Pak J Chest Med. 2023;29(04)

Original Article

journal homepage: https:/www.pjcm.net/

Pakistan Journal of Chest Medicine

Official journal of Pakistan Chest Society

Relation of positive HRCT findings and levels of different inflammatory markers in COVID patients

Syed Yar Muhammad Shah[1], Khalid Shahzad[2], Sabeel Iftikhar Ahmed[1], Khalid Ahmad[1], Muhammad Irshad Khan[2], Abdul Hameed Jamali[2], Mohammad Yasin[3] ✉

[1]Depatment of Medicine, Ayub Teaching Hospital, Abbottabad – Pakistan [2]Depatment of Medicine, Pakistan Atomic Energy Commission General Hospital, Islamabad – Pakistan [3]Depatment of Pulmonology, Ayub Medical College, Abbottabad - Pakistan

Corresponding Author:
Mohammad Yasin
Department of Pulmonology,
Ayub Medical College,
Abbottabad - Pakistan
Email:yasinmohammadjan@yahoo.com

Article History:

Received:	July 12, 2023
Revised:	Sep 25, 2023
Accepted:	Nov 11, 2023
Available Online:	Dec 02, 2023

Author Contributions:
MY conceived idea, SIA SYMS drafted the study, SIA SYMS collected data, KS MI did statistical analysis and interpretation of data, MY AHJ critical reviewed manuscript. All approved final version to be published.

Declaration of conflicting interests:
The authors declare that there is no conflict of interest.

How to cite this article:
Shah SYM, Shahzad K, Ahmed SI, Ahmad K, Khan MI, Jamali AH, Yasin M. Relation of positive HRCT findings and levels of different inflammatory markers in COVID patients. Pak J Chest Med. 2023;29 (04):423-431.

A B S T R A C T

Background: COVID-19 is an acute infectious respiratory illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that spreads rapidly and causes the pandemic. High resolution computed tomography (HRCT) chest, is a non-invasive and rapid method for diagnosing the disease and providing essential information regarding the evolution of COVID-19 pneumonia. Inflammatory markers have been an important method of assesing the severity of patients with COVID-19.

Objective: The present study was conducted with the aims to find the relation between the HRCT findings and levels of different inflammatory markers and their trends in COVID-19 patients.

Methodology: A prospective cross-sectional observational study done on patients with COVID-19 in Covid isolation unit, Ayub teaching hospital Abbottabad, from 1st September 2021 to 30th November 2022. A total of 200 patients were evaluated for HRCT findings and systemic inflammatory markers levels. Data was collected prospectively on the basis of HRCT chest scans and inflammatory markers levels by using a bioproforma containing relevant variables. Data analysis was done by using SPSS 16 and results were drawn in the form of tables, figures, bar charts and scattered diagrams.

Results: A total of 200 patients, with moderate to severe signs and symptoms of COVID-19 disease were evaluated. The age of patients was in range from 33 years to 87 years with the mean of 55 years. One hundred and five were males and 95 were females. Ninty patients had HRCT severity scores of 7-18 and 110 patients had HRCT severity score of ≥ 19 out of 25. Serum levels of systemic inflammatory markers were raised in most of the patients. About 170 patients had CRP levels more than 100mg/dL, serum ferritin levels were raised (>1000ng/mL) in 165 patients, neutrophils to lymphocyte ratio was more than 1.5 in 166 patients, ALT levels were more than 100U/L in 161 patients, D-dimers levels were significantly increased in 154 patients and 150 patients had raised levels of IL-6 i.e. more than 44pg/mL. Procalcitonin levels were also raised i.e. more than 0.25ng/mL in 134 patients.

Conclusion: The more involvement of lung lobes parenchyma with COVID-19 on HRCT, is associated with raised systemic inflammatory markers. Serum ALT, CRP, D-dimers, Neutrophils to lymphocytic ratio, IL-6 and ferritin levels were significantly raised in most of the patients with HRCT findings of severe lung lobes involvement.

