



Elevated Plasma IL-6 and CRP Levels Association with Adverse Clinical Outcomes in SARS-CoV-2 Patients: A Prospective Observational Study

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Abstract

Background: The World Health Organization named COVID-19 caused by SARS-CoV-2 a global pandemic on March 11th, 2020. CRP increased dramatically in severe COVID-19 individuals from the outset, which is a marker of lung damage and progression. This virus activates the immune system, releasing a significant number of cytokines, including IL-6. The goal of the study was to look at the relationship between biomarker levels and COVID-19 illness severity and how that correlated with outcome.

Material and Methods: A Cross sectional prospective hospital-based study done over a period of 7 months, from November 2020 to May 2021 on 250 SARS-CoV-2 patients at Department of General Medicine, JLNMCH, Bhagalpur, Bihar.

Results: Most common age group in present study having COVID-19 cases were 41 to 50 years i.e., 69 (27.60%) & males were affected i.e., 154 (58.80%) in comparison to females i.e., 96 (41.20%). In relation to distribution of symptoms among patients in present study it was found that maximum patients presented with fever, cough & sore throat i.e., 221 (88.40%), 187 (74.80%) & 193 (77.20%). Most patients suffered from moderate COVID-19 i.e., 116 (46.40%) followed by severe form i.e., 87 (34.80%) respectively. In correlation between distributions of CRP, IL6 with severity of COVID-19 results found were statistically significant with p-value <0.001.

Conclusion: Assessment of levels of various biomarkers helps in the immediate categorization of patients into risk groups following diagnosis, ensuring optimal resource allocation, especially in places where HRCT facilities are not readily available, based on the significant association with severity of lung involvement.

Keywords: COVID-19; WHO; Diabetes; RT-PCR

Introduction

The World Health Organization named COVID-19 caused by SARS-CoV-2 a global pandemic on March 11th, 2020. Coronavirus Disease (COVID-19) is a newly found coronavirus that causes an infectious disease. The majority of patients infected with the COVID-19 virus will have mild to moderate respiratory symptoms and will recover without needing any specific therapy. People over the age of 65, as well as those with underlying medical conditions such as cardiovascular disease, diabetes, chronic respiratory disease, and cancer, are at a higher risk of developing serious illness [1]. Being thoroughly informed on the COVID-19 virus, the disease it produces, and how it transmits is the greatest strategy to avoid and slow down transmission. Wash your hands frequently or use an alcohol-based rub to protect yourself and others from infection, and avoid touching your face. When an infected individual coughs or sneezes, the COVID-19 virus transmits predominantly through droplets of saliva or discharge from the nose, therefore respiratory etiquette is particularly vital (for example, by coughing into a flexed elbow) [2,3]. CRP increased dramatically in severe COVID-19 individuals from the outset, which is a marker of lung damage and progression. This virus activates the immune system, releasing a significant number of cytokines, including IL-6. IL-6 is a multi-effective cytokine that has anti-inflammatory and pro-inflammatory properties and aids in the host's defense against infections. However, excessive production while battling the virus causes a severe systemic inflammatory response known as cytokine storm [4-6]. The goal of the study was to look at the relationship between biomarker levels and COVID19 illness severity and

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how that correlated with outcome.

Material and Methods

Type of study: A Cross sectional prospective study.

Study approval: The thesis protocol had been authorized by the concerned Ethics Committee prior to the start of this investigation.

Place of study: The study was conducted at Department of General Medicine, JLNMC, Bhagalpur, Bihar.

Period of study: This study was carried out over a period of 7 months, from November 2020 to May 2021.

Sample size: The sample size for the study was taken 250.

Sampling method: Individuals were given information about the examination process and were assured that they might refuse to be examined. Before participating in the trial, the patients gave their informed written consent in the local language. Individuals were motivated to participate in the study after being informed. Separate proforma for each individual was filled. Identity of patients was not revealed. History was obtained from the patient or his/her relatives. The predesigned pretested proforma was used to collect information about epidemiological factors like age and sex. Detailed clinical data like symptoms, signs and associated illnesses, general and systemic examination is collected and included in the study. After validation by the history sheet, the age of persons was recorded on the research Proforma in completed years. All consecutive patients of COVID-19 diagnosis with RT-PCR report admitted in general medicine ward as per the inclusion and exclusion criteria was included in the study. The biochemical, radiological reports & severity or complications of all these patients was documented and correlated. **Inclusion criteria:** All patients with RT-PCR positive COVID report.

