Corona Virus Disease 2019 (COVID-19): Intensive Care Admission Prediction Model

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Research Article

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Abstract

Background: Identifying clinical-features or a scoring-system to predict a benefit from hospital admission for patients with COVID-19 can be of great value for the decision-makers in the health-sector. We aim to identify differences in patients' demographic, clinical, laboratory and radiological findings of COVID-19 positive cases to develop and validate a diagnostic-model predicting who will develop severe-form and who will need critical-care in the future.

Methodology: Patients were classified according to their clinical state into mild, moderate, severe, and critical. All their baseline clinical data, laboratory, and radiological results were used to construct a prediction-model that can predict if the COVID-19 patients will develop a severe condition that will necessitate their ICU-admission. An ensemble feature selection tool was used to identify the relative importance of each variable. The performance of the selected features compared to all features using logistic regression and area under curve test.

Results: Patients with ICU admission showed a distinct clinical, demographic as well as laboratory features when compared to pattients that did not need ICU admission. This includes elder age group, male gender and presence of comorbidities like diabetis and history of hypertension.

Out of the different demographic, clinical and laboratory charasteristics of these patients, Age at diagnosis, Lymphocyte count, C-reactive protein (CRP), lactate dehydrogenase (LDH), Albumin, Urea, and Procalcitonin levels were found to be able to predict which patients may need ICU admission.

Conclusion: Higher CRP, LDH, Age at diagnosis, Urea, Procalcitonin, and lower Albumin, Lymphocyte count are significant determinant in ICU admission for COVID-19 patients.

Background

The current pandemic of the novel 2019 coronavirus disease (COVID-19) increased the burden substantially on acute and critical care services exceeding existing hospital capacity around the world [1]. Managing the expected surges in intensive care capacity requires focused intensive care abilities and requirements to minimize loss of life and maintain control [2]. Due to the increasing numbers of recorded positive COVID-19 cases, the medical teams in the front line are in urgent need of a tool that helps their clinical judgment to identify the few that will progress to critical cases. Right now, there is no reliable, applicable, or useable clinical model or scoring system to predict if a tested positive for COVID-19 should be admitted to the hospital or asked to stay home [3]. A stratification tool for non-severe COVID-19 patients at admission can direct the resources and control the spread more efficiently and persevere the health team's power [4]. The use of prediction models for COVID-19 will support medical decision making but are still poorly reported [5]. Identifying clinical features or a scoring system to predict a benefit from hospital admission for patients with COVID-19 can be of great value for the decision-makers in the health sector world-wide as well as in the United Arab Emirates (UAE). Hence, we aim to identify differences in patients' demographic, clinical, laboratory and radiological findings between mild, severe and critical cases of COVID-19 positive cases to develop and validate a diagnostic model predicting who will develop severe form and who will need critical care in future.

Material And Method

Patients Data collection

COVID-19 positive patients admitted between March to April 2020 were recruited from Al Kuwait Hospital, Dubai, UAE. The study was approved by Ministry of Health and Prevention (MOHAP) Research Ethics Committee number (MOHAP/DXB-REC/MMM/NO.44/2020). Adult patients (above 18 years) with COVID-19 (confirmed by nasopharyngeal polymerase chain reaction; PCR positive sample) were enrolled. Complete current and past medical history, along with their demographic data, a history of a recent travel or contact with a confirmed or suspected cases were documented. The main presenting symptoms were enlisted, including (fever, cough, fatigue, anorexia, shortness of breath (SOB), sputum production, myalgias, headache, confusion, rhinorrhea, sore throat, hemoptysis, vomiting, diarrhea, nausea, anosmia, and ageusia). Risk factors for severe illness were examined, including old age, cardiovasdcular diseases (CVD), diabetes mellitus (DM), hypertension (HTN), prior stroke and or transient ischemic attack, cancer, chronic lung disease, and chronic kidney disease (CKD).