Keywords: COVID-19; HRCT; Lactate Dehydrogenase; C-reactive Protein; Interleukin-6

Introduction

The Coronavirus disease 2019 (COVID-19) outbreak, first recorded in December 2019, marks a pivotal moment in global health. Originating in Wuhan, Hubei Province, China, the disease presented initially as a cluster of atypical pneumonia cases. COVID-19, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), rapidly transcended geographical boundaries, culminating in a worldwide pandemic. This unprecedented event has drawn significant attention from the medical and scientific communities, leading to intensive research and public health measures aimed at controlling the spread and impact of the virus.[1,2]

The timely diagnosis of diseases is paramount for successful treatment, which also holds true for COVID-19. Various diagnostic methods are employed to detect COVID-19 infection, with the nasopharyngeal swab reverse transcriptase-polymerase chain reaction (RT-PCR) test being the primary technique. This test, regarded as the benchmark for COVID-19 diagnosis, aims to detect the genetic material of the SARS-CoV-2 virus.[3,4] However, the sensitivity of the RT-PCR test, estimated at approximately 71%, can be affected by several factors. These include the quality of clinical samples, the efficacy of different testing kits, and the viral load present in the patients. The presence of these variables underscores the need for additional diagnostic approaches to enhance accuracy and reliability.[5,6]

High-resolution computed tomography (HRCT) of the chest is gaining recognition as a vital non-invasive diagnostic tool in COVID-19. This method facilitates a rapid evaluation and provides essential insights into the progression of COVID-19 pneumonia. Extensive research has highlighted characteristic CT patterns observed in patients afflicted with COVID-19. These patterns include ground-glass opacities (GGO), consolidation, and pleural effusions. Identifying these radiological signs is crucial not only for diagnosing COVID-19 but also for monitoring the disease's progression. This dual role of HRCT enhances its significance in the medical management of COVID-19 patients.[7]

The reliance on HRCT has been bolstered by its ability to offer immediate and detailed imaging of the lungs, an aspect critical in managing respiratory illnesses like COVID-19. The imaging can reveal lung abnormalities that are indicative of COVID-19 pneumonia, even in cases where RT-PCR tests yield negative results. This aspect is particularly beneficial when RT-PCR testing faces limitations due to factors like the timing of the test or sample collection errors. Consequently, HRCT is an indispensable tool in the early detection and management of COVID-19, especially in symptomatic patients or those with a high clinical suspicion of infection despite negative RT-PCR results.

Inflammatory markers have been an important method of severity of patients with COVID-19.[7] Infections, and inflammatory events cause systemic reactants to be released like CRP, LDH, procalcitonin, and ferritin into the body within hours or days. The possibility of lung disease should be considered in COVID-19 patients, especially after ventilator use.8 In secondary infection, these acute phase reactants can be further increased. Inflammatory markers always correlate with disease severity.[9,10] Some studies suggest that patients with severe COVID-19 have higher levels of inflammatory markers compared to mild or moderate patients.[11].

Different research was conducted for accurate and fast diagnosis due to this COVID-19 pandemic, with intense research efforts to refine diagnostic methods and better understand the disease's complexities. While the reverse transcriptase-polymerase chain reaction (RT-PCR) test remains a cornerstone in COVID-19 diagnosis, its limitations underscore the need for supplementary approaches, such as high-resolution computed tomography (HRCT) of the chest. HRCT's capacity to swiftly and accurately assess lung abnormalities associated with COVID-19 pneumonia, even in cases with negative RT-PCR results, has positioned it as a critical tool for early detection and disease management. Furthermore, the significance of inflammatory markers in gauging disease severity cannot be overstated, as they provide valuable insights into the patient's clinical condition. Thus, this study seeks to investigate deeper into the role of HRCT and inflammatory markers in the diagnosis and prognosis of COVID-19 to contribute to the ongoing efforts to combat this global health crisis and improve patient outcome.

Objective

The present study was conducted with the aims to find the relation between the HRCT findings and levels of different inflammatory markers and their trends in COVID-19 patients.

