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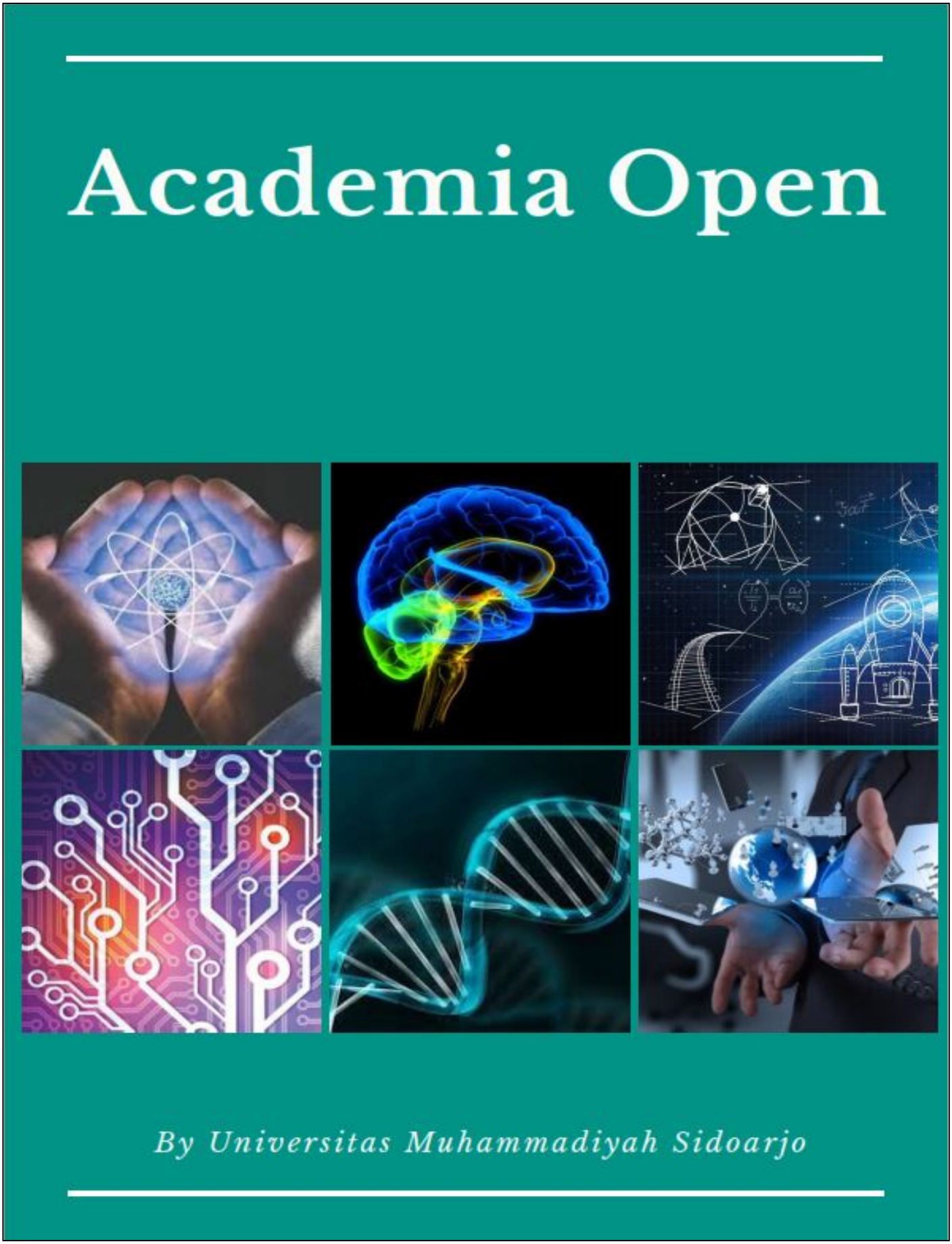

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Elevated CRP and IL6 Levels Predict Severe Cardiovascular Outcomes in COVID-19 Patients

Peningkatan Kadar CRP dan IL6 Memprediksi Hasil Kardiovaskular yang Parah pada Pasien COVID-19

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Abstract

This study explores the association between C-reactive protein (CRP) and interleukin 6 (IL-6) levels and cardiovascular complications in COVID-19 patients. Utilizing an ELISA kit for IL-6 and standard tests for CRP, we analyzed 192 samples, finding higher infection rates among the 50-69 age group, with significant prevalence of morbid obesity. Results showed a strong correlation between elevated CRP and IL-6 levels and the severity of cardiovascular complications, particularly in critical cases. These findings suggest that monitoring these biomarkers could be crucial for early intervention and managing cardiovascular risks in COVID-19 patients, potentially improving patient outcomes in clinical settings.

