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Evaluation of CRP, D-Dimer of clinical significance in Iraqi patients with COVID-19 and associated comorbidities

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***Abstract*---**Background: The pandemic of coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has caused an unprecedented global social and economic impact, and high numbers of deaths. Many risk factors have been identified in the progression of COVID-19 into a severe and critical stage, underlying comorbidities such as hypertension, diabetes, obesity, chronic lung diseases, heart, liver and kidney diseases. Aims and Methods: This study was designed to investigate Measurement of serum C-reactive protein(CRP) level, plasma D-dimer level and evaluate the levels of each one of the studied parameters between patients infected by coronavirus COVID-19 and no associated comorbidities and patients infected by coronavirus COVID-19 with associated comorbidity (Diabetes , Hypertension). Results: The mean of CRP was 19.31 ± 8.205 in control, , 96.80 ± 18.33 in HTN, 51.08 ± 16.56 in DM group, while mean of D-dimer was 560.45 ± 155.13 in control group, , 1178.86 ± 379.12 in HTN group, 1529.51 ± 530.20 in DM group of patients. Conclusion: We can conclude from the study that COVID19 patients show significant abnormalities in the laboratory biomarkers characterized by an abnormality in CRP level, plasma d-dimer level, tend to increase in COVID-19 patients with , hypertension patients compared with non- hypertension patients and diabetes patients compared with non- diabetes patients .

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Keywords---COVID-19, CRP, D-dimer, diabetes, hypertension.

Introduction

The World Health Organization labeled the coronavirus illness 2019 (COVID-19) a pandemic on March 11, 2020,. The outbreak began in Wuhan, China, in December 2019, with the first official case reported, following which the disease expanded globally, causing dramatic changes in the public health sector and healthcare delivery[1]. After severe acute respiratory syndrome (SARS) in 2002 and Middle East respiratory syndrome (MERS) in 2012, the virus was identified as genus beta coronavirus, making it the third coronavirus to cause a worldwide health disaster in the twenty-first century. Severe acute respiratory syndrome coronavirus-2 is the name of the new coronavirus (SARS-CoV-2) [1].

The virus has infected people all throughout the world, making it more contagious than earlier coronaviruses [2]. It can produce infections that vary from asymptomatic to life-threatening [3]. The COVID-19's genesis and transmission SARS-CoV-2 is thought to have spread from bats to an intermediate host (perhaps a Malayan pangolin, which has 91 percent nucleotide identity) and subsequently to humans, similar to SARS and MERS. Figure 1.3 [4].

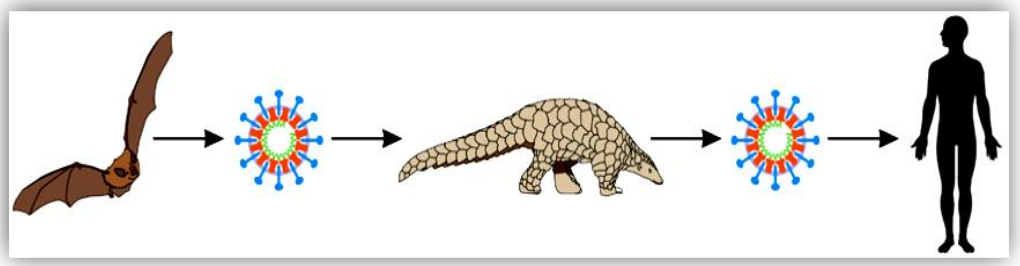

Figure 1.3: Coronavirus2 suspected of causing severe acute respiratory syndrome in humans [4]

The COVID-19 was caused by the SARS-CoV-2 virus, which is a highly transmissible and pathogenic virus that is transmitted mostly through contact with respiratory droplets [5]. Fever, cough, tiredness, anorexia, shortness of breath, and myalgia are the most prevalent symptoms. Headache, nausea, and vomiting, as well as diarrhea, nasal congestion, and sore throat, have been described [6,7,8]. According to the WHO, covid-19 infection is classified as mild disease, moderate disease (pneumonia), severe disease (severe pneumonia), and critical disease [9].

C-reactive protein (CRP) levels have been linked to severe pneumonia in some studies, and higher CRP levels have been linked to early detection of pneumonia [10]. The CRP is a hyper inflammation marker. COVID-19 has been reported to have a worse prognosis in patients with elevated CRP levels[11]. D-dimer levels have been linked to the severity of COVID-19 infection and mortality in several

recent investigations. Acutely unwell people with a variety of infectious and inflammatory disorders have high D-dimer levels [12].