Methodology

A prospective cross-sectional observational conducted at the COVID-19 isolation unit of Ayub Teaching Hospital, Abbottabad, spanning from September 1, 2021, to November 30, 2022. The research focused on a cohort of 200 patients who exhibited severe signs and symptoms of COVID-19, all of whom had previously received confirmation through PCR testing and HRCT chest scans. The evaluation of HRCT chest findings comprised an assessment of multiple parameters, including total severity score (TSS) in accordance with the classification provided by the Fleischer Society Glossary. Additionally, the presence of GGO, the appearance of a crazy paving

pattern, and the extent of consolidation in thin-section scans were meticulously examined.[12] The assessment involved the utilization of a semi-quantitative scoring system, which was instrum-ental in estimating the extent of pulmonary involvement attributed to COVID-19-related abnormalities. To achieve this, the bilateral lungs were segmented into five distinct zones based on their anatomical structure: the left upper lobe, left lower lobe, right upper lobe, right middle lobe, and right lower lobe. Each lung lobe was assigned a score on a scale of 0 to 5, reflecting the following criteria: score 0 (0% involvement), score 1 (less than 5% involvement), score 2 (5% to less than 25% involvement), score 3 (25% to less than 50% involvement), score 4 (50% to less than 75% involvement), and score 5 (75% or greater involvement). The cumulative severity score was calculated based on the sum of scores for all lung zones, yielding a total severity score ranging from 0 to 25. These scores were subsequently categorized into three severity levels: mild (< 7), moderate (7-18), and severe (≥ 19).

Concurrently, the study included an analysis of systemic inflammatory markers, which were systematically ordered for assessment. A specialized bioproforma containing pertinent variables relevant to the research was meticulously designed to facilitate data collection. Subsequently, data was prospectively gathered from patients admitted to the COVID isolation units, ensuring a robust and comprehensive dataset.

The collected data underwent a rigorous analysis employing SPSS version 16, with the results presented through various means, including tables, figures, bar charts, and scatter diagrams. This multifaceted approach to data analysis aimed to provide a comprehensive and insightful overview of the study's findings, enhancing the understanding of the relationship between HRCT chest findings, systemic inflammatory markers, and the severity of COVID-19 in the examined patient cohort.

Results

A total of 200 patients, with moderate to severe signs and symptoms of COVID-19 disease were evaluated. The age of patients was in range from 33 years to 87 years with the mean of 55 years.

Among them 105 were males and 95 were females. Among them 101 patients had smoking history, 89 were non-smokers while 10 had smoking status in past. About 103 patients had respiratory rate up to 25 per minute while 97 patients were having respiratory rate more than 25 per min. Among them 38 patients needed supplemental oxygen up to 3L/min while 162 patients required supplemental oxygen more than 3L per minute. On the

Table 1. Demographics, vitals and HRCT score of study cases.

characteristics		Frequency	Percentage%
Gender	Male	105	52.5%
	Female	95	47.5%
Smoking Status	Yes	101	50.5%
	No	89	44.5%
	Ex-Smoker	10	5%
Respiratory Rate	Up to 25/min	103	51.5%
	>25/min	97	48.5%
Oxygen Requirement/min	Up to 3L	38	19%
	>3L	162	81%
HRCT Severity Score	<7	0	0%
	7-18	90	45%
	19-25	110	55%

Table 2. Descriptive Statistics of the study

Characteristics	N	Minimum	Maximum	Mean	Std. Deviation
Age of patient in years	200	33	87	55.19	12.479
Lactate dehydrogenase	200	134	34567	1853.92	3921.739
C-reactive protein	200	22	322	193.70	76.790
Serum ferritin	200	60	6543	1784.03	948.947
D-dimers	200	88	6000	1561.93	1004.126
Alanine transaminase	200	25	1200	230.31	188.820
Nneutrophils/lymphocytes ratio	200	1.00	14.00	2.5371	1.18633
Procalcitonin	200	.009	4.000	.57534	.492814
Interleukin-6	200	8	2457	220.24	271.123
High resolution computed tomography	200	10	25	18.02	4.214

basis of HRCT chest, no patient had score less than 7 (mild lung lobes involvement), 90 patients had score within 7-18 (moderate) and 110 patients had severity score of more than 19 out of 25 (severe lung lobes involvement).

