Correlations Between Epidemiological and Clinical Characteristics, Laboratory Tests and CT Scan Reports in the Diagnosis of COVID-19: A Diagnostic Accuracy Study

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Abstract- Although the relationship between laboratory parameters, radiology, CT scan scan and clinical outcomes has not been well evaluated so far, COVID-19 is still a good challenge for this purpose. These tests can be used to diagnose, monitor, and treat COVID-19. The study was conducted from February 20 to August 31, 2020, following the referral of 340 patients with coronavirus symptoms at Chamran Hospital, Shiraz University of Medical Sciences, Shiraz, Iran. Clinical information of each patient is obtained based on patient information forms when visiting the hospital. Comparison of the relationship between lung involvement in CT scan and laboratory indicators, including biochemical and hematological factors is a suitable and reliable comparison to identify people with Covid 19. Based on the results of this study, it was found that ALT, AST, CRP, NEU, LDH, and Urea could be a suitable diagnostic method in positive RT-PCR for COVID-19. In this study, we tried to investigate the relationship between clinical and laboratory findings with CT-based quantitative score of pulmonary involvement in COVID-19 pneumonia and as a suitable and reliable method in continuing COVID-19 pandemic and diagnosis of COVID-19 infection.

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Keywords: Clinical outcomes; Laboratory findings; Coronaviruses; Coronavirus disease 2019 (COVID-19) infections; Computed tomography (CT) scan reports

Introduction

The new covid-19 coronavirus, a severe infectious disease with rapid transmission to humans, was discovered in December 2019, and its outbreak was declared by the World Health Organization as a public health emergency and has now claimed the lives of millions worldwide (1,2). Diagnosis of Covid-19 disease is performed using polymerase chain reaction tests, chest CT scans, and ELISA test kits (3,4). Research published since 2019 claims that chest CT scans, along with polymerase chain reaction tests and other laboratory parameters, have the highest efficiency in detecting Covid 19 (5,6). Therefore, chest CT scans and radiological reports have been proposed as an adjunct to polymerase chain reaction tests as a complementary method (2). No findings can completely confirm or rule out the possibility of COVID-19 (7). Some observational studies have been partially characterized Clinical, laboratory, and imaging features of Covid-19, but until

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now, few systematic studies on relating these features to each other have been published to date (8). Laboratory tests scales in most patients with COVID-19 showed a significant changes in serum pro-inflammatory cytokine levels and blood biochemical markers such as interleukins, TNF-a, LDH, AST, ALT BUN, Creatinine, D-dimers, platelet count, cardiac troponin, renal markers WBC, HB and Lymphocytes (according to Figure 1) (9,10). Evaluation of clinical features and radiological reports in severe cases of COVID-19 will help in the initial prognosis, accurate diagnosis and treatment of patients with Covid-19 (11-13). It was detecting that there are differences in the abundance of metabolic markers and biochemistry indicators in COVID-19 patients than healthy, but there is a question about the subject whether change in blood biochemistry markers are associated with CT-scan findings and the severity of COVID-19 disease? To date, most studies published in this field have examined the association between epidemiological and clinical characteristics and COVID-19 disease, and little information is available to examine the association between laboratory characteristics and CT-scan findings. (14-16). However, evaluation of lung involvement in CT scan and their relationship with laboratory indicators can be introduced as one of the best and most effective prognosis comparisons in patients with Covid 19. (17). Various studies described the epidemiological and clinical characteristics of hospitalized patients (10,18-20). However, there is a limited number of detailed analyses on blood chemicals in discharged patients. In this study, we attempted that our findings could be useful to develop future clinical research associated with COVID-19 infection. In conclusion, the aim of this study was to evaluation the relationship between laboratory parameters, CT scan reports and clinical outcomes in the diagnosis of patients with COVID-19.

