Original Research Article

Correlating CT severity score and laboratory parameters in COVID-19 patients: the Indian experience

Annu Singhal[1]*, Raja Kumar Ramar[1], Vivek C. Kottiyath[2], Nishtha Gupta[3]

[1]Department of Radiodiagnosis, Atal Bihari Vajpayee Institute of Medical Sciences and Dr. Ram Manohar Lohia Hospital, New Delhi, India
[2]Department of Radiodiagnosis, Sky Diagnostics, Kiran Garden, Uttam Nagar, Delhi, India
[3]Kasturba Medical College, Mangalore, India

*Correspondence:
Dr. Annu Singhal,
E-mail: annu.singhal@gmail.com

ABSTRACT

Background: Patients with COVID-19 infection present with myriad of symptoms to the clinicians. Many of these patients undergo HRCT chest and various lab tests during their treatment. Correlation between various lab parameters and severity of the disease on chest CT would be helpful in management of such patients. In situations where CT is not available, lab parameters may help to predict disease severity. The primary objective was to find out if there was any correlation between CT severity scores and laboratory parameters in patients having COVID-19 and if one can be extrapolated in cases where CT facilities may not be available.
Methods: This is a retrospective, descriptive, and observational study. CT severity scores were obtained in all the patients using the 25 point scale. The following lab parameters were assessed: TLC, DLC, SGOT, SGPT, CRP, D-Dimer, IL-6, Serum Ferritin and serum LDH. Correlation was done between the CT score and various lab parameters using Pearson correlation coefficient test.
Results: 285 patients with positive COVID-19 RT-PCR test were included in the study. CT score showed statistically significant positive correlation with age, TLC, Neutrophil count, SGOT, SGPT, CRP, D-dimer, IL-6, Ferritin and LDH with p-values less than 0.05. Negative correlation was seen with Lymphocyte count. Severe disease was found to be more common in older patients.
Conclusions: In our study, CRP, LDH, Serum ferritin, IL-6 and D-dimer levels were observed to have positive correlation with disease severity on CT. Thus these measured at the time of admission can be taken into consideration to predict radiological severity.

Keywords: As CT severity score, CRP, D-dimer, IL-6, Ferritin, LDH

INTRODUCTION

Coronaviruses are enveloped non-segmented positive-sense RNA viruses that belong to the family Coronaviridae. Most human coronavirus infections are mild, however, the epidemics caused by the two beta coronaviruses (SARS-CoV and MERS-CoV) have caused more than 10,000 cases in the last two decades with mortality rates of 10% and 37% for SARS-CoV and MERS-CoV respectively. A series of pneumonia cases of unknown etiology emerged in Wuhan province in China in December 2019 with a clinical presentation similar to viral pneumonia. On further evaluation, it was found to be caused by a novel coronavirus which was named 2019 novel coronavirus (2019-nCoV or COVID-19).[1] Patients with COVID-19 infection present with a myriad of symptoms, most common being fever, dry cough, and dyspnea. COVID-19 can also lead to Acute respiratory

distress syndrome (ARDS) similar to SARS-CoV and MERS-CoV. Many of these patients undergo HRCT chest to look for the extent of lung involvement. The lung involvement mainly starts as peripheral subpleural GGOs predominantly in the lower lobe bilaterally which then develop into a crazy-paving pattern due to interstitial septal thickening and subsequently lead to consolidation. On resolution, there might be residual GGOs and subpleural parenchymal bands.[2] In addition, CT severity score which involves scoring based on the extent of the lung involvement helps to provide objective data indicating the severity of the disease. A high CT severity score has been found to be an independent risk factor for poor prognosis in COVID-19.[3] Various studies have reported that old age, elevated laboratory markers like neutrophil count, C-reactive protein (CRP), lactate dehydrogenase (LDH), serum ferritin, interleukin-6 (IL-6), and D-dimer indicate poor prognosis and correlate with the disease severity. Total leukocyte count (TLC) and lymphocyte count were found to have a negative correlation with disease severity.[3–5] Correlation between these various lab parameters and severity of the disease on chest CT would be helpful in management of patients and in predicting outcome. In this study, we report the laboratory and radiological features of the patients diagnosed with COVID-19 in Delhi, India.

