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Research Article

Evaluation of ESR, TNF-α, IL-6, and CRP as Inflammatory Indicators in Patients with COVID-19 Infection

[1,]Hayder B. Abbas Al-Ghreaty

[1,]Directorate of Education in Karbala , Ministry of Education Iraq

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Abstract

Background: Coronavirus syndrome is an acute contagious respiratory inflammation caused by a strain of the coronavirus SARS-CoV-2, first found in China and then spread worldwide. Patients suffer from symptoms of varying severity, ranging from shortness of breath, low blood pressure, and oxygen deficiency to sepsis and vascular damage, which may lead to death. The excessive inflammatory response caused by acute respiratory distress syndrome is the most common cause of death, and its pathogenic causes remain unclear to date. The erythrocyte sedimentation rate (ESR) is a laboratory test routinely used in clinical examinations as an indicator of acute-phase inflammation. ESR has been used in COVID-19 to assess disease severity and predict its course, aiming to study and explore its diagnostic role compared to several other response factors. **Material and methods** :This study included two groups of patients: the first group consisted of 55 patients infected with moderate severity cases, while the second group was composed of healthy individuals 29 as a control So it case control study. **Results** : were as follows: an increase in ESR level by p< 0.01 COVID-19 infected patients compared to healthy individuals, as well as an increase in Tumor Necrosis Factor Alpha (TNF-α) levels. The study also found no significant change in liver enzymes Alanine Transaminase (ALT)and Aspartate Aminotransferase (AST)between patients and the control group, while the relationship was found between ESR and CRP(0.325). **Conclusion**: The research concluded that the erythrocyte sedimentation rate (ESR) may reflect inflammatory activity in COVID-19 patients

Corresponding Author E-mail: ha80der@gamil.com
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Introduction

COVID-19 is an acute respiratory disease caused by the SARS-CoV-2 virus strain[1]. It has caused enormous economic, social, and respiratory damages, leading to a global lockdown of most countries for nearly two year[2] .Subsequently, the World Health Organization declared this virus a pandemic, with over 250 million infected and more than 5 million deaths[3] . Ongoing studies worldwide continue to focus on prevention methods, diagnosis, disease progression prediction, and treatment. Among the various laboratory parameters in COVID-19, and the most prominent are the increase in inflammatory markers, coagulation parameter disturbances, and changes in blood parameter levels [4].These laboratory parameters are most evident in severe disease cases[5]. Many attempts have been made to establish clinical and laboratory criteria to determine the effects of the disease. Numerous studies have investigated the relationship between erythrocyte sedimentation rate (ESR) and inflammation in the acute phase, disease severity, and mortality. Although ESR has been used for years to detect many diseases and has been included among the expected findings in COVID-19 studies [6]. its benefits and necessity have not been sufficiently explored. My study examined the relationship between ESR in patients with moderate COVID-19 severity and its association with certain blood parameters, considering it an important factor in detecting COVID-19 infection.

Materials and Methods

The case-control study relied on two groups: a group infected with COVID-19 consisting of 55 patients, whose infection was confirmed by PCR testing and who were recorded multiple times as visitors to Imam Hussein Hospital in the holy city of Karbala. The results were compared with a group of 29 volunteers who served as the control group. Samples were collected during the period from September 2024 to March 2025. Eligibility criteria were used to select samples in both groups: women and men aged between 20-50 years who were diagnosed with infection through PCR testing and suffering from fever, fatigue, sneezing, and shortness of breath. They had moderate disease severity and did not require admission to the intensive care unit. Exclusion criteria included cases of viral hepatitis, obesity, pregnancy, renal failure, and rheumatic diseases. The study samples were handled according to World Health Organization guidelines. Five milliliters of blood were drawn from each patient, The erythrocyte sedimentation rate (mm/hour) was measured using the routine method, and other laboratory tests (Interleukin-6, TNF) were performed using their specific measurement kits and ELISA. The reference value for the erythrocyte sedimentation rate was 0–20 mm/hour for males and 30 mm/hour for females. and the data were collected using Excel software and then statistically analyzed using SPSS software.

Results:

Table No. (1) Showed that laboratory results for the patient and healthy groups. Significant differences were observed between the patients and the control group at the level of p.v <0.002 for ESR, while no significant differences were observed for TNF-α and interleukin 6.

Table 1 :laboratory test results				
laboratory test	**Groups**	**N**	**Mean± S. D**	**p.v**
TNF-α pg/ml	**Patient**	55	50.65±7.98	0.30
	Healthy individuals	29	39.29±5.55	
Interleukin-6 (IL-6) pg/mL	**Patient**	55	33.51±3.7	0.11
	Healthy individuals	29	20.78±2.4	
ESR mm/hr	**Patient**	55	51±6.2	0.002
	Healthy individuals	29	15±2.6	

Table No. (2) presents laboratory test results for hematological and biochemical blood samples between males and females.

