001) or myalgia (P= 0.028) were independent predictors for ICU admission **(Table 4)**.

ROC curve analysis revealed that WHO assessment scale >4 and oxygen saturation ≤90 yielded the best accuracy for the detection of the need of ICU admission (AUC= 0.850, sensitivity= 53.09, specificity= 98.88, PPV=79.9, NPV= 69.8 and AUC=0.800, sensitivity=79.1, specificity=64.04, PPV= 66.7, NPV=77 respectively). While pulse rate, serum ferritin, RR and CRP had lower AUC (0.641, 0.612, 0.738 and 0.650 respectively) **(Table 5, Fig 1)**.

Table (1): Patients' basic, demographic and clinical features.

	Group I (n = 89)	Group II (n = 81)	P
Age (years)			
Median (Min. – Max.)	49 (19 – 84)	52 (22 – 82)	0.119
Gender			
Male	50 (56.2%)	47 (58%)	0.808
Female	39 (43.8%)	34 (42%)	
Smoker	16 (18%)	10 (12.3%)	0.308
DVT/PE/stroke	0 (0%)	3 (3.7%)	^{FE}p=0.106
Cardiac problems	11 (12.4%)	13 (16%)	0.490
HTN	16 (18%)	24 (29.6%)	0.074
DM	23 (25.8%)	30 (37%)	0.116
Fever	71 (79.8%)	75 (92.6%)	0.017*
Cough	68 (76.4%)	61 (75.3%)	0.868
Dyspnea	75 (84.3%)	75 (92.6%)	0.093
Sore throat	18 (20.2%)	10 (12.3%)	0.167
Rhinorrhea	2 (2.2%)	0 (0%)	^{FE}p=0.498
Fatigue	59 (66.3%)	76 (93.8%)	<0.001*
Myalgia	45 (50.6%)	54 (66.7%)	0.033*
Headache	32 (36%)	38 (46.9%)	0.147
Anorexia	29 (32.6%)	29 (35.8%)	0.658
Malaise	32 (36%)	49 (60.5%)	0.001*
Aches and pain	37 (41.6%)	48 (59.3%)	0.021*
Diarrhea	28 (31.5%)	24 (29.6%)	0.796
Nausea	5 (5.6%)	4 (4.9%)	^{FE}p=1.000
Anosmia	23 (25.8%)	17 (21%)	0.456
Cyanosis	21 (23.6%)	54 (66.7%)	<0.001*
Loss of taste	5 (5.6%)	5 (6.2%)	^{FE}p=1.000
Blood pressure			
Systolic(mmHg)			
Mean ± SD	124.4 ± 16.9	123.9 ± 16.8	0.840
Diastolic(mmHg)			
Mean ± SD.	77.7 ± 9.5	80.6 ± 13	0.091
Pulse (beat/min)			
Mean ± SD.	91.2 ± 13	98.6 ± 17.3	0.002*
RR (breaths/min)			
Mean ± SD.	21 ± 2.6	24.8 ± 4.7	<0.001*
Temperature (Celsius)			
Mean ± SD.	37.9 ± 0.7	38.2 ± 0.7	0.028*
SpO_2 (%)			
Mean ± SD.	91.5 ± 3.8	82.6 ± 11	<0.001*
Fate			
Dead	0 (0%)	11 (13,6%)	<0.001*
Alive	89 (100%)	70 (86.4%)	

DVT= deep venous thrombosis; PE= pulmonary embolism; HTN= hypertension; DM= diabetes mellitus; RR= respiratory rate; SpO_2= saturation of peripheral oxygen.

Table (2): Laboratory and radiographic data in studied groups.

