



ORIGINAL RESEARCH PAPER

Radio-Diagnosis

CRP AND HRCT IN COVID-19: DO THEY MEET OR DEPART?

KEY WORDS: Covid-19, CT severity score, CRP, HRCT Thorax

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ABSTRACT

Background To retrospectively determine the correlation between the CT severity score and CRP levels in Covid-19 patients. **Methods** This is a retrospective original research of 247 patients (IPD and OPD) between 1st April 2021 to 31st May 2021 for Covid-19. Patients CT severity scores, HRCT Thorax findings, CRP and Demographic variables were recorded. The correlation between CT severity Score and CRP levels were determined. **Results** Mean CT severity score was 6.6 and CRP levels 33.4 mg/dl. Higher CT score and CRP levels were seen in Males (median- 7) than Females (median -5). CT severity score and CRP level showed positive correlation ($r=0.45, p<0.05$) in categories with mild CT score. Correlation was relatively weak in patient > 45 years of age than in those <45 years of age. Correlation was not significant in Severe (p value-0.59) and Moderate (p value-0.34) CT severity score group. Difference may be due to CRP level rising before the identifiable lung damage and Rise in CT severity score. **Conclusions** CRP levels shows statistically positive correlation with CT severity score only in initial (mild grade) cases of Covid-19 and hence serial evaluation of CRP in initial stages can be used to predict the Severity of Disease and CT severity score. However, a falling sequential CRP is not helpful in predicting HRCT score increase or reduction. Hence though CRP and HRCT are initially together in this clinical journey of COVID-19, finally they depart. CRP levels can therefore be not a substitute for HRCT to identify the severity and extent, the progression and regression and till date remains the gold standard as far as Covid-19 is considered.

INTRODUCTION-

Globally, as of 15 June 2021, there have been 175,987,176 confirmed cases of COVID-19, including 3,811,561 deaths, reported to WHO. As of 13 June 2021, a total of 2,187,874,534 vaccine doses have been administered. (1)

Most patients infected by SARS-CoV-2 have mild symptoms and good prognosis. However, some patients with COVID-19 progressed from severe pneumonia to pulmonary edema, acute respiratory distress syndrome, multiple organ failure, and death (2) A confirmed diagnosis of COVID-19 infection requires PCR identification of viral nucleic acid and lung imaging. Most patients have lung imaging results indicating bilateral pulmonary parenchymal ground-glass and consolidative pulmonary opacities, sometimes with a rounded morphology and peripheral lung distribution. Notably, lung cavitation, discrete pulmonary nodules, pleural effusions, and lymphadenopathy are absent. (3)

The circulating value of CRP reflects on going inflammation and/or tissue damage much more accurately than do other laboratory parameters of the acute-phase response, such as plasma viscosity and the erythrocyte sedimentation rate. Importantly, acute-phase CRP values show no diurnal variation and are unaffected by eating. (4)

At present few other studies have shown positive correlation between CT severity score and inflammatory markers. (5) The present study was done specifically to determine the relation between CT severity score and CRP.

METHODS-

Study Design And Participants

Patients were enrolled randomly from all Inpatient and Outpatient departments in Dr. Vikhe Patil Medical College and Hospital from April 1 to May 31 2021 for Covid-19. All patients were diagnosed with COVID-19 based on positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) quantitative RT-PCR using throat swab samples.

Data Collection

Demographic, HRCT Thorax, Laboratory data were collected

from electronic data record and evaluated by two researchers. CRP test was done on MISPA NANO fully automatic machine. HRCT scan was done on 16 slice GE Light speed CT machine. HRCT thorax scans were done at 140 kV and 9 mAs. Scan were evaluated at WL:450, WW:1500.

Definition

CT severity score is the percentage of lung involvement by Covid-19. Depending upon the number of lobes and percentage of each lobe involved with GGOs on HRCT, a CT Severity score is proposed as:

For percentage of each lobe involved as:

1. < 5% involvement
2. 5%-25% involvement
3. 26%-49% involvement
4. 50%-75% involvement
5. > 75% involvement.

Sum of all lobar score is done and total severity score is calculated.

Range is 0 to 25. Severity was further categorized as

Mild = <9

Moderate = 9 to 15

Severe = >15

CRP levels are obtained by Standard Laboratory procedure.

Normal range = 0 - 6 mg/

Statistical Analysis

Continuous variables were described as means and standard deviations or medians and interquartile ranges (IQR), depending on variable distributions. Continuous variables were analyzed by Student's t test or the Mann-Whitney U test as appropriate. The correlation between the continuous variables was tested by Spearman correlation analysis and t test for significance. In all the analyses, the significance level was defined as $p < 0.05$.

RESULTS-

1) Demographic Characteristics

Total of 247 patients were enrolled in our study. Of these, 155 were male and 92 were female. Demographic characteristics of the patient are summarized in the table 1.

