Original Research Article

Association of Inflammatory Markers and CT Scoring as Severity Predictors in Covid-19 Patients

Abstract-

Background- COVID-19 disease caused by SARS CoV-2 has rapidly spread worldwide and became a global concern for human health. Computed Tomography (CT) scan facility is not readily available in remote areas in developing nations like India. Previous studies have revealed the utility of CRP, LDH and other biomarkers in predicting the severity of COVID-19 pneumonia in resource limited settings and thus can help in stratification and early critical care transfer. **Objective**- The current study aimed to determine correlation between inflammatory markers with CT severity score to predict extent of COVID-19 pneumonitis. **Materials And Methods**- A total of 240 patients more than 18 years of age hospitalized with COVID-19 confirmed diagnosis either by RT-PCR test or by Rapid Antigen Test were assessed in this monocentric prospective observational study at our center, Pune, India. CT severity score and blood parameters such hemogram, hsCRP, LDH, Ferritin, IL-6 and D-dimer levels documented on the day of admission. The total CT score was the sum of five individual lobar scores and defined as: 0, none; 1–5, minimal; 6–10, mild; 11–15, moderate; and 16–20, severe lung involvement. **Results**- Mean age of patient in clinically critical cases (61.40 years) was higher than those with moderate (55 years) and non-severe clinical presentation cases (50.51years). 180 (75%) subjects were having non severe clinical presentation followed by 31 (12.9%) subjects with severe and 29 (12.1%) subjects were having critical clinical presentation on admission. hsCRP & LDH were having more correlation coefficient with CT severity score (0.599 & 0.570 respectively). The ROC analysis revealed that area under curve for hsCRP and LDH on the day of hospitalization for predicting severe lung involvement was 0.796 at 8.65 mg/dl cut-off (Sensitivity 76.9%, Specificity 74.9%) and 0.919 at cut-off of 425 U/L (Sensitivity 84.6%, Specificity 84.1%) **Conclusion**- On the basis of strong significant association with CT severity; hsCRP and LDH levels can be used to predict extent of lung involvement in chest CT in COVID-19 disease, thereby it will help in early triage and critical care transfer of patients to ensure optimal resource allocation in peripheral areas with limited facilities.

Keywords- COVID-19, hsCRP, LDH, Inflammatory markers, CT severity score.

1. INTRODUCTION

In December 2019, cluster of pneumonia cases due to unknown cause appeared in Wuhan city, Hubei province, China. In March 11, 2020 World Health Organization (WHO) proclaimed Corona Virus Disease-19 (COVID-19) as pandemic.[1] In India, first wave of COVID-19 peaked in September 2020, then it decreased steadily over 5 months. Mid-February 2021 marked the rise of overwhelming second wave of COVID-19, caused by the Severe acute respiratory syndrome coronavirus-2 (SARS CoV-2) Mutant, B.1.617.2 also known as The Delta Variant.[2] The highly infectious and increased transmissibility of this variant contributed to the sudden increase in number of cases which flooded the health care system causing exponential increase in mortality. There was no specific treatment against the COVID-19 infection leading to severe illness.

Markers like C-reactive protein (CRP), Ferritin and D-dimer are positive acute phase reactants which usually increases during acute inflammatory processes.[3] Lactate dehydrogenase (LDH) is indicator of an acute or chronic tissue damage associated with inflammation. COVID-19 patients have been related to a systemic hyperinflammation or cytokine storm, sustained by Interleukin-6 (IL-6).[4]

CRP is non-specific positive acute phase reactant and previous laboratory test methods were not sufficiently sensitive to measure blood levels of CRP within the normal range (<10 mg/L). Recently, development of high-sensitivity assays for CRP (hsCRP) has led to detection of even mild elevation of CRP, even within the normal range.[5] In April 2020, Tan C. et.al. revealed that CRP being associated with disease development showed significant rise in early stages in severe COVID-19 patients, even before the CT findings manifests. They also confirmed that CRP was an early biomarker for predicting the severity of COVID-19 with good performance.[6] In May 2020, Chen W. et.al. concluded that plasma CRP showed positive correlation with severity of COVID-19 on CT performance and higher level of CRP associated with longer inpatient duration. They suggested the use of CRP testing as an early indicator for severe illness and helpful hand for physicians to stratify patients for intensive care transfer.[7]

LDH is an inflammatory marker and has been shown to be increased during acute and severe lung damage.[8] In November 2020, Tordjman M. et.al. found that biological parameter such as LDH showed the strongest correlation with COVID-19 pneumonia CT extent while CRP was moderately correlated.[9] Strongest correlation between CRP, LDH and severity of SARS CoV-2 infection has been reported in many other studies also.[10,11] In

July 2020, Wu M. et.al. revealed that LDH is potentially useful follow up parameter in COVID-19 pneumonia which might assist in recognition of disease progression and can help in risk stratification and early intervention.[11] CT severity scores were significantly higher in patients admitted to critical care units compared to those discharged.