	Group I (n = 89)	Group II (n = 81)	P
HB(g/dl)			
Mean ± SD.	12.5 ± 1.8	12.4 ± 1.8	0.764
TLC ($x10^3$ /µl)			
Median (Min. – Max.)	7.5 (2.6 – 18.5)	8.5 (2.7 – 27)	0.485
Neutrophils %			
Mean ± SD.	71.1 ± 10.2	78.3 ± 7.7	<0.001*
N/L ratio			
Median (Min. – Max.)	4.7 (1.1 – 21.3)	5.5 (1.7 – 18.8)	0.106
Lymphocytes %			
Median (Min. – Max.)	17 (5 – 47.0)	15 (4.8 – 36)	0.196
Platelets (×10³/µl)			
Median (Min. – Max.)	223 (50 – 510)	201 (46 – 590)	0.045*
PL ratio			
Median (Min. – Max.)	206.1 (10.8 – 661.7)	174.1 (45 – 1844)	0.282
Ferritin (ng/mL)			
Median (Min. – Max.)	368 (3 – 950)	489 (17.4 – 1672)	0.012*
ALT(U/L)			
Median (Min. – Max.)	40 (6 – 243)	39 (12 – 462)	0.679
AST(U/L)			
Median (Min. – Max.)	40 (10 – 282)	41 (12 – 300)	0.833
AST/ALT			
Median (Min. – Max.)	1 (0.3 – 2.5)	1.1 (0.4 – 3)	0.657
ALT/AST			
Median (Min. – Max.)	1 (0.4 – 3)	0.9 (0.3 – 2.9)	0.784
CRP (mg/L)			
Median (Min. – Max.)	37 (0 – 227.1)	59 (0 – 217)	0.001*
Creatinine (mg/dl)			
Median (Min. – Max.)	0.9 (0.4 – 3)	1 (0.5 – 2.4)	0.161
CT chest			
Ground glass/consolidation	85 (95.5%)	51 (63%)	^{MC}p
Vascular thickening	0 (0%)	1 (1.2%)	<0.001*
All of those findings	4 (4.5%)	29 (35.8%)	
Severity			
Mild	7 (7.9%)	0 (0%)	
Moderate	37 (41.6%)	15 (18.5%)	^{MC}p
Severe	45 (50.6%)	59 (72.8%)	<0.001*
Critical	0 (0%)	7 (8.6%)	
Median (Min. – Max.)	3 (1 – 3)	3 (2 – 4)	<0.001*
WHO assessment scale			
Limitation of activities	12 (13.5%)	0 (0%)	
Hospitalized, no oxygen therapy	22 (24.7%)	0 (0%)	
Oxygen by mask or nasal prong	54 (60.7%)	38 (46.9%)	<0.001*
Non-invasive ventilation or high-flow oxygen	1 (1.1%)	32 (39.5%)	
Death	0 (0%)	11 (13.6%)	
Median (Min. – Max.)	4 (2 – 5)	5 (4 – 8)	<0.001*
Total hospital stay			
Median (Min. – Max.)	9 (0 – 15)	12 (1 – 53)	<0.001*

HB= Hemoglobin; TLC= total leucocytic count; N/L= neutrophil/lymphocyte ratio; PL= platelet / lymphocyte ratio; AST= aspartate aminotransferase; ALT= alanine aminotransferase; CRP= C-reactive protein; CT= computed tomography; WHO= World Health Organization; Min= minimum; Max= maximum.

Table (3): Correlation between SpO_2, WHO assessment scale, severity and different parameters in total sample (n=170)

	SpO_2		WHO assessment scale		Severity	
	R	p	r_s	P	r_s	P
Age (years)	-0.242	0.002*	0.146	0.057	0.282	<0.001*
Systolic blood pressure (mmHg)	-0.008	0.915	-0.036	0.640	-0.069	0.369
Diastolic blood pressure (mmHg)	-0.069	0.374	-0.027	0.727	-0.070	0.367
Pulse (beats/minute)	-0.240	0.002*	0.354	<0.001*	0.316	<0.001*
RR (breaths/minute)	-0.582	<0.001*	0.442	<0.001*	0.463	<0.001*
Body temperature (Celsius)	-0.151	0.049*	0.215	0.005*	0.281	<0.001*
HB (g/dl)	0.144	0.061	-0.134	0.081	-0.167	0.029*
TLC ($x10^3$ /µl)	-0.283	<0.001*	0.176	0.022*	0.287	<0.001*
Neutrophils %	-0.272	<0.001*	0.320	<0.001*	0.245	0.001*
N/L ratio	-0.174	0.023*	0.252	0.001*	0.281	<0.001*
Lymphocytes %	0.239	0.002*	-0.263	0.001*	-0.296	<0.001*
Platelets ($\times10^3$/µl)	0.030	0.700	-0.069	0.372	-0.068	0.381
P/L ratio	0.010	0.899	0.023	0.766	-0.007	0.931
Ferritin (ng/mL)	-0.384	<0.001*	0.395	<0.001*	0.502	<0.001*
ALT (U/L)	-0.148	0.054	0.119	0.122	0.191	0.013*
AST (U/L)	-0.080	0.298	0.106	0.171	0.176	0.022*
AST/ALT	0.003	0.971	-0.038	0.619	-0.094	0.222
ALT/AST	-0.078	0.314	0.056	0.471	0.097	0.207
CRP (mg/L)	-0.357	<0.001*	0.333	<0.001*	0.326	<0.001*
Creatinine (mg/dl)	-0.047	0.539	0.002	0.979	0.036	0.643
Total hospital stay	-0.490	<0.001*	0.558	<0.001*	0.430	<0.001*

RR= respiratory rate; HB= Hemoglobin; TLC= total leucocytic count; N/L= neutrophil/lymphocyte ratio; PL= platelet / lymphocyte ratio; AST= aspartate aminotransferase; ALT= alanine aminotransferase; CRP= C-reactive protein; CT= computed tomography.

