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Original Research Article

Correlation between chest CT severity score and C-reactive protein in COVID-19 positive patients admitted in a tertiary care hospital: a retrospective study

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ABSTRACT

Background: COVID-19 has developed into a worldwide pandemic. The early identification of patients who will become severely ill could facilitate the allocation of the limited medical resources to patients in need of aggressive treatment. Aim of the current study was to determine the correlation between COVID-19 severity with inflammatory marker CRP and CT severity score on HRCT thorax

Methods: A retrospective observational study was done in 502 hospitalized COVID-19 patients in a tertiary care hospital BMCRI, Bangalore from August 2021 to September 2021. Clinical and laboratory data of patients were collected. The correlation between clinical severity with chest CT score and CRP were determined by ANOVA test and independent sample t-test was applied among survivors and non survivors. Correlation between CTSS and CRP was analyzed by Pearson correlation analysis.

Results: In our present study we found that, out of 502 patients who fulfilled the inclusion criteria 158 patients (31.5%) were triaged as mild cases, 228 patients (45.4%) were moderate case, and 116 patients (23.1%) severe cases. There was statistical significance between CRP values and CTSS among the mild, moderate, severe cases ($p<0.001$). Both CTSS and CRP values had explicit association with clinical condition of patients. By using independent sample t-test we could derive that CRP and CTSS had strong and significant correlation with the disease severity and mortality. Pearson correlation analysis revealed strong positive correlation between CRP and CTSS in COVID-19 patients. Hence an increase in CRP caused an increase in CTSS with significant p values.

Conclusions: In our study we conclude that there is a strong positive clinical correlation between CRP and CTSS in COVID-19 patients reflecting disease severity and mortality.

Keywords: COVID-19, C-reactive protein, CT severity score.

INTRODUCTION

Corona virus disease 2019 (COVID-19), was firstly identified in a series of individuals presenting with undetermined form of pneumonia in Wuhan, China, during December 2019.[1] Since its first observation, this outbreak has became worldwide healthcare emergency. COVID-19 represents a spectrum of clinical severity ranging from asymptomatic to critical pneumonia, acute respiratory distress syndrome (ARDS) and even death posing great challenges to the global healthcare system early diagnosis of serious illness and effective early intervention are the fundamental measures for reducing mortality.[2] With waxing and waning waves globally, swift and accurate diagnosis is essential to profile patients and allocate scarce resources adequately.[3] Chest imaging may play a key role in COVID-19 diagnosis and triage, as well as stratification of disease severity. Conventional

chest radiography has limited sensitivity for COVID-19 pneumonia. Computed tomography (CT) is helpful in the diagnostic process, because the results are available almost immediately, and alternative diagnoses may be identified. In retrospective studies, sensitivity of chest CT for COVID-19 is excellent, and it may even be greater than that of polymerase chain reaction in picking up infection. In addition, using a semi quantitative CT severity score (CTSS) is reported to correlate with disease severity, and it might be used as a prognostic marker.[2] Moreover, the disease severity can be ascertained from the imaging findings, significantly supporting the clinicians in their clinical judgment and ensuring effective and timely management including intensive care.[4] The clinical course of COVID-19 pandemic is regarded as being highly variable. Though most of the patients suffered only from mild symptoms, significant percentage of patients suffered from severe illness due to viral-induced hyper inflammation with respiratory failure and need for non-invasive or invasive mechanical ventilation. Since, the evolution of clinical condition of these patients is difficult to forecast, early identification of prognostic indicators is an essential foundation to regulate treatment plans and promptly identify the severity of patients' condition.[5] Hence, identification of a simple and elective prognosticator is crucial for treating potentially critical patients, with the aim of reducing the mortality rate.[6] C-reactive protein (CRP) is a pentameric acute-phase reactant protein produced by the liver, whose level increases during an inflammatory/infectious process. The rise in CRP level either alone or in conjunction with other inflammatory markers may denote bacterial or viral infections. Multiple studies have assessed the prognostic value of CRP in both acute and chronic infections, hepatitis C, dengue, and malaria. The elevation in its levels during infections conveys the extent of tissue involvement, thus diagnosing bewildering compli-cations.[7] CT scans can have a pivotal role as an indicator of disease severity. However, more research is needed to further clarify the value of chest CT for correlation with tissue inflammation and its correlation with lab marker like CRP and in turn patient outcome. Hence in our study we aimed to determine the correlation of CRP values and CT Scores between COVID-19 clinical severity and outcome among COVID-19 patients with retrospectively.

