

Assessment of the Level of Interleukin-6 in Patients with COVID-19

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Abstract

The current study aimed to assess the level of Interleukin-6 among Covid-19 patients by using the ELISA technique. For this purpose, (100) serum samples were collected from patients infected with Covid-19 disease in the city of Kirkuk for the period from February 20, 2021 to July 8, 2021, with ages ranging from 22 to 93 years, fifty males and fifty females.

The patients were divided according to the severity of the disease into three groups, the first group had mild symptoms (19%), the second group had moderate severity (41%), and the third group was severe (40%). The results of the study showed a significant increase in the levels of interleukin-6 (61.4 ± 7.9 pg/ml) among Covid-19 patients compared to the control group (P -Value ≤ 0.05). Interleukin-6 also recorded the highest level in severe cases (106 ± 2.9 pg/ml) compared to moderate and mild cases (P -Value ≤ 0.05). Also, the level of interleukin-6 increased significantly among Covid-19 patients with diabetes, and the highest increase was recorded in severe cases, where it was (123.6 ± 5.52 pg/ml, P -Value ≤ 0.05).

Keywords

COVID-19, Corona virus, interleukin-6

I. INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by a new coronavirus first identified in Wuhan, China, in December 2019⁽¹⁾. Corona virus belongs to the genus Beta Corona, under the family Coronaviridae, which is a group of RNA viruses that cause diseases in mammals and birds^(2,3). It was first discovered in 1965 by Terrell and Benoy and the first virus to be discovered was the bronchitis virus of an adult with a cold⁽⁴⁾. Corona viruses are mainly associated with respiratory diseases, in humans and birds it primarily causes respiratory infections that can range from mild to fatal. Mild illnesses in humans include some cases of the common cold (also caused by other viruses, mostly rhinoviruses), while more deadly types can cause SARS, MERS, and Novel Coronavirus^(2,5). After the emergence of the coronavirus that causes severe acute respiratory syndrome (SARS-CoV) and the coronavirus that causes Middle East respiratory syndrome (MERS-CoV), the emerging coronavirus (SARS-CoV-2) is the seventh member of the coronavirus family to be a new member of the The genus Beta Corona virus, which results in the disease Covid-19 that infects humans

^(6,7).The common symptoms of patients were fever, shortness of breath, cough, phlegm, headache, muscle pain, chest pain, diarrhea, and pharyngitis⁽⁸⁾.

The name Corona virus is derived from the Latin word Corona, which means crown⁽⁹⁾. The new virus was named severe acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by the International Committee on Classification of Viruses (ICTV) as the name for the new virus on February 11, 2020. This name was chosen because the virus is genetically related to the coronavirus responsible for the SARS outbreak 2003. The disease it causes was named Coronavirus Disease 2019 (Covid-19) by the World Health Organization (WHO) in the International Classification of Diseases (ICD) as the name for this new disease on February 11, 2020, following the guidelines previously established with The World Organization for Animal Health (OIE) and the Food and Agriculture Organization of the United Nations (FAO) ⁽¹⁰⁾.

The innate immune response is the first step in the defense mechanism against the emerging corona virus, as host cell receptors recognize the virus's RNA and initiate a range of immune and inflammatory responses including the production of cytokines, which in turn recruit immune cells such as macrophages, neutrophils, T cells and B cells to The site of infection to increase the fight against the virus.Pro-inflammatory cytokines such as interleukin-6 play a major role in the primary response⁽¹¹⁾.Interleukin-6 is a pleiotrophic cytokine that functions as a pro-inflammatory cytokine that has a role in both innate and adaptive immune responses in defense against infection, playing a key role in the initial response against viral infection in target cells and in strengthening the immune response ^(12,13).It is produced by macrophages and monocytes in the early stage of inflammation, and is one of the major cytokines detected in COVID patients that was elevated at high levels ^(14,15). It is considered as a predictive biomarker for disease severity ⁽¹⁶⁾. Several studies have found that interleukin-6 levels were associated with mortality ⁽¹⁷⁾. Interleukin-6 is a major factor in the cytokine storm, which leads to the stimulation of acute phase proteins, where the proportion is higher in severe cases compared to mild cases ⁽¹⁸⁾. Interleukin-6 plays an important role in regulating the balance between helper T cells (CD4 + T) which includes activation of innate and acquired immunity, and killer T cells (CD8 + T) which includes regulation of immunoglobulin synthesis. It also contributes to the stimulation and differentiation of B cells, which are white blood cells that produce antibodies, and is also involved in the activation of macrophages ^(19,20).

II. MATERIALS AND METHODS

110 serum samples were collected from the city of Kirkuk for the period from February 20, 2021, to July 8, 2021, their ages ranged between 22 to 93 years, 100 samples of patients infected with COVID-19 were 50 males and 50 females. And 10 samples were from healthy subjects, representing the control group, were 5 males and 5 females.The samples recorded in this study were divided into three groups, mild symptoms (19), moderate symptoms (41), severe symptoms (40), the serum sample used to assess the level of interleukin-6 in Covid-19 patients by using the ELISA technic, by use the kit manufactured by the chines Shanghai Biological Company, to assess the level of interleukin-6, The same steps were used according

to the leaflet attached to the test kit. The results were significant at the probability value ($P \leq 0.05$).