Table (4): Univariate and multivariate Logistic regression analysis for the parameters affecting ICU (n = 81) from ward (n = 89).

	Univariate		#Multivariate	
	p	OR (95%C.I)	P	OR (95%C.I)
Pulse (beats/minute)	**0.002***	1.033(1.012 – 1.055)	0.059	0.941(0.883 – 1.002)
RR (breaths/minute)	**<0.001***	1.304(1.183 – 1.438)	0.896	1.022(0.741 – 1.409)
Body temperature (Celsius)	**0.029***	1.608(1.049 – 2.464)	0.126	2.117(0.811 – 5.530)
SpO_2(%)	**<0.001***	0.787(0.725 – 0.855)	<0.001*	2.117(0.811 – 5.530)
Neutrophils %	**<0.001***	1.092(1.051 – 1.134)	0.571	1.024(0.944 – 1.110)
Platelets ($\times10^3$/µl)	**0.073**	0.997(0.993 – 1.0)		
Ferritin (ng/ml)	**0.004***	1.002(1.001 – 1.003)	0.023*	0.995(0.991 – 0.999)
CRP (mg/L)	**<0.001***	1.014(1.007 – 1.022)	0.441	1.007(0.989 – 1.027)
Total hospital stay	**<0.001***	1.261(1.148 – 1.384)	0.244	1.197(0.885 – 1.619)
Fatigue	**<0.001***	7.729(2.826 – 21.135)	0.001*	302.979(11.51 – 7974.88)
Myalgia	**0.034***	1.956(1.051 – 3.640)	0.028*	0.075(0.008 – 0.752)
Aches and pain	**0.022***	2.044(1.109 – 3.769)	0.404	2.232(0.339 – 14.707)
Cyanosis	**<0.001***	6.476(3.304 – 12.693)	0.333	0.333(0.036 – 3.089)
WHO assessment scale	**<0.001***	62.086(8.520 – 452.415)	0.001*	320.635(10.36 – 9926.64)
CT chest(All of those findings)	**<0.001***	11.851(3.941 – 35.633)	0.094	17.515(0.614 – 500.017)
Severity	**<0.001***	4.319(2.307 – 8.083)	0.284	0.293 – 0.031 – 2.773)

RR= respiratory rate; SpO_2 = saturation of peripheral oxygen; CRP= C- reactive protein; WHO= World Health Organization; CT= computed tomography.

Table (5): Validity (AUC, sensitivity, specificity) for different parameters to discriminate ICU (n = 81) from Ward (n = 89)

	AUC	P	95% C.I	Cut off	Sensitivity	Specificity	PPV	NPV
Pulse (beat/minute)	0.641	0.002*	0.556 – 0.725	>100	41.98	83.15	69.4	61.2
SpO_2 (%)	0.800	<0.001*	0.735 – 0.865	≤90	79.01	64.04	66.7	77.0
WHO assessment	0.850	<0.001*	0.795 – 0.905	>4	53.09	98.88	97.7	69.8
Ferritin (ng/ml)	0.612	0.012*	0.527 – 0.697	>368	62.96	50.56	53.7	59.5
RR	0.738	<0.001*	0.660 – 0.816	>23	62.96	83.15	77.3	71.2
CRP (mg/L)	0.650	0.001*	0.564 – 0.736	>56	53.09	82.02	72.9	65.8