The serum lactate dehydrogenase (LDH) levels of all the patients, was in the range of 134-34567U/L with the mean of 1853.92 U/L. The minimum C-reactive protein (CRP) level was 22mg/dL and maximum was 322 mg/dL with the mean of 193.7mg/dL. Serum ferritin levels were in the range of 60-6543ng/mL with the mean of 1784ng/mL. Serum D-dimers levels was from 88-6000U/L ng/mL with the mean of 1561.93. Alanine transaminase levels were in the range of 25-1200 U/L with the mean of 230 U/L. Neutrophils to leukocytes ratio in complete blood picture was in the range of 1.0 to14.0. Procalcitonin levels were in the range of 0.009 -4.0ng/mL. Interleukin-6 levels were in the range of 8-2457 pg/mL with the mean of 220.24. HRCT severity score was in the range of 10-25 with the mean of 18.

Table 3 shows the relation of HRCT severity score to the levels of various systemic inflammatory markers. Serum LDH levels were consistently raised in different HRCT severvity scores. About 30 patients had serum CRP levels below 100mg/dL (20 in moderate and 10 in severely lung lobes involvement on HRCT chest) while 170 patients had moderately and severely raised levels of CRP within 100-200mg/dL and above 200mg/dL respectively. The raise in serum CRP levels was consistent in both moderate and severe HRCT severity scores. About 19 patients had serum ferritin levels less than 500ng/mL (10 patients with moderate and 9 patients with severe involvement of lung lobes), 16 patients had serum ferritin levels within the range of 500-1000ng/dL while 165 patients had raised serum ferritin levels of more than 1000ng/dL (including 73 patients with moderate lungs involvement and 92 patients with severe lungs involvement on HRCT chest). Only 33 patients had serum D-dimers levels less than 500ng/mL, 13 patients had levels within the range of 500-1000ng/ml and 154 patients had raised serum D-dimers level i.e. more than 1000ng/mL (including 71 patients with moderate and 83 patients with severe HRCT chest changes).

Among 200 patients, 15 had serum alanine aminotransferases (ALT) levels less than 50U/L, 24 patients had ALT levels of 50-100U/L and 161 patients had serum ALT levels of more than 100U/L (including 70 patients with moderate and 83 patients with severe HRCT chest changes).

Similar rise in the serum levels of others inflammatory markers were seen. Neutrophils to leukocytes ratio greater than 1.5 was seen in more than 166 patients, interleukin-6 levels of more than 44pg/mL was seen in 150 patients. The serum procalcitonin levels of greater than 0.25ng/mL was seen in 134 patients.

Discussion

The findings of this study, encompassing a cohort of 200 patients with severe signs and symptoms of COVID-19,

Table 3. Cross tab showing relation of HRCT severity score to levels of different inflammatory markers

HRCT Severity Score	LDH Level U/L			CRP mg/dL			Serum Ferritin ng/mL			D-Dimers ng/mL			ALT U/L			Neut/ Lym counts		IL-6 pg/mL		Pro-Calcitonin ng/mL	
	<500	500-1000	> 1000	<100	100-200	>200	<500	500-1000	> 1000	<500	500-1000	> 1000	<50	50-100	>100	≤1.5	>1.5	≤44	>44	≤.25	>.25
7-18 (Moderate)	24	31	35	20	27	43	10	7	73	17	2	71	5	15	70	13	77	25	65	34	56
19-25 (Severe)	38	30	42	10	52	48	9	9	92	16	11	83	10	9	91	21	89	25	85	32	78
Total (n)	62	61	77	30	79	91	19	16	165	33	13	154	15	24	161	34	166	50	150	66	134
	200			200			200			200			200			200		200		200	

have provided valuable insights into the relationships between various systemic inflammatory markers, HRCT chest findings, and the severity of lung involvement. These insights have important implications for understanding the disease's pathophysiology and improving its clinical management.

One key observation from this study is the age distribution of the patients, ranging from 33 to 87 years with a mean age of 55 years. This range underscores the diverse demographic affected by COVID-19, with older individuals being more prominently represented. This aligns with existing literature, which highlights the increased susceptibility of older populations to severe COVID-19 outcomes.

During the study period, 200 patients with severe sign and symptoms of COVID-19 were evaluated. The age of the patient varies from 33 years to 87 years with the mean age of 55 years.

A notable finding is that the majority of patients (162 out of 200) required supplemental oxygen of more than 3L/min, indicating the severity of the disease within the study population. This observation emphasizes the clinical significance of identifying markers that can aid in early disease severity assessment.