TABLE 1: Demographic Characteristics of Patients

		All Patients (n=247)
Age	Mean (range)	43.967 (16-83)
	Age (SD)	14.383
	≤45 years	135 (54.66)
	>45 years	112(45.34)
Sex	Male -	155 (62.7)
	Female -	92 (37.3)

The mean age was 43 ± 14.3 years; with a range of 16-83 year. 135 (54.66%) of participants were ≤ 45 years and 112(45.16 %) were > 46 years of age. Male participants were 155 (62.7 %) and 92 (37.3%) were female.

2) HRCT Thorax scan results

HRCT Thorax scans were evaluated by 2 experienced radiologists. CT Severity score was calculated for each patient. (Range= 0 -25).Mean score was 6.6 (± 5.73).Based on the CT severity score, 162 patient were in mild (<9), 64 were in Moderate (9-15) and 22 were in severe (>15) category.63 Patients showed no signs of lung involvement on HRCT.

3) CRP level results

Normal range of CRP is 0-6 mg/L. Total 78 patients had CRP within normal limits. Median was 14. Interquartile range (IQR) was 4-43.SD was 43.369.

Table 2: Characteristics of CT severity score and CRP

		CT SEVERITY SCORE	CRP (mg/L)
Total- n (247)	Mean	6.6	33.32
	Median	6	14
	IQR	0-11	4-43
Male (n=155)	Mean	7.14	38.57
	Median	7	15
	IQR	2-12	5-57
Female (n=92)	Mean	5.88	24.47
	Median	5	11
	IQR	0-10	3-31.5
CT severity Mild (<9)	Mean (SD)	3.15(2.935)	21.38(±34)
	Median	3	8
	IQR	0-5.5	3-20
CT severity Moderate (9-15)	Mean	11.54(±1.70)	46.81(±45.33)
	Median	12	32
	IQR	10-12	11-73.25
CT severity Severe(>15)	Mean	18.22(±2.09)	81(±51.23)
	Median	17	83.5
	IQR	17-19	32-130.25

4) Correlation analysis

Correlation between CRP and CT severity score showed positive correlation coefficient (r=0.46).

(p-value <0.0001). There was not much difference based on gender (Male r=0.45, Female r=0.45).

Results were not significant for correlation in severe and moderate severity categories.

TABLE 3: Correlation Analysis between CRP and CT severity Score

Correlation between CRP and CT severity score		
	r	p-value
Total (n=247)	0.46096	<0.00001
Male (n=155)	0.45857	<0.00001
Female (n=92)	0.45899	<0.00001
Age ≤ 45 years	0.49185	<0.00001
Age > 45 years	0.36873	0.00006
CT severity Category MILD (<9)	0.30176	0.0001
CT severity Category MODERATE (9 15)	0.12270	0.3340
CT severity Category SEVERE (>15)	-0.21334	0.59477

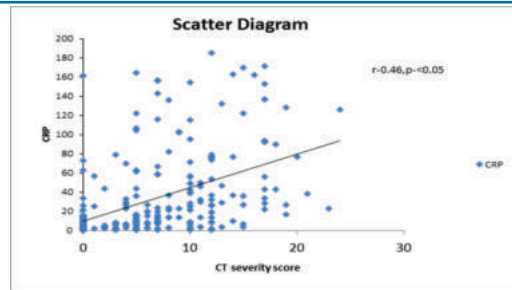


Figure 1: Scatter diagram showing Correlation between CT severity score and CRP

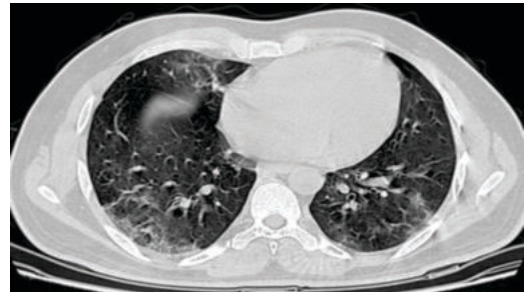


Figure 2: Axial HRCT Thorax Image of 41 year old Male patient with CRP value of 27 and CT severity score 6 .GGOs in subpleural and peripheral regions.(arrow)(WL:-450, WW :1500)

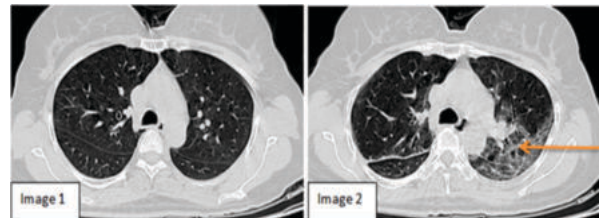


Figure 3: Axial HRCT Thorax Images of 37 old female Patient Image 1: On day 1, Minimal changes noted on HRCT (CRP - 9, CT Severity score-0). Image 2: On day 10, GGOs opacities in left posterior segment of upper lobe and apical segment of Lower lobe (Arrow) (CRP-23, CT severity score-10) (WL:-450, WW:1500)