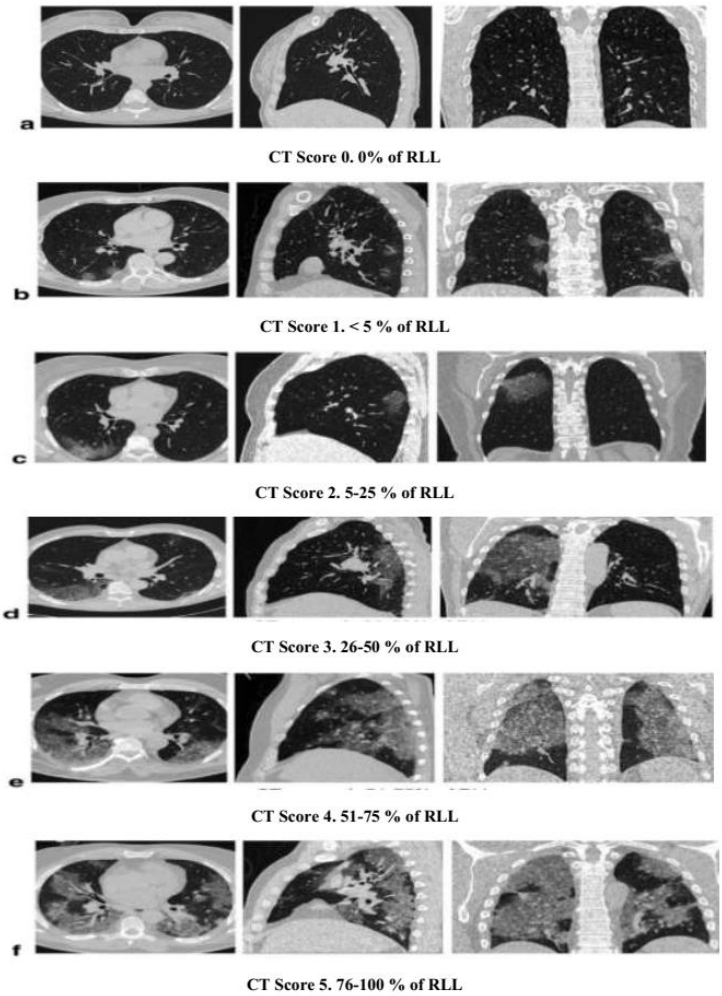

Figure 1. Different CT score of RLL involvement in COVID-19 pneumonia on axial, sagittal, and coronal images. 0% of RLL lobe involvement (a); <5% of RLL involvement (b); 20% of RLL involvement (c); 40% of RLL lobe involvement (d); 70% of RLL involvement (e); >75% of RLL involvement (f)

Materials and Methods

This study is a cross-sectional study conducted of collected data on patients of all age groups this study was conducted from February 20 to August 31, 2020, following the referral of 340 patients with coronavirus symptoms at Chamran Hospital, Shiraz University of Medical Sciences, Shiraz, Iran. In this study after obtaining permission from the ethics committee and approving the research plan, the clinical and laboratory findings of covid-19 patients were extracted from the electronic medical records of the patients. The information each patient, including the evaluation of lungs and kidney involvement in CT scan and sonography and their relationship with laboratory indicators, for the severity and prognosis of Covid 19 disease, was investigated by a trained team of physicians. The data about clinical symptoms, medical treatment, and laboratory parameters were collected by patient record, and based on the doctor's diagnosis and CT scan reports and PCR test of throat Secretions. Nasal and pharyngeal swab samples and sputum were obtained from patients on admission. We retrospectively analyzed and evaluated the epidemiological history, comorbidity, vital signs, and symptoms obtained from electronic medical records. The data collection forms were reviewed independently by two experienced physicians, and the severity of the disease is determined by the need for ICU, sepsis, involvement of the lungs and other organs, intubation, ventilation, death. The information of each case was completed using a data collection form based on the records recorded in the patient file and the examination of radiological photographs, and a sample of the data collection form was attached. Other variables studied include the need for ICU hospitalization and the time of hospitalization from the onset of symptoms to hospitalization and the need for intubation and ventilation. Problems include ARDS, Renal Injury, Septic Shock and Ventilator Associated Injury. In this study, CT scan reports are examined and the consistency of patients' deterioration based on these reports with the patient's fate in the case is examined. Inclusion criteria included, all positive coronavirus patients referred to chamran Hospital, who need to be hospitalized. Exclusion criteria included deaths before admission to the hospital and positive coronavirus patients or those who for some reason refused to visit the hospital. This project has been approved by the research ethics committee with the code of IR.SUMS.REC. 1399.S605 and project number 99-10-24-13415 by Shiraz University of Medical Sciences in Shiraz, Iran.