Objectives

Objective of current study was to determine the correlation between COVID-19 severity with inflammatory marker CRP and CT severity score.

METHODS

Study design and participants

Current study was a retrospective observational study and was conducted in Victoria hospital, BMCRI, Bangalore from August 2021 to September 2021. Data were retrieved from the medical records of adult patients who fulfilled the inclusion and exclusion criteria of the study.

Inclusion criteria

Patients aged >18 years, of either sex, admitted with confirmed COVID-19 infection by either reverse-transcriptase-polymerase chain reaction (RT-PCR) or rapid antigen testing (RAT) and who were tested for CRP and underwent high resolution computed tomography of the thorax and scored according to scoring system of Chang et al at the time of admission were included in the study.[8]

Exclusion criteria

Patients aged <18 years and who were not admitted to hospital were excluded from the study.

Table 1: CT severity score based on lung involvement.[8]

Single lobe infected percent	Score
5%	1
5-25%	2
25-50%	3
50-75%	4
>75%	5
Score	**CT severity**
<8	Mild
9-15	Moderate
>15	Severe

After obtaining approval and clearance from the institutional ethics committee of BMCRI, the patients admitted during two months (August to September 2021) fulfilling the inclusion criteria were identified from medical records and were enrolled into the study. The required data was collected from the available data source and compiled for each patient. Patients were categorized as mild, moderate or severe COVID-19 cases, based on the clinical features and the place of initial care facility was determined as per ICMR/AIIMS-COVID-19 National task force/joint monitoring group dated 22nd April 2021 (Figure 1) and treated as per standard of care.[9] Immuno turbid metric method was used for estimation of CRP and HRCT Thorax was done using Philips ingenuity 128 slice scanner and scored according to scoring system of Chang et al that was even used in patients with SARS-Cov-1.[8] To quantify the extent of disease, CT score was assigned on the basis of the area involved (Table 1). There was a score of 0–5 for each lobe, with a total possible score of 0–25. The data was compiled in the MS-Excel format into tabular forms and used in further statistical analysis.

Statistical analysis

The statistical analysis was performed using the SPSS 24.0 software. Measured data with normal distribution

are expressed as mean±standard deviation, and comparison among groups were performed using one way analysis of variance (ANOVA) and independent sample t-test. Numeration data was analyzed by Chi square test. Correlation was analyzed by Pearson correlation analysis, p value below 0.05 was considered statistically significant.

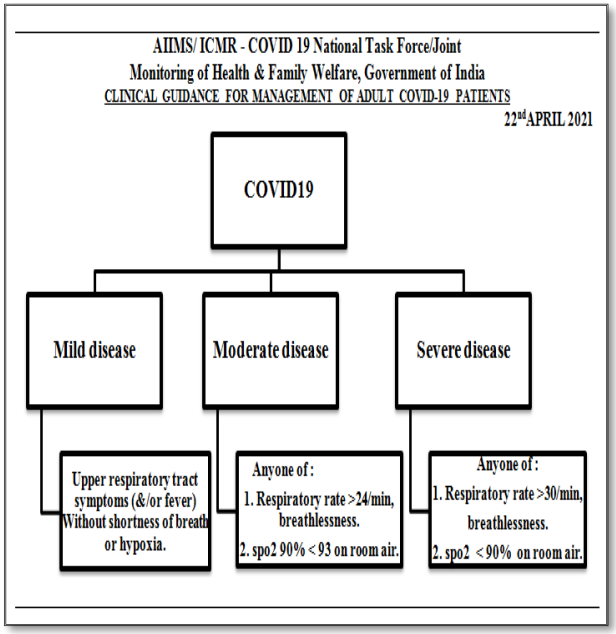

Figure 1: AIIMS/ICMR COVID-19 National task force.[9]

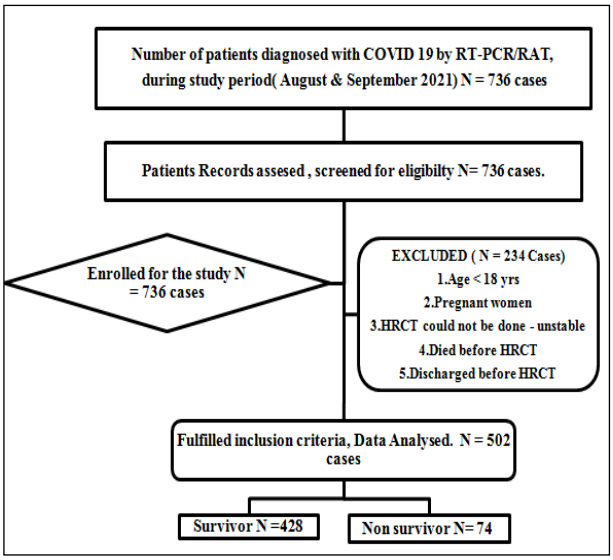

Figure 2: Study flow chart.