Patients classification

Patients were classified according to "Clinical Management of Critically Ill COVID-19 Patients" guidelines (Version 1- April 15 2020) issued by MOHAP [6]. Accordingly, patients were classified into mild illness, pneumonia, and severe pneumonia (fever or suspected respiratory infection, plus one of the following: respiratory rate > 30 breaths/min, severe respiratory distress, and $SpO2 \leq 93\%$ on room air). Severe cases that need oxygen therapy with no response to titrated oxygen therapy will require ICU treatment.

Blood and Radiological tests

Laboratory tests were retrieved that includes (1) complete blood count, including neutrophil count (NR:2-7 x10(3)/mcL), lymphocyte count (NR: 1-3 x10 (3)/mcL), heamoglobin; Hb (NR: 12-15 gm/dL), white cell count; WCC (NR: 4-11 x10(3)/mcL), and platelets count (NR:150-450 x10(3)/mcL), (2) coagulation profile, including interenational normalized ratio; INR (NR: 0.8-1.29 second), Prothrombin time; PT (NR: 9.9-12.3 seconds), (3) electrolytes, including sodium; Na (NR: 136-145 mmol/L) and potassium; K (NR: 3.6-5.1 mmol/L)), (4) renal function tests, including urea (NR: 2.5-6.5 mmol/L, creatinine (NR: 53-88 umol/L), and estimated glomerular filtration rate; eGFR (NR: 90-120 mL/min/1.73m2), (5) liver function tests, including total serum bilirubin (NR: 3-17 umol/L), alanine aminotransferase; ALT (NR:16-63 IU/L), aspartate aminotransferase; AST (NR: 15-37 U/L), alkaline phosphatase; ALP (NR: 46-116 IU/L), and albumin (NR: 34-50gm/L), (6) inflammatory markers, including C-reactive protein; CRP (NR: 0-3 mg/L), D-dimers (NR: mg/dL, lactate dehydrogenase; LDH (NR: 85-227 IU/L), procalcitonin (NR: ug/L) and ferritin (8-388 mcg/L).

For risk of severe cases, the presence of lymphopenia, neutrophilia, high ALT/AST, high LDH, high CRP, high ferritin, high d-dimer, and high pro-calcitonin, above the age and gender-matched references were used as indicators of risk. Admission chest X-Ray (presence of bilateral air consolidation), and computerized tomography (CT) scan (presence of bilateral peripheral ground-glass opacities) were documented.

Statistical Analysis

Out of the 70 data predictors input, 7 (10%) had missing data (Diarrhoea, severity-critical or not, chest X-ray, prothrombin time, LDH, INR, and ferritin levels). Out of them, five variables had missing data percentage ranging from (16% to 34%). Records that showed missing input in the five variables were excluded (20 records), and the remaining 120 records were further processed. Among the 70 variables, those who showed missing data more than 10% were excluded from prediction model generation, and the remaining 65 variables were selected. Remaining variables with missing inputs were tested whether they are missing completely at random (MCAR) using expectation-maximization (EM) method in SPSS statistical software, version 16 (SPSS, Inc., Chicago, IL, USA). Data were considered MCAR as the significance value is higher than 0.05. We replaced missing data with the estimated mean for each variable.

Feature selection

Ensemble Feature Selection (EFS): an ensemble feature selection tool (R-package) was used to identify the relative importance of each variable. It incorporates eight feature selection methods for binary classifications[7]. Features that get an accumulative score of more than 50% and 0.7 correlating with other features were selected, and its performance in comparison with all features was evaluated using receiver operating characteristics (ROC).

Results

Clinical and demographic features of patients admitted to the ICU

From the total patients cohort that consists of 119 patients, 21 patients were admitted to the ICU and 98 other patients who did not need ICU admission. For better understanding of risk factors that might determine addmittion to the ICU, the demograhic, pathological as well as the clinical features of those patients were compared to patients who did not need admission to the ICU (Table 1).

