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Estimation of D-Dimer and CRP in Serum Patients infected by COVID-19

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Abstract

Objectives: The study aimed to evaluate D-dimer and C-reactive protein (CRP) levels in patients with COVID-19, taking into account age and gender.
The study was conducted among patients attending Yarmouk Teaching Hospital.
The study included 100 blood samples from patients with COVID-19 and healthy controls. Eighty blood samples were from patients with COVID-19 and 20 from healthy controls. Serum levels of IgG and IgM antibodies, as well as D-dimer and C-reactive protein (CRP), were measured.
Results: 53 male samples and 47 female samples were recorded. The samples were divided into four age groups and statistically analyzed ($P<0.05$). There was a significant difference between the sexes and no significant difference between the four age groups. D-dimer and C-reactive protein (CRP) levels were evaluated, and a significant difference was found between patients and healthy controls ($P<0.01$).
Conclusion: There is a correlation between high levels of D-dimer and CRP in the blood with COVID-19 infection and an increased likelihood of patients being exposed to death, especially in males, which is higher than in females, and there is no difference between ages.

Keywords: D-Dimer CRP, COVID-19, Blood, Antibodies.

Introduction

D-dimer is a biomarker of fibrin formation and degradation. It is found in plasma or whole blood, where its percentage is low in healthy people, but it is high in people who have clotting problems (1).

General Concepts of D-Dimer

It is produced by the decomposition of cross-linked plasmin (1), which is formed by the sequential activity of three enzymes, which are the activated factor XIII, plasmin, and thrombin. It begins to form by converting thrombin resulting from the clotting of fathomable fibrinogen into fibrin, where apiece fibrinogen fragment consists of a homogeneous dimer consisting of three pairs of polypeptide chains, which are alpha, beta, and gamma, which are linked by disulfide bonds (2). Monoclonal antibodies that identify an antigen that manifests as cross linked dimers are used to detect it (3). Although there are several commercial tests available for detecting dimers, they can be broadly classified into three categories: latex agglutination tests, immunofluorescent tests (ELISA), and whole blood agglutination tests (3.

D-Dimer Related to COVID-19

Millions of people worldwide have died as a result of the COVID-19 pandemic during the years 2019-2022 (4). The hypercoagulable state of D-dimer caused by COVID-19 has been associated with an increased risk of stroke. Fibrin degradation product formation is bred thru the systematic degradation of blood clots thru the fibrinolytic system (5). There are several studies that have proven the validity of D-dimer levels as an indicator of COVID-19 severity with mortality rate (6-7), as it was recorded as an independent indicator of people who died from COVID-19 (8). Several studies have found that high levels of D-dimer are closely associated with severe COVID-19 disease. Zhang et al. (9) found that the probability of death in COVID-19 patients increases with high levels of D-dimer.

COVID-19 and CRP (C-reactive protein)

CRP is an acute phase protein that increases with increased inflammation and infectious diseases. It is measured clinically in the blood, as its normal concentration does not exceed 10 mg/L in healthy people. However, it was found that it rises rapidly during cases of infection with the disease (10), as its half-life is about 19 hours (11). It decreases when the inflammation ends or the patient recovers, as it is associated with inhibiting complement and activating phagocytosis, thus eliminating pathogens. It is also an indicator of severe lung diseases and is associated with infection with Covid-19, as its high levels in the blood are an indicator of pneumonia and the severity of the disease, and thus it is a strong indicator for diagnosing Covid-19 (12).

Methodology

Study Design

During the final phase of the COVID-19 pandemic, this study was conducted for the research group from September 2020 to April 2021 at Al-Yarmouk Teaching Hospital in Baghdad. The research was conducted with the consent of each individual involved or a family member present with the patient. The research adheres to the ethical code. The author confirms that there is no conflict of interest and that artificial intelligence was not used in the implementation and design of this study.

