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# The role of IL-8 as macrophage activation and C-reactive protein in disease prognosis of coronavirus disease-2019 patients

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**Abstract**---Coronavirus disease 2019 (COVID 19) may cause multi-organ involvement due to viral-induced hyper inflammation. In coronavirus disease-2019 (COVID19) cases, hyper inflammation is associated with the severity of the disease[1]. High levels of circulating cytokines were reported in severe COVID-19 patients[2, 3]. Illness prognosis and severity are predicted by interleukin-8 (IL-8) in COVID-19 patients, as well as its function as a powerful chemo attractant and activator of monocytes, lymphocytes, and neutrophils, which may attract neutrophils to infected regions and has been linked to tissue damage[4, 5]. C-reactive protein (CRP) has been identified as an essential marker that changes dramatically in severe COVID-19 patients. CRP is a liver protein that acts as an early indicator of infection and inflammation. [6]

**Keywords**--- IL-8, COVID-19, hyper inflammation.

**Introduction**

IN this study, it was aimed to determine the prognostic value IL-8 and CRP levels for the prediction of severe disease in patients with COVID-19. Severe, moderate and mild cases of COVID-19 were compared in terms of clinical and laboratory findings, as well as serum IL8 and CRP levels at hospital admission. To assess the prognostic utility IL-8 between the severe, Moderate, and mild COVID-19 groups and CRP level.

activity on neutrophils and monocytes [11] In extreme cases, the situation changes significantly. C-reactive protein (CRP), a liver protein that functions as an early predictor of infection and inflammation, was first used to identify COVID-19 individuals. [6]. During infectious or inflammatory illness states, CRP levels can activate the immune system's conventional complement cascade and affect the activity of phagocytic cells, suggesting that CRP is involved in the opsonization of infectious pathogens and dead or dying cells [12]. The exact effect of CRP in COVID-19 is unknown, although it has been reported that its level may be utilized for early detection of pneumonia [13] and assessment of severe lung infectious disorders, and it is thought to predict disease severity and guide COVID-19 care [14].

### Material and methods

This is a cross-sectional study done in Wasit Province. This study consists of three study groups, each of which consists of Eighty specimens of blood samples that have been collected from hospitalized patients infected by the coronavirus COVID-19 with the COVID-19 virus in Al Zahraa teaching hospital in the governorate of Wasit, Iraq from October 2021 to January 2022. who was diagnosed by a consultant physician based on RT-PCR and CT-scan and ten healthy non-infected subjects. Patients were subdivided according to their infected disease severity into severe, moderate and mild groups. The range of age for patients is between 20 and 80 years, subdividing to the four groups.

Peripheral blood samples were collected from each patient and controls, and the separated serum was used for CRP concentration by ARCHITECT c4000 Abbott. Serum IL-8 level concentration were measured by using Enzyme-Linked Immunosorbent Assay technique (ELISA). Data of normal distribution measured parameters were presented as mean ( $\pm$ SD) values and p.value.

### Result

In this study that present a more than two-fold higher mean concentration of IL-8 in same groups cases severity ill patients ( mean value 184.80 nmol/L (SD 20.4)) compared to patients with moderate symptoms symptoms (129.3 nmol/L (SD 30.1)) and mild symptoms (67.6 nmol/L (SD 16.0)) and healthy patients as control (15.0 nmol/L (SD 4.9)) .Also, results presents higher mean concentration of CRP in three cases groups , severely ill patients (mean value 5.8 mg\ dL (SD 3.4)) compared to patients with moderate symptoms (2.1 mg\ dL (SD 0.88)) and mild symptoms (1.3 mg\ dL (SD 0.45)) and healthy patients as control (0.3 mg\ dL (SD 0.2))

Table 1:- Mean ( $\pm$ SD) values of age of healthy controls, non-severe covid19 patients (Mild, Moderate) , and severe covid19 patients

Markers	Groups	N	Mean $\pm$ SD* (range)	Kruskal-Wallis H
IL-8 (pg/ml)	Severe	30	24.8 $\pm$ 13.6(9.5-67.5)	H=97.56 Sig. <0.001
	Moderate	25	7.7 $\pm$ 0.79 (6.0-9.1)	
	Mild	25	4.3 $\pm$ 1.85 (1.1-7.9)	
	Control	30	15.1 $\pm$ 4.9 (4.8-24.2)	

This table show that IL -8 levels were found to be elevated significantly higher than that of healthy subjects and agreement with [15] who is observed the chemokine IL 8 is being identified as a potential predictive biomarker for ARDS and one of the most important chemokines responsible for recruiting circulating neutrophils to a site of infection, e.g., chemotaxis, which is probably not affected by age also show that healthy elderly individuals show low serum levels of pro-inflammatory cytokines, but higher when compared to the younger population when infected . Our study also agreement with [16] observed Inflammatory response is an innate defense, which is less affected by age than adaptive response(Fig 1).