METHODS

Study type

The present study is a multicenter, ambispective, observational study.

Study population

A total of 285 patients were included in the study conducted at Dr. Ram Manohar Lohia Hospital and all the patients were diagnosed to have Covid-19 infection by RT-PCR between April and May, 2021. The nasopharyngeal samples were processed by using BGI'S Real Time fluorescent RT-PCR kit issued by U.S. Food and Drug administration (FDA) as per Emergency Use Authorisation ammendment (EUA) or by DiAGSure nCOV-19 Detection Assay kit developed by GCC Biotech private Ltd. RT-PCR testing was performed using Clinical Laboratory Improvement Amendments (CLIA) diagnostic standards according to the current testing guidelines.

Patients with negative RT-PCR result or with contraindication to HRCT like pregnancy were excluded from the study.

CT protocol

All the patients underwent non-contrast enhanced HRCT chest in SIEMENS SOMATOM 128 slice and GE revolution ACT scanner. Patients were placed in supine position and scanned in end inspiratory breath hold. The scanning parameters were as follows: tube voltage 120 kV, automatic tube current modulation (50 mA), pitch 0.99–1.22 mm, matrix 512×512, field of view 350×350 mm, reconstruction slice thickness 0.625 or 1.25 mm.

Image interpretation

CT severity scores were obtained in all the patients using the 25-point scale. Each lung lobe is given a score of 0 to 5 based on the percentage of lung involvement. 0, no involvement; 1, 1–5% involvement; 2, ≤25% involvement; 3, 26–50% involvement; 4, 51–75% involvement; 5, 76–100% involvement. The total CT severity score is equal to the sum of individual scores of all 5 lobes of lung with a maximum score of 25. Based on the CT severity score the disease severity was categorized into mild (CT severity score 1-7), moderate (score 8-17) and severe disease (score 18 or more).[3]

Laboratory data

The following lab parameters were collected and assessed: total leukocyte count (TLC), differential leukocyte count (DLC), serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), C reactive protein (CRP), D-dimer, Interleukin 6 (IL-6), serum ferritin and serum lactic acid dehydrogenase (LDH).

Statistical analysis

Data were coded and recorded in MS excel spreadsheet program. Statistical package for social sciences (SPSS) v21.0 was used for data analysis. Descriptive statistics were elaborated in the form of means/standard deviations and medians/IQRs for continuous variables, and frequencies and percentages for categorical variables. Linear correlation between two continuous variables was explored using Pearson's correlation (if the data were normally distributed) and Spearman's correlation (for non-normally distributed data). Statistical significance was kept at $p < 0.05$.

Ethical approval

The study was approved by Institutional Review Board and patients' consents were taken for inclusion in the study and for publication in journal.

RESULTS

In this study, the mean age of the patients was 48.63±15.18. Out of the 285 patients 167 were males and 118 were females with a clear male predominance of 1.4:1.

CT severity score

Bilateral peripheral ground glass opacities in lower lobes was the most common pattern observed. The other

common patterns observed are crazy paving pattern due to interlobular septal thickening, consolidation and subpleural parenchymal bands on resolution. The other non-common patterns like unilateral GGOs or consolidation, mediastinal lymphadenopathy and pleural effusions were also seen. The mean CT severity score was 9.82±5.37. Based on the CT severity score patients were grouped into mild (0-7), moderate (8-17) and severe (18-25). 87 patients were of the mild group, 174 patients were of moderate group and 24 patients were of severe group. (Figure1, 2, 3, 4)
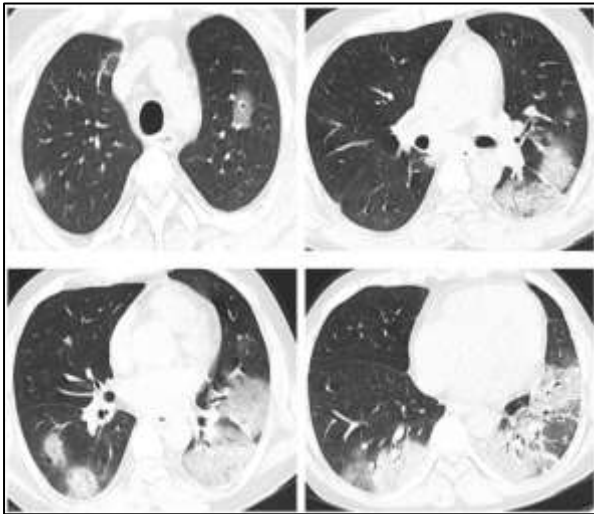