Statistical analyses

The collected data was entered and analyzed through the data collection form in SPSS software version 20. Qualitative variables were used to determine the frequency and frequency percentage and also quantitative variables were used to mean and standard deviation. To evaluate the effect of each variable as a univariate test, an independent two-sample t-test, one-way ANOVA, and chi-square will be performed for quantitative and qualitative factors, respectively. Also, the study of the effect of variables is multivariate modeled using a logistic regression model, and significance is considered at the level of 0.05. The Mann-Whitney U test was utilized to compare significant differences among continuous data. All statistical tests were two-tailed, and the *P* less than 0.05 was considered statistically significant.

Results

The demographic characteristics of all patients were listed in Table 1. The mean age of patients was 41.7, the median age 63 years (range 32-69) for critical patients which 65 % were male and 34 % were female (one-way ANOVA, $P<0.0001$). Almost 198 patients (58%) were aged ≤38 years. Generally, 183 (53%) patients had one or two types of chronic diseases, such as cancer, immune system defects, coronary heart disease (CHD), hypertension (HBP), and diabetes (DM). Hypertension 154 (45.29 %), Cardiovascular Disease 90 (26.47%) and Diabetes 178 (52.35%) were the most common Coexisting Conditions. According to the results of this study, 28 patients (9%) of patients had a familial infection or familial clusters. There was a significant difference among patients by their epidemiology history. The patients indeed presented significantly different on the most common symptoms like Fever, Dyspnea, Muscular pain, Fatigue, Shortness of Breath, Chill, Dry Cough, and Diarrhea (Table 1) (one-way ANOVA, $P=0.001$). Furthermore, the mean length of hospital stay in these patients was 14.12 days that in the critically ill patients took an average of 2.08 days longer than the total average levels, from the 340 cases with the suspicion of COVID-19 infection, 230 patients (164 males, 76 females with a positive RT-PCR test for covid-19). The most common clinical manifestations were fever, coughing, Muscular pain, and dyspnea. In this study, change CRP levels were found in patients and increased D-dimer levels were found in patients, and decreased lymphocyte count was

observed in 98 patients according to Table 2 Summary of Changes in Biomarkers Seen in Severe COVID-19 Infection. Change clinical in biochemistry parameters patients are summarized in Table 2. The results of this study show that the white blood cell (WBC) and neutrophil cell numbers were significantly higher and platelets and HB severely lower and a quite distinguishable difference on the biochemical blood test at different patients. Among patients in people with underlying diseases and high-risk groups showed significantly higher levels of serum ALT, AST, LDH than other healthy. According to Table 2, ALT, CRP, LDH, and Urea had very good precision in predicting cases with positive RT-PCR for COVID19. The result of this study RT-PCR for COVID-19 patients was positive in 252 (74%) cases and negative in 88(25%). Based on the CDC clinical scoring for covid-19 infection (10), 150 (44.11%) were classified as mild, 118 (34.70%) as severe, and 72 patients (21.17%) as critical.

Table 1. Demographic and clinical characteristics.

Demographic characteristics		Covid-19 patients (N %)
Sex: (n %)	**Male**	223 (65.48 %)
	Female	117 (34.52 %)
Age: (n %)	**0-25**	25 (7. 36 %)
	26-50	77 (22.46 %)
	51-75	183 (54.11 %)
	>75	55 (16.07 %)
Symptoms	**Fever**	211 (62.03 %)
	Coughing	157 (46.17 %)
	Dyspnea	204 (60 %)
	Diarrhea	98 (28.82 %)
	Headache	142 (41.79 %)
	Muscular pain	201 (59.11 %)
Underlying disease		154 (45.29 %)
Hypertension		90 (26.47%)
Cardiovascular Disease		98 (28.78%)
Obesity or Hyperlipidemia		178 (52.35%)
Diabetes		85 (25 %)
Chronic obstructive		77 (22.64 %)
pulmonary disease		44 (12.94 %)
Neoplasm		68 (20 %)
Chronic kidney disease		55(16.17 %)
Cancer Immunocompromised		48(14.11%)