Among them about 162 patients required supplemental oxygen of more than 3L/min, showing the severity of the disease. The evaluation of HRCT chest of the patients showed that, 90 (45%) patients had total severity score of 7-18 hence moderate involvement of lung lobes while 110 (55%) patients had severity score of more than 19 out of 25.

In our study, ALT levels had positive correlation with HRCT findings. Among 200 patients about 161 (80.5%) had ALT levels of more than 100U/L. ALT levels were raised in

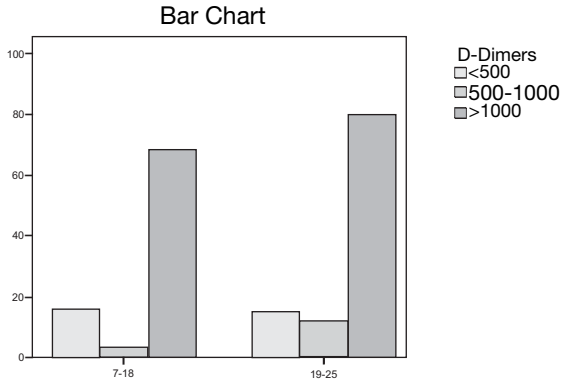

Figure 1. HRCT Score and D-dimers

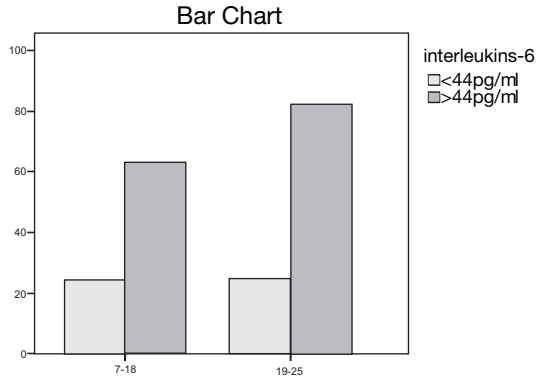

Figure 2. HRCT score and interleukins level

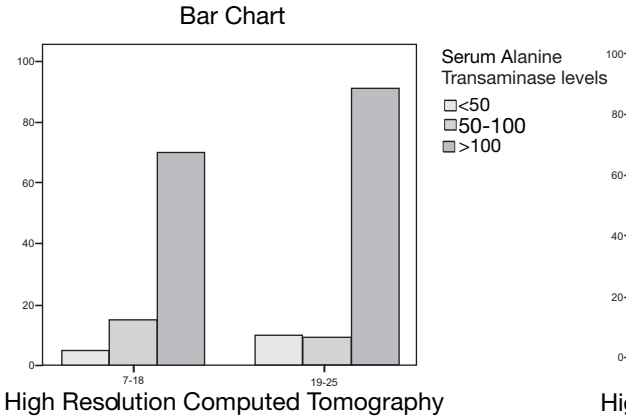

Figure 3. HRCT score and ALT levels

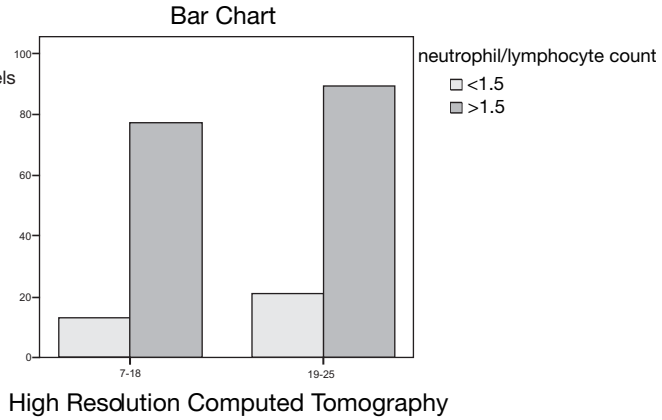

Figure 4. HRCT score and Neut/lymph count

patients with moderate and severe lung lobes involvements on HRCT scan. The findings of our study, which reveal a positive correlation between ALT (Alanine Aminotransferase) levels and HRCT (High-Resolution Computed Tomography) findings in COVID-19 patients, provide valuable insights into the complex interplay between liver function and the severity of lung involvement in this disease. One possible justification for these findings lies in the systemic nature of COVID-19. COVID-19 is not solely a respiratory illness but a multi-systemic disease that can affect various organs throughout the body. The liver, as a vital organ involved in numerous metabolic and immune functions, is susceptible to the consequences of a hyperactive immune response