Table 1
The clinicopathological and demographic characteristic of ICU admitted group compared to non admitted group

	No ICU admission	ICU admission	P value
Age of the patient (years)	44.52 ± 2.439	57.14 ± 2.49	< 0.0001
Gender			
Male	61 (62.25%)	21 (100%)	P = 0.0006
Female	37(37.75%)	0 (0%)	
Risk factors			
Elderly (> 60 years)	14 (14.28%)	6 (28.57%)	P = 0.112
CVD	2 (0.20%)	1(0.47%)	P = 0.46
DM	20 (20.40%)	10 (47.61%)	P = 0.009
Hypertension	26(26.53%)	10 (47.61%)	P = 0.05
Hemoglobin (gm/dL)	13.87 ± 0.1779	12.77 ± 0.3563	P = 0.0094
WBC (x10(3)/mcL)	6.947 ± 0.2626	8.875 ± 1.116	P = 0.0129
Platelet count (x10(3)/mcL)	234 ± 7.565	239 ± 14.61	P = 0.77
CRP (mg/l)	17.15 ± 3.419	116.5 ± 20.35	P < 0.0001
Urea (mmol/L)	4.529 ± 0.2078	9.791 ± 2.812	P = 0.0002
Creatinine (umol/L)	80.54 ± 2.947	102.8 ± 8.989	P = 0.0040
LDH (IU/L)	237.1 ± 10.84	426.5 ± 48.09	P < 0.0001
Serum bilirubin (umol/L)	10.03 ± 0.5949	13.35 ± 1.935	P = 0.0353
ALT (IU/L)	46.81 ± 3.721	50.76 ± 6.344	P = 0.6451
AST (U/L)	29.67 ± 1.724	45 ± 5.815	P = 0.0011
ALP (IU/L)	80.71 ± 3.367	75.93 ± 8.565	P = 0.5644
Albumin(gm/L)	36.5 ± 0.5812	28.77 ± 1.171	P < 0.0001

ICU; intensive care unit, p value significat > 0.05, CVD; cardiovascular diseases, DM; diabetes mellitus, WCC; white cell count, LDH; lactate dehydrogenase, CRP; C-reactive protein, ALT; Alanine aminotransferase, AST; Aspartate aminotransferase, ALP; Alkaline phosphatase

Interestingly, our results showed that patients with addmission to the ICU had significantly older age 57.14 ± 2.49 compared to no admission group 44.52 ± 2.43 years ($P < 0.0001$). Moreover, all patients in the ICU admitted group were males (100%) compared to only 62%) in the no admission group ($P = 0.0006$). Previous history of DM and history of HTN (47.61% for each) was found to be the most important risk factors and chronic medical conditions associated with the ICU admission compared to the no admission group.

Laboratory findings of patients admitted to the ICU

The Hb levels was higher at 13.87 ± 0.17 in patients that did not need ICU admission compared to the ICU admitted group at 12.77 ± 0.35 gm/dl (P=0.0094). The WCC count was in the ICU admitted group is higher at 8.87 ± 1.11 than that observed in the no admission group 8.87 ± 1.11 x10(3)/mcL (P=0.0129). Platelet count showed no statistical difference between both groups with mean platelet count in the ICU admitted group at 239 ± 14.61 vs. 234 ± 7.56 x10 (3)/mcL in the non admitted group (P=0.77) (Table 1).

Age at diagnosis, CRP, LDH, Albumin, Lymphocyte count, Urea, and Procalcitonin level can predict which patient may need ICU admission.

Better understanding of the factors that might determine patient risk for ICU admission is essential for more effective medical decision making and better selection of therapeutic strategies. For that reason, here we try to investigate different clinicopathological as well as demographic variables and their ability to predict ICU admission.

Ensemble feature selection tool sorted the 65 filtered variables for our patient cohort consist of the 120 patients according to the accumulative score of the eight feature selection methods to predict if the patient will need ICU admission, as shown in figure (1). CRP, LDH, Albumin, Age at diagnosis, Lymphocyte count, Urea, and Procalcitonin level can predict which patient may need ICU admission. The top features that scored more than 50% are CRP, LDH, Albumin, Age at diagnosis, Lymphocyte count, Urea, and Procalcitonin level.