Highlights:

- Biomarker Correlation: Elevated CRP and IL-6 levels are linked to severe cardiovascular complications in COVID-19 patients.
- Risk Management: Monitoring these biomarkers helps in early intervention and managing cardiovascular risks.
- Demographic Insights: The highest infection and complication rates are among the 50-69 age group with significant obesity.

Keywords: COVID-19, Cardiovascular Complications, CRP, IL-6, Biomarker Monitoring

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Introduction

Coronaviruses belong to the family Coronaviridae in the order Nidovirales and are RNA viruses that cause sickness. In December 2019, it was first discovered in Wuhan, China, and the illness swiftly spread throughout the world. Named coronaviruses because they are enclosed, nearly spherical, and have an average diameter of 120 to 160 nanometers. They are also ornamented with spike proteins, which, when seen under an electron microscope, give them the look of a crown. These viruses are distinguished by their very large genome (about 28-32 kb) [1]. Humans and a range of different animals including (ducks, pigeons, cows, pigs, ferrets, and bats) act as hosts for coronaviruses. Its clinical symptoms are severe respiratory infections in addition to intestinal symptoms, and when infected, it may result in negative effects on many organs of the body. HCoVHKU1, HCoV-NK63, HCoV-OC43, HCoV-229E, MERS-CoV, SARS-CoV and SARS-CoV-2 that infect humans, have been identified. Of these, only three viruses could cause death: SARS-CoV, MERS-CoV, and SARSCoV-2 [2].

COVID-19 infection can lead to long-term difficulties due to many physiological factors, however the specific processes behind these consequences are still not fully understood. SARS-CoV-2 has both a direct and indirect pathogenic impact. Given that the virus depends on ACE2 for infecting the target cell, ACE2 is present in numerous cells throughout the body, the virus will directly impact the organs it invades [3]. The virus can directly harm organs that contain cells with the ACE2 enzyme, such as the respiratory system, heart, blood vessels, pancreas, and others, leading to long-term consequences. Furthermore, the indirect impact of infection may be attributed to several factors such as immune system dysfunction, acute infections, blood coagulation, hypoxia, and acid-base imbalance. Additionally, it is worth noting the adverse psychological impacts experienced by the patient [4]. While, the Individuals who already have cardiovascular disease (CVD) seem to be more susceptible to contracting COVID-19 and are more likely to experience a more severe form of the illness with unfavorable clinical consequences. The extent of this sensitivity may differ depending on the geographical region. Medical studies and scientific studies have substantiated that COVID-19 has detrimental impacts on the cardiovascular system, exacerbating the severity of the condition and leading to mortality [5]. The most frequently reported cardiovascular consequence in COVID-19 is acute myocardial damage, characterized by elevated levels of cardiac enzymes, notably high-sensitivity cardiac troponin I (cTnI), and aberrant electrocardiographic findings [6]. Empirical data indicates that an increased cardiac troponin level is an unfavorable indication for most patients requiring critical care. COVID-19 primarily impacts the respiratory system, but it can also have direct or indirect effects on the cardiovascular system, as outlined by Tveit *et al*.[7].

Coronary artery disease and the worldwide COVID-19 pandemic are both impacted by IL-6 signaling. In addition to being associated with inflammatory states promoted by obesity, smoking, and cardiovascular risk factors, this proatherogenic cytokine reaches increased blood levels after the cytokine storm generated by SARS-CoV-2 [8]. In common parlance, "long COVID" describes signs and symptoms that continue or become worse following acute COVID-19. The chronic symptoms of COVID-19 may be exacerbated by the possibility of IL-6 hyperactivation in the host immunological pathway. Patients with COVID-19 have elevated levels of interleukin-6, and this level of concentration rises anytime a patient's condition becomes critical enough to necessitate admission to the intensive care unit [9], [10].

Methods

A. Study Design

Study design: The study was carried out in the Al-Hussein Teaching Hospital, the Nasiriyah Heart Center, and several isolation centers in Thi-Qar Governorate. It was a case-control study that was done at the hospital level. A total of 192 blood samples from patients with 50 as control sample, a basic random sample method was employed.