Sample Criteria and Procedures

This study included adolescents and adults of various ages. The sample size was 100, including patients and healthy individuals, ranging in age from 14 to 82 years, including 53 males and 47 females. Comprehensive information and data were collected on laboratory aspects of the individuals included in the study sample, such as gender, age, and previous or first-time COVID-19 infection. Laboratory samples were collected after blood was drawn and separated using a centrifuge, serum was taken, and some tests were performed, such as measuring the levels of IgG and IgM related to COVID-19, as well as measuring the level of D-dimer using the Afias device, and assessing the level of CRP in patients' serum using the Cobas 311 device. Figure (1)

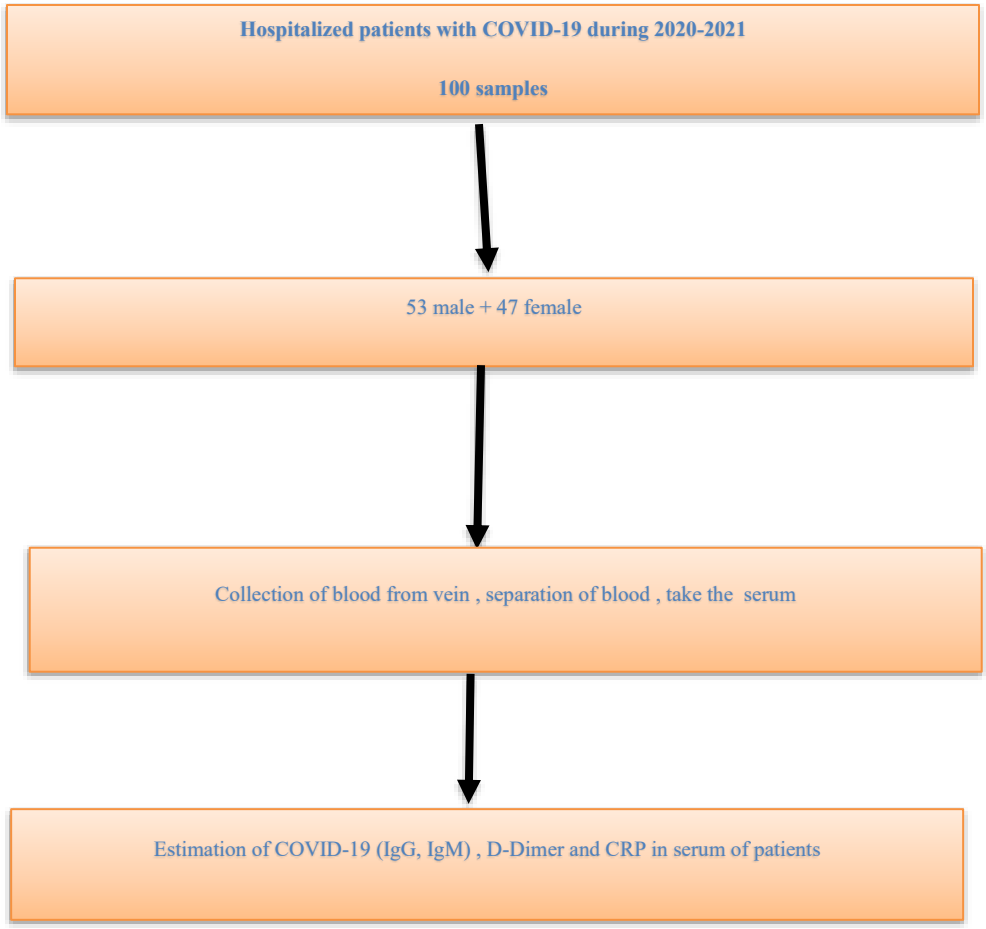


Figure (1): Flow diagram of study

Statistical analysis

Data were statistically analyzed using the program Statistical Analysis System -SAS (13). and compared the significant differences between the averages using the Duncan test (14) polynomial.

Results

From September 2020 to April 2021, 100 samples of COVID-19 patients were recorded at Yarmouk Teaching Hospital, where 80 blood samples were taken from a person infected with COVID-19 and 20 samples from healthy individuals. A high statistically significant difference was recorded between the two groups in terms of evaluating the antibodies IgG, IgM, D-dimer, and CRP ($p<0.01$). Table 1 and Figure No. (2)

Table (1): Differences between normal sample and abnormal samples.

