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Intensive care unit admission and mortality risk prediction in covid19 patients with spectrum of comorbidities using clinical laboratory and CT severity score

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ABSTRACT

Introduction: Treatment of patients with COVID-19 in intensive care unit (ICU) has been a significant challenge. Early detection of COVID-19 related severity is critical for timely management of such patients. This retrospective observational study aimed to evaluate clinical characteristics such as laboratory parameters, associated comorbidities, computed tomography (CT)-based semi-quantitative score, and cumulative correlative measurement of critically ill COVID-19 patients to assess the requirement for early ICU admission.

Materials and methods: Data from the treatment record of COVID-19 patients with severe pneumonia was collected at a tertiary care governament medical institution from 1st May, 2020 to 30th May, 2020. Binary logistic regression analysis, specificities and sensitivities of maximum D-dimer, ferritin, other laboratory measures, and CT-based semi-quantitative score for outcome cutoffs were calculated to predict early indicators of ICU admission and mortality.

Results: Of 200 severe COVID-19 patients, 48% had comorbidities while 40% had mortality. The ICU admission rate was 43.5%, in which non-invasive ventillation and mechanical ventilation support were 27.5% and 16% respectively. Hypertension was reported for the most prevalent comorbidities (48%) followed by diabetes mellitus (24%), respiratory diseases (10.5%), renal diseases (5%), and chronic heart diseases (10%). Optimal cutoff for ICU requirement was 17.2 for neutrophil lymphocyte ratio (NLR), 727 ng/mL for ferritin, 2.2 mg/L FEU for D-dimer and 362.5 mg/L for C-reactive protein (CRP). Significantly higher risk of death was reported for patients having CT score of 14.5 ($p<0.0001$).

Conclusion: Cutoff values of NLR, ferritin, D-dimer and CRP, and CT score along with medical history of comorbidities of COVID-19 patients help to determine early indicators of ICU admission and mortality.

Keywords: COVID-19**,** severe acute respiratory syndrome**,** D-dimer, CT score, C-reactive protein

INTRODUCTION

Early identification of severe complications in COVID-19 patients is of clinical importance. Reports imply the prevalence of severe COVID-19 ranging from 15.7-26.1% among admitted cases which were associated with abnormal computed tomography (CT) findings and laboratory parameters. COVID-19 manifestations are conquered by comorbidities like gastrointestinal and respiratory symptoms. However, several patients also encompass other comorbidities such as hypertension, diabetes, cardiovascular illness, and renal complications that can influence the related illness. Therefore 25-50% of patients with COVID-19 represent with pre-existing comorbid complications.[1] Cancer, diabetes mellitus, hypertension, chronic respiratory illness and cardiovascular complications portray 5.6%, 7.3%, 6.0%, 6.3% and 10.5% mortality of COVID-19 patients. Diabetes/hyperglycemia results in neutrophil dysfunction, poor chemotaxis, defective macrophage mononuclear function, and impairment of the cellular immunity.[2] In COVID-19, there is over-activation of T-cells, which leads to severe immune dysfunction.[3] COVID-19 patients with diabetes at older age >60 years, with hypertension, chronic cardiac, lung or renal diseases, obesity, patients with organ transplantation receiving persistent immunosuppressants, and with genetic or acquired immunodeficiency conditions represent poor clinical and mortality outcomes. Hence, diabetes with hypertension and coronary heart disease needs to be assessed and managed in COVID-19 patients.[4]

COVID-19 patients with myocardial injury (MI) who were admitted to ICU have showed significantly higher levels of MI biomarkers.[5] Likewise, highest proportion of COVID-19 patients with pneumonis (90%) have demonstrated elevated D-dimer levels as major indication of significantly increased coagulopathy.[6] Major mechanisms that affects ischemia and thrombosis processes involves systemic pro-inflammatory cytokine responses which directly contribute to rupture of plaques by local

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inflammation, induction of procoagulant factors, and hemodynamic changes. Increased D-dimer levels have also demonstrated increased in-hospital mortality.

Preparing intensive care units is an integral part of COVID-19 pandemic. Despite requirement of large number of ICU facilities for COVID-19 patients is critical during the outbreak of COVID-19, early signal are not known. We hypothesized that identifying early signals may help public health policy or early decision making and in advance hospital facility preparation for timely ICU admissions. This could help healthcare systems to adapt quickly for future outbreak more rapidly, including second pandemic of COVID-19. Hence, the current study aims to evaluate whether chest CT along with comorbidities, and laboratory parameters of COVID-19 has an incremental role to predict requirement of ICU facility on time.