The last few weeks' clinical and epidemiological data on COVID-19 reveal that certain comorbidities enhance the likelihood of infection, leading to severe lung injury and death. Hypertension, cardiovascular disease, and diabetes are the most prevalent comorbidities recorded so far [13]. Furthermore, a significant number of COVID-19 patients and other disorders in admitted ICU cases suggests that comorbidities may be a risk factor for COVID-19 patients[14].

Diabetes and COVID-19

Due to reduced phagocytic cell capacities, people with diabetes are more susceptible to infections. In diabetic patients, several other factors can enhance the risk of COVID-19. Mendelian randomization study found a higher level of ACE-2 receptors to be causally associated to diabetes; this may predispose patients with diabetes to SARS-CoV-2 infection [15]. Furin is a type 1 membrane-bound protease that is overexpressed in diabetics [16]. This proprotein convertase helps the virus get inside the host cell by reducing SARS-reliance CoV-2's on human proteases. The massive quantities of furin activate the SARS-CoV-2 spike (S) protein, which binds to ACE-2 receptors. This pre-activation of the S protein permits the virus to enter the cell and avoid detection by the human immune system [17]. As a result, a dysregulated immune response characterized by increased ACE-2receptors and furin expression may result in greater lung inflammation and reduced insulin levels. For diabetic individuals, the virus's easy entrance creates a life-threatening situation[15,16]. Furthermore, decreased T-cell activity and higher levels of interleukin-6 (IL-6) play a key role in the development of COVID-19 illness in diabetics [18].

Hypertension and COVID-19

The COVID-19 infection is linked to uncontrolled blood pressure, as well as a high case fatality rate (CFR). In China, 23% of hypertensive COVID-19 cases were recorded with 6% CFR, with the number steadily increasing due to pandemic fear [19]. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) are commonly used to treat hypertension in individuals. When taken in large doses, these inhibitors upregulate expression of the ACE-2 receptor, increasing vulnerability to SARS-CoV-2 infection [20]. Higher levels of receptor cell expression in the lungs render the infection more vulnerable, increasing the risk of severe lung damage and respiratory failure [21]. The aim of this study was to compare the levels of serum CRP, plasma D-dimer, and each of the examined parameters between patients infected with coronavirus COVID-19 who had no related comorbidities and patients infected with coronavirus COVID-19 who had associated comorbidities (Diabetes , Hypertension).

Methods

This is a case-control study conducted at medical city Department /AL-Shifa Crisis center during the period from January 2022 to the end of April 2022. The

study involved 110 patients infected by coronavirus COVID-19 who were diagnosed by Consultant physician based on RT-PCR and CT- scan and associated comorbidity Patients were subdivided according to the comorbidity. The range of the age for patients between (30-75 years).

Group 1: The control group consisted of 40 patients infected by coronavirus COVID-19 with no associated comorbidities,
Group 2: 35 patients infected by coronavirus COVID-19 with a history of diabetes mellitus .
Group 3: 35 patients infected by coronavirus COVID-19 with a history of hypertension.

Inclusion criteria

Patients aged 30-75 years old who were admitted and before commencing any therapy for the coronavirus COVID-19.

Exclusion criteria

Patients who have had influenza-cold viral infection, chronic liver diseases, chronic kidney diseases.

Ethical approval

This study was carried out after approvals were obtained from:

1. 1.The scientific committee of the Biochemistry Department, College of Medicine, University of Baghdad.
2. Ministry of Health/ Medical City.
3. Vocal consent from each patient or her/ or his relative.

Blood Sampling

5 milliliters of blood sample was collected from the peripheral vein of each patient and control and subdivided into two parts**:**

1. The first one included 1.8 milliliters transferred into sodium citrate tube to obtain plasma for measurement of D-dimer.
2. 2-The second part transferred into gel plain tube that allows to clot for 15 minutes and then centrifuged for 10 minutes at 3000 rpm, to obtain serum sample. The separated serum for measurements of ,CRP level.

Statistical Analysis

The data was interpreted using SPSS version 25.0 software, frequency, percentage, mean and stander deviation were used to describe data.
ANOVA test was used to evaluate the difference in mean level of numeric data between more than2 variables. Histogram figures were used to show mean of studied biomarkers between the groups. Chi-square test used to test association between qualitative variables.

Result

CRP, D-dimer with difference groups

A statistical significant difference in mean level of CRP and D-dimer between the groups, p<0.00 and <0.00. The mean of CRP was 19.31 ± 8.205 in control, , 96.80 ± 18.33 in HTN, 51.08 ± 16.56 in DM group, while mean of D-dimer was 560.45 ± 155.13 in control group, , 1178.86 ± 379.12 in HTN group, 1529.51 ± 530.20 in DM group of patients. as presented in table 1.