A significant difference was found in ESR between males and females, while no significance was reached for the other parameters.

Table 2: Laboratory parameter results				
laboratory test	Groups	Gender	Mean± S. D	P. value
WBC	Patient	Male	15.04±5.2	.358
		Female	16.51±5.3	
	Healthy individuals	Male	7.22±2.	
		Female	7.44±3.1	
Lymph.%	Patient	Male	0.26±0.4	.333
		Female	0.23±0.3	
	Healthy individuals	Male	0.04±0.1	
		Female	0.26±0.3	
AST u/l	Patient	Male	47.35±5.4	.577
		Female	53.90±6.9	
	Healthy individuals	Male	26.08±13.18	
		Female	23.85±3.02	
ALT u/l	Patient	Male	42.79±4.9	.350
		Female	71.84±5.9	
	Healthy individuals	Male	26.84±3.7	
		Female	28.25±4.5	
TNF-α pg/ml	Patient	Male	54.37±6.2	.141
		Female	48.68±4.8	
	Healthy individuals	Male	51.84±7.7	
		Female	23.86±2.3	
IL-6 pg/ml	Patient	Male	34.55±3.01	.613
		Female	32.97±4.8	
	Healthy individuals	Male	16.50±2.3	
		Female	26.04±3.54	
Neutro.%	Patient	Male	0.26±0.40	.237
		Female	0.23±0.37	
	Healthy individuals	Male	0.04±0.16	
		Female	0.26±0.30	
ESR	Patient	Male	49±5.2	.02
		Female	52±3	
	Healthy individuals	Male	16±3.6	
		Female	17±2.1	

Table No. (3) illustrates the correlation relationships between ESR, CRP, TNF-α , and IL-6 relationship was found between ESR and CRP(0.325*), while no correlation was found between TNF-α and IL-6.

Table 3:correlation		
parameter	ESR mm/hr	
	P.value	(r)
TNF-α pg/ml	> 0.01	0.049
(IL-6) pg/mL	> 0.01	0.133
CRP mg/dl	< 0.01	0.325*

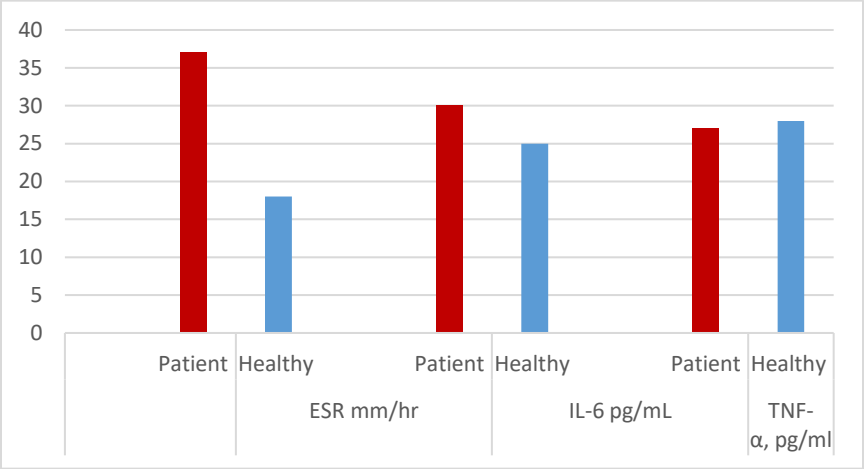

Figure 1: represents a gradual curve showing a comparison between ESR, TNF-α, and IL-6 in individuals infected with COVID-19 and healthy individuals. Elevated levels of ESR were observed in COVID-19 patients compared to healthy individuals.

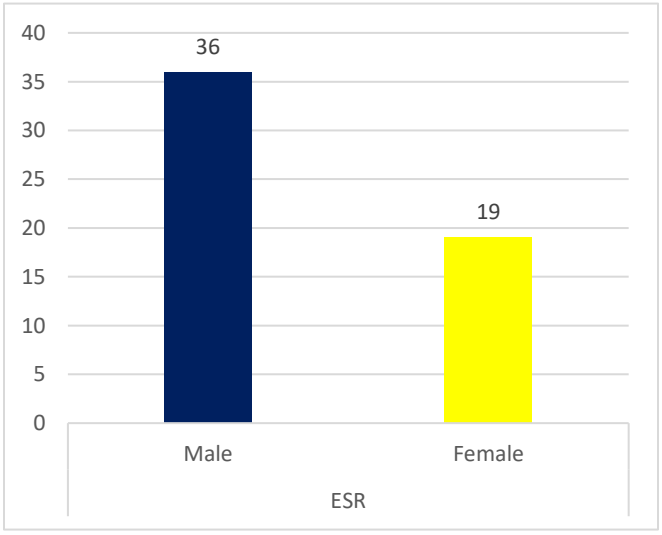

Figure 2: shows the variation in ESR levels between males and females in patients infected with COVID-19 An increase in ESR levels was observed in males.

