CORRELATION BETWEEN SERUM C-REACTIVE PROTEIN LEVEL WITH SEVERITY OF THE DISEASE IN COVID-19 PATIENTS

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Abstract

Background: To find the levels of serum CRP in confirmed Covid-19 patients and to compare their levels in patients with mild to moderate disease and patients with severe disease who required ICU care for management.

Methods: A Cross sectional study was carried out on 100 confirmed cases of Covid-19, in whom Serum levels of Random sugar (RBS), Creatinine, Urea, C- reactive protein (CRP) were measured.

Results: The levels of serum Urea, Creatinine were significantly increased in group II when compared to group I, and the levels of CRP were significantly increased with p value <0.0001 in group II when compared to group I.

Conclusion: Findings of our study suggest that determination of biochemical parameters like CRP at the time of hospitalization helps in predicting the severity of disease and need for ICU for better treatment management and prevention of adverse outcome.

Keywords: Severe acute respiratory syndrome, Covid-19, C- reactive protein, Intensive care unit.

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has become the focus of attention worldwide. It is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).¹ First case of COVID-19 was reported in late December 2019 in Wuhan, China, since then it has aggressively spread across the world and dramatically impacted people's health and daily life.² This outbreak has been a challenge for clinicians and researchers alike.

COVID-19 infection has a variable clinical presentation from asymptomatic to milder symptoms, including fever, dry cough, dyspnoea, myalgia, sore throat and headache, to more severe and emergent manifestations including confusion, chest pain, hypoxemia, pneumonia and other complications requiring intensive care unit (ICU) admission and mechanical ventilation.³⁻⁵ Diarrhoea, anosmia and ageusia as well as neurologic manifestations have also been reported in a few studies.⁶⁻⁸ As the number of infected and fatal cases is rising across the globe, there is a pressing need to investigate the clinical, radiological, and laboratory characteristics, and more importantly, the mortality risk factors in severe COVID-19 patients.

In an effort to aid medical management, researchers all over the globe have been toiling hard to search for predictors of COVID-19 disease severity to identify and stratify them accordingly. Insights into disease pathogenesis and methods to rapidly discern and assess COVID-19 infection are evolving. Laboratory biomarkers are economical, faster and feasible to obtain. As such, they have been the

preferred modality to monitor and predict outcomes and prognosis of disease.⁹⁻¹¹ Understanding the variation and profile of specific biomarkers as a function of different COVID-19 outcomes would help in the development of a risk stratified approach in the care of patients with this illness. With the surge in COVID-19 cases across the globe due to its highly contagious nature, there have been numerous studies reporting on the predictors of disease severity in COVID-19 patients.

CRP is an acute-phase, nonspecific marker of inflammation/infection which has been found to broadly correlate with disease severity and treatment response across a variety of infectious and noninfectious conditions. Elevated CRP levels have been previously reported in severe acute respiratory syndrome, Middle East respiratory syndrome, H1N1 influenza.¹⁹⁻²¹ Recent studies have reported that CRP levels are elevated in patients with COVID-19 and may correlate with severity of disease and disease progression.¹² As such, CRP holds promise as a potential prognostic biomarker. The aim of the study is to evaluate the clinical utility of CRP in predicting the severity of COVID-19 and need for intensive care and further complications.

Material and Methods

Source of Data: A cross sectional study was carried out on 100 Confirmed positive cases of Covid-19. All the cases were confirmed Covid-19 positive by real time reverse

transcriptase polymerase chain reaction (RT-PCR) assay in nasal and pharyngeal swab specimen.

Data collection: After taking informed consent, Cases were subjected to medical examination and blood investigations. General health characteristics such as Age, Sex, history of travel, exposure to any other patient with similar illness were noted. History of Diabetes, hypertension and any other co morbid condition was recorded.

Biochemical investigations: A random blood sample of about 3ml was drawn from all the patients recruited for the study. Serum was separated by centrifugation and used for estimation of RSG, Serum Creatinine, blood urea and CRP.

Methods of Estimation: RSG: Glucose Oxidase Peroxidase, Serum Creatinine: Kit based Jaffe's method, Blood Urea: Modified Berthelot's Method. CRP: Turbidimetric Method using a reagent kit Tubilaxex,

Statistical analysis: The data was collected, compiled and analyzed using SPSS statistical package version 21.00. Pearson's correlation test was performed to examine various correlations. Unpaired t-test was used for two group comparison. For all the tests, p value of < 0.05 was considered as statistically significant. Results were expressed as Mean, SD, and range values for continuous data, number and percentage for discrete data.