Samples of venous and arterial blood were drawn from COVID-19 patients as well as the control group using the following technique: Each sample was obtained in approximately seven milliliters; six milliliters were then put into a gel tube and let to stand at room temperature for about half an hour. The gel tubes underwent five minutes of centrifugation at a rate of 4000 revolutions per minute. After that, the serum sample was separated into three parts, each of which had around 500 µl, and kept in a deep freezer at -20°C.

B. Criteria for Selection and Exclusion

This research project includes individuals who have been diagnosed with COVID-19 and were admitted to Imam Hussein Teaching Hospital, Nasiriyah Heart Center, and some isolation centers in Thi-Qar Governorate for both sexes up to the age of more than 69 years, except for patients who did not provide a sufficient sample and the patients whose data we could not obtain well.

C. Interleukin-6 Quantification

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IL-6 was quantified using an ELISA kit (reference AEK0051,component number EK106/2-24 EK106/2-48 EK106/2-96, China), according to the manufacturer's instructions [9]. The other laboratory test CRP,were performed by following the standard procedures [11].

D. Statistical Analysis

Version 26 of the Statistical Package for the Social Sciences (SPSS) was utilized to conduct the statistical analysis. To compare the groups statistically, independent sample T test for mean comparison between patients and control group and one way ANOVA for mean comparison between groups.

Results and Discussion

A. Results

This study focuses on individuals diagnosed with COVID-19 and encompasses a total of 192 samples. These samples are categorized based on the degree of the infection, with 35 instances classified as critical, 53 cases as severe and 54 cases as moderate and 50 samples serving as a control group. Figure (1) illustrates this.

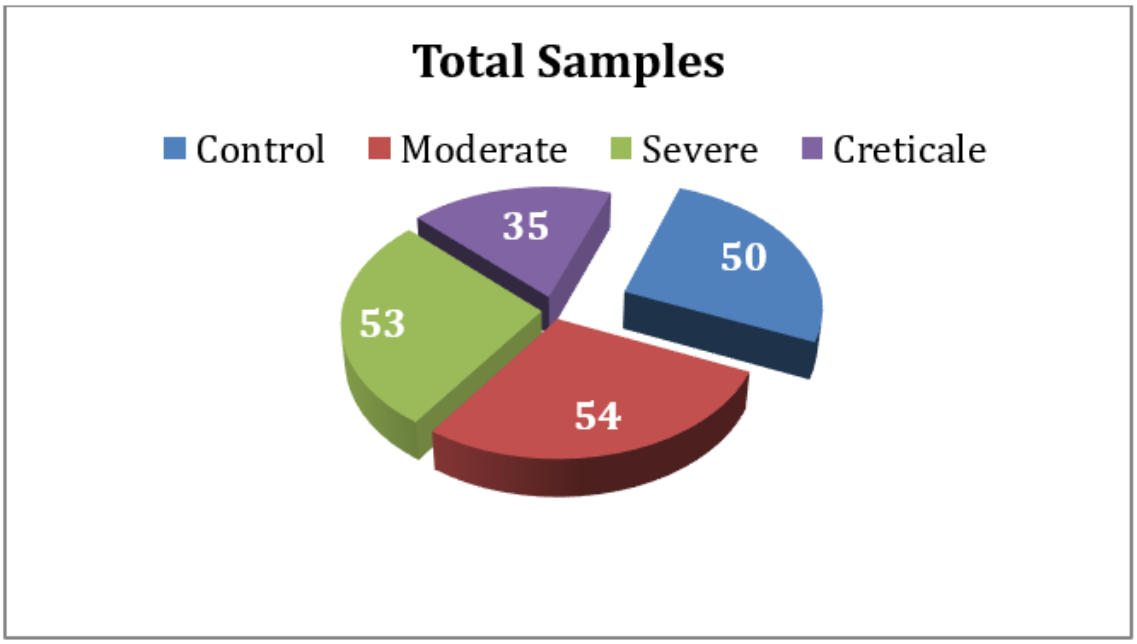

Figure 1. ***D isplays all study samples, including patients and the control group***

Figure (2) illustrates the breakdown of COVID-19 patients in this study based on their age and gender. The age group with the highest prevalence of COVID infection among both males and females is between 50-69 years, whereas the age group with the lowest prevalence is under 30 years.