MATERIALS AND METHODS

This is an observational study, collected the data from medical records retrospectively. The study was carriedout during 1st May 2020 to 30th May 2020 at government general hospital, Kurnool medical college, Kurnool, Andhra Pradesh.

All the data in this study were collected from the Medical Record of patients positive for SARS-CoV-2 in Real-time Polymerase Chain Reaction (RT-PCR) test and included a total of 200 patients. The study involved 200 patients, who presented to Emergency Room with COVID-19 infection confirmed by real time-PCR in nasal-pharingeal swabs and underwent immediate chest CT due to dyspnea.

Inclusion criteria included severe clinical symptoms of COVID-19 pneumonia, with respiratory rate >30 breaths/min, severe respiratory distress, and SpO_2 levels less than 90%.

Criteria for ICU admission: Need for mechanical ventilation and vasopressors, PaO_2 <50 mmHg on room air or SpO_2 <90% on supplemental oxygen of 6Lpm, confusion, leukopenia, thrombocytopenia, uremia, multilobar infiltrates, hypotension requiring fluid resuscitation, hypothermia, and quick sequential organ failure assessment (qSOFA) score >2 were set major criteria for ICU admission.

Further, thresholds for transferring deteriorating patients for Extracorporeal Membrane Oxygenation (ECMO), severe hypoxemia (PaO_2/FiO_2 ratio <80 mmHg), uncompensated hypercapnia (pH, 7.2) and worsening of hemodynamic status included.

Investigations : Data of medical record collected consisting investigations such as baseline complete hemogram, liver and renal function tests, baseline electrocardiogram (ECG), chest radiograph (CT and X-ray), and arterial blood gas (ABG). Individual records were labeled with the highest level of care a patient received during hospital stay as (1) ward hospitalization (non-ICU), and (2) ICU admission.

Statistical analysis: Statistical analyses performed using SPSS, version 22.0 (IBM Corp., Armonk, NY, USA). Mean, frequency, percentage, median, and range values were calculated for data presentation. For statistical significance, measures of effect, odds ratios with 95% confidence interval (CI) and a 2-sided p value ≤0.05 were applied. Binary logistic regression was used to identify the predictors of severity of COVID-19. The specificities and sensitivities at admission and highest D-dimer, ferritin, and other biochemical, hematological, and radiological measures for each outcome cutoff were calculated to identify early ICU admission indicators.

RESULTS

Of 200 study participants with severe COVID-19 disease, 120 (60%) were managed in ICU and remaining 80 (40%) hospitalized patients did not need ICU-level care (Table 1). The mean ferritin on admission was 600.14 ng/mL, and the maximum observed value was 1500 ng/mL. A ferritin of >500 ng/mL on presentation was seen in 120 (60%) patients, and 110 (55%) patients had a maximum ferritin ≤500 ng/mL during hospital stay. The mean presentation and maximum ferritin was significantly different in alive and dead patients with COVID-19 (p<0.001). Of 80 (40%) patients admitted to the ICU, ferritin's mean presentation was 727.14 ng/mL. The 120 (60%) patients who survived had median presentation of ferritin 271 ng/mL. Whereas ferritin levels (mean±SD) in discharged patients were observed as 42.5±28.5.

Mean D-dimer at admission was 0.845 mg/L FEU, and the maximum value over admission was 18.4 mg/L FEU. A D-dimer of ≤0.14 mg/L FEU on presentation was observed in 40 (20%) patients, while 160 (80%) patients had D-dimer >0.14 µg/dL during admission. D-dimer (µg/dL) levels in discharged patients were observed as 0.21±0.32 while it was 0.75±0.65 in expired patients (p<0.001). Of 80 (40%) patients who were admitted to ICU, the mean presentation of D-dimer was 2.2 mg/L FEU and remaining 120 (60%) patients who survived had median presentation 0.7 mg/L FEU.

The NLR ratio was 6.031 in discharged patients and 17.2 in expired patients. The cutoff of the NLR ratio was 17.2 for ICU admissions. The mean CRP at admission was 26, and the maximum value over admission was 800. CRP levels were observed as 26.5 in discharged patients. Of 80 (40%) patients

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who were admitted in ICU had mean presentation of CRP as 362.5 and remaining 120 (60%) patients who survived had median presentation 26.5. The cutoff of CRP was 362.5 for ICU admissions. The mean length of hospital stay was 21.8 days for discharged patients and 12.1 days for expired patients ($p<0.05$).