Exclusion criteria: All patients with RT-PCR negative COVID report.

Data entry and analysis: All of the data was tabulated and analyzed using statistical software (SPSS version 21.0). As needed, data was presented as a mean with standard deviation or as proportions. The following statistical significance tests were used along with the mean, standard deviation, and variance. For statistical significance testing, the "Chi-square Test" and "Fisher's exact test" were utilized.

Test of Significance for proportional differences. The statistical instrument employed to test for significance of observed mean differences was the Student's T-test. One-Way ANOVA is a statistical test that compares the means of two or more groups, two or more interventions, and two or more change scores. Finally, the estimated value was compared to the tabulated value at a specific degree of freedom to determine the significance level. If the "p-value" was found to be greater than 0.05, it was judged non-significant, and if it was less than 0.05, it was regarded significant. The probability of error was considered significant at 0.05, whereas it was very significant at 0.01 and 0.001. Each biomarker's ROC (receiver operating characteristic curve) was created and utilized to demonstrate diagnostic ability.

Result

A Cross sectional prospective study conducted at a tertiary care centre of northern India over a period of 7 months, from November 2020 to May 2021 on 250 patients of COVID-19.

Table 1 shows that most common age group in present study

Table 1: Distribution of patients according to age.

Age group	No. of patients	Total (%)
12-20	12	4.80%
21-30	35	14.00%
31-40	56	22.40%
41-50	69	27.60%
51-60	55	22.00%
61-70	23	9.20%
Total	250	100%

Table 2: Distribution of patients according to gender.

Gender	No. of Patients	Percentage
Male	154	58.8
Female	96	41.2

Table 3: Clinical presentation of COVID-19 cases studied.

Clinical presentation	No. of patients	Percentage
Fever	221	88.4
Cough	187	74.8
Sore throat	193	77.2
Headache	84	33.6
Dyspnea	124	49.6
Abdominal pain	61	24.4
Diarrhea	77	30.8
Vomiting	49	19.6
Myalgia/ arthralgia	31	12.4
Conjunctival injection	19	7.6

Table 4: Degree of severity of COVID-19 patients studied.

Degree of severity	No. of patients	Percentage
Mild	47	18.8
Moderate	116	46.4
Severe	87	34.8
Total	250	100.00%

Table 5: Distribution of biomarkers level in studied population.

Variables	CRP	IL-6
Distribution	8.09 ± 8.02	15.33 ± 16.79

Table 6: Correlation between distributions of CRP, IL-6 with severity of COVID.

Severity	CRP	IL-6	t- statistics	p-value
Mild	06.57 ± 04.21	08.91 ± 05.11	5.588	p<0.001
Moderate	08.99 ± 03.64	12.87 ± 06.27	8.462	p<0.001
Severe	14.24 ± 06.87	17.68 ± 8.71	4.903	p<0.001

having COVID-19 cases were 41 to 50 years i.e., 69 (27.60%) followed by 31 to 40 years i.e., 56 (22.40%) respectively. Mostly males were affected i.e., 154 (58.80%) in comparison to females i.e., 96 (41.20%) (Table 2).