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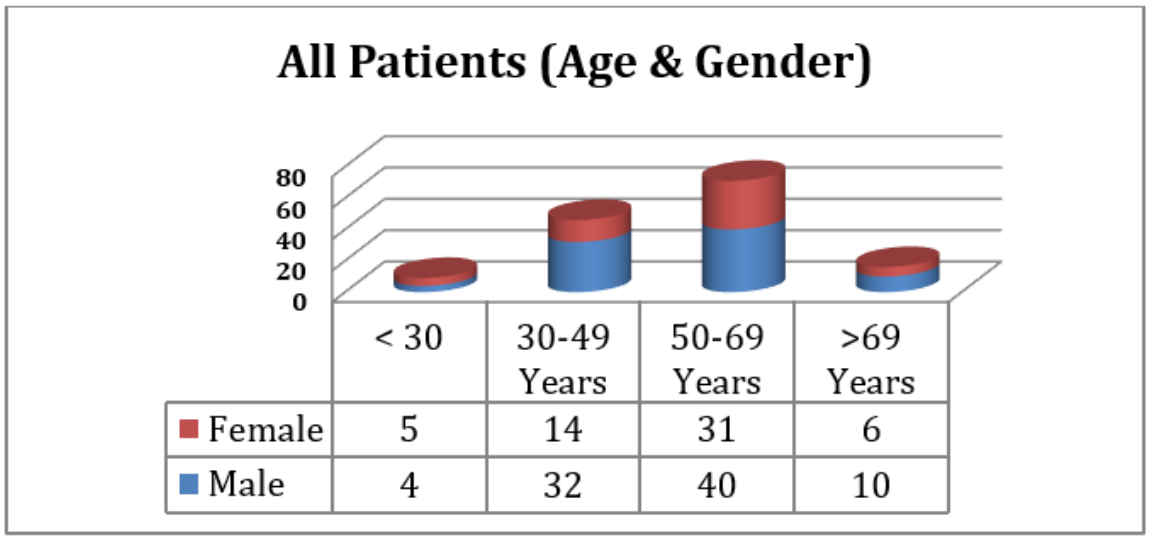

Figure 2. ***Age and gender of COVID-19 patients' distribution***

1. Demographic Characteristics of the Study Samples

Table (1) displays the attributes of the study population based on demographic criteria. The present findings exhibited notable variations based on age, gender, body mass index, specific chronic illnesses among certain individuals, and COVID-19 -related disease problems, with a statistical significance level of less than 0.05.

In this investigation, the maximum number of COVID-19 infections was observed in the third age category (50-69 years), with only 9 patients falling into the first age group (<30 years). The male patient population constitutes 60.56% (86 individuals), while the female patient population comprises 39.43% (56 individuals). Out of all the patients, 46.5% were diagnosed with morbid obesity, 33.1% had a high BMI, and just 20.4% had a normal BMI. The study found that 75.4% of COVID-19 patients did not have chronic conditions. Among those who did, 8.5% had chronic high blood pressure, 5.6% had diabetes, and 5.6% had other health concerns. 4.9% of the participants in the research had multiple chronic conditions, including chronic heart disease. The distribution of patients based on the severity of the disease did not yield statistically significant findings. However, there were 54 instances classified as moderate, 53 cases classified as severe, and 35 cases classified as critical.

Complications arising from COVID-19 infection were observed in 19% of the patients included in this study. Among the patients, the biggest percentage experienced a myocardial infarction, accounting for 5.6% of the total number. This was followed by cardiac arrhythmia, which affected 4.2% of the patients. The prevalence of patients with this disease was equivalent. The incidence of heart failure and pulmonary embolism was 2.8% for both groups, while 3.5% of all patients experienced multiple problems targeted in this investigation.

Age Groups		Characteristics		
		Frequency	Percent	Chi-square Sig.
	< 30 Years	9.00	6.300	< 0.001
	30-49 Years	46.0	32.40	
	50-69 Years	71.0	50.00	
	> 69 Years	16.0	11.30	
	Total	142	100.0	
Gender				
	Male	86.0	60.6	0.012
	Female	56.0	39.4	
	Total	142	100	
BMI				
	Normal	29.0	20.4	0.001
	Over	47.0	33.1	
	Obesity	66.0	46.5	
	Total	142.0	100	

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Chronic Disease				
	non	107	75.4	< 0.001
	HBP	12.0	8.50	
	DM	8.00	5.60	
	Heart Problems	8.00	5.60	
	Mix	7.00	4.90	
	Total	142	100	
Severity				
	Moderate	54.0	38.0	0.089
	Severe	53.0	37.3	
	Critical	35.0	24.6	
	Total	142	100	
Complication				
	Non	115	81.0	< 0.001
	MI	8.00	5.60	
	HF	4.00	2.80	
	Arrhythmia	6.00	4.20	
	PE	4.00	2.80	
	MIX	5.00	3.50	
	Total	142	100	

Table 1. ***Demographic Characteristics of COVID-19 P atients***

2. C-reactive Protein and Interleukin-6 Level in COVID-19 Patients

When assessing immunological parameters in individuals infected with COVID-19 and comparing them to the parameters observed in the control group, a notable and statistically significant elevation was observed in the infected individuals' levels. The concentrations of C-reactive protein and interleukin 6 in the blood of patients were found to have dramatically increased to a level below 0.05, as compared to the control group. Table 2 displays this information.

