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CORRELATION BETWEEN C-REACTIVE PROTEIN (CRP) LEVELS AND CHEST CT SEVERITY SCORES IN COVID-19 PATIENTS: A RETROSPECTIVE STUDY

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Abstract:
Introduction: CRP levels and Chest CT severity scores, the outcomes of which might prove utilitarian to the clinicians worldwide in the detection, risk stratification as well as early treatment of COVID 19 patients. Objective of the study is to determine the correlation between COVID-19 severity with inflammatory marker CRP and chest CT severity score.
Methodology: A hospital based cross sectional study were conducted in a tertiary care for the period of two months from August 2022 to September 2022 by Department of Medicine. The study population was in patients with COVID 19 infection who were tested positive for COVID 19 infection by RT PCR test, whose CRP levels were tested and chest CT imaging done. The sample size was 180 and the sampling technique was simple random sampling.
Results: Among 180 participants majority were males (65.6%). Most of the participants belonged to working age group (79%). The most prevalent co morbidity was Diabetes Mellitus (48.9%). The mean CRP level was 57.17 mg/dl with standard deviation of 57.96. The mean Chest CT Severity score was 10.7 with standard deviation of 4.78. The correlation coefficient was found to be 0.26 by Spearman's rank coefficient method, showing mild positive correlation between Chest CT Severity Scores and CRP levels
Conclusion: The present study showed that a weak positive correlation exists between Chest CT Severity Scores and CRP levels (r value=0.26), making it a useful tool for predicting the severity and prognosis of the illness.

Key words: CRP, Chest CT severity scores, COVID-19, Retrospective study

Introduction:

COVID-19, a disease caused by SARS-CoV2 Virus, was declared a global pandemic by World Health Organization on March 11 2020[1]. Although respiratory system is primarily affected, other

systems are also involved[2]. Early diagnosis of the infection forms the most crucial step in the treatment of the infection[3].

C – Reactive Protein (CRP) is an acute inflammatory protein that may rise in significant folds at sites of infection or inflammation[4]. CRP levels which measures the systemic inflammation shows strong association with AKI, VTE, critical illness and mortality in COVID-19[5]. There are documentations that show severe COVID-19 disease is associated with higher levels of inflammatory markers compared to mild disease; hence tracking of these markers may help in early detection and prediction of disease progression[6].

Radiological investigations, in particular the thin slice chest computed tomography (CT) scan plays a critical role in diagnosis, management and follow up of COVID-19 patients[7].The 25 point CT Severity score correlates well with disease severity and as well as with inflammatory markers, duration of hospital stay and oxygen requirement in patients diagnosed with COVID-19[8]. Hence this present study is undertaken to correlate the CRP levels and Chest CT severity scores, the outcomes of which might prove utilitarian to the clinicians worldwide in the detection, risk stratification as well as early treatment of COVID 19 patients.

Aim: To find the correlation between CRP levels and Chest CT Severity scores in COVID-19 patients.

Objective: To determine the correlation between COVID-19 severity with inflammatory marker CRP and chest CT severity score

Methodology:

Study area and participants:

The present Hospital based cross sectional study were conducted in a tertiary care hospital for period of two months study period from August 2022 to September 2022 by Department of Medicine.

The study population was in patients with COVID-19 infection.

Inclusion Criteria: Inpatients who were tested positive for COVID-19 infection by RT-PCR test, whose CRP levels were tested and chest CT imaging done.

Exclusion criteria: Patients who were diagnosed positive by other methods like Rapid Antigen Testing.

Sample size and sampling:

The sample size was 180 and the sampling technique was simple random sampling. The sample size was calculated based on the study done by Yilmaz A et al.[9] where the r-value was found to be 0.436. With a level of significance of 5% and power of 80%, the required sample size was calculated to be 180.