In relation to distribution of symptoms among patients in present study it was found that maximum patients presented with fever, cough & sore throat i.e., 221 (88.40%), 187 (74.80%) & 193 (77.20%) respectively, followed by dyspnea and headache i.e., 124 (49.60%) &

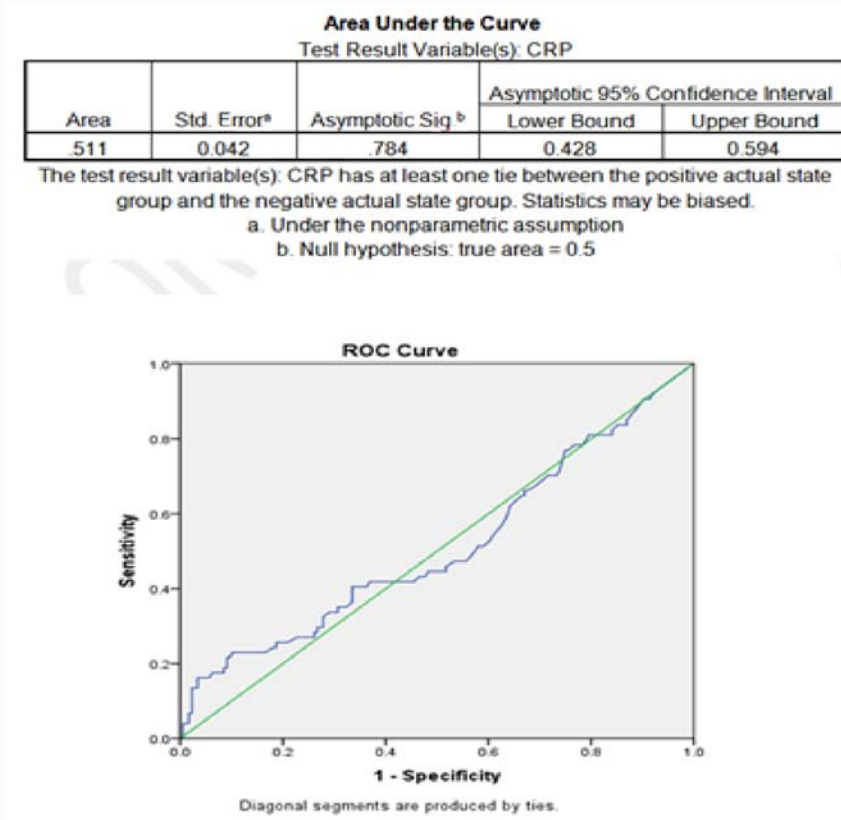


Figure 1: ROC curve of CRP.

84 (33.60%) (Table 3).

According to recent WHO guidelines [6] most patients were suffered from moderate COVID-19 i.e., 116 (46.40%) followed by severe form i.e., 87 (34.80%) respectively (Table 4).

T-statistic =6.152, Degrees of freedom =498, Two-tailed probability <0.001, Written as $t(498)=6.152$, $p<0.001$, Conclusion at the 0.05 critical alpha level: The difference is significant (Table 5).

In correlation between distributions of CRP, IL-6 with severity of COVID-19 results found were statistically significant with p-value <0.001 (Table 6).

Discussion

A Cross sectional prospective hospital-based study done over a period of 7 months, from November 2020 to May 2021 on 250 SARS-CoV-2 patients. Present study found that most common age group in present study having COVID-19 cases were 41 to 50 years i.e., 69 (27.60%) followed by 31 to 40 years i.e., 56 (22.40%) respectively & mostly males were affected i.e., 154 (58.80%) in comparison to females i.e., 96 (41.20%). In a study similar to this one, Gupta et al. [2], found that the average age of patients with severe lung involvement is 54.1 years, while the average age of patients with non-severe lung involvement is 52 years, but there was no significant relationship between the severity of lung involvement and the age of the patients. There were 133 male patients and 67 female patients.

In present study, it was found that maximum patients presented with fever, cough & sore throat i.e., 221 (88.40%), 187 (74.80%) & 193 (77.20%) respectively. Similarly, Revzin et al. [7], mentioned fever, cough, and sore throat occurrence was 88%, 68% & 61%. Most

patients were suffered from moderate COVID-19 i.e., 116 (46.40%) in the present study. Guler et al. [8] study found severe cases were 66 i.e., 64.57% in comparison to mild/moderate cases i.e., 47 (35.43%).

ROC curve results in present study suggest a pathogenic role of IL-6 than CRP in the pathophysiology of SARS-CoV-2 infection (Figure 1 and 2). Guler et al. [8], & Sultan et al. [9], also found comparable results.