Table 2. Comparing the laboratory findings of COVID-19 patients between Positive and Negative cases

Parameters	Total (n=340)	RT-PCRforCOVID-19		*P*
		Positive (n=252)	Negative (n=88)	
WBC	6962.8±2127	4343±1002	6994±1982	<0.0001
NEU	48.1	62.2	45.7	<0.0001
LYM	45.8	39.1	52.1	<0.0001
POSITIVE CRP a	39	57	29	<0.0001
ESR	27.2±8.6	32	20	0.486
AST	28.6±8.6	32.1±8.01	21.24± 8.1	0.533
ALT	32±7.1	38.8±2.1	25.2±5.9	0.926
LDH	385.6±125	471.2±110.2	361.6±94.1	0.0001
SAA	28.2±8.01	36.1±8.5	24.8±4.9	0.0001
Urea	43.12±32.41	66.81±53.83	42.78±33.42	0.001
Creatinine	1.39±0.95	1.69±0.95	1.97±9.32	0.877
CK-MB	899.35± 255.21	1033.45±1754.19	216.38±474.51	0.0001
D-dimer	0.4 ±1.5	0.5±2.9	0.3±0.7	0.0001
Blood urea Nitrogen	35	58-70	8-24	0.001

WBC: white blood cell; NEU: Neutrophil; LYM Lymphocyte AST: aspartate aminotransferase; ALT: alanine aminotransferase; LDH lactate dehydrogenase; ESR: erythrocyte sedimentation rate; CRP: C reactive protein; CK-MB, creatine kinase-muscle and brain type; SAA; serum amyloid A

The results of this study (Table 3) in CT features, scoring, screening patients show the most common patterns of disease included GGO, observed in 152 patients (44.7%), followed by crazy-paving pattern 68 (20%) and parenchymal consolidations in 78 (22.9%) (Figure 2). Features and characteristics related to CT were found as follows: fibrosis (n=57; 16.76%), subpleural lines (n=43; 12.46%), pleural effusion (n=28; 8.23%), precordial effusion (n=8; 2.35%), and mediastinal lymphadenopathy (n=27; 7.94 %), COPD thinking of ILD, ILS (n=30; 8.82 %). The findings of this study also shown lobar involvement, lesion distribution, and localization in the pulmonary parenchyma. Pathological involvement in the left lower lobe (LLL) in 157 patients (46.17%) was most common, and right lower lobe (RLL) in 143 patients (42.05 %). The mean of involvement lung lobes and CT scores were shown in (Figure 3) (Table 4).

Table 3 Frequency of main patterns and features in covid-19 patients.

CT features in COVID-19 patients		N%	*P*
Main CT	**pattern**	152/340 (44.7%)	< 0.0001
	Crazy paving	68/340 (20%)	0.0003
	Consolidation	78/340 (22.9%)	0.0021
	Mixed GGO and consolidation	94/340 (27.64%)	0.0001
Related	**features**	57/340 (16.76%)	< 0.0001
	Fibrosis	43/340 (12.46%)	0.0024
	Sub pleural lines	28/340 (8.23%)	0.422
	Pleural effusion	8/340 (2.35%)	0.210
	precordial effusion	27/340 (7.94 %)	0.321
	mediastinal Lymphadenopathy		
	COPD thinking of ILD, ILS	30/340 (8.82 %)	0.541