Figure 1: Axial CT sections of the chest in lung window in a 29-year-old male. Multiple peripheral ground-glass opacities with consolidations predominantly in bilateral lower lobes. CT severity score was 14/25. This patient had elevated levels of CRP, IL-6, and LDH.
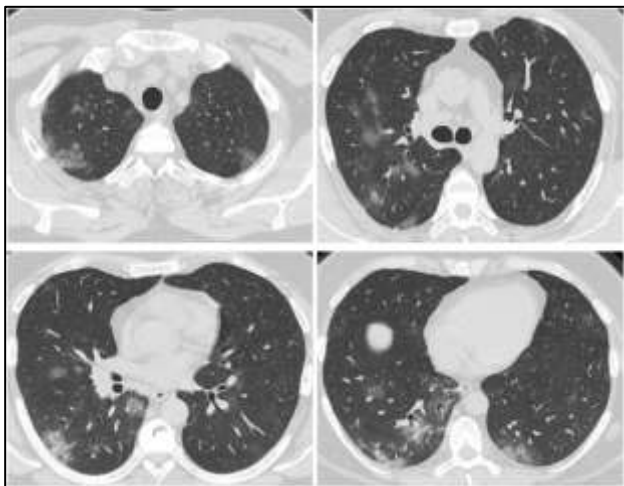

Figure 2: Axial CT sections of the chest in lung window in a 51-year-old male. Multiple peripheral, as well as central patches of GGOs with interlobular septal thickening, were seen. CT severity score – 10/25. This patient had elevated levels of CRP, IL-6, and LDH.

CT severity score versus age

The CT severity score had a positive correlation with the age of the patients (p – 0.004, r – 0.17). The mean age of the mild group was 45.2±17.6, moderate group was 49.8±13.8 and severe group was 52.6±13.7 years. The mean age of the severe group was relatively higher compared to mild and moderate groups.
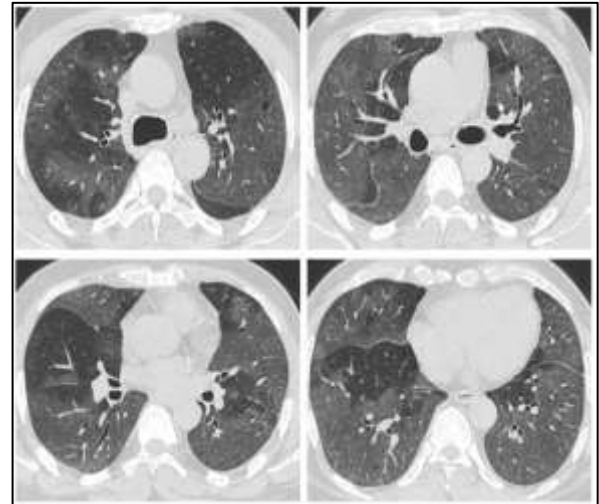