triggered by the SARS-CoV-2 virus. When COVID-19 progresses to severe stages, the body often mounts an exaggerated immune response, someti-mes referred to as a "cytokine storm." This immune over-activity can lead to widespread inflamma-tion and tissue damage, affecting not only the lungs but also other organs, including the liver. ALT is an enzyme primarily found in liver cells, and its presence in the bloodstream at elevated levels is indicative of liver cell damage or inflammation. In patients with moderate and severe lung involvement observed on HRCT scans, it is plausible that the systemic inflammatory response triggered by COVID-19 is more pronounced. This heightened inflammation can extend beyond the respiratory system and impact the liver, causing an increase in ALT levels. This observation underscores the interconnectedness of COVID-19's impact on different organ systems. Additionally, factors such as medications used in the treatment of severe COVID-19 cases, as well as the potential for secondary bacterial infections, can contribute to liver injury and further elevate ALT levels. These factors add complexity to the relationship between ALT levels and lung involvement on HRCT scans.

It's important to emphasize that elevated ALT levels

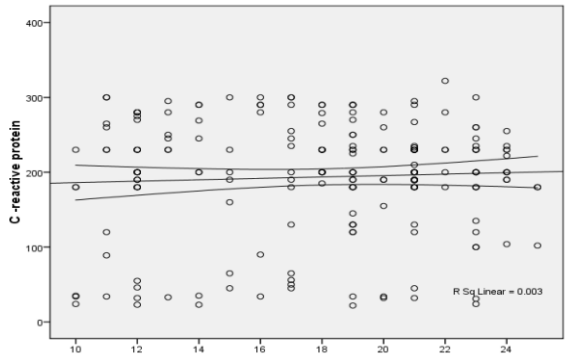

Figure 5. Correlation of HRCT severity score and CRP levels

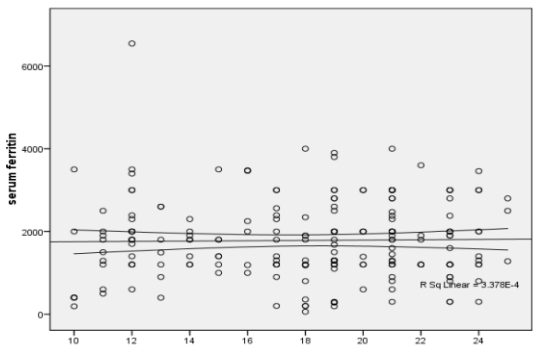

Figure 6. Correlation of HRCT severity score and serum ferritin levels

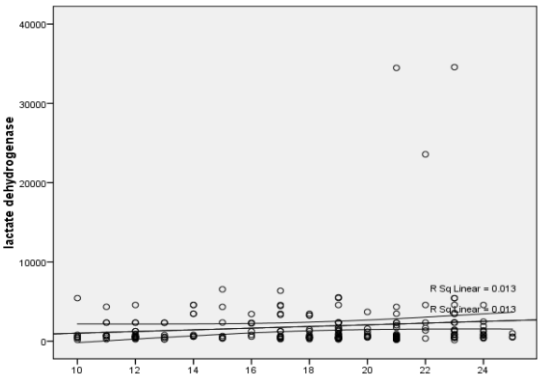

Figure 7. Correlation of HRCT severity score and LDH levels.