Parameters	Mean & Std.		T-test Value
	Control	Patients	
CRP	3.075±0.778	83.69±34.18	< 0.001
IL-6	27.90±7.888	157.9±142.9	< 0.001

Table 2. ***CRP and IL-6 Levels in COVID-19 Patients and the Control Group***

3. C-reactive Protein and Interleukin-6 Levels in COVID-19 Patients According to S ex

Table (3) demonstrates statistically significant variations in CRP and IL-6 levels based on gender, with a greater increase observed in males compared to the average levels in females.

Parameters	Mean & Std.		T-test Value
	Male	Female	
CRP	89.31±33.60	75.05±23.55	0.015
IL-6	181.1±139.2	122.2±142.5	0.016

Table 3. ***CRP and IL-6 Levels in COVID-19 Patients According to S ex***

4. C-reactive Protein and Interleukin-6 Levels in COVID-19 Patients According to Age Groups

When performing statistical analysis on the variations in the mean standards given in Table (4) according to different age groups. Statistically significant changes were seen at a significance level of less than 0.05 between age groups in the mean levels of CRP and IL-6. The third age group exhibited the greatest increase in both biomarkers.

Age Groups Parameters		Mean & Std.	ANOVA Sig.	LSD Sig.
CRP	<30 Years	82.31±42.87	0.372	$NS^{1,2}$, $NS^{1,3}$, $NS^{1,4}$,

	30-49 Years	76.90±46.14		$NS^{2,3}$, $NS^{2,4}$, $NS^{3,4}$
	50-69 Years	88.14±40.10		
	> 69 Years	73.51±49.43		
IL-6	<30 Years	131.1±13.94	0.032	NS1,2, NS1,3,NS11,4, NS2,3,NS2,4, 0.0023,4
	30-49 Years	125.6±108.2		
	50-69 Years	172.1±146.9		
	> 69 Years	101.8±175.5		

Table 4. ***CRP and IL-6 Levels in COVID-19 Patients According to Age Groups***

5. C-reactive Protein and Interleukin-6 Levels in COVID-19 Patients According to Chronic Diseases

Table (5) displays statistically significant variations, with a significance level of less than 0.05, for each criterion contained in it based on the chronic conditions experienced by COVID-19 patients. The group of patients with chronic cardiac problems exhibited the most significant rise in average CRP and IL-6 levels, whereas the group of patients without any chronic conditions displayed the least significant increase.

Chronic Disease Parameters		Mean & Std.	ANOVA Sig.	LSD Sig.
CRP	Non	78.72±22.56	<0.001	NS1,2, 0.0381,3,0.0011,4,NS1,5, 0.0011,6, NS2,3,NS2,4, NS2,5, 0.0012,6,NS3,4, NS3,5, 0.0013,60.0134,5, 0.0014,6, 0.00135,6
	HBP	95.66±42.26		
	DM	100.3±32.40		
	Heart problems	117.7±41.75		
	Mix	81.00±144.6		
	Control	3.075±0.778		
IL-6	Non	135.2±136.3	<0.001	NS1,2, 0.0091,3,0.0011,4,NS1,5, 0.0011,6, NS2,3,0.0012,4, NS2,5, 0.0012,6,NS3,4, NS3,5, 0.0013,60.0164,5, 0.0014,6, 0.00135,6
	HBP	147.5±99.69		
	DM	246.0±109.5		
	Heart problems	348.1±154.9		
	Mix	203.5±144.6		
	Control	27.90±7.886		

Table 5. ***CRP and IL-6 Levels in COVID-19 Patients According to Chronic Diseases***

6. C-reactive Protein and Interleukin-6 Levels in COVID-19 Patients According to Severity

Table (6) demonstrates a positive correlation between the severity of COVID-19 infection and the elevated levels of CRP and IL-6. Patients with a critical infection had the greatest level of both criteria. The group with the lowest increase in their levels was the moderate group. These results are highly significant and have achieved statistical significance at the level of $p<0.05$.

