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Correlation between Serum Ferritin and HRCT Score in COVID-19 Patients with Pneumonia in Tertiary Care Hospital, Jharkhand

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Abstract
Aim: This study was aimed to measure serum ferritin and correlate it with HRCT score in diagnosed cases of COVID-19 patients with pneumonia.
Study Design: An observational study.
Place and Duration of Study: Department of Biochemistry, Sheikh Bhikhari Medical College and Hospital, Hazaribag, Jharkhand, between 28th April 2021 and 27th May 2021.

Methodology: We included 126 patients (74 men, 42 women; age range 18-99 years) with documented COVID-19 were reviewed. All patients underwent RT-PCR tests and had a non-contrast HRCT scan done at presentation. Estimation of serum ferritin was analyzed by using chemiluminescence method. The subjects were divided into three groups; mild, moderate and severe on the basis of HRCT score. Each group's HRCT score correlated with serum ferritin. The details were recorded on a pre-structured performa. The Pearson correlation coefficient test was used for correlations, and p value less than 0.05 was defined as statistically significant. The data was analyzed using Statistical Package for the Social Sciences (SPSS).
Results: Out of 126 patients, 60 patients were included in the mild group, 48 were included in the moderate group and 18 were included in the severe group. CT severity score was found to be positively correlated with ferritin levels ($p < 0.001$). Strong positive correlations were found between CT scores and serum ferritin in mild ($r = 0.84$), Moderate ($r = 0.92$, and severe group ($r = 0.082$).
***Conclusion**: Serum ferritin levels were very strongly correlated to HRCT score in COVID19 patients.*
***Keyword**: COVID-19, Serum ferritin, HRCT score, Correlation.*

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I. Introduction

On March 13, 2020, the World Health Organization (WHO) declared the novel coronavirus outbreak to be a pandemic [1]. By March 30, 2021, 127,349,248 confirmed cases of COVID-19, including 2,787,593 deaths,
were reported to the World Health Organization (WHO) [2]. The disease may trigger a broad inflammatory process and cause sepsis, septic shock, and multiple organ dysfunction syndrome, which requires mechanical ventilatory support [3]. Elevated ferritin levels may be predictive of an imminent inflammatory reaction in COVID-19 or be associated with viral spread in the human body and affect iron metabolism [4]. The nasopharyngeal swab RT-PCR test has been the diagnostic test used as the standard of reference for disease confirmation [5]. The test is a powerful tool; however, there is a small but significant proportion of false-negative results reported [6]. A non-contrast high-resolution CT chest imaging plays a pivotal and essential role in the early disease detection, particularly in patients with false-negative RT-PCR results, as well as in managing and monitoring the course of disease [7]. To our knowledge, ours is the first comprehensive study to describe the correlation of chest CT severity scores and the serum ferritin in patients with COVID-19 disease in the Jharkhand region. We hope the results of this study will contribute to clinicians' comprehension and treatment plan of COVID-19.

II. Material And Methods

2.1 Study Population

The observational study was carried out at the Department of Biochemistry, Sheikh Bhikhari Medical College and Hospital, Hazaribag, Jharkhand, from 28th April 2021 to 27th May 2021. A total of 126 COVID-19 patients (74 men, 42 women; age range 18-99 years) enrolled from Isolation and COVID-19 ward of Sheikh Bhikhari Medical College and Hospital, Hazaribag, Jharkhand. All patients underwent RT-PCR tests and had a non-contrast HRCT scan done at presentation. All patients were divided into mild, moderate and severe groups on the basis of HRCT score. Mild group included 48 patients (HRCT score ≤7), moderate group included 60 patients (HRCT score 8 to 17) and severe group included 18 patients (HRCT score ≥18) were included and exclusion criteria: patients less than 18 years old, patients with negative RT-PCR results, suboptimal HRCT scan due to significant motion artefacts, or CT with atypical findings for COVID-19 pneumonia.

2.2 Analysis of serum ferritin

Serum analysis for ferritin was determined on a fully automated autoanalyzer (Abbott Architect 1000i), which works on Chemiluminescent Microparticle Immunoassay technology using non-radiometric chemiluminescent method. The blood sample was collected, as per the standard protocol. The concentrations of serum ferritin were expressed in ng/mL.

2.3. Statistical Analysis.

Statistical data were analyzed using SPSS version20.0. The Pearson correlation coefficient test was used for correlations. The strength of the correlation (r) was defined as follows: $|r|<0.20$, very weak; $0.20\leq|r|<0.40$, weak; $0.40\leq|r|<0.60$, moderate; $0.60\leq|r|<0.80$, strong; $0.80\leq|r|<1.0$,very strong. All quantitative variables were expressed as mean value ± standard deviation. One-way ANOVA test was used to compare the differences between the groups. A "p value" below ≤0.05 was considered statistically significant and $p < 0.001$ considered statistically highly significant.