Many previous studies had demonstrated the significant strong linear regression of CRP and LDH with regard to the severity of pulmonary lesions on CT scan in COVID-19 patients.[6][7][9-13] Therefore, we aimed to analyze the relationship between inflammatory blood variables with extent of CT lesions in COVID-19 pneumonia and to find best cut-off values for blood parameters correlating with extent of lesions in chest CT to explore most useful prognostic factor for early, accurate and individualized assessment of COVID-19 patients.

2. MATERIALS AND METHODS

2.1 Study design and Participants

Our study was approved by Institutional Ethics Committee. The study was conducted in accordance with the Declaration of Helsinki. Informed consent was waived off being an observational study. It was monocentric prospective observational study conducted for 8 months duration at a tertiary care centre. Adult patients aged more than 18 years of age admitted in hospital with COVID-19 confirmed diagnosis either by Reverse transcription polymerase chain reaction (RT-PCR) test or by Rapid Antigen Test were included in our study. A total of 240 hospitalised patients who underwent CT thorax and biomarkers such as complete blood count, hsCRP, LDH, Ferritin, IL-6 and D-dimer quantification on the day of admission, were enrolled.

2.2 Clinical Data Collection

Using electronic and laboratory records of the patients, Epidemiological, Clinical and laboratory data was obtained. Detailed clinical information including demographics, signs and symptoms, comorbidities and significant past history was recorded. Patient were categorized clinically as Non-severe, Severe and Critical based on WHO COVID-19 Clinical Management (Living guidance) Guidelines.[14] Confidentiality of recorded data was maintained throughout the study period.

2.3 HRCT image acquisition

High-resolution computed tomography (HRCT) thorax was performed on the day of hospitalisation using Philips Ingenuity Core 128 Slice MDCT machine. CT severity scores

documented in all patients who had done HRCT thorax at our center. Each of the five lung lobes were visually scored for the degree of lung involvements using a 4-point- scale: 0, no involvement; 1, 1–25% involvement; 2, 26%-49% involvement; 3, 50%- 75% involvement; 4, 76%-100% involvement. The total severity CT score (the extent of pulmonary disease) was the sum of the five individuals lobar scores. The total severity CT score (parenchymal involvement) was the sum of the five individual lobar scores and defined as follows: 0, none; 1–5, minimal; 6–10, mild; 11–15, moderate; and 16–20, severe involvement of the lung.[15] **(Figure 1)**

2.4 Statistical Analysis:

All statistical analyses were performed using IBM SPSS Statistics version 20 (SPSS Inc., New York, USA). Quantitative data are presented as means ± standard deviations (SD), Qualitative data are presented as frequencies. The unpaired t test was used to compare normally distributed continuous variables between groups. The relationship between two scale variables was evaluated by Pearson's rank correlation coefficient. A value of two tailed $P<0.05$ was considered significant.

3. Results:

Presenting Characteristics

In our study mean age of study sample was 52.42 years (SD -15.28) with maximum 87 years & minimum 20 years old. There were 158 patients (65.8%) under 60 years old and 82 patients (34.1%) were more than 60 years old. Average age of patient having severe lung involvement was 55.8 years (SD ± 13.5). There were 156 male patients (65%) and 84 female patients (35%) of total study population.

Out of 240 study sample, 122 patients had an underlying disease. Diabetes (35%) was most common comorbid condition followed by hypertension (31.6%), cardiovascular disease (12%), COPD/Asthma (4.5%) and malignancy (3.7%) among study sample. Most of the study population (65.8%) presented to emergency room on day 4 to day 5 of symptoms with a median duration of 4 days. The most common symptoms at the onset of illness were Fever (66.6%), Cough (59%), Fatigue (56%), Dyspnoea (38.3%) and Myalgia (28.35%) followed by Headache (15%), Rhinorrhea (14.5%), Anorexia (10%), Diarrhea (8.7%), Ageusia (4.1%) and Anosmia (3.8%). **(Table 1)**

As per WHO COVID-19 Clinical Management Guidelines,[8] 180 (75%) patients with Non severe, 31 (12.9%) patients with Severe and 29 (12.1%) patients were having

Critical clinical presentation on admission. hsCRP and LDH levels showed significant positive correlation with the clinical severity **(Table 2)**.

Laboratory results showed raised hsCRP levels (Normal range- up to 0.7mg/dl) in 179 patients (74.6%) and elevated LDH levels (Normal range 120-246 U/L) in 141 patients (58.8%). Mean values of hsCRP and LDH in clinically critical COVID-19 disease were 11.0 mg/dl and 541.8 U/L respectively. The mean chest CT severity score of the patients in this study was 6.48 with a maximum number (n=77) having severity score between 1 and 5 followed by 76 cases having severity score between 6 and 10. Among study sample, 5.4% patients had severe lung involvement (CT score >15).

Correlation between CT severity and biological variables

Mean values of hsCRP and LDH associated with severe CT score were 11.34 mg/dl and 666.6 U/L respectively. As CT severity increases, mean values of hsCRP and LDH increases and vice versa **(Figure no.2 & 3).** The mean value of hsCRP in moderate cases was slightly higher compared to severe cases, the reason being a smaller number of severe cases compared to moderate cases**.** hsCRP & LDH were having strong correlation coefficient with CT score (Pearson correlation 0.599 & 0.570 respectively; $P<0.001$) (**Table no.3**).