Severity Parameters		Mean & Std.	ANOVA Sig.	LSD Sig.
CRP	Moderate	64.66±12.03	<0.0001	0.0011,2, 0.0011,30.0011,4, ns2,3, 0.0012,4, 0.0013,4
	Severe	92.86±36.47		
	Critical	99.14±40.43		
	Control	3.075±0.778		
IL-6	Moderate	32.87±11.92	<0.001	0.0011,2, 0.0011,3NS1,4, 0.0012,3, 0.0012,4, 0.0013,4
	Severe	170.2±66.57		
	Critical	332.2±146.1		
	Control	27.90±7.886		

Table 6. ***CRP and IL-6 Levels in COVID-19 Patients According to Severity***

7. C-reactive Protein and Interleukin-6 Levels in COVID-19 Patients According to Complications

The study findings revealed statistically significant disparities ($P < 0.05$) in CRP and IL-6 concentrations across patients with distinct clinical conditions as consequences arising from infection. The cohort of COVID-19 patients who experienced obstruction exhibited the most elevated levels of C-reactive protein (CRP) and interleukin-6 (IL-6), whereas the cohort of patients without any illness complications displayed the lowest values consult table (7) for additional information.

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Complication Parameters		Mean & Std.	ANOVA Sig.	LSD Sig.
CRP	Non	77.20±31.23	<0.001	0.0011,2, 0.0161,3, 0.0161,4,0.0091,5, 0.0111,6, 0.0011,7,NS2,3, NS2,4, NS2,5,NS2,6, 0.0012,7, NS3,4,NS3,5, NS3,6, 0.0013,7,NS4,5, NS4,6, 0.0014,7,NS5,6, 0.0015,7, 0.0016,7
	MI	116.1±39.17		
	HF	111.0±27.28		
	Arrhythmia	105.1±29.83		
	PE	113.7±41.41		
	MIX	109.4±35.71		
	Control	3.075±0.778		
IL-6	Non	125.7±118.8	<0.001	0.0011,2, 0.0011,3, NS1,4,0.0011,5, 0.0031,6, 0.0011,7,NS2,3, NS2,4, NS2,5,NS2,6, 0.0012,7, 0.0203,4,NS3,5, NS3,6, 0.0013,7,0.0034,5, NS4,6, 0.0014,7,NS5,6, 0.0015,7, 0.0016,7
	MI	303.5±176.1		
	HF	352.5±202.7		
	Arrhythmia	190.3±81.74		
	PE	402.2±117.8		
	MIX	275.8±157.0		
	Control	27.90±7.886		

Table 7. ***CRP and IL-6 Levels in COVID-19 Patients According to Complication***

B. Discussion

The current study included 142 people with COVID-19 infection and 50 samples as a control group. Infections were distributed among patients according to gender, and the percentage of male patients infected with COVID-19 was 60.6%, while 39.4% were females. The results of the current study agree with most previous studies, including the study Su *et al* [12], it differs from the results of a study Al Hijaj *et al*.[13], in Basra, which recorded a higher infection rate among females instead of males. Moreover, the study Mukherjee and Bahan, [14], stated that even if the infection rate was equal between males and females, the infection would be more severe and dangerous in males. Among the most important factors that lead to an increase in infection among males compared to females, including hormonal factors, as scientific research confirms that sex hormones contribute to increasing males' susceptibility to infection with COVID-19 [15]. It is believed that the presence of ACE2 receptors in testicular tissue in men increases the likelihood of exposure to the virus and the development of infection [16]. Social and professional factors play a major role in increasing infection in males, as males are exposed to the virus, such as work that requires physical presence and interaction with others. In addition, men may have a higher proportion of social gatherings that expose them to the risk of infection than women [17]. It should be noted that these factors vary according to the cultural, social, and demographic context of each region.

Depending on age, the current study recorded that the age group ranging from (50 to 69 years) includes the largest number of COVID-19 patients, their percentage to the total study population being 50%, and their infection is more serious. While the lowest percentage of patients is 6.3% within the age group (less than 35 years). This result is consistent with Mushtaq *et al*. [18] and differs with Davies *et al*.[19], which stated that the most common detection of COVID cases is in age groups under 50 years old, because they are more socially active, which increases the chances of exposure to the virus. The high rate of infection in advanced age groups, as shown in the results of the current study, may be attributed to several important factors, including the immune system and chronic diseases [20]. Older people may have an immune system that is less able to fight infection and thus increases the likelihood of developing serious symptoms resulting from infection. Moreover, the presence of underlying medical conditions such as respiratory diseases, diabetes, and cardiovascular disease can increase the risk of infection.

