Original Article

Correlation between C-reactive Protein (CRP) Level and Clinico-radiological Profile in COVID-19 Patients Admitted in a Tertiary Care Hospital in Eastern India

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Background : Coronavirus disease 2019, first reported in December 2019 mainly presented with the symptoms of Cough, Fever, Shortness of breath, Myalgia, Weakness and anosmia. C-reactive Protein (CRP) is an acute-phase reactant protein which is synthesized by the liver in response to raised levels of interleukin-6 (IL-6) which is a biomarker of inflammation.

Methods : This was a prospective observational study, done on 110 COVID-19 patients after applying inclusion and exclusion criteria. Detailed history, vaccination status, presence of comorbidities and thorough clinical examination was performed. Serum CRP levels was assessed and Computed Tomographic scan (CT scan) of Thorax was done. CORADS scoring and CT severity grading as per CT scan was done. All the above parameters were recorded in the preformed proforma and data was entered in excel spreadsheet and was analysed using SPSS v26 software.

Results : Majority were males (56.3%) and majority were from 61-80 years of age. Majority (57.3%) patients were non-smokers. Hypertension was the most common associated comorbidity (86.4%)(r=0.743, p=0.000). There is a strong positive correlation between CRP levels and CTSS in COVID 19 patients and a strong negative correlation between the CRP levels and outcome of COVID-19 patients (r= -0.449, p=0.000).

Conclusion : Elevated serum CRP value is associated with disease progression and poorer outcome.

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Key words : Acute phase reactant, COVID-19, Severe COVID, CORADS.

Coronavirus disease 2019, also known as COVID-19 was first reported in Wuhan, China, in December, 2019. Patients of COVID-19 mainly present with the symptoms of cough, fever, shortness of breath, myalgia, weakness and anosmia[1]. Cases are diagnosed based on Nucleic Acid Amplification by RTPCR test from oropharyngeal or nasopharyngeal swab. High Resolution Computed Tomography (HRCT) scan of thorax has high sensitivity in detecting COVID-19 among people[2].

The hallmark feature of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection is the systemic inflammatory response to COVID-19 and most hospitalized patients with COVID-19 have abnormal inflammatory biomarkers[3]. C-reactive Protein (CRP) is an acute-phase reactant protein which was first described by Tillet and Francis and is synthesized

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Editor's Comment :
- There is an association between inflammatory biomarker, serum CRP and the chest CT severity scores among COVID 19 patients. Elevated serum CRP value on admission is associated with severe disease and poorer outcome. In these patients, prompt treatment and optimal monitoring is mandatory to reduce morbidity and mortality.

by the liver in response to raised levels of interleukin-6 (IL-6), a biomarker of inflammation[3]. Elevated CRP concentrations are seen in cardiovascular diseases like Myocardial Infarction, Acute Kidney Injury (AKI), inflammatory rheumatic diseases such as rheumatoid arthritis and gout, and with incident Venous Thrombo-Embolism (VTE)[3]. C-reactive Protein has also been previously associated with severe disease in patients with H1N1 influenza pneumonia[4].

Previous studies have shown that there is a good correlation between CT Severity Scores (CTSS), severity of clinical disease and blood CRP values among patients diagnosed with COVID-19. Since CRP is an acute phase reactant hence its values increase greatly during inflammation and indicate the severity of disease. With an increase in inflammation there is also activation of the coagulation cascade in the body leading to formation of microthrombi as identified by

postmortem studies[1,5].

In low resource areas like our country, CRP can used as a substitute for CTSS for determining the severity of the disease. Hence, it was decided to carry out this study to find out the utility of serum CRP as a marker of severity of COVID-19 disease as well as the distribution pattern of the disease in this part of Eastern India.

MATERIALS AND METHODS

This study was a prospective observational study on 110 COVID 19 patients which was conducted after approval from Institutional Ethics Committee (IEC). Participants who gave consent for the study and were haemodynamically stable were included in the study. Detailed history, vaccination status, presence of comorbidities and thorough clinical examination was performed with relevant biochemical and radiological investigations. Serum CRP levels was assessed for all patients. Computed Tomographic scan (CT scan) of Thorax was done. CORADS scoring and CT severity grading as per CT scan was done. Duration of Hospital stay and clinical outcome of the patient was assessed. All the above parameters were recorded in the preformed proforma after taking written consent from all patients/relatives. Data was entered in excel spreadsheet and was analysed using SPSS v26 software. P-value of <0.05 was considered as statistically significant and Pearson correlation have been used to show correlation between various parameters.