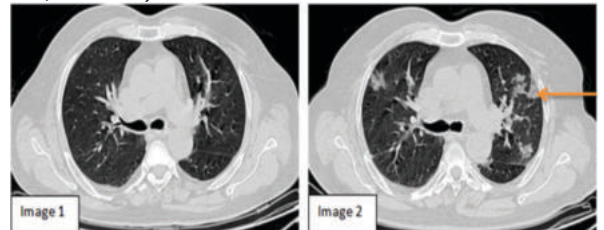


Figure 4: Axial HRCT Thorax Images of 52 year old male Patient Image 1: On day 3, Minimal changes noted on HRCT (CRP -9, CT Severity score-0). Image 2: On day 9, GGOs opacities in left posterior segment of upper lobe and apical segment of Lower lobe (Arrow) (CRP-23, CT severity score-7) (WL:-450, WW:1500)

DISCUSSIONS-

The main pathological changes of COVID-19 are lung and immune system damage (6). Serous, fibrin exudate and clear membrane form in the alveolar cavity and congestion and edema appear in the lung (7). HRCT lung may be used to identify the characteristic imaging of lung changes: multiple small patch shadows and stromal changes are observed in the early stage and the lung exudate is obvious (8) [https:// www. ncbi. nlm. nih. gov/ pmc/ articles/ PMC7146693/ -bib0150](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7146693/-bib0150), which then develops into multiple ground-glass shadows and infiltrating shadows in both lungs(9).

CRP is a type of protein produced by the liver that is elevated

in response to inflammation. Many clinical studies demonstrated that altered levels of some blood markers might be linked with the degree of severity and mortality of patients with COVID-19 (10).

In this study we have specifically correlated the CRP levels with CT severity score of patient. We found that CRP and CT severity score are positively correlated. ($r=0.46$, $p<0.00001$) (Fig -3 and 4). Mean, Median and Interquartile range were higher in males as compared to females. However, Correlation coefficient showed no difference between genders. (Male: $r=0.45$, Female: $r=0.45$).

Correlation was relatively weak in patient >45 years of age ($r=0.36873$) than <45 years of age ($r=0.49185$). According to Lamin B et al (11), analyses of biochemistry plasma inflammatory markers showed that >65 years patients had increased CRP in the early phase of symptom onset, which were not consistent with our findings.

Based on the CT severity Categories, CRP levels were elevated in severe [mean (SD) - 81 (± 51.23)] than in moderate [mean (SD) - 46.81 (± 45.33)] and mild [mean (SD) - 21.38 (± 34)] cases. But correlation was not significant in severe (p value-0.59) and moderate (p value-0.34) group. Possible explanation of these findings can be explained by pathological and radiological changes with disease progression.

According to Hans et al (12), Covid-19 is characterized by cytokine storm in early phase of disease with striking increase in CRP and IL-6 level. In late stage there is diffuse alveolar damage which is reflected as increased CT severity score.

The plasma half-life of CRP is about 19 hours. When the stimulus for increased production completely ceases, the circulating CRP concentration falls rapidly, at almost the rate of plasma CRP clearance. (13)

Hence in severe category, patient may be in late phase of disease where CRP levels may be declining while diffuse alveolar damage is still on going. So time difference in peak severity of CRP level and CT severity Score may be the reason for such a result.

Tan et al (14) divided patients in two groups, Mild and Severe. They divided course of illness into Initial (0-8 days), progression (4-12 days), Peak (8-16 days) and Recovery (11-25 days) stages. The CRP in the severe group at the progression stage was higher than that in the mild group but was decreased although with no statistically significant differences at the peak and recovery stages. Detecting serial levels of the CRP in every 3-4 days in initial stages may be useful in predicting lung involvement, severity and CT severity score. Above finding suggest that elevated levels of CRP in initial stages of disease leads to overproduction of inflammatory cytokines in patients with COVID-19 causing lung damage which is reflected as increased CT severity score.

In summary, this study provides evidence that CRP and CT severity score are positively correlated, with serial evaluation of CRP in initial stages of disease predicting the severity of Disease and CT severity score. CRP levels shows statistically positive correlation with CT severity score only in initial [mild grade] cases of Covid-19 and hence serial evaluation of CRP in initial stages can be used to predict the Severity of Disease and CT severity score. However, a falling sequential CRP is not helpful in predicting HRCT score increase or reduction. Hence though CRP and HRCT are initially together in this clinical journey of COVID-19, finally they depart. CRP levels can therefore be not a substitute for HRCT to identify the severity and extent, the progression and regression and till date remains the gold standard as far as Covid-19 is considered.

Conflict of Interest-

The authors declare that they have no conflict of interest.

Abbreviations-

- CRP- C- reactive Protein
- CT - Computed Tomography
- GGO- Ground Glass Opacities
- HRCT- High Resolution Computed Tomography
- IPD - In patient Department
- IQR- Inter Quartile Range
- OPD- Out patient Department
- WHO- World Health Organization
- SARS- CoV- Severe acute respiratory syndrome -Corona Virus
- RT-PCR- Reverse Transcriptase- Polymerase Chain Reaction

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