Table 1. Baseline Characteristic and associated comorbidities

Admission details	ICU (N=120) n (%, IQR)	Non-ICU (N=80) N (%, IQR)	Overall (N= 200) n (%, IQR)	p value
Age 18-34	2 (1.67%) {32.25-34}	5 (6.25%) {25.5-32}	8 (3.5%) {26-32}	< 0.0001
Age 35-54	22 (18.33%) {45-51.70}	25 (31.25%) {39-51}	47 (23.5%) {40-51}	0.97
Age 55-64	49 (40.83%) {56-60.25}	28 (35%) {56-61.25}	77 (38.5%) {56-61}	0.06
Age > 65	47 (39.17%) {68-76.5}	22 (27.5%) {67-73}	69 (34.5%) {67-75}	0.002
Males	90 (75%)	62 (77.5%)	152 (76%)	0.02
Females	30 (25%)	18 (22.5%)	48 (24%)	0.02
Fever	108 (90%)	72 (90%)	80 (90%)	1.0
Cough	74 (61.67%)	48 (60%)	122 (61%)	<0.0001
Fatigue/Weakness	30 (25%)	21 (26.25%)	51 (25.5%)	0.27
Sore Throat/Throat Pain	17 (14.17%)	11 (13.75%)	28 (14%)	0.96
Nausea/Vomiting	5 (4.17%)	5 (6.25%)	10 (5%)	0.52
Total Comorbidities			96 (48%)	
Hypertension	58 (48.3%)	38 (47.5%)	96 (48%)	0.0001
Diabetes Mellitus	26 (21.67%)	22 (27.5%)	48 (24%)	0.0004
Chronic Pulmonary Disease	12 (10%)	9 (11.25%)	21 (10.5%)	0.005
Chronic Cardiac Disease	14 (11.67%)	6 (7.5%)	20 (10%)	0.001
Chronic Liver Disease	3 (2.5%)	1 (1.25%)	4 (2%)	0.25
Chronic Kidney Disease	6 (5%)	4 (5%)	10 (5%)	0.3
Inpatient Complications				
AcuteKidney Injury(AKI)	10 (8.33%)	-	10(5%)	-
Dialysis Required due to AKI	10 (8.33%)	-	10 (5%)	-
Encephalopathy	4 (3.33%)	-	4 (2%)	-
Myocarditis	9 (7.5%)	1 (1.25%)	10 (5%)	0.04
Shock	12 (10%)	2 (2.5%)	14 (7%)	0.01
Sepsis/Secondary Bacterial Infection	14 (11.67%)	-	14 (7%)	-
CV Stroke	3 (2.5%)	1 (1.25%)	4 (2%)	0.25
Need for vasopressors	30 (25%)	2 (2.5%)	32 (16%)	0·123
Mechanical ventilation	32 (26.67%)	-	32 (16%)	-
NIV	55 (26.67%)	-	55 (27.5%)	-
Outcomes				
Intubated (at least once)	48 (40%)	-	48 (24%)	-
Median average length of Hospital stay in days	16 (0 to 30d)	6 (0 to 16d)	11 (0 to 30 day)	NA
Death-Male	44 (36.67%)	12 (15%)	56 (28%)	0.005
Death-Female	17 (14.17%)	7 (8.75%)	24 (12%)	0.009

Receiver operator curve: The area under curve (AUC) for ferritin at admission was 0.598, with an optimal cutoff of 727 ng/mL in predicting the cause of mortality. A ferritin positive predictive value of 35.5% and a negative predictive value of 76.5% for the predictor of mortality was observed. Hence, the AUC for maximum ferritin was 0.598, with optimal cutoff of 727 ng/mL in predicting the ICU requirement. The AUC for D-dimer at admission was 0.880, with optimal cutoff of 2.2 mg/L FEU to predict the cause of mortality. The analysis demonstrated 60% of positive (PPV) and 85% of negative

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predictive value (NPV) of D-dimer to predict mortality. The AUC for maximum D-dimer was 0.880 with cutoff of 2.2 mg/L FEU to predict the ICU requirement. The AUC for C-reactive protein (CRP) at admission was 0.65, with optimal cutoff of 362.5 mg/L in predicting the cause of mortality. To predict mortality based on CRP levels was reported 70% for the PPV and 90% for NPV. The AUC for maximum CRP was 0.65 with optimal cutoff of 362.5 mg/L to predict ICU requirement. The AUC for NLR at admission was 0.66 while PPV was 30% and NPV was 90% to predict the mortality. The AUC for maximum NLR was 0.66 with optimal cutoff of 17.2 predicting the ICU requirement (Table 2).