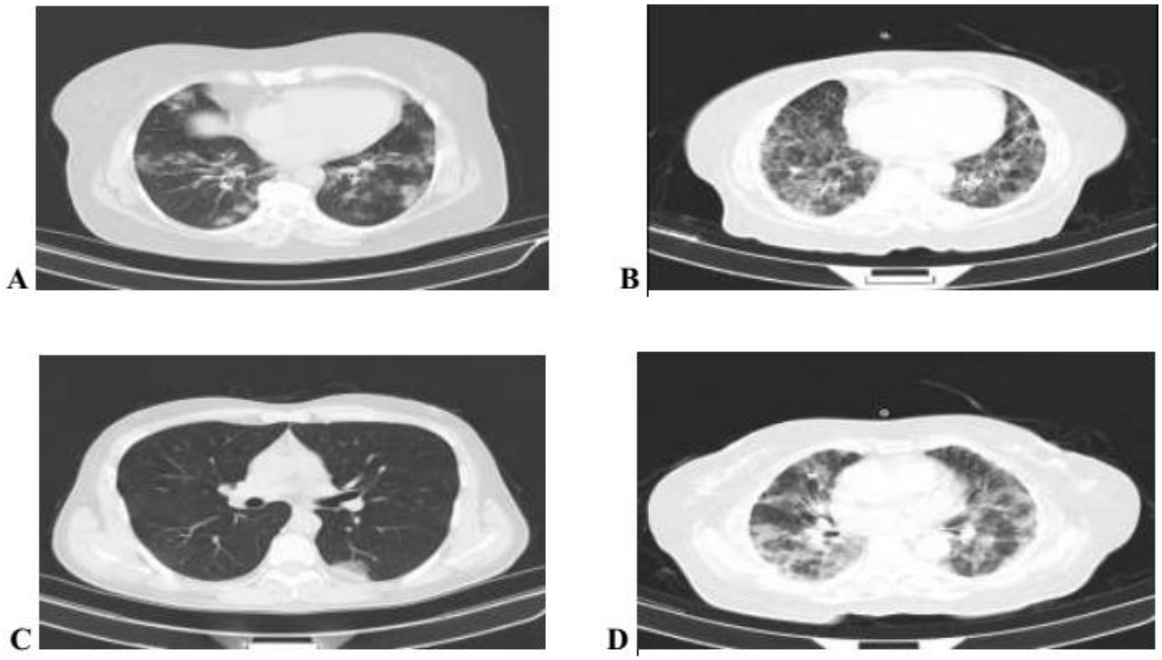

Figure 2. Chest CT findings of COVID-19 pneumonia on axial images. GGO (A); crazy-paving pattern (GGO with superimposed inter-and interlobular septal thickening) (B); consolidation (C); GGO, crazy-paving pattern and consolidation (D)

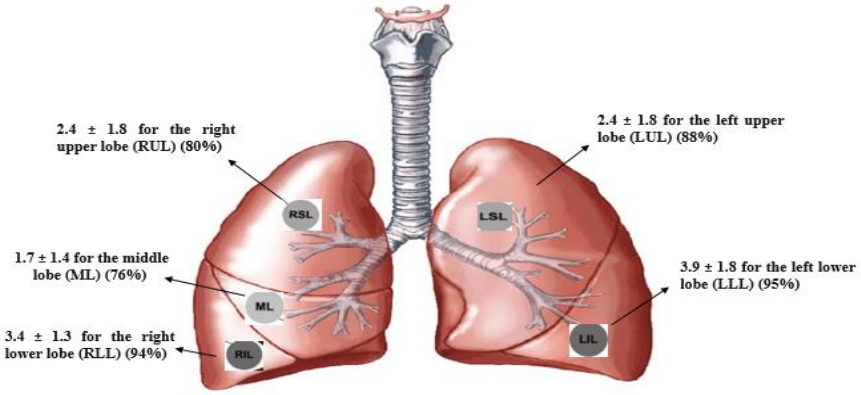

Figure 3. Lobar CT scores of patients Covid-19, data are expressed as mean value±SD (% of occurrences of involvement for each lobe) (*****P*<0.0001). RUL, right upper lobe; ML, middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe

Table 4. Frequency of involvement of each lobe with related CT score.