Correlation analysis (Scatter dot plot) indicated that chest CT severity score showed significant positive correlation with hsCRP and LDH ($P< 0.05$) **(Figure 4)**.

Cut-off values of biological variables to predict lung lesion on chest CT (ROC analysis) (Figure 5).

ROC curve showed that inflammatory markers such as hsCRP and LDH were having sufficient credibility (Area under curve i.e. AUC > 0.7) to detect severe CT severity score (CT score >15/20). hsCRP and LDH had a good sensitivity and specificity for prediction of severe CT severity score (>15/20) and hence can be considered as a strong predictor of CT severity. If one parameter lies above or below the cut-off values i.e., hsCRP > 8.65 mg/dl and LDH > 425 U/L, severe CT severity grade was detected with 76.9% and 84.6 sensitivity respectively. **(Table 4)**.

CLINICAL OUTCOME

Out of 240 patients, 27 patients died and 213 patients were discharged. There was significant positive correlation between CT score and age, hsCRP and LDH ($P< 0.05$). It means that, as value of CT score increases, the value of blood markers also increases. From our study we also inferred that mean values of CT score, hsCRP and LDH was significantly

higher on admission among those who died due to Covid-19 in comparison with those discharged (P<0.05).

Discussion

Over the past 2 years, many studies evaluated the epidemiology, clinical characteristics, radiological and laboratory parameters of varying severities of COVID-19 infection. Being declared COVID-19 as a global pandemic, India went through the 2nd wave that had been significantly worse than 1st COVID wave. RT-PCR test is the gold standard for confirmed diagnosis of COVID-19. Moreover, CT scan facility is not available in all health care centres and remote areas to assess the extent of lung lesions and treatment options also differs in accordance with the chest CT severity. Therefore, it stands rational to evaluate the condition of patients on time by using biochemical markers. The present study on Indian population consolidated parameters such as hemogram, hsCRP, LDH, Ferritin, IL-6 and D-dimer to evaluate their relations with the chest CT severity scores on the day of hospitalization in COVID-19 disease for early recognition of disease severity and optimum management of critical illness.

Our population revealed relatively middle age population (mean 52.4 years). Average age of patient having severe lung involvement was 55.8 years. This is in par with study done by Gupta P. et.al.[16] with average age of 54.1 years and 52 years in patient having severe and non-severe lung involvement respectively. Our study showed male predominance (Male 65%) which is similar to study by Tordjman M et.al.,[9] which had a male predominance of 64.8% and study by Gupta P et.al,[16] in his study in Indian population, found male predominance of 66.5%.

The clinical spectrum of COVID-19 syndrome varies remarkably, going from asymptomatic forms to ARDS (acute respiratory distress syndrome) requiring hospitalization, critical care support. In our study, fever was the most common presentation (66.6%) followed by cough (59%), fatigue (56%) and dyspnoea (38.3%). This is in correlation with some of the international studies done in different countries which suggested fever was the most common presentation followed by cough.[6,17-19] In our study population, 50.8% patients had one or more coexisting comorbid illness such as diabetes, hypertension, cardiovascular disease, obstructive airway disorder or malignancy. Diabetes and Hypertension were the most

common comorbidities seen in Covid-19 patients in our study which is comparable to study done by Bhandari S et.al.[20] and Kurri N et.al.[21] in Indian population.

As per the results, mean CT severity score in clinically critical cases (13.2759 ±1.43) was higher than moderate and mild cases. This is similar to the study done by Bellos I et.al.[22] in Greece, which showed a mean CT severity score of 12.60 ± 4.35 among critical Covid-19 patients. In our center, HRCT Thorax was done for all patients during COVID-19 first wave to segregate into non-Covid ward, isolation ward or critical care admissions. Patients with higher CT severity score should be monitored continuously as they are potential candidates for critical care shift.

Mean values of Age, CT score, NL ratio, hsCRP and LDH were significantly higher on admission among those who died due to COVID-19 disease in comparison with those discharged ($P< 0.05$), while there was no significant difference in mean values of IL-6, Ferritin, D-dimer with respect to clinical outcome ($P>0.05$). From the inflammatory markers we studied; hsCRP & LDH showed strong correlation coefficient with CT severity score (Pearson correlation 0.599 & 0.570 respectively, $P=0.00$)