Table 2. The receiver operating characteristic curves for mortality in severe COVID-19 Pneumonia

Variables	Cutoff	AUC	Sensitivity	Specificity	PPV	NPV
NLR	17.2	0.660	80%	50%	30%	90%
CT scores	14.5	0.7	50%	90%	60%	90%
Neutrophils, $\times10^9$/L	3.2	0.5	80%	40%	30%	90%
Lymphocyte, $\times10^9$/L	1.5	0.4	35%	65%	25%	80%
S-ferritin	727.14	0.598	55%	65%	35.5%	76.5%
D- dimer	2.2	0.880	72%	88%	60%	85%
WBC, $\times10^9$/L	4.5	0.49	83%	32%	60%	85%
CRP	362.5	0.65	75%	65%	70%	90%
ALT (IU/L)	180	0.880	35%	70%	45%	75%
AST (IU/L)	190	0.4	35%	65%	50%	70%

Abbreviations: AUC:area under curve; CRP: C-reactive protein; ESR:erythrocyte sedimentation rate; WBC:white blood cell; L:lymphocyte; N:neutrophils; NLR:granulocyte/lymphocyte ratio; PPV:positive predictive value; NPV: negative predictive value.

Co-morbidities and ICU requirement: Patients with comorbidities accounted for 48% of all cases, whereas fatal cases accounted for 40%. Hypertension was the most prevalent (48%) comorbidities, followed by T2DM (24%), and respiratory diseases (10.5%). In total 80 expired cases, the major comorbidity for predicting death in COVID-19 patients was observed with hypertension (40%). Significantly higher frequencies of lymphopenia, and increased levels of CRP, and LFT parameters were observed among critical COVID-19 patients between ICU and non-ICU admitted patients ($p<0.05$).

Table 3. T-Test analysis of laboratory parameters

Group Statistics					
		N	Mean/median/percentage	Standard Deviation	P value
AGE	Non-ICU	80	53.2058	14.1227	0.35(ns)
	ICU	120	56.2058	11.2616	
D-Dimer Normal: >0.5 (mg/L FEU)	Non-ICU	80	0.687772277	1.6349	<0.001**
	ICU	120	2.193617	2.726	
S.Ferritin Normal: 20–250-male; 10-20-male	Non-ICU	80	271.268198	287.916	<0.001**
	ICU	120	727.1465	474.045	
C-reactive protein (CRP)	Non-ICU	80	26.5	22.5	<0.001**
	ICU	120	362.5	285.5	
NLR	Non-ICU	80	6.03166	-	0.07(ns)
	ICU	120	17.12692	-	
Lymphocytes(10^3/uL)	Non-ICU	80	1.1	0.6	0.89 (ns)
	ICU	120	1.2	1.2	
ALT (IU/L)	Non-ICU	80	41.5	6.7	< 0.001
	ICU	120	186.5	85.2	
AST (IU/L)	Non-ICU	80	44.5	4.5	< 0.001
	ICU	120	195.5	72.8	

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INR	Non-ICU	80	1.03	0.20	
	ICU	120	1.04	0.13	
P/F (mmHg)	Non-ICU	80	236	97	<0.001**
	ICU	120	153	66	
Glasgow coma scale	Non-ICU	80	15 [3 - 15]	-	
	ICU	120	15 [3 - 15]	-	-
SOFA score	Non-ICU	80	9 [6 - 12]	-	
	ICU	120	10 [7 - 13]	-	-
Troponin, ng/L	Non-ICU	80	13·1 [8·0 - 28·6]	-	
	ICU	120	43·1 [16·4 - 96·0]	-	-
APACHE II score	Non-ICU	80	15 [7 - 20]	-	<0.001
	ICU	120	20 [13 - 24]	-	
Erythrocyte sedimentation rate, mm/h	Non-ICU	80	68.38	38.08	0.43
	ICU	120	59.56	32.46	
The mean global CT score	Non-ICU	80	8.5	8.8	<0.001
	ICU	120	14.5	10.6	
CT chest	Non-ICU= multifocal GGO+ patchy, distributed peripherally	80	40%	-	-
	ICU= crazy-paving pattern, consolidation, Subpleural lines and fibrosis	120	60%	-	-