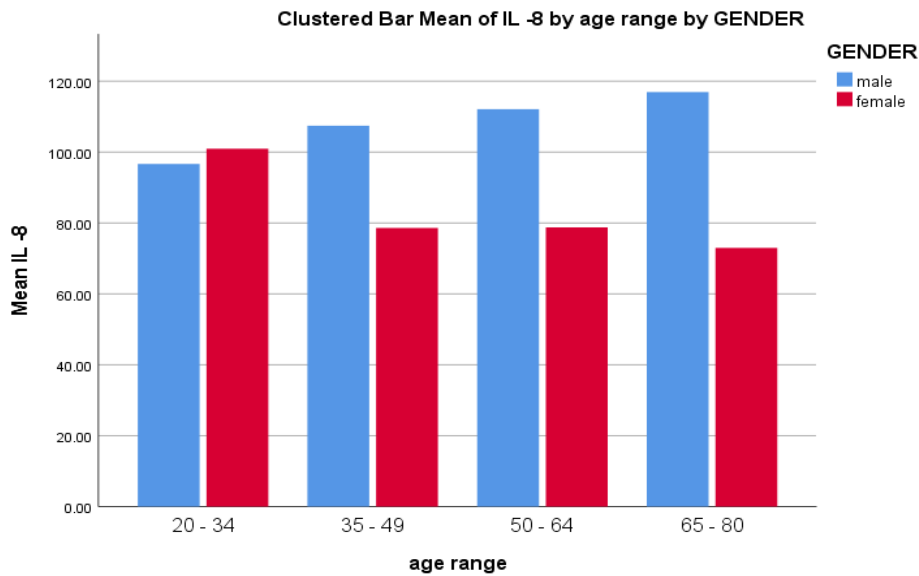


Figure 1:- comparison IL-8 according to the age group and gender

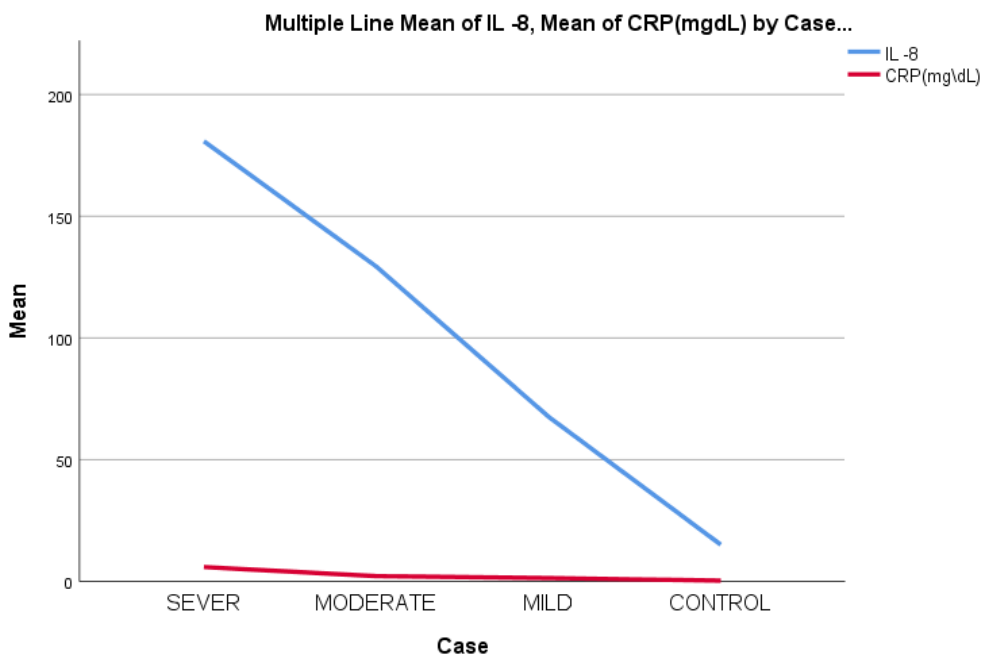


Figure 2 :- correlation between IL- 8 and CRP according to severity.

This indicates that a severe form of COVID19 is associated with an increased CRP catabolism. Additionally, closely correlated to IL-8 ( $r = 0.7$ ,  $p < 0.0001$ , Fig. 2 ). Analysis of IL-8 in serum revealed significantly higher levels in severe cases compared to mild cases (Table 2), and the levels of CRP correlated to IL-8 ( $r = 0.8$ ,  $p < 0.0001$ ).

### Conclusion

Serum IL-8 levels are associated with the severity of COVID-19. Our findings suggest that IL-8 could be used as a prognostic marker. Serum levels of IL8 correlated with CRP levels with the overall clinical disease levels at different stages of the same COVID19 patients. Thus, both may act as a biomarker or as guide for COVID-19 disease prognosis and target for COVID-19 treatment in patients with COVID-19–related hyper inflammatory syndrome.

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