During the current study, the results showed that there is a positive relationship between the number of COVID-19 infections and body mass index. This result is consistent with [21]. Much research indicates that obesity contributes to increasing the risk of infection with the COVID-19 virus and causes its symptoms to develop seriously. There are some reasons that explain this relationship. Obesity is considered a chronic inflammatory condition [22]. Obesity leads to a distortion in the immune response, and when infected with COVID-19 , it can cause an excessive immune response and serious lung infections [23]. There is no doubt that obesity affects the functioning of the respiratory system, and obese people may suffer from difficulty in proper ventilation and may have an accumulation of fat in the lungs, which increases respiratory complications [24]. Obesity is usually accompanied by many types of chronic diseases and thus the possibility of increasing the risk of contracting COVID-19 .

COVID-19 patients were divided in this study based on the severity of the disease, and among them were 54 moderate cases, 53 severe cases, and 35 critical cases (38%, 37.3%, 24.7%, respectively), and there was no

statistically significant relationship between them. This may be since these samples were collected in isolation centers, and that most COVID-19 patients who have a mild or moderate infection do not visit hospitals, as do severe and critical cases that require immediate intervention due to shortness of breath and lack of oxygen, as well as severe inflammatory symptoms resulting from their infection. Of course, the percentages of severity of COVID-19 infection vary in different countries, due to many factors such as the health policies in place, the health care system, circulating strains, the level of vaccination, and demographic factors [25].

Although respiratory disease is the predominant clinical manifestation of COVID-19 , the enormous burden of disease means that a significant number of patients with COVID-19 may develop pre-existing cardiovascular disease or develop new cardiac dysfunction during the course of the illness Bansal, [26]. Therefore, the current study sheds light on cardiovascular complications resulting from COVID-19 infection. The results of this study recorded that 19% of COVID-19 patients had complications due to infection, and 5.6% of them had myocardial infarction, 4.2% arrhythmia, 2.8% heart failure, 2.8%. % pulmonary embolism, 3.50%, mixed disease complications. This result is consistent with Xiong *et al*.[17], where the percentage of heart patients was reported to be approximately 17%, which constitutes a risk factor and leads to death during infection.

The occurrence of myocardial infarction cases may be attributed to clotting problems that accompany COVID-19 infection for many reasons, including the cytokine storm Schmid *et al*.[27]. Strikingly, more than 70% of deaths associated with COVID-19 are attributable to thrombosis-related complications such as pulmonary embolism, strokes, and multi-organ failure [28]. Coagulation disturbances during COVID infection may be due to activation of hypoxia-associated coagulation factors such as tissue factor (an important player in stimulating the coagulation cascade), cytokine storm, neutrophil activation and release of neutrophil extracellular traps, immobility, and ICU-associated risk factors. Under normal circumstances, the pro- and anticoagulant systems are strictly regulated. Infection with SARS-CoV-2 appears to upset this delicate balance, leading to a blood-clotting state in some patients. The causes of the prothrombotic state in COVID patients appear to differ from classical disseminated intravascular coagulation with elevated plasma fibrinogen levels and D-dimers in patients [29]. Some evidence supports the existence of complex interactions between the innate immune response, coagulation, fibrinolytic pathways, and the vascular endothelium, leading to a prothrombotic state. Overall, hyperinflammation appears to be associated with a variety of mechanisms that include alveolar epithelialization, endothelial dysfunction, complement activation, monocytes/macrophages, cytokine storm, dendritic cell toxicity, platelets, and coagulant autoantibodies that contribute to microthrombus formation [30].

COVID-19 patients have relatively increased fast heart rates [31]. Arrhythmia is one of the major complications of COVID-19 [32]. Mechanistically, a number of ion channels could be negatively affected in COVID-19 , leading to changes in cardiac conduction and/or repolarization properties, as well as calcium handling, potentially leading to arrhythmias [33]. Many antimicrobials used as potential therapeutic agents for COVID-19 , such as chloroquine, hydroxychloroquine, and azithromycin, may induce QT prolongation on electrocardiography with potential proarrhythmic effects [34]. In addition to worsening cardiomyopathy and previous conduction disturbances and causing arrhythmic events. SARS-CoV-2 may also cause electrophysiological abnormalities in patients with no prior history of heart disease under a variety of mechanisms [35]. Moreover, high temperatures during COVID-19 infection may have an impact on heart rate [36].