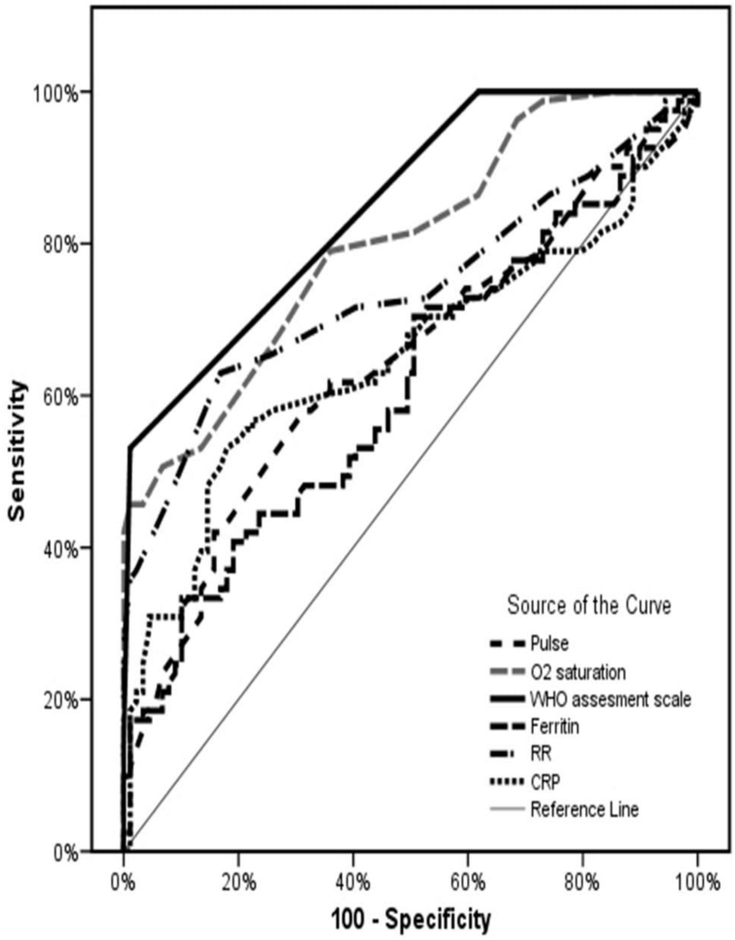

Figure (1): ROC curve for different parameters to discriminate factors determining ICU admission (n = 81) from WARD (n =89)

DISCUSSION

This study involved a retrospective evaluation of prospectively gathered data from 170 Egyptian patients who were either home isolated, hospitalized in a ward, or referred to an ICU. Initially, on the basis of demographic data, there were no significant variations in gender or age here between the two groups. Age did have a statistical correlation with both oxygen saturation and severity of illness; this was in the same line with prior researches encompassing age in the Covid-19 severity scores and even assumed it as one of the predictors of deaths; meanwhile, age could not be considered an independent factor for ICU admission in the present research work **[18, 19]**.

Although 8 of 11 dead patients had a history of either one or more of the following conditions;

diabetes mellitus, hypertension, deep venous thrombosis, or ischemic heart disease, there was no significant difference in preexisting medical factors between the two evaluated groups. On the contrary, predisposing illnesses such as cancer, chronic kidney disease, chronic lung disease, diabetes mellitus, hypertension, and others, have been identified as risk factors for severity, intubation risk, and death in earlier researches **[3, 14]**. This disparity could be attributable to the current study exclusion criteria, which included both cancer patients and chronic chest patients.

Since the emergence of the pandemic, a wide range of symptoms and signs have been recorded, all of which are non-specific for COVID-19, though fever, fatigue, malaise, myalgia, body aches, and cyanosis were seen in a higher percentage of ICU patients than in-home isolated or ward admitted patients. Furthermore, fatigue and myalgia were found to be independent predictors for ICU admission need. In accordance with our result, Li et al 2020 concluded that muscle and joint pain are predictors of the severity of COVID-19 **[20]**.

Unlike previous studies that linked bradycardia to community-acquired pneumonia **[21]** or the severity of COVID-19 **[22]**, ICU patients had significantly higher respiratory rates, body temperatures, and pulse rates. Furthermore, only two ICU admitted patients had bradycardia, while the majority had either normal or increased pulse rates. This increase in pulse rate can be attributed to many influences, including increased body temperature (as pulse increases 9.46 beats/min/°C in female patients and 7.24 beats/min/°C in male patients for every 1°C increase in body temperature) **[23]**, cardiac affection caused by COVID-19 infection **[24]**, and associated inflammation. Moreover, in this study, 4 out of 11 dead patients had arrhythmia and ischemic heart attack. So pulse rate can be used as a rapid, simple, and bedside indicator of disease severity. Therefore, this finding highlights the importance of conducting ECG as a routine for COVID-19 infected patients.

Oxygen saturation, in previous studies, was proved to be associated with severity and mortality **[25]** and is incorporated in various COVID-19 management protocols. This is the same as in this study, where it was one of the independent predictors of ICU admission, with moderate sensitivity and specificity, at a cutoff value ≤ 90.