Categories		Covid-19 patient n%	CT mean score±SD	*P*
Lung Lobe	**Right upper lobe (RUL)**	272(80%)	2.4 ± 1.8	0.0001
	Middle lobe (ML)	258 (76%)	1.7 ± 1.4	0.0001
	Right lower lobe (RLL)	143 (42.05 %)	3.4 ± 1.3	0.0001
	Left upper lobe (LUL)	299 (88%)	2.4 ± 1. 8	0.0001
	Left lower lobe (LLL)	157 (46.17%)	3.9 ± 1.8	0.0001

According to the average global CT, the score was 12.3±11.1. All patients did show parenchymal involvement at CT reports, and there are not any patients, therefore, scored as 0. In comparisons between lung lobes, the mean CT score was significantly higher in RLL than in ML and RUL (*P*<0.0001), and the mean CT score was significantly higher in LLL than in LUL (*P*<0.0001) (Figure 3), also the distribution of parenchymal abnormalities in pathological findings were posterior in 118 patients (34.70%) and anterior in 68 patients (20 %). In the 50 patients (16.8%), there was the involvement of both anterior and posterior areas. Regarding the results of this study and investigation of CT features, demonstrated the GGO pattern was most prevalent in early-phase disease and late-phase disease, while crazy-paving and consolidation patterns were most common in late-phase, also fibrosis were significantly common in late-phase. The pleural effusion and lymphadenopathy in patients were rarely observed in the late phase. CT score in late-phase was significantly higher than in early-phase patients (*P*<0.0001). CT score between age range groups statistically significant difference was found (*P*=0.0018), in this way CT score was significantly higher in age range >75 than in other age groups (*P*=0.001).

Furthermore, the results of this study indicated statistically significant correlations between CT score with SAA (*P*<0.0001, r=0.4314), LDH (*P*<0.0001, r=0.3214), Cardiac troponin (*P*<0.0001, r=0.6714), Renal biomarkers Urea & creatinine (*P*<0.0001, r=0.3314), CRP (*P*<0.0001, r=0.6314), D-dimer (*P*<0.0001, r=0.6427), lymphocyte count (*P*=0.0001, r=0.1630) levels. Univariate and multivariate analyses of 340 patients in this study show that 48 patients (11.17 %) died during a mean follow-up of 14.1±4.8 days (range 1-26 days), all of which indicated at least one or more of the previously mentioned underlying diseases. The mortality rate was significantly higher in patients ≥75-year-old (n=39; 11.47%) and among critical patients (12/12; 100%). The univariate analysis CT score in this patients indicated a higher risk of death in patients with a CT score ≥18 (HR, 8.23; 95% CI, 2.17-25.63; *P*<0.0001), and significantly correlated with increase of age (HR,1.02;95% CI,1.01-1.21; *P*=0.001), HDL (HR, 1.01; 95% CI, 1.03-1.07; *P*<0.001), Cardiac troponin (HR,

1.003; 95% CI, 1.10-1.00; *P*<0.001), Urea (HR, 1.06; 95% CI, 1.03-1.07; *P*<0.001), creatinine (HR, 1.01; 95% CI, 1.00-1.01; *P*<0.001) CRP (HR, 1.06; 95% CI, 1.03-1.07; *P*<0.001) and D-dimer levels (HR,1.011; 95% CI, 1-1.08.001; *P*=0.0001). Table 5 show the correlations between Clinical Findings, laboratory tests and CT reports.

In this study, we investigated the correlation of clinical and laboratory findings with CT-based quantitative score of pulmonary involvement in COVID-19 pneumonia, that we realized CT scan findings may be predictive of patients 'outcomes and had a correct correlate with laboratory findings and disease severity.

Table 5. Correlations between CT reports, Clinical Findings and laboratory tests.

laboratory tests	CT SCORE	
	r	***P***
WBC	r=0.1520	0.0001
NEU	r=0.2630	0.0001
LYM	r=0.1630	0.0001
POSITIVE CRP [a]	r=0.6314	<0.0001
ESR	r=0.6314	<0.0001
AST	r=0.3517	<0.0001
ALT	r=0.5310	<0.0001
LDH	r=0.3211	<0.0001
SAA	r=0.4319	<0.0001
Urea & Creatinine	r=0.3314	<0.0001
TROPONIN	r=0.6714	<0.0001
CK-MB	r=0.3214	<0.0001
D-dimer	r=0.4214	<0.0001
Blood urea Nitrogen	r=0.6427	<0.0001