Heart failure is a common disease state that can be encountered at different stages during a COVID-19 patient presentation. New or existing heart failure in the setting of COVID-19 can present a set of unique challenges that can complicate presentation, management, and prognosis. A careful understanding of the hemodynamic and diagnostic implications is essential for the appropriate triage and management of these patients. Abnormal cardiac biomarkers are common in COVID-19 and can stem from a variety of mechanisms that involve the viral entry itself through the ACE2 receptors, direct cardiac injury, increased thrombotic activity, stress cardiomyopathy, and others. The cytokine storm observed in this pandemic can be a culprit in many of the observed mechanisms and presentations. A correct understanding of the two-way interaction between heart failure medications and the infection, as well as the proposed COVID-19 medications and heart failure, can result in optimal management.

Interleukin-6 is a pleiotropic cytokine that is produced in response to tissue damage due to viral infections, and has pro- and anti-inflammatory effects [37]. The results of this study found that the level of enterokine-6 is very high in COVID-19 patients compared to the control group. This result is consistent with the study for Zhu *et al*.[38], which supported that this significant increase is related to the severity of the disease. The reason may be that elevated IL-6 occurs due to lung damage [39]. The results of this study also showed that the level of IL-6 increases more in patients who suffer from chronic heart problems, as a study Nguyen *et al*. [40]and Liu *et al*.[41] reported that there is a relationship between cardiovascular diseases and a high level of IL-6, and it can be used as an indicator of the severity of the disease, as it was found in this study shows that the level of IL-6 increases significantly in patients who have had pulmonary embolism, heart failure, myocardial infarction, arrhythmia, and common complications resulting from COVID-19 , in addition to that its level has a significant positive relationship with the severity of the disease. When the virus enters epithelial cells through its binding to the ACE2 receptor located on their membranes, the innate immune system is stimulated, including interleukin 6, thus generating cytokines and other chemokines that cause immune attack [42]. Then many inflammatory secretions and red blood cells enter the alveoli infected with the virus, and thus shortness of breath occurs in the patient [43]. The underlying mechanism is that acute inflammation induced by IL-6 affects coagulation factor levels, which will subsequently modify venous thromboembolism. Therefore, IL-6 plays an important role in the pathogenesis of venous thromboembolism in

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COVID-19 patients, and excessive signal transduction can promote the development of coagulation cascade and venous thromboembolism [41].

Liver cells produce C-reactive protein, a protein that is active in inflammatory conditions and whose production can be stimulated by a group of inflammatory mediators, including interleukin-6, and has a lifespan of approximately 19 hours [44]. The results of the current study showed that the level of CRP in the blood was excessively high in COVID-19 patients. The summary of the results for CRP and IL-6 concentrations in patients' blood significantly increased compared to the control group and Males had a greater increase than females, the statistically significant changes (below 0.05) in CRP and IL-6 levels were observed between age groups, with the third group showing the greatest increase also, patients with chronic cardiac problems had the most significant rise in average CRP and IL-6 levels, while patients without chronic conditions had the least significant increase. Moreover, there was a positive correlation between the severity of COVID-19 infection and elevated CRP and IL-6 levels. COVID-19 patients with obstruction had the highest CRP and IL-6 levels, while patients without complications had the lowest values. This result is consistent with almost all previous studies, including the study. High CRP indicates severe inflammation and is associated with kidney damage and cardiac injury [45]. CRP suppresses the release of nitric oxide, leading to endothelial dysfunction [46]. Moreover, high CRP level is associated with damaged tissue, lipoproteins, programmed cell death, and is involved in complement activation and tissue damage. Interestingly, it is present in atherosclerotic plaques but not in normal vessel wall [47]. Some studies show that CRP can stimulate the expression of adhesion molecules and chemokines in human endothelial cells, and there is evidence that it works synergistically with lipopolysaccharide to induce tissue factor production, so CRP is considered an amplifier of inflammation [48]. For these reasons, it can be believed that a high level of CRP in the blood of COVID-19 patients could be a dangerous indicator of the development of cardiovascular diseases in them.

Conclusion

Elevated levels of CRP and IL-6 were found in infected Patients compared to the control group, with males exhibiting a greater increase also Patients with complications and severity had the highest levels, while those without had the lowest. Significant differences were seen based on age and chronic conditions so these findings may contribute to understanding the impact of COVID-19 on various demographic and health factors.

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