III. Results

A total of 126 inpatients were declared COVID-19 positive during the study duration. Out of these, 48
patients (mean age = 45.6 ± 12.6 years) were included in the mild group, 60 patients in moderate group (mean age= 56.4 ± 11.9 years) and 18 patients (mean age = 64.4 ± 8.6 years) in severe group on the basis of HRCT score as shown in Table 1 and Table 2. This study also showed a significant difference in age p= 0.03 shown in table 2, gender p= 0.01, shown in Table 3 and serum ferritin level p= 0.001, shown in Table 2 between the groups..

Table 1: Individual lobar scores based on percentage of lung involvement.

Lobar involvement	Score
5% or less	1
5%–25%	2
26%–49%	3
50%–75%	4
>75%	5

Table 2: HRCT score, Age and serum ferritin levels in mild, moderate and severe groups

Groups	HRCT Score	Age (mean, SD) (years)	Serum ferritin (mean, SD) (ng/ml)
Mild (n=48)	≤ 7	45.6 ± 12.6	286 ± 154
Moderate (n=60)	8-17	56.4 ± 11.9	783 ± 350
Severe(n=18)	≥18	64.4 ± 8.6	1187±710
P value		0.03	0.001

$p < 0.05$ statistically significant and $p < 0.001$ highly significant

Table 3
Gender distribution in Groups

Groups	Male	Female
Mild	40	8
Moderate	54	6
sever	16	2

p value= 0.01
p <0.05 statistically significant and p <0.001 highly significant

Mild, moderate and severe group had significant correlation between HRCT score and Serum ferritin. Mild group had p value 0.001 and r = 0.86 as shown in figure 1, Moderate group had p value 0.001 and r = 0.94 as shown in figure 2 and severe group had p = 0.001 and r = 0.85 as shown in figure 3.