Data collection procedure: After obtaining institutional ethical clearance, a pre-designed structured questionnaire was used. The COVID-19 patients diagnosed by RT-PCR test and who have undergone CRP level tests and Chest CT scans were included in the study. Sociodemographic details, vaccination status, co morbidities if any, disease severity, symptoms, oxygen saturation levels, CRP value at the time of admission, chest CT severity score and the disease outcome was collected according to the prepared data extraction sheet from the existing hospital records and studied to find the relationship between CRP values at the time of admission and Chest CT severity scores

Statistical Analysis

The data obtained was entered in Microsoft Excel. The entered data was analyzed in IBM SPSS and summarized using mean and standard deviation. The relationship between CRP levels and CT

Severity scores was evaluated using Spearman's rank correlation coefficient or Pearson's correlation coefficient based on the distribution of data.

Ethical considerations

Ethical clearance was obtained from the institutional ethics committee (IEC). A waiver of informed consent was requested to the ethics committee as the study involves only secondary analysis of existing data and no risks to the participants. The confidentiality of the data obtained was maintained throughout the course of the study.

Results:

Among 180 participants majority were males (65.6%). Most of the participants belonged to working age group (79%). The most prevalent co morbidity was Diabetes Mellitus (48.9%) followed by systemic hypertension (36.7%). It was found 33.3% of the participants were smoker and alcoholic. In the study group, 18.88% of patients were vaccinated while 81.11% were not (Table: 1).

The oxygen saturation at the time of admission of the participants is summarised in (Figure: 1). The mean oxygen saturation was 93.48% with a standard deviation of 6.04. The values ranged from the minimum value of 63% to maximum value of 100%.

Out of 180 participants, 148 patients were discharged and 18% of participants succumbed to the disease. Most of the patients came with mild severity 48.3%. The mean Chest CT Severity score was 10.7 with standard deviation of 4.78 and the lowest score being 1 and the greatest being 25.The most common scores were between the ranges of 8 to 17 with 118 entries (Table: 2).

The mean CRP level was 57.17 mg/dl with standard deviation of 57.96 and 230 mg/dl being the largest and 1 mg/dl being the lowest values. Most of the entries were in the group 0-20 mg/dl (Figure: 2). The correlation coefficient was found to be 0.26 by Spearman's rank coefficient method, showing mild positive correlation between Chest CT Severity Scores and CRP levels (Figure: 3).

Table 1: Socio-demographic details of the participants (n=180)

Variables	No. of patients (n)	Percentage (%)
Gender:		
Male	118	65.6
Female	62	34.5
Age distribution:		
20-40	13	7.3
41-60	79	43.9
61-80	72	40
>80	16	8.8
Co-morbidities:		
Diabetes	88	48.9
Hypertension	66	36.7
CAD	20	11.2
CKD	4	3.2
Addictions:		
Only Smoking	47	26.2
Only Alcohol	33	18.3
Both (Smoking and Alcohol)	60	33.3
None	40	22.2
Vaccination status:		
COVID-Vaccine 1st dose	23	12.77
COVID-Vaccine 2nd dose	11	6.11

Not vaccinated	146	81.11

Table 2: Clinical characteristics and outcome of the study participants

Clinical characteristics	Frequency (n)	Percentage (%)
Disease Severity:		
Suspect	4	2.3
Mild	87	48.3
Moderate	74	41.1
Severe	15	8.3
Symptoms:		
Fever	153	85
Cough	97	53.89
Breathlessness	65	36.11
Headache	24	13.33
Rhinorrhoea	10	5.56
Anosmia	51	28.33
Sore throat	27	15
Diarrhoea	30	16.67
Nausea and vomiting	29	16.11
Myalgia	86	47.78
Chest CT score:		
0-8	44	24.4
8-17	118	65.6
17-25	18	10
Disease Outcome:		
Discharged	148	82
Diseased	32	18