groups	No.	M.±St. E. (IgG)	M.±St. E. (IgM)	M.±St. E. (D-Dimer)	M.±St. E. (CRP)
(abnormal)	80	4.92 ± 0.55^{a}	6.31 ± 0.70^{a}	599.75 ± 74.46^{a}	40.33 ± 3.96^{a}
(Normal)	20	0.49 ± 0.08^{b}	0.11 ± 0.05^{b}	140.20 ± 20.71^{b}	5.26 ± 0.64^{b}
Significant		**	**	**	**

** =($P<0.01$), groups=2(Normal) / groups=1(abnormal)

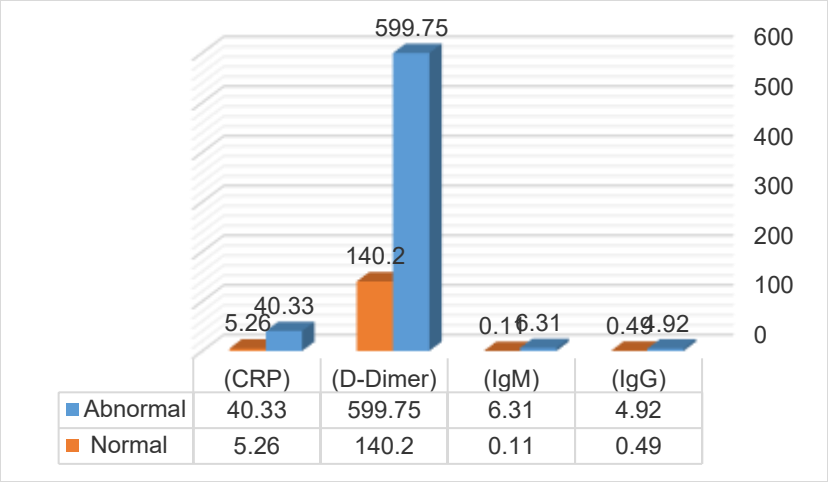


Figure (2): *Differences between normal sample and abnormal samples*

The results related to gender showed that there was no statistically significant difference between males and females with regard to measuring the level of IgG and IgM antibodies, while there was a significant difference between the sexes with regard to D-dimer and CRP. (P<0.05) (Table 2 and Figure 3).

Table (2): The differences between male and female.

Gender	No.	M.±St.. E. (IgG)	M.±St. E. (IgM)	M.±St. E. (D-Dimer)	M.±St. E. (CRP)
1 (male)	53	3.55±0.55[a]	6.20±0.94[a]	639.20±101.37[a]	40.51±5.54[a]
2 (female)	47	4.58±0.81[a]	3.79±0.73[a]	359.70±62.02[b]	25.21±3.64[b]
Significant		n.s.	n.s.	*	*

n.s.= No Significant, * =(P<0.05) Gender:1= male / gender:2= female

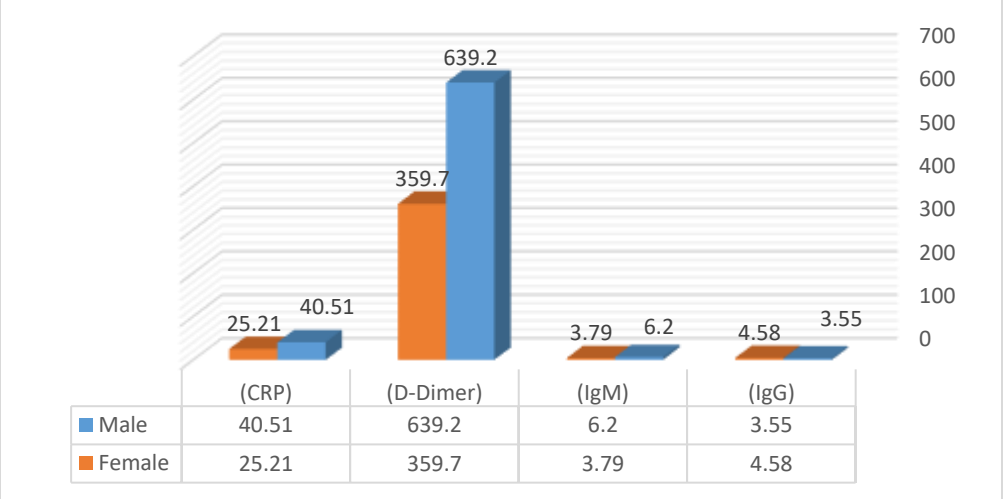


Figure (3): *Differences between male and female*

The results related to age, which were divided during the study into four age groups, are shown in Table No. (3), where the results were recorded as no significant difference between the four age groups.