Discussion

According to the findings of the present study, it seems that there is a significant relationship between chest CT scan characteristics and changes in clinical parameters with outcomes of COVID-19 cases. Based on these results, ground Glass Opacity (GGO) and consolidation were the most common chest CT scan findings, which were a match to other researches (21,22). The most common location of abnormalities was lower zone involvement that was observed more than upper zone, which was consistent with findings of other studies (19,23). An investigation carried out on other patients shows that CT reports will be more obvious when revealed longer the onset of symptoms (24). In this study, radiological patterns have a correlation with the stages of the development disease, which was in match to the studies (24,25). Result of our study indicated ALT, AST, CRP, NEU, LDH, and Urea have very good accuracy in predicting cases with positive RT-PC R for COVID-19, respectively. Also, liver injury is more prevalent in severe cases compared to mild cases of COVID-19. This study was similar to the study Chen *et al*., Another study indicated that 2-11%of patients with COVID-19 had ALT and AST levels during the progression of COVID-19 disease (19). In comparison to the normal range, in patients with positive RT-PCR COVID19, the rate of WBC and LYM counts was decreased, and NEU counts increase, which is in line with another study (26). The COVID -19 Virus is extensive through the respiratory system and infected immune cells and causing changes in the number of peripheral white blood cells such as lymphocytes (27). Various studies proposed the substantial decrease in the number of lymphocytes following infection with the coronavirus that influence immune cells and prevent immune action (28). Also, other reports show that high neutrophil count and LDH level in COVID-19 patients were autonomous predictors of an adverse clinical outcome (29). The results of laboratory parameters in this study, such as ALT, CRP, AST, LDH, and NEU, indicated that there could be used to foretell the presence of COVID-19 disease, while WBC was poorly predicted of the disease. This information is matched to findings reported by Wang *et al*., (30) and Gao *et al*., (31). Thus, some laboratory parameters can use to screening cases with positive RT-PCR forCOVID-19. Overall, the Clinical course of the COVID-19 disease is unforeseeable due to the heterogeneity of its manifestations and multi-organ failure. At present, there are no prognostic biological markers to identify Covid 19 patients and estimate their associated mortality. It seems that predicting CT scan reports of disease progression and its relationship with laboratory-clinical findings may be useful in patient

triage and symptomatic treatment of patients (32). In this study, we used a previous CT score for confirming this presumption, that it was based on the lobar Involvement expanse of as reported by Pan *et al*., (33). The results of the study showed correlation CT scoring with laboratory parameters, age, dyspnea at admission, and the presence of pre-existing comorbidities like coronary arteries and diabetes. Information of mortality rate in this study has approved the outstanding importance of age and its rate in patients older than 75 years. our finding in the study substantially assessment CT parenchymal reports and may reflect short and high-term outcome through direct visualization of anatomic damages than with non-specific laboratory parameters and inflammatory biomarkers. Based on clinical criteria provided by the WHO (34) and as expected, finding of this study indicated the correlation of disease severity with CT reports and laboratory parameters, so CT scores were significantly confirmed high correlation between imaging findings and clinical stages, however, the diagnostic role of CT scan and its correlation to laboratory parameters is controversial and debated. Although, CT is as a first line test, but highly sensitive imaging method like CT associated with specific clinical parameters, might be beneficial to speed up diagnostic and therapeutic workflow.

Considering the significant difference in CT scoring and laboratory parameters, can hope to model or predict the results of coronavirus testing based on routine laboratory tests. In conclusion, based on the results of this study, it was found that ALT, AST, CRP, NEU, LDH, and Urea could be a suitable diagnostic method in positive RT-PCR for COVID-19. In this study, we tried to investigate the relationship between clinical and laboratory findings with CT-based quantitative score of pulmonary involvement in COVID-19 pneumonia and as a suitable and reliable method in continuing COVID-19 pandemic and diagnosis of COVID-19 infection.Thus, expected future studies can indicated better clarify impact on clinical decision-making and larger clinical trials.

Limitation

Differences between Iran's National Guideline for COVID-19 and guidelines of other countries, in addition to usual limitations of cross sectional studies, were among the most important limitations of this study. We performed a retrospective analysis evaluation in a relatively limited cohort of patients, but the severity of the current health care emergency implies that a prospective evaluation would have been extremely complex and longer to complete.

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