Figure 3: Axial CT images in lung window in a 70-year-old male. Diffuse and confluent GGOs are noted throughout bilateral lung fields involving all 5 lobes. CT severity score –24/25. This patient had elevated levels of TLC, SGOT, SGPT, CRP, d-dimer, S. Ferritin, IL-6, and LDH, and a reduced percentage of lymphocytes in DLC.
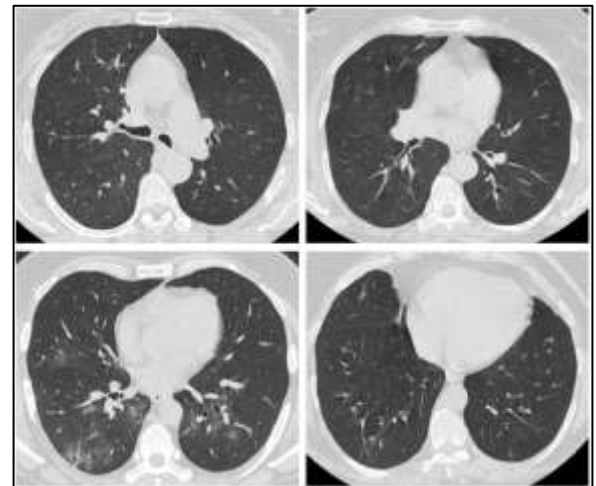

Figure 4: Axial CT images in lung window in a 70-year-old female. Few patches of GGO were noted in the central and peripheral distribution in the bilateral lower lobes and right middle lobe. Ct severity score 5/25. This patient had normal TLC, SGOT, SGPT, CRP, D-dimer, IL-6, S. Ferritin, LDH however had a low percentage of lymphocytes in DLC.

Table 1: Correlation of CT severity grades with biochemical parameters (significant p<0.05).

	Mild		Moderate		Severe		Total	mild versus mod	Mild versus severe	Mod versus severe
	Mean	SD	Mean	SD	Mean	SD	P value	P value	P value	P value
Age	45.17	17.57	49.81	13.79	52.63	13.73	0.026	0.020	0.032	0.391
TLC	7084.71	2753.29	7836.67	3707.63	10044.44	3912.61	0.004	0.111	0.001	0.011
DLC-P	63.27	11.85	73.02	9.73	79.94	9.10	0.000	0.000	0.000	0.009
DLC-L	29.92	10.61	21.63	9.00	15.83	8.87	0.000	0.000	0.000	0.016
SGOT (0-49)	47.17	26.46	47.34	17.53	56.13	7.46	0.603	0.968	0.330	0.328
SGPT (0-46)	48.88	27.91	48.72	21.25	55.33	11.96	0.804	0.974	0.533	0.513
CRP (0.0 to 6.0)	10.00	12.45	37.12	30.35	65.20	31.78	0.000	0.000	0.000	0.000
D dimer (<0.5)	0.36	0.39	0.53	0.47	5.26	19.25	0.002	0.853	0.001	0.001
IL-6 (0.0 to 7.0)	33.29	72.19	44.99	107.27	36.43	40.25	0.812	0.531	0.918	0.767
Ferritin (10.0 - 291.0)	288.57	500.19	362.85	328.38	518.97	354.94	0.242	0.341	0.106	0.261
LDH (114-240)	296.28	113.25	449.24	192.69	646.25	227.45	0.000	0.001	0.000	0.032

Table 2: Change in the pattern of biochemical parameters with CT severity scores (significant p<0.05).

		CT group			Total	Chi-square value	p-value
		Mild	Moderate	Severe			
Sex	F	41.4%	42.0%	37.5%	118	0.172	0.917
	M	58.6%	58.0%	62.5%	167		
SGOT group	Normal	68.3%	60.0%	16.7%	68	5.882	0.053
	Abnormal	31.7%	40.0%	83.3%	44		
SGPT group	Normal	53.7%	43.1%	16.7%	51	3.266	0.195
	Abnormal	46.3%	56.9%	83.3%	61		
CRP group	Normal	57.4%	15.7%	0.0%	63	50.050	0.000
	Abnormal	42.6%	84.3%	100.0%	178		
D dimer group	Normal	88.1%	71.7%	40.0%	158	19.180	0.000
	Abnormal	11.9%	28.3%	60.0%	56		
IL-6 group	Normal	66.7%	26.6%	16.7%	45	19.202	0.000
	Abnormal	33.3%	73.4%	83.3%	70		
Ferritin group	Normal	70.8%	57.8%	20.0%	73	9.128	0.010
	Abnormal	29.2%	42.2%	80.0%	49		
LDH group	Normal	39.1%	14.3%	0.0%	15	6.571	0.037
	Abnormal	60.9%	85.7%	100.0%	54		

Total leukocyte count (TLC)

The mean TLC in our study was 7738±3387 cells/ml. TLC showed a positive correlation with CT severity score (r – 0.18, p – 0.006). There was significant difference in the TLC values of severe group when compared to mild (p – 0.001) and moderate (p - 0.011) groups.