C-reactive protein is produced by liver secondary to ongoing inflammation and key protein of the acute phase response. It appears in blood within 6–10 hours after tissue damage with a plasma half-life of 19 hours and is produced without a memory response.[23] In our study mean hsCRP level in critical and severe cases was significantly higher than mean hsCRP in non-severe cases ($P<0.05$). Mean hsCRP of dead patients was significantly higher than discharged patients ($P<0.05$). Similar observations were noted in various studies. Saleemi S et.al.[17] found that patients with severe Covid-19 had higher CRP levels. Tan C. et.al.[6] reported that CRP in severe patients increased significantly at the initial stage of disease and CRP predicted early Covid-19. Huang Y et.al.[24] concluded that CRP was significantly elevated in non-survival group compared to survival group of Covid-19 patients. hsCRP showed strong significant positive correlation with CT severity score (Pearson correlation: 0.599, $P<0.001$). Sun D. et.al.[10] found hsCRP having significant positive correlation with total lesion CT score group ($P=0.001$). Similarly, Li R. et.al.[19] in their study showed significant positive correlation of CT score with CRP ($r=0.616$, $P<0.001$) and concluded that CRP is expected to predict disease severity and prognosis of COVID-19 infection. Canovi S. et.al.[25] demonstrated the significant progressive increase in CRP and LDH levels along with other biomarkers, as more and more parenchymal worsening on CT scan. These results are also in correlation with studies published by, Tordjman M et.al.,[9] Zhang J. et.al.,[18] Orlacchio A et.al.[26] All these studies were supportive of significant

positive correlation of CRP with CT severity score. Tordjman M. et.al.[9] also suggested that along with LDH, CRP can be used to predict parenchymal extent of the pneumonia.

We also studied another biomarker Lactate dehydrogenase i.e. LDH, to determine whether they have any significant contribution in assessing the COVID-19 severity. LDH is found in high concentrations in lung tissue (isozyme 3) and therefore patients with severe COVID-19 pneumonia can be anticipated to have high LDH levels in the circulation, as a severe form of interstitial pneumonia, often leading to acute respiratory distress syndrome (ARDS), is the hallmark of the disease.[4] Wu MY et.al.[11] reported that LDH levels in severe COVID-19 patients were higher than those with non-severe patients. Yang C. et.al.[27] also mentioned that there is increased likelihood of severe Covid -19 infection in patients with increased LDH levels. Huang Y. et.al.[24] also noticed that LDH and other inflammatory markers are significantly increased in non-survival group. Mean LDH level in patients with higher CT severity was found to be higher than those with lesser CT severity scores. LDH and CT severity was having a strong significant positive correlation (Pearson correlation=0.570, $P<0.001$**).** Wu MY et.al.[11] demonstrated that increase or decrease of LDH was indicative of radiographic progress or improvement, respectively. Feng Z et.al.[28] and Dogan HO et.al.[29] also found strong positive correlation between CT severity score and LDH. Tordjman M et.al.[9] reported that with a cut-off value LDH> 380, severe pneumonia on CT can be detected with 100% sensitivity while in our study we found severe lung lesions on chest CT detected with 84.6% sensitivity at a cut-off value LDH> 425. They concluded that LDH was the biomarker having strongest correlation with CT severity score (r=0.67) while CRP was moderately correlated (r=0.52). This is in contrast to our study, where we found hsCRP as having strongest correlation(r=0.599) compared to LDH (r=0.570).

Limitation of the present study was the small sample size along with less clinically critical cases. More such studies are required on Indian population to formulate optimum guidelines.

Conclusion

We found that inflammatory markers we studied, had significant positive correlation with CT severity score and clinical severity of COVID-19 disease. hsCRP had strong significant positive correlation with CT severity score followed by LDH. Inflammatory markers especially hsCRP and LDH along with CT severity score can help clinicians to triage the patients in emergency room. These markers can guide clinicians to identify the patients with possible critical outcomes, hence assisting in early recognition of disease progression and

timely critical care transfer especially in remote peripheral areas where CT scan facility is unavailable.

References:

1. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020 [Internet]. Who.int. [cited 2021 Sep 16]. Available from: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020
2. Ranjan R, Sharma A, Verma MK. Characterization of the second wave of COVID-19 in India [Internet]. bioRxiv. 2021 [cited 2021 Aug 27]. p. 2021.04.17.21255665. Available from: https://www.medrxiv.org/content/10.1101/2021.04.17.21255665v1.full
3. Jain S, Gautam V, Naseem S. Acute-phase proteins: As diagnostic tool. J Pharm Bioallied Sci. 2011;3(1):118–27.
4. Henry BM, Aggarwal G, Wong J, Benoit S, Vikse J, Plebani M, et al. Lactate dehydrogenase levels predict coronavirus disease 2019 (COVID-19) severity and mortality: A pooled analysis. Am J Emerg Med [Internet]. 2020;38(9):1722–6. Available from: http://dx.doi.org/10.1016/j.ajem.2020.05.073
5. Helal I, Zerelli L, Krid M, ElYounsi F, Ben Maiz H, Zouari B, et al. Comparison of C-reactive protein and high-sensitivity C-reactive protein levels in patients on hemodialysis. Saudi J Kidney Dis Transpl [Internet]. 2012 [cited 2022 Mar 15];23(3):477–83. https://www.sjkdt.org/temp/SaudiJKidneyDisTranspl233477-6656342_182923.pdf
6. Tan C, Huang Y, Shi F, Tan K, Ma Q, Chen Y, et al. C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. J Med Virol. 2020;92(7):856–62.
7. Chen W, Zheng KI, Liu S, Yan Z, Xu C, Qiao Z. Plasma CRP level is positively associated with the severity of COVID-19. Ann Clin Microbiol Antimicrob [Internet]. 2020;19:1–7.