Table 1: mean difference of CRP and D- dimer in the studied groups

		Mean ± SD	SE	p-value
CRP	control	19.13 ± 8.205	1.29	< 0.00*
	HTN	96.80 ± 18.33	3.1	
	DM	51.08 ± 16.56	2.80	
D- Dimer	control	560.45 ± 155.13	24.52	< 0.00*
	HTN	1178.83 ± 379.12	64.08	
	DM	1529.51 ± 530.20	89.62	

*p-value ≤ 0.05

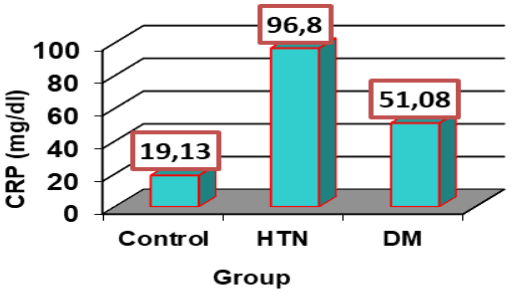

Figure 1: Comparison between difference groups in CRP

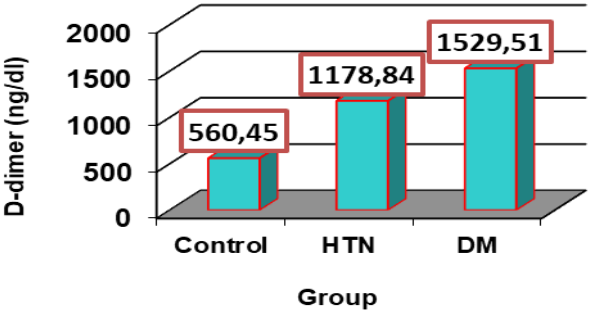

Figure 2: Comparison between difference groups in D-dimer

Discussion

The present study found that the mean value of serum CRP activities of diabetic patients (51.08 ± 16.56) was significantly higher than that of non -diabetic patients (19.13 ± 8.205) (figure 1).These findings are in agreement with that reported by Debi et al., 2022 [22] who found the diabetic patients showed higher levels of CRP than the non-diabetic patients. This might have happened due to inflammatory reactions and related tissue destruction. Oxygen saturation (SpO2 < 90%) is significantly decreased in these types of patients indicating that CRP levels are increased in severe lung injury patients [23] COVID-19 infects the lungs via binding to the ACE-2 inhibitor[24] . The severity of COVID-19 illness worsens in individuals with high glucose levels due to a strong pro-inflammatory cytokine response, weakened innate immunity, and downregulated angiotensin 2-converting enzyme (ACE-2) [25] .

In this study found that the mean value of inflammatory marker serum CRP activities of HTN patients (96.80 ± 18.33) was significantly higher than that of non–HTN (51.08 ± 16.56) (figure 1).These findings are in agreement with that reported by Zeng et al., 2021[26] who found the HTN patients showed higher levels of CRP than the non-HTN patients. inflammation associated with HTN synergizes cytokine storm and worsens host immune surveillance in SARS-CoV-2 infection[27,28]. the mean value of serum CRP activities of HTN patients was higher than that of diabetic and control patients.

The development of COVID-19 diseases has been linked to an irregular coagulation activity with elevated D-Dimer [29,30]. The present study found that the mean value of serum D-dimer activities of diabetic patients (1529.51 ± 530.20) was significantly higher than that of non -diabetic patients (560.45 ± 155.13) (figure 2).These findings are in agreement with that reported by Debi et al., 2022 [22] who found the diabetic patients showed higher levels of d-dimer than the non-diabetic patients. D-dimer may be a sign of serious virus infection along with thrombosis and pulmonary embolism. A virus infection can cause sepsis and coagulation problems which are also frequent in the development of severe diseases. Furthermore, the increment of D-dimer may be considered as an indirect expression of an inflammatory response, as inflammatory cytokine may induce an imbalance in coagulation and fibrinolysis in the alveoli which can stimulate the fibrinolysis mechanism and raise D-dimer levels [31]

The study found that the mean value of serum D-dimer activities of HTN patients (1178.83 ± 379.12) was significantly higher than that of non -HTN (560.45 ± 155.13) (figure 2).These findings are in agreement with that reported by Osmanet al., 2022and Andina et al., 2021[32,33] who found the HTN patients showed higher levels of D-dimer than the non-HTN patients. The mechanism in patients with higher D-dimer could be that systemic pro-inflammatory cytokine responses induce the production of procoagulant factors and hemodynamic changes [34] .

Conclusions

It can be conclude from the study that COVID19 Patients with hypertension, diabetes mellitus should be carefully managed and these patients need to be closely monitored , This is due to the increase in CRP level, plasma D-dimer level observed in hypertension patients compared with non- hypertension patients and diabetes patients compared with non- diabetes patients which can be considered strong predictors of clinical deterioration.

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