*significant; ns= not significant ; ** highly significant

NIV and mechanical ventilator-associated support were 27.5% and 16%, while ICU duration was 9.5 and 11.5 days, respectively. The major correlates with ICU mortality were mechanical ventilator, acute kidney injury (AKI) (Odds Ratio [OR], 12.47), and acute respiratory distress syndrome (OR, 6.52)(Table 4).

Table 4. Unadjusted and adjusted Risk Ratios (RR) and 95% Confidence Intervals (CI) for associations between baseline socio-demographic and baseline comorbidity[1] and COVID-19 mortality

Baseline Characteristics	N (%) Mortality	RR (95% CI)	Adjusted RR[2] (95% CI)
Age			
18–64 years (n = 131)	23(11.5)	Ref	Ref
65 years and older (n = 69)	57 (28.5%)	1.96 (1.37–2.82)$^{\omega}$	1.97 (1.31–2.95)$^{\omega}$
Sex			
Female (n = 48)	24 (12%)	Ref	Ref
Male (n = 152)	56 (28%)	1.23(0.81–1.88)	1.32 (1.04–1.70)$^{\omega}$
Cardiovascular Comorbidity[3]			
No (n =180)	60 (30%)	Ref	Ref
Yes (n =20)	20 (10%)	1.35 (0.92–1.99)	1.12 (0.75–1.68)
Pulmonary Comorbidity[4]			
No (n = 179)	59(29.5)	Ref	Ref
Yes (n = 21)	21(10.5%)	0.96 (0.54–1.68)	0.86 (0.51–1.45)
Renal Comorbidity[5]			
No (n =190)	70 (35%)	Ref	Ref
Yes (n = 10)	10 (5%)	1.22 (0.73–2.05)	1.27 (0.90–1.78)
Type 2 Diabetes			
No (n =152)	32(16%)	Ref	Ref
Yes (n = 48)	48(24%)	1.02 (0.68–1.51)	0.86 (0.62–1.21)
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No (n = 104)	0 (0)	Ref	Ref
Yes (n = 96)	80 (40%)	1.19 (0.82–1.74)	1.37 (1.07–1.74)$^{\omega}$

$^{\omega}p<0.05$. [1]A total of 48% of 200 patients had at least one comorbidity upon hospitalization including cardiovascular, pulmonary, or renal comorbidity, diabetes. Presentation with any comorbidity was associated with 1.56 times the mortality risk (95%CI:0.87–2.82). [2]All socio-demographic and comorbidity factors were included in the fully-adjusted model. [3]Hypertension, Heart Failure, Stroke or Transient Ischemic Attack, Coronary Artery Disease. [4]Asthma, Chronic Obstructive Pulmonary Disease (COPD), Obstructive Sleep Apnea, Interstitial Lung Disease. [5]Chronic Kidney Disease (CKD) or End-stage Renal Disease (ESRD).

Elevated D-dimer, ferritin, lower SpO_2, and decreased lymphocyte counts were the most prevalent top predictors of ICU admission and death (OR 1.83). In assessing ICU admittance, the combination of lung consolidation volume on CT at ER presentation had significant incremental advantage over the laboratory results. The top predictors of mortality and ICU admittance were reported for cardiac failure (OR, 33.5; CI, 4.99–224.45], D-dimer (OR, 6.31; CI, 0.79–22.26), ferritin (OR, 5.78; CI, 1.65–20.28), chronic obstructive pulmonary disease (COPD) (OR, 9.23; CI, 1.89–45.01), SpO_2 (OR, 4.80; CI, 1.32–17.45), heart rate (OR, 7.73; CI, 1.27–46.90), and age (OR, 4.90; CI, 1.17–20.50). Medical history of cardiac diseases, COPD, and increased heart rate upon appearance were inimitable top predictors of death and ICU admission (Table 4). These cumulative inferences may help to evaluate the earliest COVID-19 related signals to anticipate ICU bed requirement. This data will aid health officials in predicting future outbreak, such as the second phase of COVID-19, or deciding on increased social interventions.