8. Poggiali E, Zaino D, Immovilli P, Rovero L, Losi G, Dacrema A, et al. Lactate dehydrogenase and C-reactive protein as predictors of respiratory failure in CoVID-19 patients. Clin Chim Acta. 2020;509:135–8.
9. Tordjman M, Mekki A, Mali RD, Monnier H, Neveu S, Chassagnon G, et al. Determining extent of COVID-19 pneumonia on CT based on biological variables. Respir Med. 2020;175(106206):106206.
10. Sun D, Li X, Guo D, Wu L, Chen T, Fang Z, et al. Ct quantitative analysis and its relationship with clinical features for assessing the severity of patients with COVID-19. Korean J Radiol. 2020;21(7):859–68.
11. Wu MY, Yao L, Wang Y, Zhu XY, Wang XF, Tang PJ, et al. Clinical evaluation of potential usefulness of serum lactate dehydrogenase (LDH) in 2019 novel coronavirus (COVID-19) pneumonia. Respir Res. 2020;21(1):1–6.
12. Wang L. C-reactive protein levels in the early stage of COVID-19. Med Mal Infect [Internet]. 2020 [cited 2022 Feb 21];50(4):332–4. Available from: https://www.ncbi.nlm.nih.gov/labs/pmc/articles/PMC7146693/
13. Yang S, Shi Y, Lu H, et al. Clinical and CT features of early stage patients with COVID-19: a retrospective analysis of imported cases in Shanghai, China. Eur Respir J 2020; 55: 2000407 [https://doi.org/10.1183/13993003.00407-2020]
14. World Health Organization. (2021). COVID-19 clinical management: living guidance, 25 January 2021. World Health Organization. https://apps.who.int/iris/handle/10665/338882.
15. Hu Y, Zhan C, Chen C, Ai T, Xia L. Chest CT findings related to mortality of patients with COVID-19: A retrospective case-series study. PLoS One. 2020;15(8):e0237302.
16. Gupta P, Halani A, Samuel T, Singh DP. Association of inflammatory biomarkers with radiological severity for COVID-19 patient risk stratification: An Indian perspective. Asian J Med Sci. 2021;12(4):1–7.
17. Saleemi S, Skaff F, Albaiz F, Almaghrabi R, Alrabiah F, Alhajji M. Radiology Features of Chest Imaging and Its Correlation to Clinical Severity in Patients with COVID-19. Int J Med Imaging. 2020;8(2):35.
18. Zhang J, Meng G, Li W, Shi B, Dong H, Su Z, et al. Relationship of chest CT score with clinical characteristics of 108 patients hospitalized with COVID-19 in Wuhan, China. Respir Res. 2020;21(1):1–11.
19. Li R, Liu G, Huang X, Jia C, Xia Z, Song W, et al. Dynamic changes in clinical and CT characteristics of COVID-19 cases with different exposure histories: A retrospective study. BMC Infect Dis. 2020;20(1):1–14.

20. Bhandari S, Rankawat G, Bagarhatta M, Singh A, Singh A, Gupta V, et al. ClinicoRadiological Evaluation and Correlation of CT Chest Images with Progress of Disease in COVID-19 Patients. J Assoc Physicians India. 2020;68(7):34–42.
21. Kurri N, Tyagi B, Singhal E, Gupta N, Agarwal AK, Gupta V, et al. Assessing the Impact of Inflammatory Markers and CT Severity Score on Disease Severity of COVID-19 Patients Admitted to ICU at a Tertiary Hospital. 2021;69(December 2019):41–5.
22. Bellos I, Tavernaraki K, Stefanidis K, Michalopoulou O, Lourida G, Korompoki E, et al. Chest CT severity score and radiological patterns as predictors of disease severity, ICU admission, and viral positivity in COVID-19 patients. Respir Investig. 2021;59(4):436–45.
23. Jain S, Gautam V, Naseem S. Acute-phase proteins: As diagnostic tool. J Pharm Bioallied Sci. 2011;3(1):118–27
24. Huang Y, Lyu X, Li D, Wang L, Wang Y, Zou W, et al. A cohort study of 676 patients indicates Ddimer is a critical risk factor for the mortality of COVID-19. PLoS One [Internet]. 2020;15(11 November):1–11.
25. Canovi S, Besutti G, Bonelli E, Iotti V, Ottone M, Albertazzi L, et al. The association between clinical laboratory data and chest CT findings explains disease severity in a large Italian cohort of COVID-19 patients. BMC Infect Dis. 2021;21(1):157.
26. Orlacchio A, Gasparrini F, Roma S, Ravà MS, Salvatori E, Morosetti D, et al. Correlations between chest-CT and laboratory parameters in SARS-CoV-2 74 pneumonia: A single-center study from Italy. Medicine (Baltimore). 2021;100(14):e25310.
27. Yang C, Ma X, Wu J, Han J, Zheng Z, Duan H, et al. Low serum calcium and phosphorus and their clinical performance in detecting COVID-19 patients. J Med Virol. 2021;93(3):1639–51
28. Feng Z, Yu Q, Yao S, Luo L, Zhou W, Mao X, et al. Early prediction of disease progression in COVID-19 pneumonia patients with chest CT and clinical characteristics. Nat Commun. 2020;11(1):1–9.
29. Doğan HO, Bolat S, Büyüktuna SA, Sarıismailoğlu R, Çetinkaya N, Doğan K, et al. The use of laboratory parameters and computed tomography score to determine intensive care unit requirement in COVID-19. Turkish Journal of Biochemistry [Internet]. 2021;0(0). Available from: http://dx.doi.org/10.1515/tjb-2020-0359