Selected features outperform the total features in predicting which patient may need ICU admission

Next, we used the efs_eval function of the EFS tool to evaluate the performance and validity of the EFS method using logistic regression compared to using all other features represented in ROC curves and AUC, as shown in figure (2).

Higher CRP, LDH, Age at diagnosis, Urea, Procalcitonin, and lower Albumin, Lymphocyte count are significant determinant in ICU admission for COVID-19 patients

Comparing the level of each of the selected features between COVID-19 patients who were admitted to ICU and those who didn't show that Higher CRP, LDH, Age at diagnosis, Urea, Procalcitonin, and lower Albumin, Lymphocyte count are significant determinant in ICU admission for COVID-19 patients, as shown in figure 3.

Discussion

The pandemic of (COVID-19) which began at the end of 2019 represent an international public health emergency [8]. Most of patients with this disease suffer from mild to moderate illness [9]. However, small percentage of those patients suffer from more sever illness that can rapidly progess into more critical form. This includes acute respiratory distress syndrome (ARDS) and acute respiratory failure, in addition to metabolic acidosis, coagulopathies, and septic shock [10]. Depending on patient characteristics and the studied population, ICU admission vary between 5 to 16% of the total number of patients [11]. The wide spread of the disease led to a rapid overwhelming of the public health system of different countries including the intensive care units [12] with some countries reaching to a critical care crisis [13].

Till now, there is limited data that describe the clinical charasteristics as well as the risk factors and clinical course of patients that might have critical illness from COVID-19 infection [14, 15]. For that reason, better understnaing and identification of risk factors that might predispose for ICU admission might be essential for more more active medical decision making that might lead to optimal clinical practice with the aim of improving patients outcome.

Our results showed a significant difference in the pre-admission demographic, clinical as well as laboratory characteristics of the ICU admitted group when compared to non admitted group. Indeed, the association between ICU admission and elder age group was previously described in several reports that also showed the median age of critical/death groups to be higher than that of non-critical group groups [16–18]. Similarly, presence of comorbidities that includes previous history of DM and HTN was among the main determinant of ICU amiddion. These results also goes with other reposts which also showed the presence of several comorbidies like DM, HTN, CVD and respiratory illnesses as a major risk factor for critical/mortal covid19 disease [16].

Interesingly, and among more than 65 filtered variables, our results identified 8 parameters that can predict patient admission to the ICU. This includes age at diagnosis, lymphocyte count, and level of CRP, LDH, albumin, urea, and procalcitonin.

Many of those parameters were recently found to play a role in the prediction of COVID19 patient severity and outcome. This includes elder age group (above 60 years), higher CRP levels as well as low lymphoctype count [12]. Similarly, LDH levels as well as procalcitonin were also found in another report to be among the markers that can predict severity and mortality in COVID 19 patients [19, 20].

Conclusion

The present study has clearly demonstrated the accuracy of our approach in identifying factors that can predict the COVID 19 patient outcome. For that reason the stratification of patients according to the parameters discovered by our model might provide a simple and efficient system for patients risk stratification. This system might help clinicians and health care providers to deliver more efficient medical care for COVID 19 patient. Those factors, in addition to the fact that this report is the first report that use in house patient cohort from UAE highlight the importance of implementation of such method in the stratification of our own patients into high or low risk groups for ICU transfer might be essential for more efficient use of our own resources and infrastructes available to deal with the COVID 19 outbreak.

Declarations

Ethical Approval and Consent to participate: The study was approved by the Scientific Research Committee MOHAP/DXB-REC/MMM/NO.44/2020 and certify that the study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments ethical standards.

Consent for publication: All authors have agreed to the publication and to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data availability statement: Data can be provided upon request on individual basis

but it is not available publicly.

Competing interests: All authors declare no conflict of Interest related to the current manuscript.

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Authors' information: as per title page.