Ethics :

This study was conducted after getting approval from Institutional Ethics Committee (IEC).

RESULTS

Out of 110 patients, 62 (56.3%) were males and 48 (43.6%) were females. 63 (57.2%) were from 61-80 years of age. Most of the male (64.5%) and female patients (68.8%) who were hospitalized were above 60 years of age (Table 1).

In 63 (57.3%) patients were non-smokers while 47 patients (42.7%) were smokers (Table 2).

Hypertension was the most common associated comorbidity seen in 95 (86.4%) patients, followed by Type 2 Diabetes Mellitus in 75 (68.2%) patients (Table 3).

Mean CRP levels were 91.25±32.948 mg/dl while mean CTSS was found to be 16.24±6.486. There is a strong positive correlation between CRP levels and CTSS in COVID-19 patients and is statistically significant (r=0.743, p=0.000) (Table 4).

Table 1— *Distribution of COVID patients according to age and gender*

Age	Gender			
	Male		Female	
	No of Patients	Percentage	No of Patients	Percentage
Below 21	0	0.0%	0	0.0%
21-40	5	8.1%	1	2.1%
41-60	17	27.4%	14	29.2%
61-80	36	58.1%	27	56.2%
Above 81	4	6.5%	6	12.5%

Table 2 — *Smoking status of COVID patients*

Smoking Status	No. of Patients	Percentage
NO	63	57.3%
YES	47	42.7%

Table 3 — *Distribution of co-morbidities of COVID patients*

Comorbidities	No of Patients	Percentage
Hypertension :		
Present	95	86.4
Absent	15	13.6
Type 2 Diabetes :		
Present	75	68.2
Absent	35	31.8
Ischemic Heart Disease :		
Present	38	34.5
Absent	72	65.5
Chronic Respiratory Disease :		
Present	20	18.2
Absent	90	81.8

Table 4 — *Correlation between CRP levels and CT Severity score*

Parameters	Mean Value ± SD	r value	p value
CRP levels	91.25±32.948	0.743	0.000
CT Severity Score	16.24±6.486		

There is a strong negative correlation between the CRP levels and outcome of COVID-19 patients and is statistically significant. (r= -0.449, p=0.000) (Table 5)

DISCUSSION

The current study explores the benefit of using serum CRP value as an indicator of severity of COVID-19 disease. When there is clinical suspicion of COVID-19 with initial negative RT-PCR testing, WHO had advised the use of chest imaging as diagnostic tool. CT scan is an appropriate means to assess individual disease severity[6]. In the current study a previously validated score based on lobar extent of the disease as reported by Pan, *et al* has been adopted to quantify the disease severity[7]. The liver synthesizes various acute phase proteins like CRP. Serum CRP levels

Table 5 — *Correlation between CRP levels and Outcome*

Parameters	r value	p value
CRP levels	-0.449	0.000
Outcome		

increase during inflammatory responses. It is stated by Liu, *et al* that severe cases of COVID-19 exhibited higher levels of CRP[8].

In the present study, age of most of the patients is above 60 years (57.2%). Comparable findings were observed in studies by Wang, *et al* and Francone, *et al* in which the study population comprised of a relatively older age[9,6]. Existing literature has mentioned that presence of comorbidities such as Hypertension, diabetes, Coronary Artery Diseases and Chronic Lung diseases makes the prognosis grim[6,10]. In our study the most prevalent comorbidity was hypertension similar to the study by Guan, *et al* in which hypertension followed by diabetes were the two most frequent comorbidity among the patients. In our study, majority of the patients were non-smokers in accordance with the finding of low prevalence of smokers among patients hospitalized with COVID-19 in a multicentred study by Meini, *et al*[11].