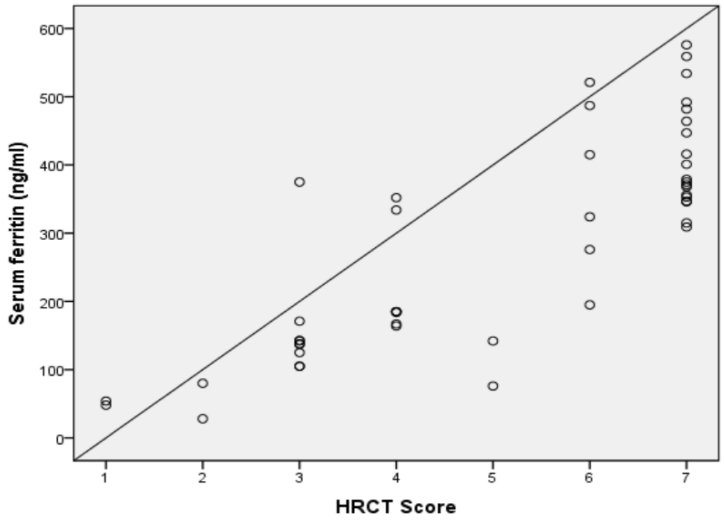

Fig 1- The correlations of HRCT scores and serum ferritin in Mild group

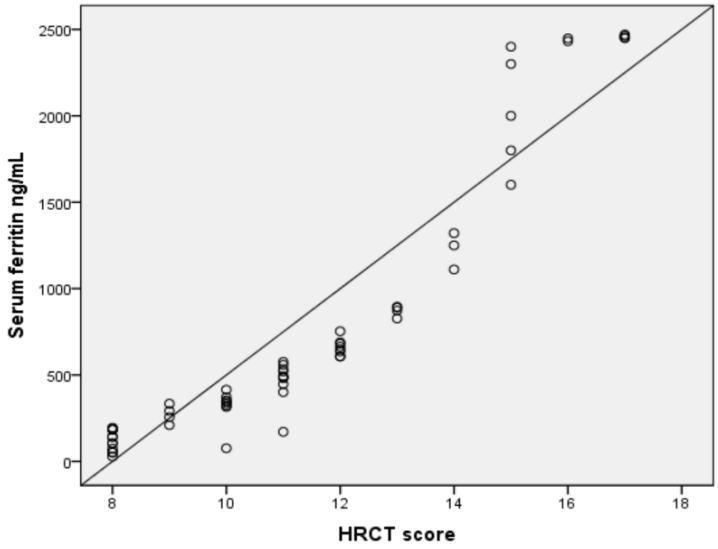

Fig 2- The correlations of HRCT scores and serum ferritin in Moderate group

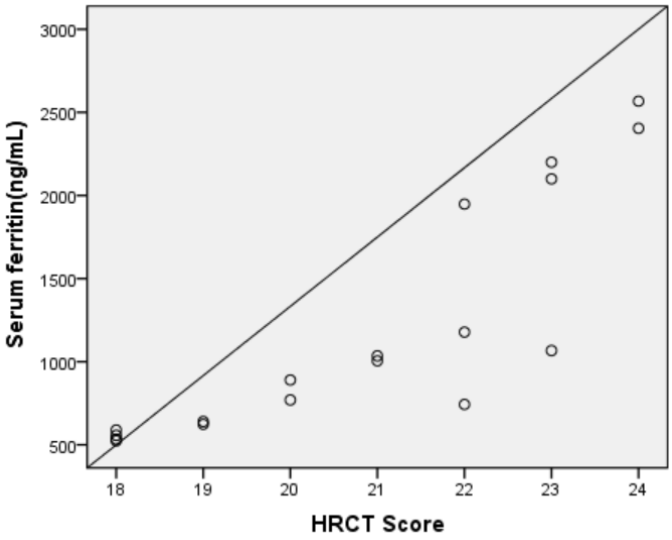

Fig 3- The correlations of HRCT scores and serum ferritin in Severe group

IV. Discussion

In developing countries like India, the role of Serum ferritin is more important in risk stratification and prognostic indication as it is a relatively inexpensive test widely available. The current study showed significantly strong correlation between HRCT score and serum ferritin. Our study also showed serum ferritin levels in the severe group were higher than compared to moderate and mild groups suggesting that the serum ferritin level may be a biomarker of disease severity and progression in patients with COVID-19. Serum ferritin is a vital mediator of immune dysregulation, and its level was closely linked to the severity of the disease [8]. Recent data have reported that patients with COVID-19 also have elevated levels of ferritin due to the inflammatory process. Hyperferritinemia has been accepted as an acute-phase reaction parameter that is used by clinicians to assess therapeutic response. In contrast, current research suggests that higher ferritin levels can be detected during an acute-phase response and may also play an important role in inflammation regarding development of a cytokine storm [9]. CT scan can be a useful tool in evaluating the individual disease burden [10]. Death rate in cohort was significantly increased among patients with severe CT findings, as noted in other studies [11]. Ghufran et al, study showed oxygen requirements increase with the increasing CT severity. The progressive increase in oxygen requirement can be due to the direct damage of the lung by the virus causing inflammatory changes in the alveolar wall that limit oxygen exchange, leading to acute respiratory distress, pulmonary fibrosis, and eventually death[12]. Moreover, significant pulmonary thromboembolic effects were also found on autopsies from patients who died from COVID-19 disease [13–15]

The WHO advised the use of chest imaging as part of diagnostic workup of COVID-19 disease whenever RT-PCR testing is not available, in case of delayed test results or when there is a clinical suspicion of COVID-19 with initial negative RT-PCR testing[16] There was a high statistical significance between both elevated serum ferritin and serum LDH and CT staging using the Kruskal-Wallis test where ferritin was increased in 18.4% in the mild stage, 63% in the moderate, and 100% in the severe stage[17]. Our study found that comparison between sex and different CT stages showed significant difference in the mild stage, moderate stage and in the severe stage. Severe disease was mostly seen in males (93.4%). Studies suggest that such distribution can be attributed to many factors like disparity in behavior and the possible protective effect of estrogen [18]. The most severe disease and the highest mortality rates were found in the older age group. This can be affected by different factors like the stage of the pandemic when the study was carried out, presence of patients' comorbidities, maturity and preparation of the healthcare system, and existence of elderly nursing homes services where disease can spread faster [19]. Also, a comparison between age and CT scoring showed that there was a statistically significant correlation between the two factors using the Kruskal Wallis test[17]. The estimated increase in severity with age is reported in several cases, with reports that the mean age is between 50 and 60 years [20]. Liu et al. revealed that patients over 60 years tend to develop respiratory failure. This demonstrated that elderly patients with COVID-19 had more severe disease compared to younger patients [21]. The present study also found that elderly COVID-19 patients tended to have more severe disease than younger patients. Additionally, the fatality rate was higher in the elderly population (53.3% in patients in their 60s). The higher mortality rate in the elderly population might be explained by an increase in comorbidities with advancing age. This is agreed with the previous report that the older patient with COVID-19 tends to become more severe [22].

V. Conclusion

Serum ferritin and chest CT findings laboratory test results were worsening in COVID19 patients, with very strong positive correlations between CT severity scores and serum ferritin levels.

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COMPETING INTERESTS

None.

AUTHORS' CONTRIBUTIONS

" Hemanti designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. 'Rajiv kumar Mahli' managed the analyses of the study and managed the literature searches. All authors read and approved the final manuscript."

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