Tables:

Table 1- Demographics Of patients with SARS CoV2 infection

Variable		Total (%) (N=240)	Critical (N=29)	Severe (N=31)	Non severe (N=180)
Sex	Male	156 (65%)	18 (62.1%)	21 (67.7%)	117 (65%)
	Female	84 (35%)	11 (37.9%)	10 (32.2%)	63 (35%)
Comorbidities	Diabetes mellitus	84 (35%)	20 (68.9%)	9 (29%)	54 (30%)
	Hypertension	76 (31.6%)	12 (41.3%)	11 (35.5%)	53 (29.4%)
	Cardiovascular disease	29 (12%)	6 (20.6%)	2 (6.5%)	21 (11.7%)
	COPD/ Asthma	11 (4.5%)	1 (3.4%)	2 (6.5%)	8 (4.4%)
	Malignancy	9 (3.7%)	2 (6.9%)	1 (3.2%)	6 (3.3%)
Symptoms	Fever	160 (66.6%)	18 (62.1%)	21 (67.7%)	121 (67.2%)
	Cough	142 (59%)	22 (75.9%)	18 (58%)	102 (56.7%)
	Fatigue	135 (56%)	13 (44.8%)	18 (58%)	104 (57.8%)
	Dyspnea	92 (38.3%)	21 (72.4%)	21 (67.7%)	50 (27.8%)
	Myalgia	68 (28.3%)	1 (3.4%)	8 (25.8%)	59 (32.8%)
	Headache	36 (15%)	3 (10.3%)	3 (9.7%)	30 (16.7%)
	Rhinorrhea	35 (14.5%)	2 (6.9%)	0 (0%)	32 (17.8%)
	Anorexia	24 (10%)	2 (6.9%)	1 (3.2%)	21 (11.7%)
	Diarrhea	21 (8.7%)	2 (6.9%)	2 (6.5%)	17 (9.4%)
	Ageusia	10 (4.1%)	2 (6.9%)	2 (6.5%)	6 (3.3%)
	Anosmia	9 (3.8%)	1 (3.4%)	2 (6.5%)	6 (3.3%)
Clinical €Outcome	Discharge	213 (88.7%)	6 (20.7%)	30 (96.8%)	177 (98.3%)
	Death	27 (11.3%)	23 (79.3%)	1 (3.2%)	3 (1.7%)

Table 2 - Correlation of clinical severity with hsCRP and LDH

Variable		hsCRP	LDH
Clinical severity	Pearson Correlation	.530[¥]	.496[¥]
	Sig. (2-tailed)	.000	.000

[¥]Correlation is significant at the 0.01 level (2-tailed)

Table 3 - Correlation of CT severity (CT score) with inflammatory markers

Variable		Il-6	Ferritin	D-dimer	hsCRP	LDH	NL ratio
CT Score	Pearson Correlation	.188[€]	.328[€]	.262[€]	**.599[€]**	**.570[€]**	.390[€]
	Sig. (2-tailed)	.003	.000	.000	.000	.000	.000

[€]Correlation is significant at the 0.01 level (2-tailed)

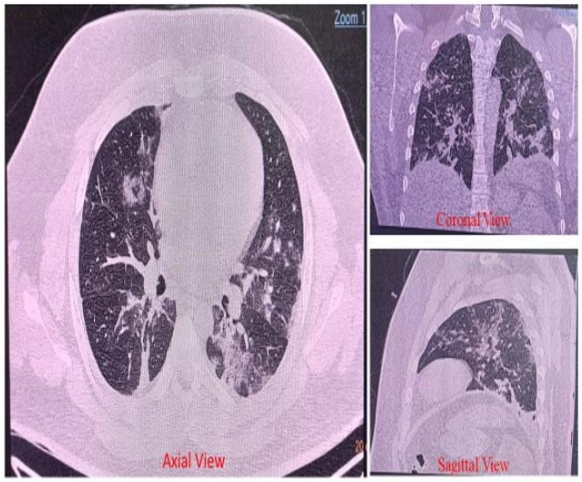
Table 4 - Receiver operating curves (ROC) characteristic for CT severity in COVID-19 patients

Variable	AUC	Cut Off	Sensitivity	Specificity
hsCRP	0.796	8.65	76.9	74.9
LDH	0.919	425	84.6	84.1