In a retrospective monocentric observational analysis by Gupta et al. [2], 121 individuals with increased CRP were identified, 31 of whom had severe lung involvement and 90 of whom did not. In contrast, 79 patients with normal CRP levels were found, 10 of whom had severe lung involvement and 69 of whom did not. There is a strong link between CRP levels and the severity of lung disease ($p=0.0346$, RR of 2.02, Odds Ratio of 2.37).

CRP is a non-specific acute-phase protein generated by IL-6 in the liver and a sensitive biomarker of inflammation, infection, and tissue damage, according to a study by Liu et al. [10]. There is a link between isolated levels of LDH, CRP, and ferritin and lung involvement severity. CRP levels have clinical relevance as a marker for severe illness and increasing inflammation, according to our findings.

The study by Soraya et al. [11] also discovered that IL-6, a significant pro-inflammatory mediator for inducing the acute phase response, has been intensively examined as a predictive biomarker in sepsis and diverse acute organ injuries. Sabaka et al. [12] study very similar to present study found CRP levels in mild and critical cases were 8.92 & 7,069 mg/l, also IL-6 levels were 7.3 & 26.3 pg/ml respectively.

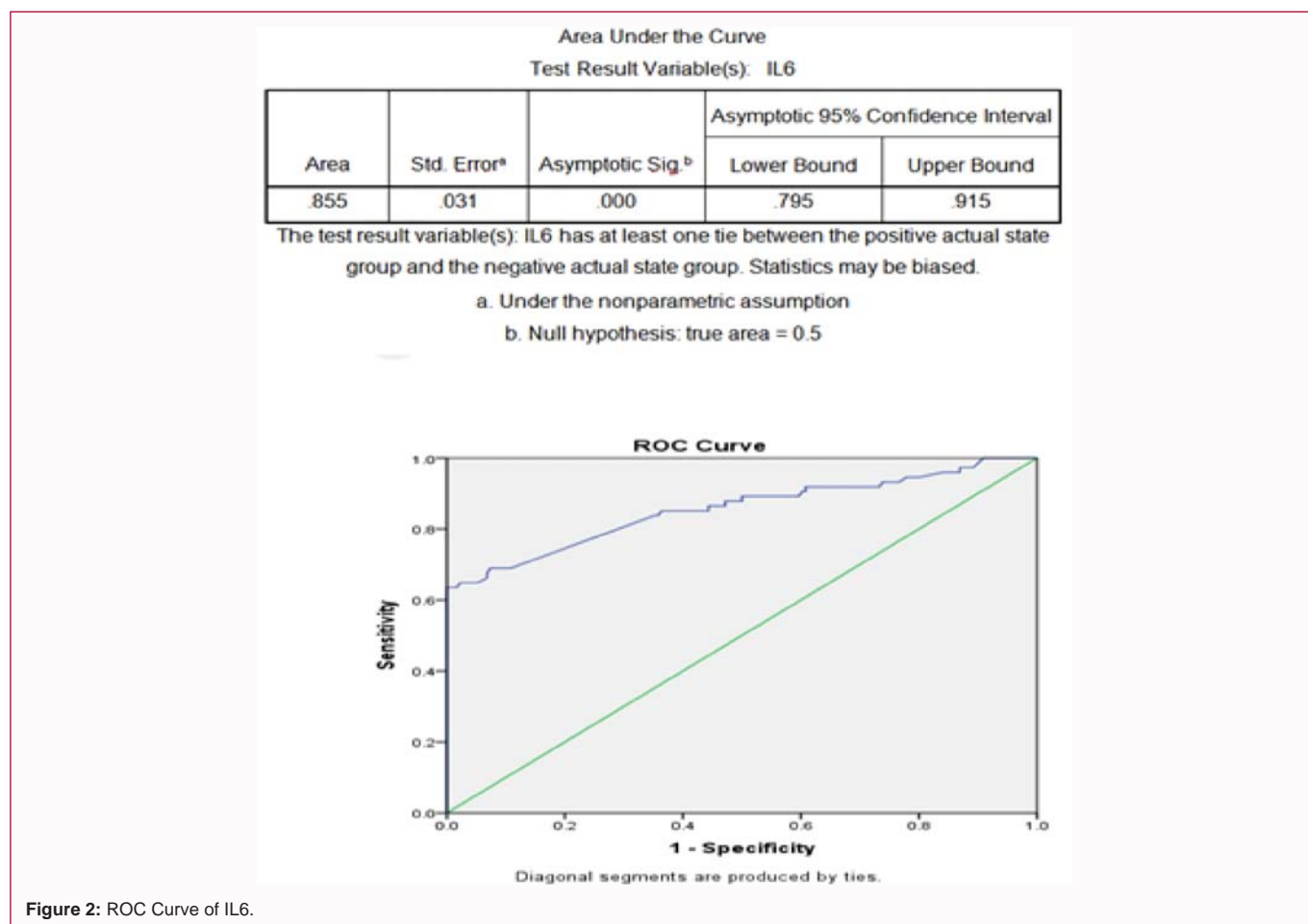


Figure 2: ROC Curve of IL6.

Conclusion

The relevance of IL-6 as a predictive biomarker in sepsis and various acute organ injuries has been extensively researched. It is a significant pro-inflammatory mediator for induction of the acute phase response. In our research, there was a substantial link between IL-6, CRP, and illness severity. Assessment of levels of various biomarkers helps in the immediate categorization of patients into risk groups following diagnosis, ensuring optimal resource allocation, especially in places where HRCT facilities are not readily available, based on the significant association with severity of lung involvement.

References

- World Health Organization. COVID-19 weekly epidemiological update, 23 February 2021.