Figure 1: Oxygen saturation at the time of admission

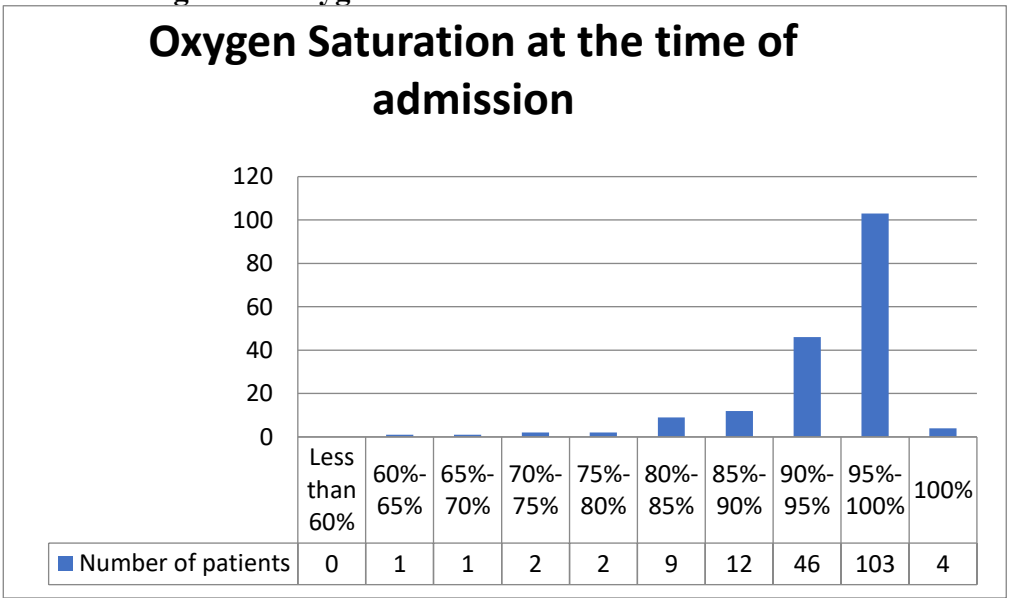


Figure 2: Frequency distribution of CRP levels