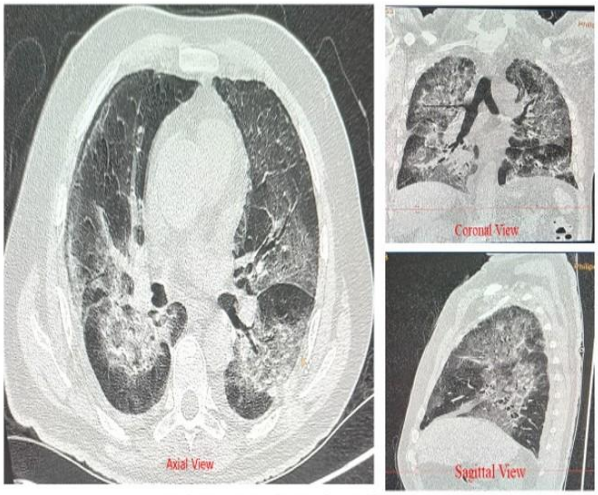
Abbreviations

AUC- Area under curve, CT - Computed tomography, COPD- Chronic obstructive pulmonary disease, COVID – Coronavirus disease, SARS CoV 2- severe acute respiratory syndrome coronavirus 2, CRP- C-reactive protein, HRCT- High-resolution computed tomography, hsCRP- High sensitivity C-reactive protein, LDH- Lactate dehydrogenase, MDCT- Multi-detector computed tomography, RT-PCR – Reverse transcription polymerase chain reaction, WHO- World health organization

Figure 1



CT Thorax images showing "Mild" CT severity grade.



CT Thorax images showing "Severe" CT severity grade.