RESULTS

This study was done from the data of patients admitted over a period of two months between August 2021 and September 2021. It was during the peak of the second wave in Bangalore Karnataka, India. Total 736 cases were admitted to our hospital with RT-PCR COVID-19 positive report during two months period, out of which 502 patients fulfilled our inclusion and exclusion criteria. The data was compiled in the MS-Excel format into tabular forms and used in further statistical analysis.

Table 2: Clinical and laboratory characteristics.

Descriptive statistics					
Variables	**N**	**Minimum**	**Maximum**	**Mean**	**SD**
Age (years)	502	18.0	92.0	48.084	14.3218
SOB (days)	449	0.0	7.0	3.034	2.1530
Cough (days)	428	0.0	7.0	3.496	1.8461
Fever (days)	415	0.0	9.0	4.261	2.5386
Myalgia (days)	283	0.0	7.0	2.410	2.4032
Sore throat (days)	280	0.0	8.0	2.520	2.5183
Headache (days)	158	0.0	4	1.580	1.5182
Diarrhea (days)	42	0.0	3	1.250	1.4250
Vomiting (days)	30	0.0	3	1.650	1.5890
PR (BPM)	502	72.0	136.0	96.131	14.1778
RR (CPM)	502	14.0	34.0	19.781	5.9913
SPO2 in RA	502	60.0	99.0	92.064	8.0681
CRP (mg/dl)	502	3.0	153.0	62.233	43.1098
CTSS	502	2.0	25.0	11.307	5.8669

Out of 502 patients, we found that 348 (69.3%) were males and 154 (30.7%) were females, with mean age 48.084±14.32 years. The most common complaints of the patients were shortness of breath (N=449, 89.4%), cough (N=428, 85.25%), fever (N=415, 82.66%), myalgia (N=283, 56.4 %), sore throat (N=280, 55.8%), headache (N=158, 31.47%), diarrhea (N=42, 8.36%), vomiting (N=30, 5.97%). Most of the patients in our sample population had one or other underlying comorbid condition. They mostly suffered from diabetes mellitus (N=232, 46.21%), hypertension (N=210, 41.83%), obstructive airway disease (N=98, 19.52%), ischemic

heart disease (N=95, 18.9%), chronic kidney disease (N=72, 14.34%), cerebrovascular accident (N=65, 12.9%), hypothyroid (N=52, 10.35%), chronic liver disease (N=15, 2.9%), malignancy (N=8, 1.59%).

Table 3: Mean value of CRP among clinically mild, moderate, severe diseases.

Grade	CRP (mg/dl)						
	N	Mean	SD	Minimum	Maximum	Range	P value
Mild	158	13.620	8.0868	3.0	33.0	30.0	<0.001
Moderate	228	67.978	26.5669	35.0	134.0	99.0	
Severe	116	117.155	16.0930	85.0	153.0	68.0	
Total	502	62.233	43.1098	3.0	153.0	150.0	

Table 4: Mean value of CTSS among clinically mild, moderate, severe diseases.

Grade	CTSS						
	N	Mean	SD	Minimum	Maximum	Range	P value
Mild	158	4.316	2.4025	2.0	11.0	9.0	<0.001
Moderate	228	12.281	1.7561	8.0	15.0	7.0	
Severe	116	18.914	2.9328	16.0	25.0	9.0	
Total	502	11.307	5.8669	2.0	25.0	23.0	

Table 5: Mean value of CRP among the ward, HDU, ICU admissions.

Ward/HDU/ ICU	CRP (mg/dl)						
	N	Mean	SD	Minimum	Maximum	Range	P value
Ward	214	28.112	28.3429	3.0	120.0	117.0	<0.001
HDU	156	64.917	25.0890	40.0	126.0	86.0	
ICU	132	114.379	20.1542	55.0	153.0	98.0	
Total	502	62.233	43.1098	3.0	153.0	150.0	

Table 6: Mean value of CTSS among the ward, HDU, ICU admissions.