CT-chest findings of COVID-19 cases: 40% patients (n=80) with chronic COVID-19 showed focal appearance in the form of reticular and interlobular septal thickening with or without ground-glass opacities (GGO) in 80 (40%) cases. These patients mostly involved posterior component, inferior lobe of lungs, while other 120 (60%) cases showed crazy-paving appearance with or exclusive of GGO. The mean global CT score was 14.5 in 120 cases admitted to ICU. Univariate analysis shows significant high risk of death for patients having CT score of 14.5 (CI, 6.19–19.5; $p < 0.0001$).

Table 5. Binary Logistic Regression Analysis of Predictives of COVID-19 Severity

Variables	B	SE	p-value	95% CI	
Age	0.071	0.028	0.11	1.01	1.13
Sex	0.56	0.55	0.315	0.58	5.2
BMI	− 0.14	0.099	0.138	0.71	1.04
Smoking	− 0.27	0.52	0.6	0.26	2.1
Co-morbidities					
• Diabetes mellitus	1.6	0.74	0.032	1.14	21.5
• Hypertension	1.18	0.7	0.093	0.82	12.9
• Ischemic heart disease	− 20.5	40,192	1.0	0.0	-
Fever	1.03	0.85	0.230	0.52	15.04
Cough	0.24	0.49	0.621	0.48	3.37
Dyspnea	1.6	0.56	0.004	1.64	15.2
Sore throat	0.96	0.53	0.069	0.92	7.4
Malaise	0.69	0.53	0.196	0.7	5.7
Diarrhea	− 21.04	40,192	1.0	0.0	—
Headache	0.56	0.55	0.315	0.58	5.2
Hemoglobin (g/dL)	− 0.102	0.231	0.66	0.57	1.4
WBC ($x10^3$ mm^{-3})	− 0.130	0.136	0.338	0.67	1.14
Lymphocytic count ($x10^3$ mm^{-3})	− 0.002	0.001	0.014	0.99	1.0
CRP (mg/dL)	0.085	0.022	< 0.001	1.04	1.13
ESR (mm/h)	0.056	0.014	< 0.001	1.03	1.08
Ferritin (ng/mL)	0.023	0.005	< 0.001	1.01	1.03
Serum creatinine (mg/dL)	2.09	1.47	0.156	0.44	148.03
Albumin (g/dL)	− 9.9	1.89	< 0.001	0.0	0.002

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ALT (IU/L)	0.159	0.045	< 0.001	1.07	1.28
AST (IU/L)	0.75	0.2	< 0.001	1.42	31.9
CT Chest findings	4.9	0.94	< 0.001	0.001	0.04

Abbreviations: B:regression coefficient; SE:standard error; CI:confidence interval; BMI:body mass index; WBC:white blood cellcount; CT:computed tomography; CRP:C-reactive protein; ESR:erythrocyte sedimentation rate; ALT:alanine aminotransferase; AST:aspartate aminotransferase.

Binary logistic regression analysis of indicators: Predictors of severity for COVID-19 in the study patientswere presence of diabetes mellitus as a comorbidity (CI, 1.14–21.5; p=0.032), dyspnea (CI, 1.64–15.2; p=0.004), lymphopenia (CI, 0.99–1.0; p=0.014), increased inflammatory markers such as CRP (CI, 1.04–1.13), ESR (CI, 1.03–1.08), and ferritin (CI, 1.01–1.03) with p<0.001, abnormal liver parameters such as albumin (CI, 0.0–0.002), ALT (CI, 1.07–1.28) and AST (CI, 1.42–31.9) with p<0.001 for all cases (Table 5).

Correlation analysis of laboratory biomarkers with CT score: D-dimer (R =−0.25; p<0 .01) was correlated negatively with the CT score. Whereas ferritin levels did not correlate with CT score (R=0.11; p=0 .15). This implies that a considerable rise in CT score combined with a rise in D-dimer is an indication of lung damage and advancement.

DISCUSSION

This study holistically combined blood laboratory and CT results at ER presentation to predict ICU admission in patients with COVID-19 pneumonia. Considering that most COVID-19 deaths had more lymphopenia, it's plausible to infer that the lymphocyte count is a fast and readily accessible laboratory test that can forecast COVID-19 disease severity. Our study reported no signifcant difference in neutrophil-to-lymphocyte ratio (NLR) between dead and surviving groups of COVID-19 patients. The lymphocyte counts lower than 0.8×10^9/L were associated with COVID-19 severity and number of neutrophils higher than 3.5×10^9/L may be associated with the poor clinical outcome. Yang et al. (2020) reported for elevated NLR may predict COVID-19 prognosis.[7] Our study results also demonstrates the incidence of COVID-19 related mortality 10.4% in patients of age more than 40 years having NLR >17.