Figure 2

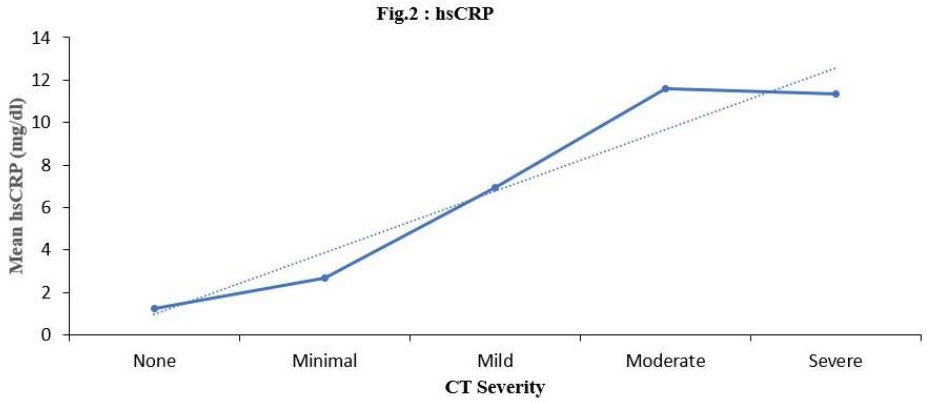


Figure 3

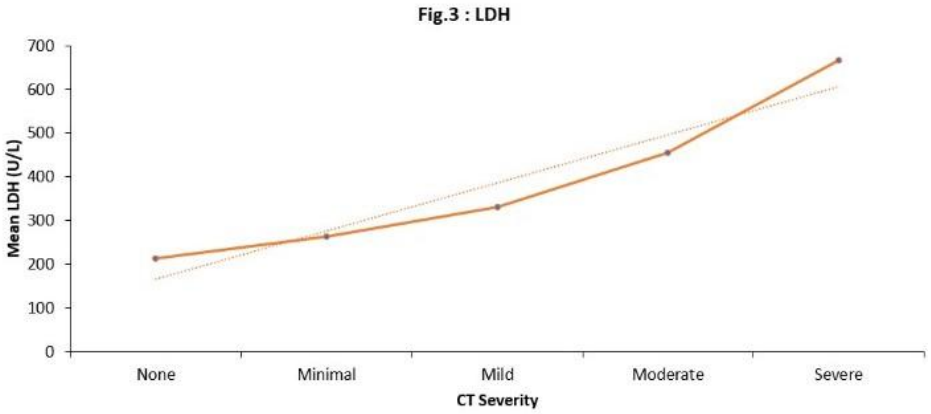


Figure 4

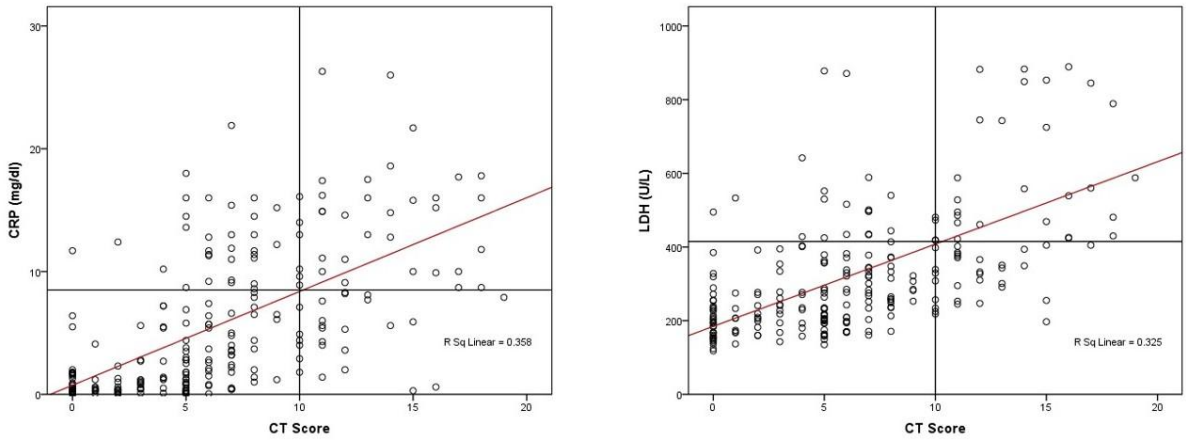


Figure 5

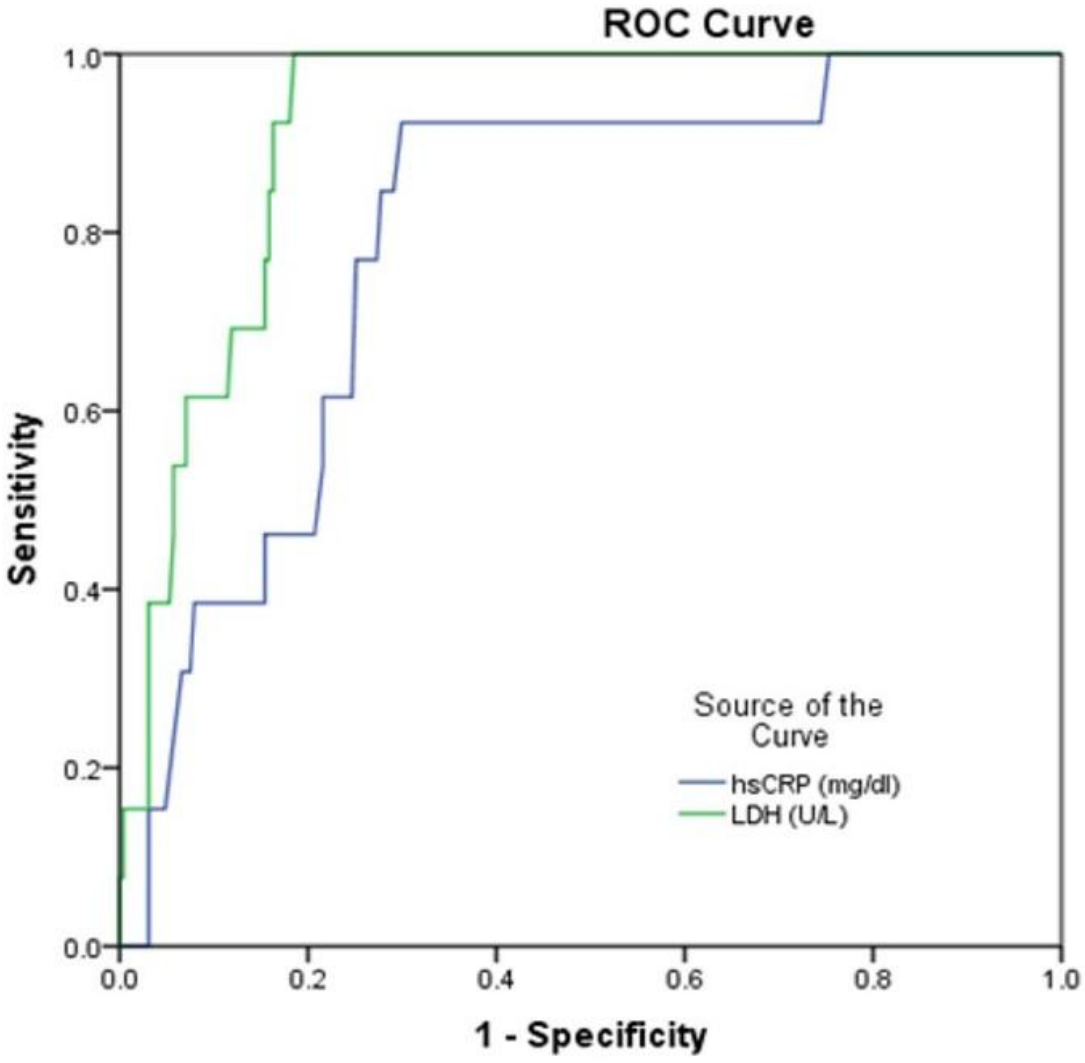


Figure Legends

Figure 1 - Axial, Coronal and Sagittal view of CT thorax showing extent of parenchymal

Involvement

Figure 2 - Correlation between CT severity and hsCRP

Figure 3 - Correlation between CT severity and LDH

Figure 4 - Correlation analysis between CT scores and markers i.e. hsCRP and LDH

Figure 5 - ROC curve analysis of hsCRP and LDH