Ward/HDU/ ICU	CTSS						
	N	Mean	SD	Minimum	Maximum	Range	P value
Ward	214	6.229	3.9060	2.0	15.0	13.0	<0.001
HDU	156	12.628	2.0039	8.0	21.0	13.0	
ICU	132	17.977	3.6118	10.0	25.0	15.0	
Total	502	11.307	5.8669	2.0	25.0	23.0	

Table 7: Mean CRP values and CTSS among survivors and non survivors.

Variables	Survivors/ non survivors						P value
	Survivors			Non survivors			
	N	Mean	SD	N	Mean	SD	
CRP	428	52.680	38.9387	74	117.486	15.9968	<0.001
CTSS	428	9.808	4.8447	74	19.973	3.1053	<0.001

On arrival, patients were categorized into mild, moderate or severe COVID cases, based on the clinical features and provided with standard of care respectively as per ICMR/AIIMS-COVID 19 national task force/joint monitoring group dated 22nd April 2021 (Figure 1). Out of 502 patients, 158 patients were (31.5%) mild case, 228 patients (45.4%), moderate case, and 116 patients (23.1%) severe case. Of which 214 (42.6%), 156 (31.1%), 132 (26.3%) patients were admitted to ward, HDU (high dependency unit), ICU respectively. ANOVA test was used to compare CRP values and CTSS among patients categorized as mild, moderate, severe diseases clinically, which showed Statistically significant, p value <0.001. CRP values and CTSS increased as the clinical severity increased and were highest among severe cases (Table 3-4). Also ANOVA test was used to compare CRP values and CTSS among the Ward, HDU, ICU admission which was statistically significant with p<0.001. CRP values and CTSS were highest among ICU admitted cases, though very few cases in ward and HDU had

raised values of both CRP and CTSS which showed correlation with each other (Table 5-6).

There was also significant correlation of CRP values and CTSS among survivors and non survivors. Higher values of both CRP and CTSS were observed among non survivors. The mean CRP values and CTSS among survivors and non survivors which showed statistically significant p value is depicted in (Table 7). By using Pearson correlation value, the correlation between CRP and CTSS was done (Table 8, Figure 3) and we found, there is a strong positive correlation between CRP and CTSS in COVID-19 patients (N=502). An increase in CRP caused an increase in CTSS with significant p values.

Table 8: Correlation between CRP and CTSS.

Correlations			
Variable		**CRP (mg/dl)**	**CTSS**
CRP (mg/dl)	Pearson correlation value	1	0.843**
	P value		0.000

**Correlation is significant at the 0.01 level (2-tailed).

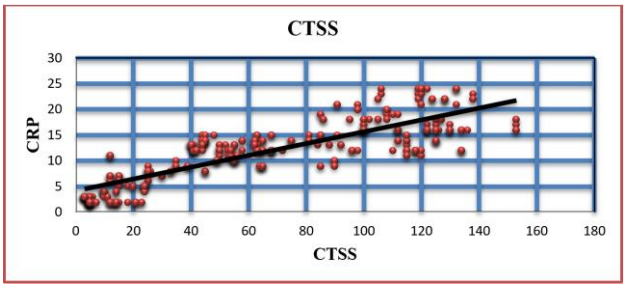

Figure 3: Pearson-correlation between CRP and CTSS.

DISCUSSION

COVID-19 has developed into a worldwide pandemic, early identification of severe illness is critical for controlling it and improving the prognosis of patients with limited medical resources. Early monitoring of key indicators is an important basis to guide treatment strategies, and early assessment of the severity of patients' condition. The present study was carried out retrospectively with an aim to correlate the clinical severity with inflammatory marker CRP and CT severity score. Liu and collaborators found a significant correlation between CRP and the severity of COVID-19 and suggested its use in predicting disease severity as independent -risk factor.[6]

Chen and colleagues performed an observational retrospective study on 76 cases infected by SARS-CoV-2.[10] They disclosed a positive correlation between serum CRP level and pulmonary affection on CT chest, regardless of age and lymphocytic count. Moreover, the serum CRP increased significantly by 23.40 mg/l in the moderate and severe CT affection. A Study by Zhang et al consisted of 108 hospitalized patients with confirmed COVID-19, 87 patients (81%) had elevated CRP levels. Correlation analysis indicated that chest CT score had significantly positive correlations with systemic inflammatory markers. [11] In a Swedish multicenter study, admission CRP level >100 mg/l was found to be associated with increased ICU admissions and 30 day mortality, irrespective of morbidity. They concluded CRP may be simple, early marker for prognosis in ICU admission.[12]