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Figures

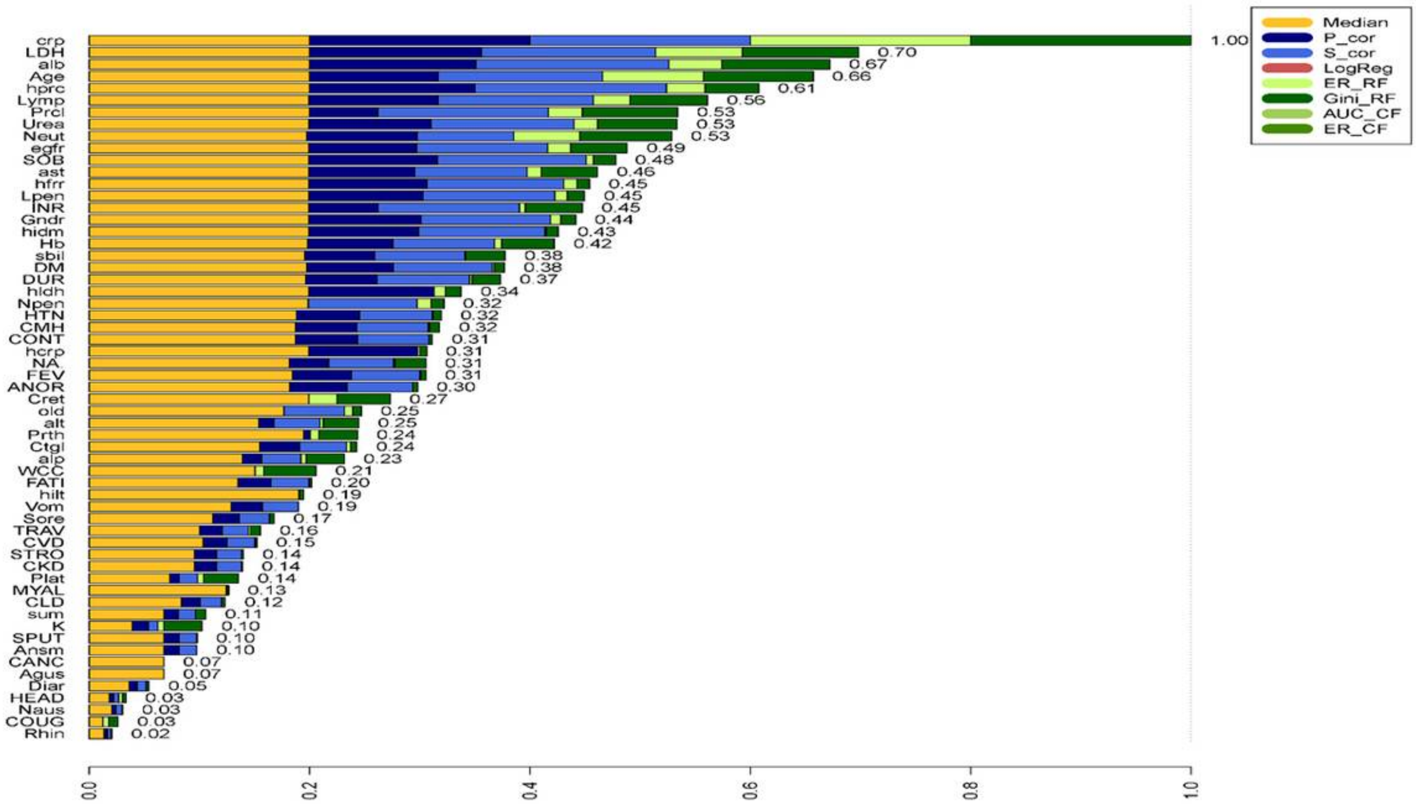

Figure 1

Shows the ensemble feature selection tool sorted the 65 filtered variables to predict if the patient will need ICU admission. Age at diagnosis, CRP, LDH, Albumin, Lymphocyte count, Urea, and Procalcitonin level can predict which patient may need ICU admission.