The AUC for maximum ferritin was 0.598, with an optimal cutoff of 727 ng/mL in predicting the mortality. This suggests that inflammation plays a role leading to mortality in younger vs older cases. Zhou et al. (2020) reported increased levels of serum ferritin in non-survivors in comparision to surviving COVID-19 patients.[8] Hyperferritinemia has also shown to activate macrophages, resulting in an increase in the release of pro-inflammatory cytokines causing inflammation which is primarily responsible for the organ damage.

D-dimer is produced by the synthesis and breakdown of crosslinked fibrin and indicates coagulation and fibrinolysis activity. COVID-19 was linked to hemostatic problems and high D-dimer levels, particularly in instances of mortality. The AUC for D-dimer at admission was 0.880 with cutoff of 2.2 µg/dL in predicting the cause of mortality while it was 0.598 for serum ferritin which represents poor ability to discriminate prediction for the cause of death than D-dimer levels. Similarly, Tang et al. (2020) also observed abnormal coagulation results, especially markedly elevated D-dimer in death with Covid-19.[9]

Our study found that D-dimer increased significantly at early stage in severe COVID-19 patients. D-dimer (R=−0.25; p<0 .01) was correlated negatively with the CT score (p<0.05). Although ferritin (R=0.11; p=0.15) was also correlated negatively with the CT score, no statistical significance was observed (p>0.05). This suggests that a significant increase in CT score along with D-dimer represents early signals of lung deterioration and progression.

These results are in line with and reinforce data from prior studies that evaluated CT's contribution in predicting ICU admission.[10,11] For comparison with CT, we considered several biomarkers of severity of COVID-19 pneumonia, including serum D-dimer, CRP, and lymphocyte counts, predicting ICU admission.[12,13] According to Gattinoni et al. (2020) consolidation and its extent characterizes two phenotypes of CARDS named type L (low elastance, ventilation to perfusion ratio, lung weight, and recruitability), and type H (high elastance, ventilation to perfusion ratio, lung weight, and recruitability) are best identified by CT, involving diverse pathophysiological mechanisms and requireother treatment options.[14] In case of type H, include intubation, positive end-expiratory pressure and extracorporeal membrane oxygenation that pertain to the ICU environment. In our study, CT image texture features of the affected lung improved significant ICU admission prediction compared with blood laboratory

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markers. Overall, the pathologies correlates well with the CT texture features for triage of patients with COVID-19 pneumonia.

Inclusion of CT to patients with COVID-19 pneumonia may have a practical value for individual patient's management and help plan and organize the Health Systems response COVID-19 pandemic.

CONCLUSION

Among all the study patients, 48% had comorbidities with 40% of mortality. Hypertension was the most evident comorbidity (48%), followed by T2DM (24%), and respiratory diseases (10.5%). The ICU admission rate was 43.5% in all 200 severe COVID-19 patients. NIV and mechanical ventilator support were 27.5% and 16%, while ICU duration was 9.5 and 11.5 days, respectively. The AUC for maximum ferritin was 0.598, with an optimal cutoff of 727 ng/mL in predicting the ICU requirement while it was 0.880 for D-dimer, with an optimal cutoff of 2.2 µg/dL. The AUC for maximum CRP was 0.65, with an optimal cutoff of 362.5 in predicting the ICU requirement While it was 0.66 for NLR at admission with an optimal cutoff of 17.2. The CT patterns of disease included GGO which was observed in 40% of patients followed by crazy-paving, parenchymal consolidations (60%). Results showed that the D-dimer was correlated negatively with the CT score ($p<0.01$), whereas ferritin had no significant difference with CT score. This suggests that a significant increase in CT score along with D-dimer is signal of lung deterioration and disease progression and demonstated significantly higher risk of death in patients with a CT score of 14.5.

Elevated D-dimer, ferritin, lower SpO_2, and decreased lymphocyte counts and medical history of heart diseases, COPD and increased heart rates were the most prevalent top predictors of ICU admission and death. These informations will help health systems to anticipate a future epidemic, including the second wave of COVID19, or decide additional social measures.

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