Results:

A total of 100 patients with confirmed COVID-19 infection were enrolled in this study. Among the total patients enrolled for the study, 23 were females and 77 were males, the average age being 51-65 years. To assess the clinical utility of CRP in predicting hospital outcome, Covid-19 Patients were divided into two groups- Group I Covid-19 patients with mild to moderate disease (n=83) Group II Covid-19 patients with severe illness who required ICU admission for the management. (n=17)

Table 1: Distribution of patients according age, serum levels of RBS, urea, creatinine, and CRP

	Group	Mean	SD	p (value)
Age (years)	1	63.21	11.23	>0.05
	2	52.69	12.96	
RBS (mg/dl)	1	172.65	83.21	>0.05
	2	152.32	80.27	
Urea (mg/dl)	1	38.65	21.32	<0.05
	2	30.12	10.28	
S. Creatinine (mg/dl)	1	1.39	0.53	<0.05
	2	0.84	0.26	
CRP (mg/L)	1	59.63	32.14	0.0001
	2	36.23	23.62	

There was no significant difference in the age, and SRG level between Group I and group II (p value>0.05).

The levels of serum Urea, Creatinine were significantly increased in group II when compared to group I, and the levels of CRP were significantly increased with p value <0.0001 in group II when compared to group I.

Discussion:

Covid-19 is a pandemic infectious disease which has spread rapidly across the globe and became an urgent public health challenge. According to WHO's report, the pandemic will continue at least for years¹². Clinical and epidemiological features have been reported by many studies,^{13,14} but the knowledge about the biochemical parameters predicting the severity and mortality of the disease is reported by very few studies. Thus the aim of this study is to find out the predictive value of CRP in assessing the severity of COVID-19, need for intensive care and associated mortality.

We found statistically higher levels (p value<0.0001) of CRP in group 2 patients who were in ICU when compared to group 1 patients. Our findings are in accordance with previous studies.^{15,16-19} High levels of inflammatory markers are critical indicators of underlying systemic vasculitis and dysregulation of coagulation mechanism that leads to parenchymal lesions in vital organs. CRP is a non-specific acute phase reactant induced by IL-6 in the liver. Elevated CRP levels are directly correlated with level of inflammation and disease severity. Hence, it is an important biomarker in diagnosis and assessing the severity of infectious diseases.²⁰

In one retrospective study, CRP and IL-6 values on admission were independent predictors of disease severity, while in a small prospective study IL-6 and CRP levels correlated with the development of respiratory failure.^{21,22} Another small retrospective study reported a correlation between mortality and CRP values in diabetic patients with COVID-19.²³ Few researchers have reported a direct association between the level of CRP with the

inflammation and severity of disease,²⁴⁻²⁵ suggesting that CRP levels can be most effective and sensitive biomarker in predicting the COVID-19 disease progression.

The findings of our study suggest that determination of serum CRP along with the other routine laboratory tests is useful for predicting high risk and need for ICU care in the early stage to prevent the adverse outcome of Covid-19 disease.

Conclusion:

Study of biomarkers is essential for identifying high risk categories following Covid-19 diagnosis for optimal resource allocation, to improve the clinical management and prevention of serious complications. CRP is widely available, easy to obtain, and inexpensive. Our study advocates that determination of biochemical parameters like CRP at the time of hospitalization helps in predicting the severity of disease and need for ICU care, leading to better treatment management and prevention of adverse outcome.

References:

1. Corona viridae Study Group of the International Committee on Taxonomy of Viruses. The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. *Nat Microbiol* 2020; 5:536-544.
2. Zhu NA, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020; 382:727-733. <https://doi.org/10.1056/NEJMoA2001017>.
3. W-jG, Z-y N, Hu Y, et al. Clinical characteristics of corona virus disease 2019 in China. *N Engl J Med* 2020.
4. The Novel Corona virus Pneumonia Emergency Response Epidemiology T. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) — China, 2020. *China CDC Weekly* 2020; 2:113-22.
5. Zaim S, Chong JH, Sankaranarayanan V, et al. COVID-19 and multi organ response. *Curr Probl Cardiol* 2020; 45:100618.
6. Giacomelli A, Pezzati L, Conti F, et al. Self-Reported olfactory and taste disorders in patients with severe acute respiratory coronavirus 2 infection: a cross-sectional study. *Clin Infect Dis* 2020; 71:889-90.
7. Pan L, Mu M, Yang P, et al. Clinical characteristics of COVID-19 patients with digestive symptoms in Hubei, China: a descriptive, cross-sectional, multicenter study. *Am J Gastroenterol* 2020; 115:766-737.
8. Kaur N, Gupta I, Singh H, et al. Epidemiological and clinical characteristics of 6635 COVID-19 patients: a pooled analysis. *SN Compr Clin Med* 2020:1048-52.
9. Whittaker A, Anson M, Harky A. Neurological manifestations of COVID-19: a systematic review and current update. *Acta Neurol Scand* 2020; 142:14-22.
10. Vasileva D, Badawi A. C-reactive protein as a biomarker of severe H1N1 influenza. *Inflamm Res* 2019;68(1):39-46. <https://doi.org/10.1007/s00011-018-1188-x> PMID: 30288556
11. Herold T, Jurinovic V, Arnreich C, et al. Elevated levels of IL-6 and CRP predict the need for mechanical ventilation in COVID-19. *J Allergy Clin Immunol* [Internet] 2020; Available from: <https://doi.org/10.1016/j.jaci.2020.05.008> PMID: 32425269
12. Huang Y, Lyu X, Li D, Wang L, Wang Y, Zou W, et al. (2020) A cohort study of 676 patients indicates D-dimer is a critical risk factor for the mortality of COVID-19. *PLoS ONE* 15(11): e0242045.
13. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020; 395(10223): 497-506
14. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med*. 2020; 02: 25-29.
15. Ullah W, Thalambedu N, Haq S, Saeed R, Khanal S, Tariq S et al. Predictability of CRP and D-Dimer levels for in hospital outcomes and mortality of COVID-19. *Journal of Community Hospital Internal Medicine Perspectives*. 2020; 10(5):402-408.
16. Wang F, Zhang H, Sun Z. The laboratory tests and host immunity of COVID-19 patients with different severity of illness. *JCI Insight*. 2020;5(10):e137799.
17. Tomlins J, Hamilton F, Gunning S, Sheehy C, Moran E, Mac Gowan A. Clinical features of 95 sequential hospitalised patients with novel coronavirus 2019 disease (COVID-19), the first UK cohort. *J Infect*. 2020; 81(2):e59-e61.
18. Velavan TP, Meyer CG. Mild versus severe COVID-19: Laboratory markers. *International Journal of Infectious Diseases*. 2020; 95: 304-307.
19. Ponti G, Maccaferri M, Ruini C, Thomasi A, Thomari O. Biomarkers associated with COVID-19 disease progression. *Critical Reviews in Clinical Laboratory Sciences*. <https://doi.org/10.1080/10408363.2020.1770685>.
20. Chalmers S, Khawaja A, Wieruszewski PM, et al. Diagnosis and treatment of acute pulmonary inflammation in critically ill patients: the role of inflammatory biomarkers. *WJCCM* 2019; 8:74-96.
21. T. Haitao, J. V. Vermunt, J. Abeykoon et al., "COVID-19 and sex differences: mechanisms and biomarkers," *Mayo Clinic Proceedings*, vol. 95, no. 10, pp. 2189-2203, 2020.
22. Sproston NR, Ashworth JJ. Role of C - reactive protein at Sites of Inflammation and Infection. *Front Immunol*

- 2018; 9:754. <https://doi.org/10.3389/fimmu.2018.00754> PMID: 29706967
23. Koozi H, Lengquist M, Frigyesi A. C-reactive protein as a prognostic factor in intensive care admissions for sepsis: A Swedish multicenter study. *J Crit Care* 2020; 56:73–9. <https://doi.org/10.1016/j.jcrc.2019.12.009> PMID: 31855709
24. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China [Internet]. *Intensive Care Medicine*. 2020; 46:846–8. Available from: <https://doi.org/10.1007/s00134-020-05991-x> PMID: 32125452
25. Chen Y, Yang D, Cheng B, et al. Clinical Characteristics and Outcomes of Patients With Diabetes and COVID-19 in Association With Glucose-Lowering Medication. *Diabetes Care* [Internet] 2020; Available from: <http://dx.doi.org/10.2337/dc20-0660>.