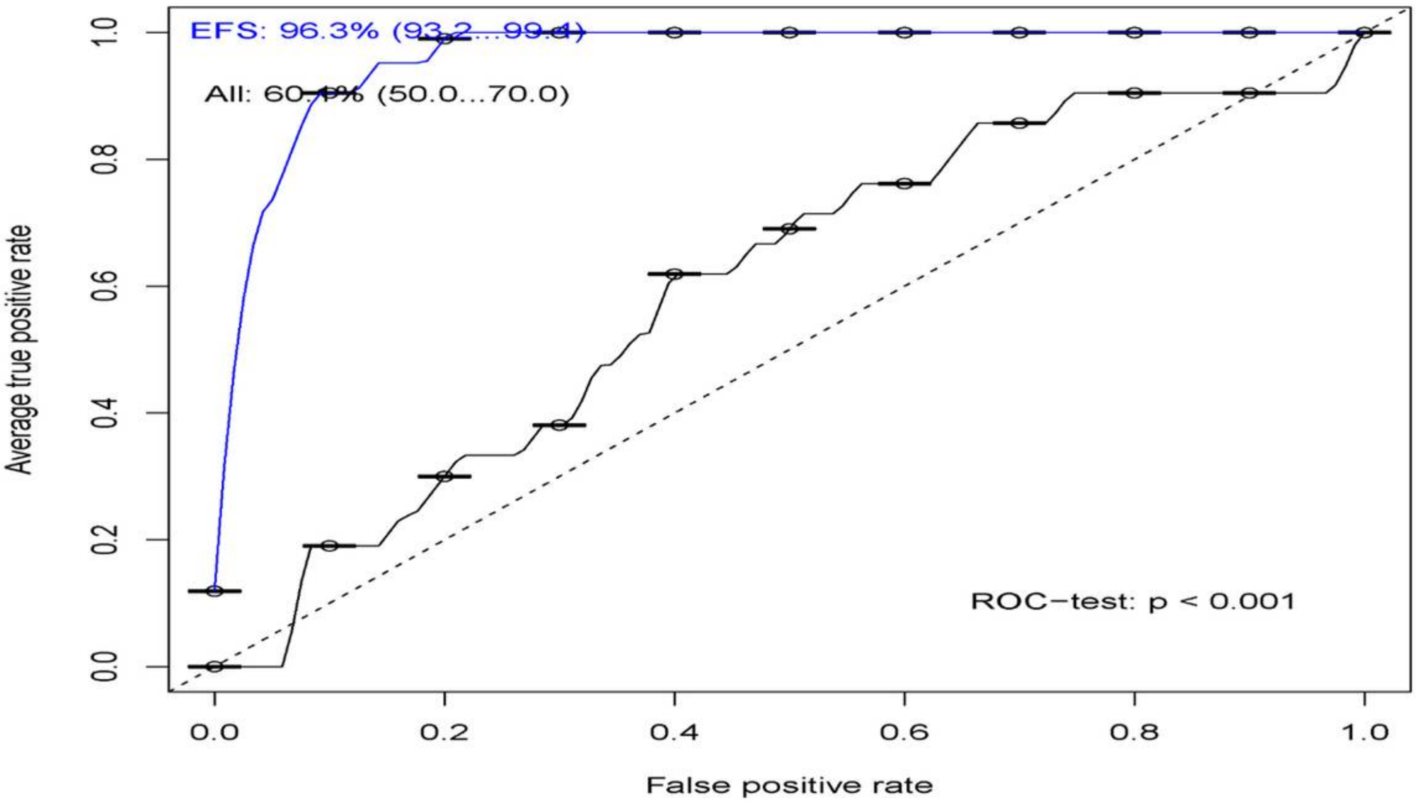

Figure 2

Shows the efs_eval function of the EFS tool to evaluate the performance and validity of the EFS method using logistic regression compared to using all other features represented in ROC curves and AUC.