Differential leukocyte count

The percentage of neutrophils and lymphocytes were evaluated for all the patients. The mean percentage of neutrophils was 70.1±11.7% and of lymphocyte was 24.1±10.6%. The neutrophil percentage showed positive correlation with CT severity score (r – 0.45, p – 0.001) and lymphocyte percentage showed negative correlation with CT severity score (r=-0.43, p – 0.001). There was significant difference between mild, moderate and severe groups in the neutrophil and lymphocyte percentage (p – 0.001 and 0.001 respectively). As the grade increased-neutrophil percentage increased and as the grade decreased- lymphocyte percentage increased.

SGOT and SGPT

SGOT and SGPT had a mean value of 47.8±20.9 and 49.1±23.5 IU/L respectively in this study. Both SGOT and SGPT showed a positive correlation with the CT severity score with p values of 0.017 and 0.035 respectively.

C reactive protein

In our study the mean CRP of the patients was 31.8±30.9 mg/dl. CRP levels showed the highest positive correlation with the CT severity score (r=0.601, p – 0.001). The mean CRP of mild group was 10.0±12.5 mg/dl, moderate group was 37.1±30.4 mg/dl and severe group was 65.2±31.8 mg/dl. There was significant difference between the CRP values of the three groups (p – 0.001) with highest in the severe group and lowest in the mild group.

D-dimer

In our study the mean D-dimer value was 0.9±5.9 µg/ml. It showed significant positive correlation with the CT severity score (r = 0.34, p – 0.001). The mean d-dimer value of mild group was 0.4±0.4 µg/ml, moderate group was 0.5±0.5 µg/ml and severe group was 5.3±19.3 µg/ml. There was significant difference between the d-dimer of severe group when compared to mild and moderate group (p – 0.001 and 0.001 respectively) (Table 1).

Interleukin – 6 (IL-6)

The mean IL-6 value in our study was 40.1±91.0 pg/ml. It showed significant positive correlation with CT severity score (r – 0.35, p – 0.001), however no significant difference was noted between mild, moderate and severe groups.

Serum ferritin

The s. ferritin level in our study was 346.4±408.2 µg/L. There was significant positive correlation between s. ferritin and CT severity score (r=0.39, p – 0.001), however no significant difference was noted between mild, moderate and severe groups.

Lactate dehydrogenase (LDH)

In our study the mean LDH value was 409.7±193.5 IU/L. LDH values showed the second highest positive correlation with CT severity score (r=0.53, p – 0.001) next to CRP. The mean LDH value of mild group was 296±113.3 IU/L, moderate group was 449.2±192.7 IU/L and severe group was 646.3±227.5 IU/L. There was significant difference between the LDH values of mild, moderate and severe group (p – 0.001).

The values of CRP, d-dimer, Il-6, S. Ferritin and LDH were abnormal in 100%, 60%, 83%, 80% and 100% of the patients in severe group respectively. This proportion is significantly high compared to mild and moderate groups indicating that more severe the disease, more abnormal the biochemical parameters. As the grading of CT score is increasing, CRP, D-dimer, LDH, TLC, DLC-P is also seen to be increasing significantly (highlighted p<0.05) (Table 2).