The level of serum ferritin had been posited as one of the predictors of poor outcome in COVID-19 sufferers. Higher levels of serum ferritin were associated with higher odds of ICU admission through both univariate and multivariate analyses in this work, which was comparable to earlier studies that found an association between raised ferritin count and fatality, but with a lower cut off value (300 ng/ml) vs (368 ng/ml) in our study **[1, 14]**.

The link between the severity of infection and lymphopenia had been hypothesized, although it is not disease-specific as it can take place with any viral infection **[26]**. Though some of our patients had lymphopenia, lymphocyte percentage and N/L ratio did not show any significant difference between the two studied groups while they were strongly correlated with the severity of the disease and oxygen saturation, this result is corroborated by previous studies **[27, 28]**. Consistent with previous research **[29]**, the percentage of neutrophils throughout ICU patients seemed to be comparatively high and was positively correlated with the severity of illness, and it was one of the crucial variables in univariate regression analysis. It can still be clarified by the virus's capabilities to wreck epithelial walls, distorting airway surfactant, and consequently results in secondary bacterial infection **[30]**.

Among ICU patients, the platelet count had declined sharply, which was in line with prior research that attributed thrombocytopenia to both the seriousness of covid-19 & myocardial affection **[31]**. On the other hand, a study by **Qu et al** revealed that patients with a higher platelet count and P/L ratio had an even worse fate. This divergence could be related to the small sample size of 30 patients in their study **[32]**. But, after performing univariate and multivariate analyses, platelet count cannot be regarded as an independent predictor of severity.

ALT and AST were analyzed for the recognition of liver cellular injury; they were found to be raised within many patients in both groups, and they had a positive correlation with the degree of illness severity, but no significant difference was recorded between the both tested groups. As a result, ALT and AST could not be included among the factors determining ICU admittance, in conversely to a previous study **[33]**, which recommended ALT and AST as factors determining both ICU transferring hence the need for mechanical ventilation. This difference could be due to sample size dissimilarities.

CRP is a non - specific indicator of inflammation which arises in infection or inflammation **[34]**, has already been postulated as a key predictor of COVID-19 infection as well as intensity, and even some publications have consistently demonstrated its rising before other hematological indicators **[35]**. Even though CRP, in our study, was considerably higher in the ICU group and revealed an evident correlation with both oxygen saturation and severities, it could not be considered an independent forecaster of ICU admission since it was one of the crucial variables in univariate but not multivariate analysis, in contrast to previous studies **[36, 37]**.

Numerous studies have illustrated the practical value of CT chest not just as a detector of disease severity but also as a diagnostic instrument in areas with limited resources **[38]**, and this is the same in this study as a higher proportion of cases who mandated ICU admission had worse CT signs of infection.

On the one hand, our study had some strength; first, it was a multicenter study; second, it was a prospective study. On the other hand, there were some limitations, such as missing data that forced us to erase D dimer & other tests indicating coagulation profile, as well as the small sample size, necessitating further research with a larger cohort to validate our results.

In conclusion, in Egypt, fatigue, myalgia, oxygen saturation, pulse, and respiratory rates, ferritin and CRP; within these limited resources; are simple, rapidly monitored predictors of severity and the demand for ICU admission among COVID-19 sufferers.

Abbreviations:

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2
ALT: alanine aminotransferase
AST: aspartate aminotransferase
COVID-19: coronavirus disease 2019
CRP: C- reactive protein
CT: computed tomography
DM: diabetes mellitus
ICU: intensive care unit
NLR: Neutrophil-to-lymphocyte ratio
PCR: polymerase chain reaction
ROC: receiver operating characteristic
SpO2: Saturation of peripheral oxygen
TLC: total leucocytic count
PLR: Platelet–to–lymphocyte ratio
AUC: area under curve
PVC: premature ventricular contractions
WHO; world health organization; RR= respiratory rate
HB: hemoglobin
HTN: hypertension
PE: pulmonary embolism
DVT: deep venous thrombosis
PPV; positive predictive value
NPV= negative predictive value

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Conflict of interest

The authors declare that they have no competing interests.

Ethical consideration

All included patients approved for participation before enrollment, data included in this research was accessed by the contributing authors, reviewed and agreed on the final manuscript. Tanta University Ethical committee of scientific research approved the study.

Highlights

SARS-CoV-2 pandemic around the world increased the need for medical supplies to alleviate this burden.
Many countries as Egypt have limited supplies especially critical care units (ICUs) and ventilators.
The aim of our work is to investigate the prognostic value of combined clinical, laboratory, and imaging results on admission in predicting critical COVID-19 cases that will need extra care and ICUs.

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