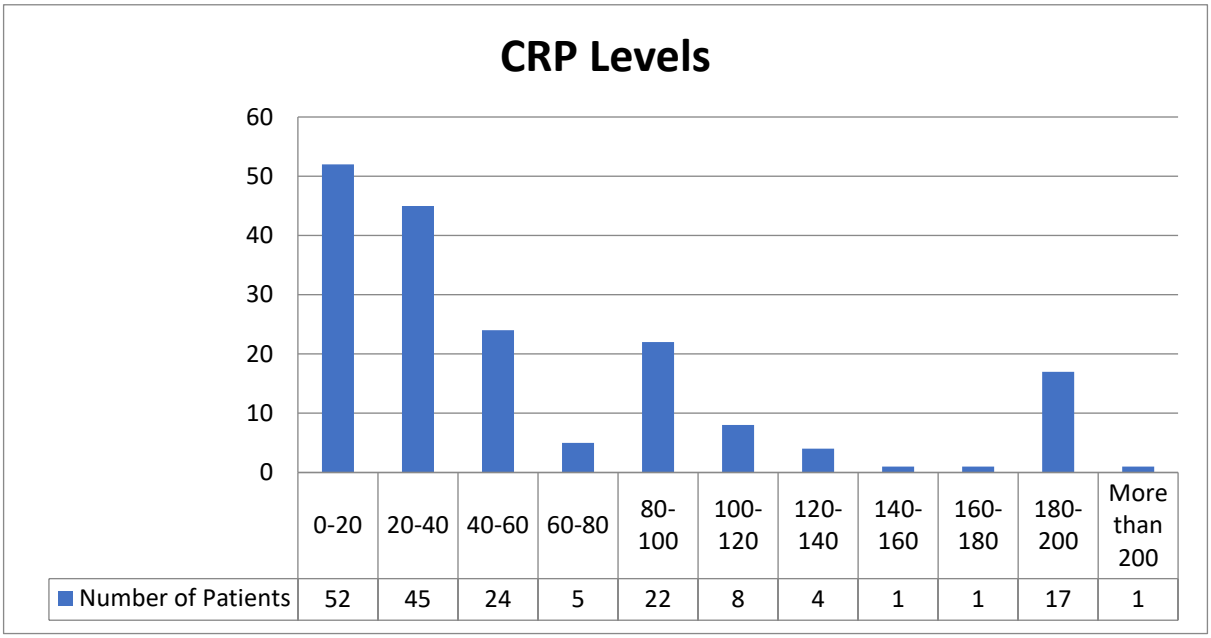
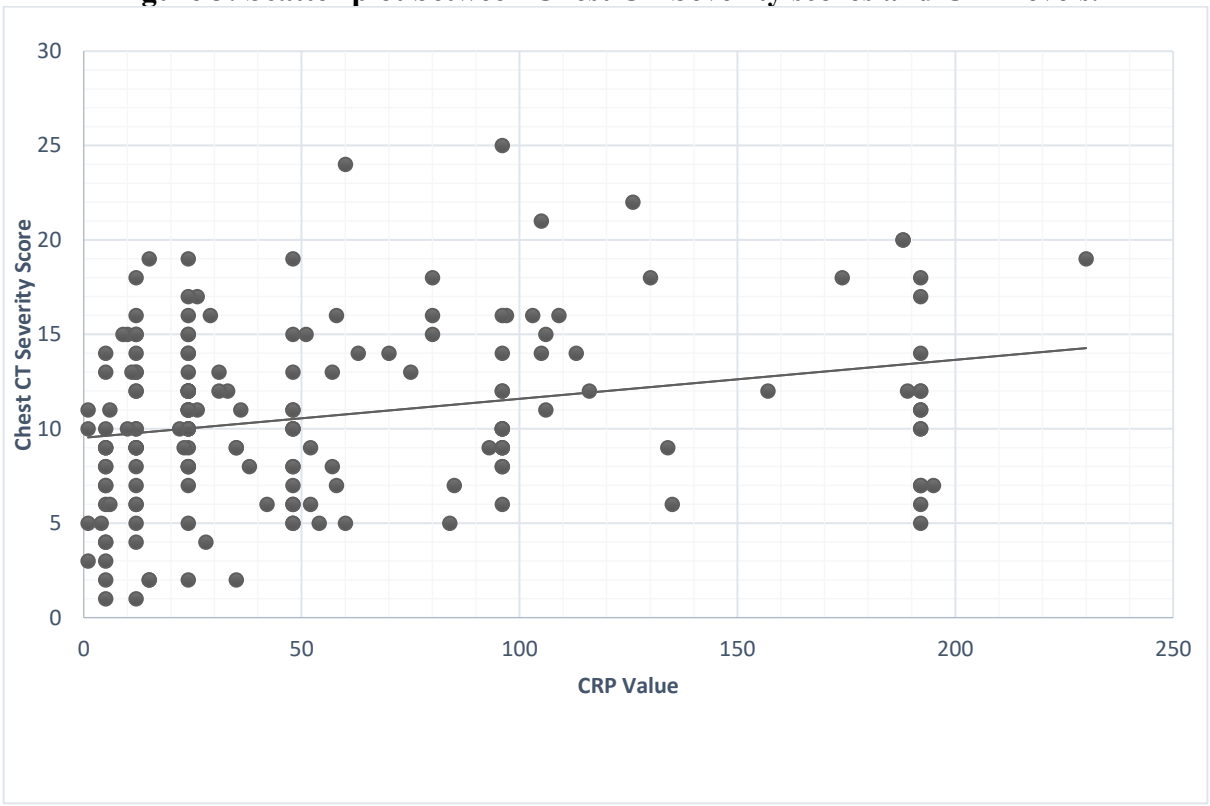


Figure 3: Scatter plot between Chest CT Severity scores and CRP levels.