DISCUSSION

The classical feature of COVID-19 pneumonia, as seen in our study, is the presence of GGOs with or without consolidation in peripheral and lower lobe predominant distribution.[4] COVID-19 pneumonia starts by alveolar hyaline membrane injury and interstitial edema which appear as GGOs on CT which then progresses to consolidation due to alveolar filling with exudates. This is followed by activation of both B and T cells leading to formation of inflammatory cytokines which leads to inter-lobular septal thickening giving rise to crazy paving pattern and then lead to fibrosis.[6] CT chest can be used to predict the disease severity based on semi-objective analysis of it by calculating CT severity score and correlation of it with clinical and laboratory findings can help in clinical decision making.[4]

In our study, CT severity score had a positive correlation (r – 0.16, p – 0.004) with the age of the patient. In other words, higher the age of the patient more severe was the disease. The severe group had more proportion of older patients as compared to mild and moderate groups. In similar studies by Zhou et al, Francone et al and Saeed et al, they found similar positive correlation between age of the patient and CT severity score or disease severity.[3–5]

There was a significant positive correlation (r – 0.18, p – 0.006) between CT severity score and total leukocyte count (TLC). Leukocytosis was more common in severe group and had high TLC values compared to mild and moderate group. Zhou et al in their study found a similar positive correlation between disease severity and TLC levels.[3]

Neutrophil percentage in DLC had a positive correlation (r – 0.45, p – 0.001) with CT severity score and was significantly higher in severe group than moderate and mild group. Lymphocyte percentage had a negative correlation (r=-0.43, p – 0.001) with CT severity score and was significantly low in severe group compared to other groups. Hence, neutrophilia and lymphopenia can be considered for predicting disease severity. In a similar study by Saeed et al they showed significant negative correlation between CT severity and lymphopenia (p – 0.0001).[5] Zhou et al in their study showed positive correlation between neutrophilia and disease severity (p<0.05).[3]

CRP is a non-specific acute-phase protein and is a sensitive biomarker of inflammation, infection, and tissue damage. CRP is elevated in COVID-19 pneumonia due to inflammatory changes occurring in the lung. CRP showed the single highest positive correlation (r – 0.601, p – 0.001) with CT severity score in our study. There was significant difference in the CRP values of the 3 group with severe group having the highest values. This implies that CRP levels, either independently or in combination with other biochemical parameters, can predict the CT severity and in turn the disease severity. Many other similar studies showed positive correlation between CRP levels and disease or CT severity, and CRP can be used as an independent prognostic indicator. The similar studies mentioned above were by Saeed et al (p<0.0001, r – 0.556), Francone et al (p<0.001, r – 0.62), Yilmaz et al (p – 0.0001, r – 0.39) and Liu et al (p<0.001).[4,5,7,8]

D-dimer is a by-product of coagulation and fibrinolysis and D-dimer levels are elevated due to the haemostatic abnormalities associated with COVID-19 pneumonia. In our study d-dimer values had a positive correlation (p – 0.001, r – 0.34) with CT severity score and the d-dimer values were the highest in the severe group. D-dimer independently or along with other biochemical markers is a reliable prognostic indicator in COVID-19 pneumonia. Saeed et al in their study showed that D-dimer values were significantly high in severe group.[5] Krishna et al in their study showed that mortality was significantly high in patients with raised d-dimer values.[9] Francone et al and Yilmaz et al in their studies have shown significant correlation between CT or disease severity with d-dimer values.[4,7]

IL-6 is a multifunctional cytokine and is considered to be the primary trigger for cytokine storm in COVID-19 pneumonia. IL-6 levels had a positive correlation (p – 0.001, r – 0.35) with CT severity score in our study which was similar to the study by Liu F et al. who showed positive correlation between IL-6 level and disease severity with a p<0.001.

Ferritin is secreted by the macrophages which account for the main immune cells present in lung parenchyma and hence S. Ferritin is increased in COVID-19 pneumonia. In our study, S. Ferritin levels had significant positive correlation (r – 0.39, p – 0.001) with CT severity score. Saeed et al and Yilmaz et al in their study found a positive correlation between S. Ferritin levels and CT severity score (p<0.0001 and p – 0.0001 respectively). El Bakry et al in their study found that S. Ferritin was significantly elevated in critically ill patients and it can be used to predict short term outcome in them.[10] These findings were similar to our study in which more severe the disease higher was the S. Ferritin level.