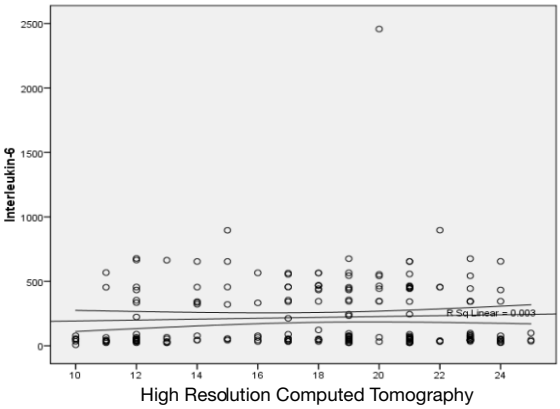

Figure 8. Correlation of HRCT severity score and interleukin-6 level.

should not be viewed in isolation as a marker of COVID-19 severity. Instead, they should be considered within the broader clinical context, taking into account other indicators of disease progression and organ involvement. Nevertheless, our study's findings highlight the need for vigilance in monitoring liver function in COVID-19 patients, especially those with moderate to severe lung involvement, to ensure comprehensive management of this complex and dynamic disease. Further research is warranted to explore the precise mechanisms underlying these correlations and their clinical implications fully.

C-reactive protein is an acute phase reactant, raised in systemic infections and severe infections[13]. In our study CRP has a positive correlation with the HRCT chest severity score. About 170 (85%) patients had raised CRP levels of more than 100mg/dL. The observed positive correlation between C-reactive protein (CRP) levels and HRCT chest severity scores in our study aligns with the well-established role of CRP as an acute phase reactant that increases in response to systemic infections and severe inflammatory conditions, including COVID-19. In severe cases of COVID-19, the body's immune response can become dysregulated, leading to a heightened inflammatory state characterized by the release of various inflammatory mediators, including CRP. This elevated CRP level reflects the magnitude of the systemic inflammation accompanying severe lung involvement, as seen on HRCT scans. The high percentage of patients (85%) with raised CRP levels exceeding 100 mg/dL further underscores the significance of CRP as an indicator of the inflammatory response in severe COVID-19 and its utility in assessing disease severity. These findings emphasize the value of CRP as a readily available and informative biomarker for monitoring the progression and severity of COVID-19.

The findings of our study, indicating a positive correlation between IL-6 levels and HRCT chest findings in COVID-19 patients, are consistent with the established role of IL-6 as a potent pro-inflammatory molecule. IL-6 is known to orchestrate a cascade of inflammatory responses and can induce the production of other inflammatory mediators. In severe COVID-19 cases, the virus can trigger an excessive immune response, leading to widespread inflammation and lung parenchymal lesions, often accompanied by symptoms like dyspnea. The observation that 75% of patients in our study had IL-6 levels exceeding 44 pg/mL underscores the prominence of this inflammatory marker in severe cases of COVID-19. The positive correlation between elevated IL-6 levels and the severity of lung involvement on HRCT scans highlights the pivotal role of IL-6 in driving the pathological changes seen in the lungs of these patients. These findings underscore the potential utility of IL-6 as a valuable biomarker for assessing disease severity and guiding clinical management in COVID-19 patients with respiratory distress.[14]

Neutrophil to lymphocyte ratio is an inflammatory biomarker that is associated with poor clinical outcomes in malignant and cardiovascular diseases when elevated.[15] The normal ratio is 1.5 (i.e. 60/40 on blood picture), in current study about 166 (83%) patients had ratio more than 1.5. It is positively correlated with HRCT chest severity.

The findings in our study regarding procalcitonin, D-dimers, and ferritin levels are indicative of the complex interplay between systemic inflammation and severe lung involvement in COVID-19.[16] Procalcitonin, typically recognized as a specific biomarker for bacterial infections, was elevated in 67% of our patients, suggesting that bacterial co-infections or secondary infections might occur in a significant proportion of severe COVID-19 cases. This elevation in procalcitonin levels correlated with the severity of lung changes observed on HRCT scans, underscoring its potential as a marker of

both bacterial infections and the extent of pulmonary damage in COVID-19 patients. Likewise, elevated D-dimers (found in 77% of patients) and ferritin levels (found in 82.5% of patients) in those with severe lung lobe changes on HRCT scans highlight the association between coagulation abnormalities and systemic inflammation, further emphasizing the multifa-ceted nature of severe COVID-19 and the importance of monitoring these biomarkers for comprehensive disease assessment and management. These findings collect-ively contribute to our understanding of the intricate pathophysiology of severe COVID-19 cases.
Serum LDH levels had a mix pattern with normal LDH levels in some patients having high HRCT severity score while raised LDH levels in other patients with severe lungs involvement on HRCT.