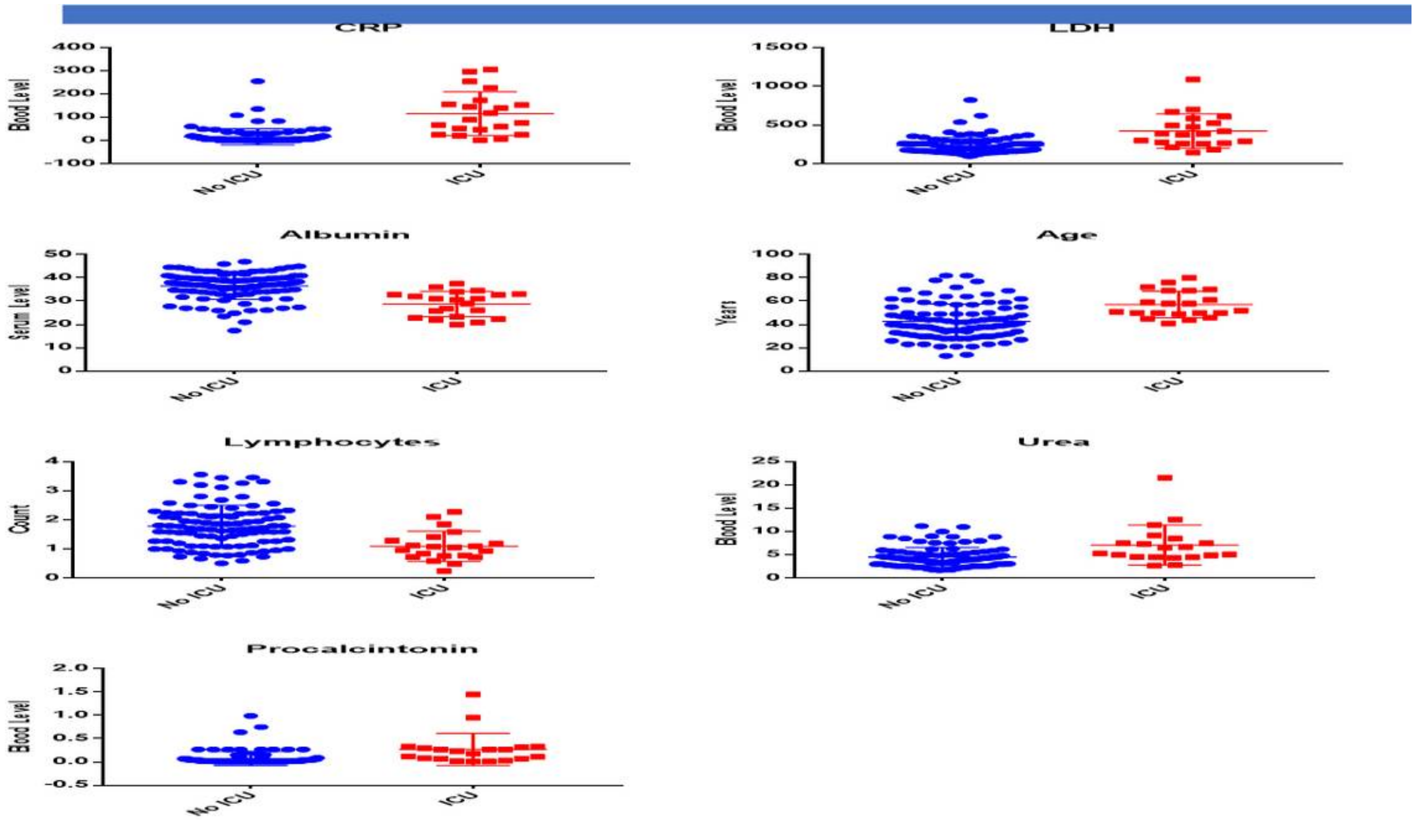

Figure 3

Comparison of the level of the selected features between COVID-19 positive patients admitted to ICU and those who didn't need ICU.

Supplementary Files

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