In the current study there is statistically significant correlation between serum CRP levels and Chest CT severity scores (p<0.0001, r=0.743), which is consistent with the findings of the research by Saeed *et al* (p<0.0001, r=0.556) and Francone, *et al* (p<0.0001, r= 0.6204)[6,7]. Thus in centres which are lacking CT facility, serum CRP value of the patient can be utilized to anticipate severe COVID-19 disease and initiate prompt management such as intravenous steroid at the earliest. In the present study serum CRP value is significantly negatively correlated to outcome of COVID-19 patients, which is equivalent to the finding of significant increase inflammatory markers like CRP in more severe COVID-19 illness in a study by Hachim, *et al*[12,13].

The current study takes into account a short sample size. So, the results cannot be universalized. Also, multiple serum CRP value measurements at regular intervals could be done to augment the findings of this study.

To conclude with, the current study establishes an association between inflammatory biomarker namely serum CRP and radiological parameter particularly the Chest CT severity scores among COVID-19 patients. Elevated serum CRP value is associated with disease progression and poorer outcome. Thus, careful monitoring of COVID-19 patient is mandatory to avert mortality. Future research should be directed to consider a large sample size and to obtain serial data for analysis.

References

1   Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review. *JAMA* 2020; **324(8):** 782-93. doi:10.1001/jama.2020.12839

2   Ai T, Yang Z, Hou H, Zhan C, Chen C, Lv W, Tao Q, Sun Z, Xia L — Correlation of Chest CT and RT-PCR Testing for Coronavirus Disease 2019 (COVID-19) in China: A Report of 1014 Cases. *Radiology* 2020; **296(2):** E32-E40. doi: 10.1148/radiol.2020200642. Epub 2020 Feb 26. PMID: 32101510; PMCID: PMC7233399.

3   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. *Eur Heart J* 2021; **42(23):** 2270-9. doi: 10.1093/eurheartj/ehaa1103. PMID: 33448289; PMCID: PMC7928982.

4   Vasileva D, Badawi A — C-reactive protein as a biomarker of severe H1N1 influenza. *Inflamm Res* 2019; **68:** 39-46.

5   Sproston NR, Ashworth JJ — Role of C-Reactive Protein at Sites of Inflammation and Infection. *Front Immunol* 2018; **9:** 754. doi: 10.3389/fimmu.2018.00754. PMID: 29706967; PMCID: PMC5908901.

6   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. *Radiology Research and Practice* 2021; 2021.

7   Francone M, Iafrate F, Masci GM, Coco S, Cilia F, Manganaro L, *et al* — Chest CT score in COVID-19 patients: correlation with disease severity and short-term prognosis. European Radiology 2020; **30(12):** 6808-17.

8   Pan F, Ye T, Sun P, Gui S, Liang B, Li L, *et al* — Time course of lung changes on chest CT during recovery from 2019 novel coronavirus (COVID-19) pneumonia. *Radiology* 2020 Feb 13.

9   Liu F, Li L, Xu M, Wu J, Luo D, Zhu Y, *et al* — Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19. Journal of clinical virology. 2020 Jun 1; 127:104370 The Paradox of the Low Prevalence of Current Smokers Among COVID-19 Patients Hospitalized in Nonintensive Care Wards: Results From an Italian Multicenter Case–Control Study. *Nicotine and Tobacco Research* 2021; **23(8):** 1436-40.

10   Wang G, Wu C, Zhang Q, Wu F, Yu B, Lv J, *et al* — C-reactive protein level may predict the risk of COVID-19 aggravation. In Open forum infectious diseases 2020 May (Vol. 7, No. 5, p. ofaa153). US: Oxford University Press.

11   Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, *et al* — Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *European Respiratory Journal* 2020; **55(5).**

12   Meini S, Fortini A, Andreini R, Sechi LA, Tascini C — The Paradox of the Low Prevalence of Current Smokers Among COVID-19 Patients Hospitalized in Nonintensive Care Wards: Results From an Italian Multicenter Case-Control Study. *Nicotine Tob Res* 2021; **23(8):** 1436-40. doi: 10.1093/ntr/ntaa188. PMID: 32964233; PMCID: PMC7543586.

13   Hachim IY, Hachim MY, Hannawi H, Naeem KB, Salah A, Hannawi S — The inflammatory biomarkers profile of hospitalized patients with COVID-19 and its association with patient's outcome: A single centered study. *Plos one* 2021; **16(12):** e0260537.