Nalini et al, concluded that inflammatory markers were elevated in all patients (survivors and non-survivor) admitted to ICU. However, their elevation was not found to have a strong correlation to the disease severity. CTSS showed a strong and significant correlation with the disease severity and mortality.[13] Xiong et al several laboratory parameters, specifically the ESR, CRP and LDH, showed significant positive correlation with the severity of pneumonia quantified on initial CT.[14] A recent study was conducted by Marimuthu et al concluded that judicious use of COVID‑19 biomarkers could help in disease prognostication and thereby provide guidance to device appropriate management strategies.[15]

Most of the studies were conducted in western population where inflammatory biomarkers were correlated with HRCT Severity scores, there is not much data regarding Indian population, though we are one of the highest in numbers of COVID-19. Additionally, the early identification of patients who will become severely ill could facilitate the allocation of the limited medical resources to patients in need of aggressive treatment. Keeping these above studies in mind and their correlation between inflammatory markers, CTSS and their severity progress of COVID-19, in our study we aimed to determine the correlation between COVID-19 severity with CRP and HRCT severity score. We chose CRP alone in our study among the inflammatory markers as CRP is a simple test, not expensive as compared with tests like IL 6, D-dimer, procalcitonin, ferritin levels and was used earlier in pre-COVID era as an inflammatory marker for various infectious diseases. CRP levels are correlated with the level of inflammation, and its concentration level is not affected by factors such as age, sex, and physical condition.[16] SARS‑CoV‑2 binds to the cell surface receptor of ACE‑2 by the spike glycoprotein and enters the cell cytoplasm, where it releases RNA genome and replicates, resulting in the formation of new viral particles.[17] Then, the cell disintegrates and the virus spreads to other cells. The immune deregulation initiated by pyroptosis (pro‑inflammatory form of apoptosis) with rapid viral replication leads to massive release of inflammatory mediators.[18] When inflammation or tissue damage happens, CRP can be significantly increased in serum, which usually is used as an important biomarker in the current clinical practice. CRP is an important index for the diagnosis and assessment of severe pulmonary

infectious diseases. Matsumoto's study also showed the value of CRP levels in severe pneumonia.[19]

The main pathological changes of COVID-19 are lung and immune system damage. Serous, fibrin exudates and clear membrane form in the alveolar cavity and congestion and edema appear in the lung.[20] CT dynamic monitoring may be used to identify the characteristic imaging of lung changes: multiple small patch shadows and stromal changes are observed in the early stage, which then develops into multiple ground-glass shadows infiltrating in both lungs.[21] CT scan examination, as a quick and simple method to screen for pulmonary infection, cannot only determine the presence of pulmonary infection but it can also provide a reference for determining the type of pathogen, with unique diagnostic advantages.[22] According to Zhong Nanshan's latest research, the sensitivity of COVID-19 diagnosis with CT scan alone was 76.4%, and the application of CT scan in COVID-19 was evaluated as useful.[23] In our present study we found that, out of 502 patients who fulfilled the inclusion criteria 158 patients (31.5%) were triaged as mild cases, 228 patients (45.4%) were moderate case, and 116 patients (23.1%) severe cases clinically according to AIIMS/ICMR guidelines. ANOVA test was used to compare CRP values and CTSS among the mild, moderate, severe cases clinically, which showed statistically significant correlation ($p<0.001$). Both CTSS and CRP values had explicit association with clinical condition of patients, hence proved to be prognosticating factors in COVID-19 patients. We also found that among 502 patients, in hospital mortality rate was 14.7% By using independent sample t test we could derive that CRP and CTSS had strong and significant correlation with the disease severity and mortality. By using Pearson correlation value, the Correlation between CRP and CTSS was done. An increase in CRP caused an increase in CTSS with significant p values. Here by, in our study we conclude that there is a strong positive correlation between CRP and CTSS in COVID-19 patients.

Limitations

Limitations of current study were; **i**t is a retrospective observational study and study period was of short duration. Results obtained were from small sample size. It is a limiting factor for generalizing the results. Multi centre trials with a large population may be needed to conclude the external validity.

CONCLUSION

In this present retrospective observational study, we found that there is a strong positive clinical correlation between CRP and CT severity score in COVID-19 Patients. Also CRP levels were positively correlated with CTSS in reflecting disease severity and mortality. Our findings may be useful as an earlier indicator for severe illness and help physicians to stratify patients accordingly. Independent use of inflammatory marker like CRP may help to monitor severity of illness and stratify patients accordingly without waiting for radiological evaluation and it's scoring and helpful in places where CT is not available. Larger studies could throw more light on the impact of treatment protocols guided by the biomarkers on the eventual outcomes due to this severe viral infection.

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