- Gupta P, Halani A, Samuel T, Singh DP. Association of inflammatory biomarkers with radiological severity for COVID-19 patient risk stratification: An Indian perspective. *Asian J Med Sci.* 2021;12(4):1-7.
- Bagchi S. The world's largest COVID-19 vaccination campaign. *Lancet Infect Dis.* 2021;21(3):323.
- Wouters OJ, Shadlen KC, Salcher-Konrad M, Pollard AJ, Larson HJ, Teerawattananon Y, et al. Challenges in ensuring global access to COVID-19 vaccines: Production, affordability, allocation, and deployment. *Lancet.* 2021;397(10278):1023-34.
- Singh J, Singh J. COVID-19 and its impact on society. *Electr Res J Soc Sci Human.* 2020;2(1).
- Andrade C. COVID-19: Humanitarian and health care crisis in a third world country. *J Clin Psychiatry.* 2020;81(3):20com13383.
- Revzin MV, Raza S, Warshawsky R, D'agostino C, Srivastava NC, Bader AS, et al. Multisystem imaging manifestations of COVID-19, part 1: Viral pathogenesis and pulmonary and vascular system complications. *Radiographics.* 2020;40(6):1574-99.
- Guler SA, Ebner L, Aubry-Beigelman C, Bridevaux PO, Brutsche M, Clarenbach C, et al. Pulmonary function and radiological features 4 months after COVID-19: First results from the national prospective observational Swiss COVID-19 lung study. *Eur Respir J.* 2021;57(4):2003690.
- Sultan OM, Al-Tameemi H, Alghazali DM, Abed M, Ghniem MN, Hawiji DA, et al. Pulmonary CT manifestations of COVID-19: Changes within 2 weeks duration from presentation. *Egypt J Radiol Nucl Med.* 2020;51(1):105.
- 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. *J Clin Virol.* 2020;127:104370.
- Soraya GV, Ulhaq ZS. Crucial laboratory parameters in COVID-19 diagnosis and prognosis: An updated meta-analysis. *Med Clin (Engl Ed).* 2020;155(4):143-51.
- Sabaka P, Koščálová A, Straka I, Hodosy J, Lipták R, Kmotorková B, et al. Role of interleukin 6 as a predictive factor for a severe course of COVID-19: Retrospective data analysis of patients from a long-term care facility during COVID-19 outbreak. *BMC Infect Dis.* 2021;21(1):308.