III. RESULT AND DISCUSSION

The results of the statistical analysis showed a significant increase in the mean of IL-6 in COVID-19 patients when compared with the control group, where it was (61.4 pg/ml, 7.03pg/ml, respectively, P value ≤ 0.05) as shown in Table (1).

Table (1): Mean IL-6 level in covid-19 patients and control group

Standards	patients	control group	P. value
IL-6	61.4 \pm 7.9pg/ml	7.03 \pm 2.0 pg/ml	0.0003

Cytokines play an important role in eliminating pneumonia-causing pathogens that can be synthesized by many other immune or non-immune cells. However, if their level becomes too high, tissue damage and host death can occur. Therefore, the presence and quantity of cytokines can give a clear indication of the understanding of the pathogen and immune response of the host ⁽²¹⁾. This increase indicates the effect of the pneumonia in the patient group on the level of cytokines, this inflammatory response can become detrimental if it is excessive or not sufficiently balanced by anti-inflammatory agents ⁽²²⁾. The results of the current study agreed with what researchers found in London, where a study in London found that patients with Covid-19 disease show elevated levels of interleukin-6 ⁽²³⁾, and this matches what was reported by an Egyptian clinical study in individuals with Covid-19 disease about High levels of pro-inflammatory cytokines, including interleukin-6 ⁽²⁴⁾.

The results of the statistical analysis also showed significant increase in the mean of IL-6 in COVID-19 patients according to the severity of the disease, where the average in the following cases (severe symptoms, moderate symptoms, mild symptoms) were as follows (106 pg/ml, 38.8 pg/ml, 16.4 pg/ml, respectively, p value ≤ 0.05) as shown in Table (2).

Table (2): Mean level of IL-6 in covid patients according to severity of disease

Standards	mild symptoms	moderate symptoms	severe symptoms	P. value
IL-6	16.4 \pm 0.62pg/ml	38.8 \pm 1.3pg/ml	106 \pm 2.9 pg/ml	0.0006

The results of the current study are consistent with those in Wuhan, China, the first descriptive primary study evaluating the immunological characteristics of patients with laboratory confirmed COVID infection, where the study found that serum concentrations of IL-6 in most Severe cases were significantly higher than those in moderate and mild cases,

and the cytokine storm corresponded to disease severity ⁽²⁵⁾, and researchers in Italy also found that in severe cases of COVID patients had high levels of IL-6⁽²⁶⁾, the present findings are also consistent with a study in India that found that COVID patients were associated with moderate increases in a wide range of cytokines including IL-6 that were significantly associated with disease severity ⁽²⁷⁾.

The results of the statistical analysis also showed a significant increase in the mean of interleukin-6 in Covid-19 patients with diabetes, (severe symptoms, moderate symptoms, mildsymptoms) were as follows (123.6 pg/ml, 48.53 pg/ml, 17.46 pg/ml, respectively, p value ≤ 0.05) compared with patients without diabetes (97.60 pg/ml, 35.67 pg/ml, 15.91 pg/ml, respectively, p value ≤ 0.05) as shown in Table (3).

Table (3):Mean level of IL-6 in covid patients with and without diabetes

Standards	severity of disease	with diabetes	Without diabetes	P. value
IL-6	mild	17.46 \pm 1.31pg/ml	15.91 \pm 0.64 pg/ml	0.0003
	moderate	48.53 \pm 3.89 pg/ml	35.67 \pm 1.46 pg/ml	0.0003
	severe	123.6 \pm 5.52pg/ml	97.60 \pm 3.07 pg/ml	0.0003

Studies have shown that people with diabetes have a dysregulated innate and adaptive immune response and have chronic low-grade inflammation making them more susceptible to a cytokine storm ⁽²⁸⁾, in which diabetes-induced changes in immune cell function lead to the production of proinflammatory cytokines ⁽²⁹⁾. This is caused by activated immune cells escaping the anti-inflammatory action of interleukin-10, which leads to an excessive response to pro-inflammatory cytokines. This occurs under certain conditions including hyperglycemia in individuals with type 2 diabetes ⁽³⁰⁾, This increases inflammation in individuals with diabetes, based on elevated levels of cytokines including interleukin-6 ⁽³¹⁾. These findings suggest a greater response to proinflammatory cytokines in patients with diabetes than in non-diabetics ⁽³²⁾. A study conducted in Italy also agreed with the results of the current study, which revealed that the average interleukin-6 increased significantly in Covid patients with diabetes when compared to patients without diabetes, where high blood sugar was associated with a high level of interleukin-6, which indicates the presence of inflammatory signs, Correcting hyperglycemia reduces levels of interleukin-6, which reduces the risk of severe outcomes ⁽³³⁾, so when infected with the Corona virus, this pre-existing inflammation in diabetics can be exacerbated, predisposing to hyperinflammatory syndrome or cytokine storm, which is the most common factor. significance in disease progression ⁽³⁴⁾, so it has been suggested that COVID patients with diabetes are more susceptible to an 'inflammatory storm', which is associated with rapid deterioration and higher mortality risk ⁽³⁵⁾.

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