In the process of tissue breakdown LDH converts lactate to pyruvate and increased levels of LDH are seen in patients with severe COVID-19 pneumonia. In our study, LDH levels had the 2nd highest positive correlation (r – 0.53, p – 0.001) with CT severity score. There was significant difference in the LDH values of mild, moderate and severe groups with severe group having the highest levels followed by moderate and the mild group. Magdy et al in their study found that LDH levels were elevated in severe and critically ill patient, similarly our study also shows elevated levels of LDH in severe cases.[11] El Bakry et al in their study found that LDH was elevated more in severe group followed by moderate and then mild groups.[10] Our study findings were in concordance with the above-mentioned studies.

Yuan et al in their study found out that the mean CT severity score of those who died of COVID-19 pneumonia was higher compared to those recovered.[12] Similarly, in our study the mean CT severity score was higher in critically ill patients than with mild disease and those with higher CT severity score showed raised biochemical markers also.

CONCLUSION

CT plays an important role in assessing the disease severity in COVID-19 pneumonia and in guiding further management. CT severity score had significant positive correlation with laboratory markers of severity like CRP, LDH, D-dimer, S. Ferritin, IL-6, TLC and Neutrophil count, and it had negative correlation with Lymphocyte count. This implies that CT severity score is closely related to the disease severity. Alternatively, these laboratory parameters can be used to predict the CT severity in situations where CT is not available. CRP and LDH values which had the highest correlation with CT severity score can be used independently or together to predict the CT severity.

REFERENCES

1. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020;395(10223):497-506.
2. Time Course of Lung Changes at Chest CT during Recovery from Coronavirus Disease 2019 (COVID-19). Radiology. Available at: https://pubs.rsna.org/doi/full/10.1148/radiol.2020200370. Accessed on 12 November 2021.
3. Zhou S, Chen C, Hu Y, Lv W, Ai T, Xia L. Chest CT imaging features and severity scores as biomarkers for prognostic prediction in patients with COVID-19. Ann Transl Med. 2020;8(21):1449.
4. Francone M, Iafrate F, Masci GM, Coco S, Cilia F, Manganaro L, et al. Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. Eur Radiol. 2020;30(12):6808-17.
5. Correlation between Chest CT Severity Scores and the Clinical Parameters of Adult Patients with COVID-19 Pneumonia. Available at: https://www.hindawi.com/journals/rrp/2021/6697677/. Accessed on 12 November 2021.
6. Pan F, Ye T, Sun P, Gui S, Liang B, Li L, et al. Time Course of Lung Changes at Chest CT during Recovery from Coronavirus Disease 2019 (COVID-19). Radiology. 2020;295(3):715-21.
7. Yilmaz A, Sabirli R, Seyit M, Ozen M, Oskay A, Cakmak V, et al. Association between laboratory parameters and CT severity in patients infected with Covid-19: A retrospective, observational study. Am J Emerg Med. 2021;42:110-4.
8. Liu F, Li L, Xu M, Wu J, Luo D, Zhu Y, et al. Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19. J Clin Virol Off Publ Pan Am Soc Clin Virol. 2020;127:104370.
9. Krishna BSG, Krishna PP, Sankar VR, Raghu K, Kumar AS, Srikanth M, et al. Laboratory Markers Versus Ct Severity Score In Predicting Mortality In Covid 19. Eur J Mol Clin Med. 2021;7(10):1824-31.
10. Chest CT manifestations with emphasis on the role of CT scoring and serum ferritin/lactate dehydrogenase in prognosis of coronavirus disease 2019 (COVID-19) | Egyptian Journal of Radiology and Nuclear Medicine. Available at: https://ejrnm.springeropen.com/articles/10.1186/s43055-021-00459-4. Accessed on 15 November 2021.
11. Comparative evaluation of semi-quantitative CT-severity scoring versus serum lactate dehydrogenase as prognostic biomarkers for disease severity and clinical outcome of COVID-19 patients. Egyptian Journal of Radiology and Nuclear Medicine. Available at: https://ejrnm.springeropen.com/articles/10.1186/s43055-021-00493-2. Accessed on 15 November 2021.
12. Yuan M, Yin W, Tao Z, Tan W, Hu Y. Association of radiologic findings with mortality of patients infected with 2019 novel coronavirus in Wuhan, China. PloS one. 2020;15(3):e0230548.