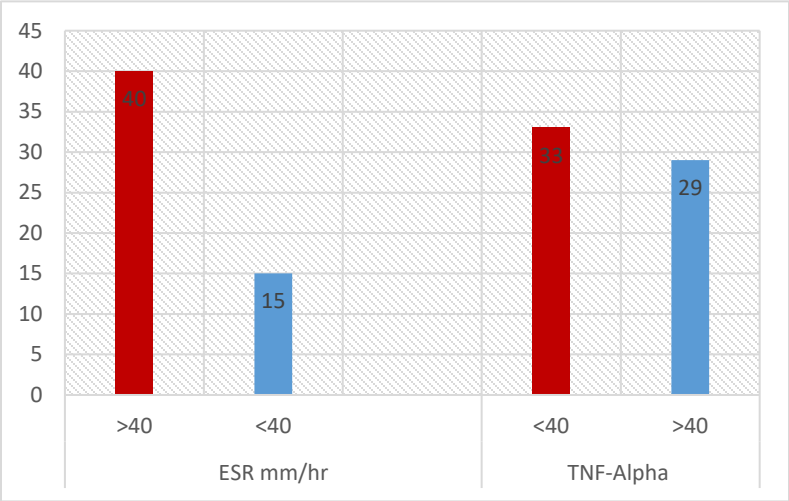

Figure 3: illustrates the normal and abnormal levels of ESR and TNF-α according to age. An increase in ESR levels was observed in those over 40.

Discussion

The erythrocyte sedimentation rate (ESR) is an important indicator that signifies the presence of an acute inflammatory condition[7]. However, the highly contagious disease caused by the SARS-CoV-2 virus still has unclear interactions with the immune system after entering the human body, except for comprehensive research on the virus's structure and gene sequencing[8].In the current study, it was found that the erythrocyte sedimentation rate (ESR) became significantly faster in many cases of COVID-19 infection during hospitalization[6]. Patient age was also associated with sedimentation rate speed, but this is not necessarily a causal relationship[9]. In this study, C-reactive protein (CRP) had a positive effect on the erythrocyte sedimentation rate. This may be due to the fact that coronavirus infection enhanced the occurrence of inflammatory storms in patients, enabling the human body to mount a nonspecific resistance to combat the virus. Here, C-reactive protein plays a positive role in the inflammatory response[10]. Additionally, studies showed that continuous measurement of the inflammatory marker CRP can be used as a predictive indicator in the presence of infection. CRP was also found to have a positive effect on erythrocyte sedimentation rate (ESR)[11]. The explanation for this is that the new coronavirus infection caused a significant increase in C-reactive protein, which leads to an increase in the erythrocyte sedimentation rate (ESR), which can stimulate connective tissue diseases.

A study found a significant increase in interleukin-6 concentration compared to healthy individuals. The role of interleukin 6 and its receptor was described. Interleukin 6 is one of the main mediators of the inflammatory and immune response resulting from viral infection. Therefore, many patients suffer from a lethal immune response with continuous damage caused by cytokines, leading to the leakage of macrophages and monocytes into the alveoli[9].Upon infection, the infected cells particularly enhance the production of all cytokines and chemokines in large quantities, which then leads to a cytokine storm. Endothelial cells and capillaries may be affected, causing oxygen deficiency and increased infection. Among the findings, our

study found lower TNF-α in patients diagnosed with a positive corona test, which aligns with a study conducted on 21 patients with severe COVID-19 compared to the average infection severity in patients. Interferon was considered a risk factor for the development of pulmonary fibrosis in people infected with COVID-19 [12]. Our study found an elevation in C-reactive protein levels in COVID-19 patients, which may be a result of the body's inflammatory response to the infection, indicating the presence of inflammation or tissue damage[13] .

The study found that the erythrocyte sedimentation rate (ESR) was higher in males than in females, and that this increase is also associated with age[14]. which is consistent with some published research indicating elevated erythrocyte sedimentation rates in COVID-19 infection [15]. Furthermore, the higher incidence rate in males compared to females may be attributed to the mechanism of the angiotensin-converting enzyme 2 (ACE2), which is the main receptor invaded by the COVID-19 virus and is positively regulated by androgen receptors[10][16] .

Conclusion: The research concluded that the erythrocyte sedimentation rate (ESR) may reflect inflammatory activity in COVID-19 patients.

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