Discussion:

The key findings of the study showed that the correlation coefficient that exists between Chest CT severity scores and C-Reactive Protein levels is +0.26, indicating a weak positive correlation. A study conducted by Qunying Lin et al.[4] showed an r-value of 0.49 between the two parameters. While a study conducted by Atakan Yilmaz et al.[9] showed a moderate positive correlation between CT Score and CRP levels with an r-value of 0.436 with $p<0.001$ where the sample size was 130. In another study conducted among 168 COVID-19 patients admitted in the ICU by Mohammed Esmaeil Hejazi et al.[10], a significant correlation was established between CT Scan features and CRP levels. Furthermore, a study by Saeed GA et al.[8] among 1062 suspected COVID-19 patients the

correlation coefficient was found to be 0.556 again showing a positive correlation between the two parameters that were studied. While the correlation coefficient was calculated to be 0.62 in a study conducted among twenty-seven patients by C Tan et al[11].At the same time a study by Jin Zhu et al. among 25 patients showed a significant correlation between the two parameters under study.[12]

In the present study, it was found the majority were males (65.56%) which is in concordance with a study conducted by Sharma et al[14] and Bhandari S et al.[14] 62.7% were male. The reason could be due to more chance of getting indulging in addictions like smoking and alcohol which could have aggravated the condition. In a country like India especially in rural females don't seek proper healthcare services and another boon like fear of the disease and the lack of awareness of disease prevention. This could be the result of gender bias or the fact that females are less likely to contract viruses, which could be explained by their immunity to the X chromosome and sex hormones, which are crucial for both innate and adaptive immunity.[14,15] This emphasises the need for improving awareness in the community through proper health education and the distribution of pamphlets to all the patients in the patients waiting area. Most of the participants belonged to the working age group (79%) which is of main concern as it ultimately affects the country's economy Numerous factors, including the patients' comorbidities, the state of the healthcare system, and the pandemic's stage, can be blamed for this.[13,14,15]

Most participants (48.33%) had mild severity at the time of admission, but it was closely followed by number of patients with moderate disease (41.11%) This finding was also found to have positive statistically significant correlation with CTSS ($p = 0.045$). On coming to the immunisation status of the participants 18.88% of the participants have taken at least one dose of vaccine against COVID-19 infection the reason for not complete immunization could be due to mixed opinion, fear of vaccine and lack of family support. Diabetes Mellitus was the most common co morbidity among the participants (48.88%), the participants had one or more comorbidities which is less when compared to the study conducted by Sharma et al.[13] which could be due to practices followed and the geographic distribution of the participants. fever was the most common symptom (85%) presented. 82% of the patients were discharged following treatment while 18% of the participants succumbed to the disease.

The average of the correlation coefficients mentioned above obtained through the other studies mentioned was 0.52, which was greater than that was obtained following the current study (r value=0.26) whereas in study conducted by Sharma et al[14] Mean of CRP was significantly higher in the severe group (11.7) as compared to mild (5.3) and moderate (5.2) group. It is comprehensible from the above discussion that the results of the present study showed a lesser degree of positive correlation compared to the others which could be attributed to a variety of reasons including a number of variables as well as to a few limitations of the study, which the study was not free of. A few variables that could be attributed include the study population, laboratory evaluation methods, sample size, clinical profile etc to mention a few. In cases where an RT-PCR test is not available or in patients who have negative test findings, the WHO advises chest imaging for suspected COVID-19 patients.[16]

A few limitations of the study include, the study being a retrospective study, inclusion of Chest CT Severity scores computed from different centres, inability to obtain CT Severity scores and CRP levels at the same point of time and during multiple points of the disease progression. These limitations could be ascribed to economic constraints of conducting multiple Chest CT Scans and CRP value evaluations. Considering these facts, still CRP Levels and Chest CT Severity scores should be considered to have a positive correlation with the disease severity and progression and is reasonable to consider these parameters for the evaluation of these patients. It is Hospital based cross-sectional study, temporarily cannot be maintained. Association between comorbidities have not been found because of smaller sample size hence the findings cannot be generalised. It is

recommended to carry out further studies in the regard with larger sample sizes and better standardization to reach into conclusive evidence regarding the accurate correlation between the two parameters studied. In order to make this more reflective of the general population, a multi-center study can be performed with more participants. More research between rural and urban to find the multiple confounders is needed.