Table (3): The four age groups dependent in study

Age	No.	M.±St. E. (IgG)	M.±St. E. (IgM)	M.±St. E. (D-Dimer)	M.±St. E. (CRP)
1	23	2.97±0.74[a]	6.16±1.51[a]	537.30±116.63[a]	34.39±7.18[a]
2	33	3.99±0.78[a]	4.79±1.04[a]	519.30±128.09[a]	36.44±6.78[a]
3	27	4.14±1.06[a]	3.90±0.78[a]	372.96± 40.20[a]	24.54±5.05[a]
4	17	5.37±1.36[a]	5.97±1.88[a]	659.94±212.91[a]	39.75±9.30[a]
Significant		n.s.	n.s.	n.s.	n.s.

Discussion

Our research results indicate that the level of D-dimer in patients infected with Covid-19 recorded a significant increase in all infected patients, while it recorded normal levels in healthy individuals (15) This is consistent with the indicators of physiological responses in the group of patients (16-17). Another study showed a relationship between D-dimer and COVID-19, as it was associated with deep vein thrombosis in patients with COVID-19 (17). This increase in D-dimer levels is consistent with our study. Other results indicate that D-dimer is an indicator of heart disease in COVID-19 patients in the event of blood clotting (18). This is linked to the need for patients to use anticoagulants (19-20). This in turn strengthens our results, but we need to study a larger sample to further validate these results, as future studies may determine the ability of D-dimer to diagnose other related critical points such as stroke and length of hospitalization. A study conducted on a number of patients with COVID-19 reported that D-dimer levels exceeding 1 microgram/ml are an indicator of poor prognosis (21). The observation of elevated D-dimer levels in patients with COVID-19 has been used to confirm a physiological component of the syndrome, namely thromboembolism, indicating the high rates of venous thromboembolism that characterize some patients with COVID-19. Other reports have indicated an association with a pulmonary physiology similar to that of pulmonary vascular disease (22-25). However, these observations remain reliable, indicating acquired thrombosis caused by COVID-19. D-dimer is also a highly non-specific marker of deep vein thrombosis and may be more associated with manifestations of inflammation than thrombosis, as indicated by (26-27). Other studies have found a correlation between D-dimer levels and levels of inflammatory markers such as CRP (28). However, D-dimer levels are currently used to determine therapeutic doses for COVID-19 patients in some centers. There are many studies that have been found on the difference between males and females in terms of D-dimer and its relationship to COVID disease (29,30). Multiple changes have been proposed for the differences between the sexes, including the shielding upshot of E2 and the difference in the natural defenses, for instance the difference in the level of cytokines or functions related to T cells, as well as the difference in the lining of the blood vessels, but none of these factors have been proven until now (31). In a study conducted on COVID patients, a similar difference was found between the sexes in the level of D-dimer, as it was higher in males than females (32). This is consistent with our study, and the reason for this is that males are more likely to suffer from serious diseases compared to females. Also, blood clotting is one of the prominent characteristics of COVID patients (33), as is the ability to form a clot (34). These are all factors that may be possible in explaining this difference between the sexes.

CRP is a well-established indicator of total infections and stark infection as an critical protein that has a close association with phosphocholine in pathogens and host cell membranes and acts as a stimulating ligand for phagocytosis (35). Before the COVID pandemic, CRP was associated with bacterial infections (36-37) as well as viral infections (38-41). Advanced studies have shown that elevated CRP levels in COVID-19 patients lead to an increased incidence of pulmonary failure, severe respiratory distress, and myocardial injury in multiple series (42-44). This is in patients with COVID-19, as this protein is a biomarker, as the concentration of CRP in COVID-19 patients reflects the severity of the disease and the magnitude of the acute inflammatory response (45).

Conclusion

There is a correlation between high levels of D-dimer and CRP in the blood with COVID-19 infection and an increased likelihood of patients being exposed to death, especially in males, which is higher than in females, and there is no difference between ages. This importance in the levels is considered a predictive indicator of the deterioration of the patients' condition, which may be useful in developing visions to improve the condition of patients in the future.

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