Conclusion

The more involvement of lung lobes parenchyma with COVID-19 on HRCT, is associated with raised systemic inflammatory markers. Serum ALT, CRP, D-dimers, Neutrophils to lymphocytes ratio, IL-6 and ferritin levels were significantly raised in most of the patients with HRCT findings of severe lung lobes involvement. Procalcitonin eves were found to be raised in most of the patients suggesting the presence of secondary bacterial infections. LDH was not raised in all the patients having severe lung lobes involvement on HRCT.

Strength and Limitations

The first study to be done in this region to show the trends of systemic inflammatory markers with the findings on HRCT chest. Various inflammatory markers were evaluated to check the relation with HRCT chest findings in COVID-19 patients. The limitation of the study is that, HRCT scans and systemic inflammatory markers were obtained on the time of admission only.

References

1. Alsharif W, Qurashi A. Effectiveness of COVID-19 diagnosis and management tools: A review. Radiography. 2021;27(2):682-7.
2. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DK, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Eurosurveillance. 2020;25(3):2000045.
3. Fang Y, Zhang H, Xie J, Lin M, Ying L, Pang P, et al. Sensitivity of chest CT for COVID-19: comparison to RT-PCR. Radiol. 2020;296(2):E115-7.
4. Saeed GA, Gaba W, Shah A, Al Helali AA, Raidullah E, Al Ali AB, et al. Correlation between chest CT severity scores and the clinical parameters of adult patients with COVID-19 pneumonia. Radiol Res Pract. 2021;2021:1-7.
5. 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.
6. Zhou X, Pu Y, Zhang D, Xia Y, Guan Y, Liu S, Fan L. CT findings and dynamic imaging changes of COVID-19 in 2908 patients: a systematic review and meta-analysis. Acta Radiol. 2022, 63, 291–310.
7. Mahat RK, Panda S, Rathore V, Swain S, Yadav L, Sah SP. The dynamics of inflammatory markers in coronavirus disease-2019 (COVID-19) patients: A systematic review and meta-analysis. Clin Epidemiol Glob Health. 2021;11:100727.
8. Zhu T, Wang Y, Zhou S, Zhang N, Xia L. A comparative study of chest computed tomography features in young and older adults with corona virus disease (COVID-19). J Thorac Imaging. 2020; 35(4):W97-101.
9. Tan C, Huang Y, Shi F, Tan K, Ma Q, Chen Y, et al. Creactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. Clin Chim Acta. 2020;506:145-148.
10. Li YX, Wu W, Yang T, Zhou W, Fu YM, Feng QM, et al. Characteristics of peripheral blood leukocyte differentialcounts in patients with COVID-19. Chinese J Intern Med. 2020; 59(5):372-4.
11. 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; 21:859-68
12. Yang R, Li X, Liu H, Zhen Y, Zhang X, Xiong Q, et al. Chest CT Severity Score: An Imaging Tool for Assessing Severe COVID-19. Radiol Cardiothorac Imaging 2020; 2:e200047.
13. Volanakis JE. Human C - reactive protein: Expression, Structure, and Function. Mol Immunol. 2001;38:189–97.
14. Sanli DE, Altundag A, Kandemirli SG, Yildirim D, Sanli AN, Saatci O, et al. Relationship between Disease Severity and Serum IL-6 Levels in COVID-19 Anosmia. Am J Otolaryngol. 2021;42:102796.
15. Lucijanic M, Cicic D, Stoos-Veic T, Pejsa V, Lucijanic J, Dzankic AF, et al. Elevated Neutrophil-to-Lymphocyte-Ratio and Platelet-to-Lymphocyte

Ratio in Myelofibrosis: Inflammatory Biomarkers or Representatives of Myeloproliferation Itself? Anticancer Res. 2018;38 (5): 3157-63;.

16. Tao M, Zheng D, Liang X, He Q, Zhang W. Diagnostic Value of Procalcitonin for Bacterial Infections in Patients Undergoing Hemodialysis: A Systematic Review and Meta-Analysis. Ren Fail. 2022;44(1): 81–93.