Conclusion:

The present study showed that a weak positive correlation exists between Chest CT Severity Scores and CRP levels (r value=0.26), making it a useful tool for predicting the severity and prognosis of the illness. Considering the background of few limitations of the study, it could be concluded that it is reasonable to employ the parameters under the study for the diagnosis and management of COVID-19 patients and further studies should be carried out in this regard.

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References:

1. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Bio Medica: Atenei Parmensis. 2020; 91(1):157.
2. Yuki K, Fujiogi M, Koutsogiannaki S. COVID-19 pathophysiology: A review. Clinical immunology. 2020 Jun 1; 215:108427.
3. Hosseini ES, Kashani NR, Nikzad H, Azadbakht J, Bafrani HH, Kashani HH. The novel coronavirus Disease-2019 (COVID-19): Mechanism of action, detection and recent therapeutic strategies. Virology. 2020 Dec 1;551:1-9.
4. Sproston NR, Ashworth JJ. Role of C-reactive protein at sites of inflammation and infection. Frontiers in immunology. 2018 Apr 13; 9:754.
5. Smilowitz NR, Kunichoff D, Garshick M, Shah B, Pillinger M, Hochman JS, Berger JS. C-reactive protein and clinical outcomes in patients with COVID-19.European heart journal. 2021 Jun 14; 42(23):2270-9.
6. Luan Y, Yin C, Yao YM. Update advances on C-reactive protein in COVID-19 and other viral infections. Frontiers in Immunology. 2021 Aug 10:3153
7. World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: interim guidance, 13 March 2020. World Health Organization; 2020.
8. Saeed GA, Gaba W, Shah A, Al Helali AA, Raidullah E, Al Ali AB, Elghazali M, Ahmed DY, Al Kaabi SG, Almazrouei S. Correlation between chest CT severity scores and the clinical parameters of adult patients with COVID-19 pneumonia. Radiology research and practice. 2021 Jan 6; 2021.
9. Yilmaz A, Sabirli R, Seyit M, Ozen M, Oskay A, Cakmak V, Goren T, Turkcuer I.Association between laboratory parameters and CT severity in patients infected with Covid-19: A retrospective, observational study. The American Journal of Emergency Medicine.2021 Apr 1; 42:110-4
10. Hejazi ME, Malek Mahdavi A, Navarbaf Z, Tarzamni MK, Moradi R, Sadeghi A, Valizadeh H, Namvar L. Relationship between Chest CT scan Findings with SOFA score, CRP, Comorbidity, and Mortality in ICU Patients with COVID-19. International Journal of Clinical Practice. 2021 Dec: 75(12):e14869
11. Tan C, Huang Y, Shi F, Tan K, Ma Q, Chen Y, Jiang X, Li X. C-reactive protein correlates with computed tomographic findings and predicts severe COVID-19 early. Journal of medical virology. 2020 Jul; 92(7):856-62.

12. Zhu J, Chen C, Shi R, Li B. Correlations of CT scan with high-sensitivity C-reactive protein and D-dimer in patients with coronavirus disease 2019. Pakistan journal of medical sciences. 2020 Sep; 36(6):1397.
13. Sharma S, Aggarwal A, Sharma RK, Patras E, Singhal A. Correlation of chest CT severity score with clinical parameters in COVID-19 pulmonary disease in a tertiary care hospital in Delhi during the pandemic period. Egypt J Radiol Nucl Med. 2022;53(1):166.
14. Alam S, Muid S, Akhter A, Rahman A, Emran MA, Mostakim MT. HRCT chest evaluation of COVID-19 patients: experience in combined military hospital Dhaka Bangladesh. *JBCPS.* 2020;38:21–8.
15. Beeching NJ, Fletcher TE, Fowler R. Coronavirus disease (COVID-19): BMJ best practise. *Nat Microbiol.* 2019;5(4):536–44.
16. World Health Organization. Use of chest imaging in COVID-19: a rapid advice guide.[Online] 2020.[cited on May 12]:Avaiable from URL: https://www.who.int/publications/i/item/use-of-chest-imaging-in-covid-19).