

Assessment the Correlation of D-dimer and Ferritin Level in Patients Infected with Covid-19 in Anbar Governorate of Iraq

Safaa A.L. Al Meani^{1*}, Ali H. Abdulkareem¹, Mohammed O. Ibrahim², Mohammed M. Ahmed¹, Mahmood Yassin Mukhlif³

¹University of Anbar/ College of Science/Department of Biotechnology/Iraq

²Ministry of Health, Anbar health department, Ramadi teaching hospital, Iraq

*Corresponding Author: Email: sc.safaa-meani@uoanbar.edu.iq

ABSTRACT

In total, 366 patients (193 males and 173 females) were screened with 366 D-dimer and ferritin. The current study showed that the infection with Covid-19 is affected by the patients age, the age group (less than 40) years was the most affected, where the rate of infection being (56.01%). also, the study showed the sex factor was an effect on spread infection where the men infection was more than women. The study also appeared that the caused a significant increase ($p < 0.001$) in the D-dimer level in both sex and age. A significant increasing showed in ferritin level compared with the healthy group.

Keywords: COVID-19, ferritin, d-dimer

Correspondence:

Nusaree Sripath

¹ College of Public Health Sciences, Chulalongkorn University, Bangkok, Thailand

*Corresponding author: Nusaree Sripath email-address:

nusaree.spk@gmail.com

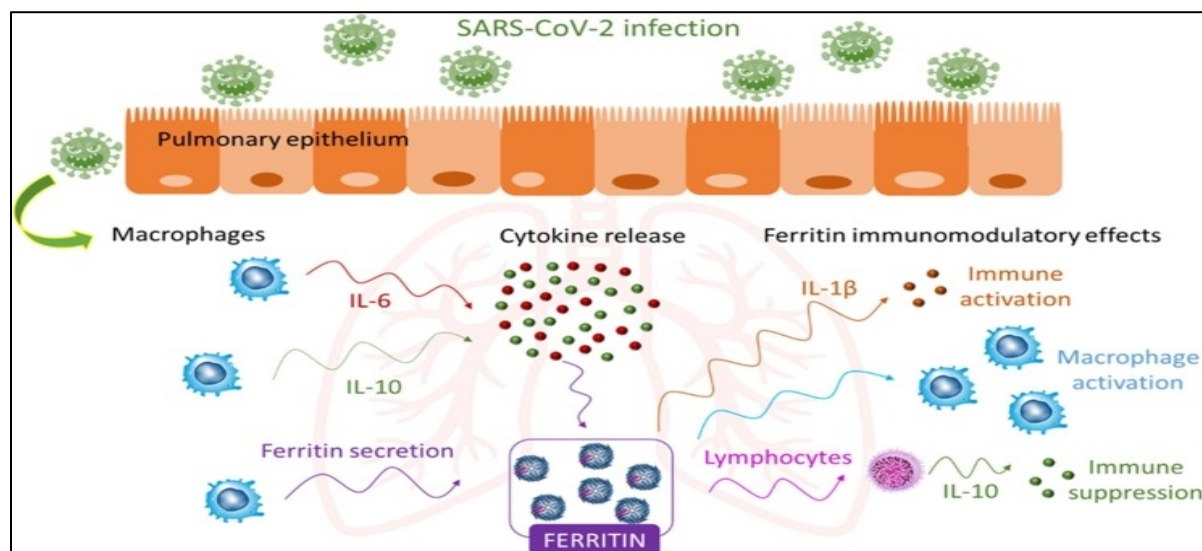
INTRODUCTION

Pandemic Corona virus is an outbreak of a novel detected virus that spread rapidly, with systemic or local pneumonia complications occurring globally, then called as SARS-CoV-2 in China [1]. In February/2020, (WHO) called this disease as (Covid-19) [2]. D-dimer is a particular cross-linked fibrin metabolite formed by a plasma fibrinolytic enzyme[3]. The elevated D-dimer concentration represents secondary fibrinolysis. D-dimer has been used to diagnose and determine deep vein thrombosis (DVT) of the lower extremities, pulmonary embolism (PE), disseminated intravascular coagulation (DIC), surgical trauma and malignant tumors[4].

Some inflammatory markers have been reported in studies in COVID-19 patients, such as procalcitonin, C-reactive protein, (ESR), and serum amyloid A. Ferritin, however has received little recognition, It has been shown that high ferritin is related with other complications of other viral diseases such as dengue fever [5]. In addition to ARDS, sepsis is found in all deceased patients with corona virus [6]. Disseminated

intravascular coagulation is also one of the major underlying causes of death in these patients (DIC). Coagulopathy intake, which should be avoided to minimize mortality, occurs in DIC with a decrease in fibrinogen levels and a rise in D-dimer levels. Fibrinogen and D-dimer have also been stated to have a predictive value for the mortality of non-Covid sepsis patients who are secondary to DIC complications[7].

The ferritin level increasing is a potential role of this protein during inflammation following the development of COVID-19 disease[8]. In controlling pro-inflammatory and anti-inflammatory mediators, there are complex mechanisms between ferritin and cytokines because cytokines can induce ferritin expression, but ferritin may also induce the expression of pro- and anti-inflammatory cytokines, as shown in Fig. 1. The current study aims to understand the correlation of D-dimer with age and sex during infection with the coronavirus and the impact of the infection on certain blood parameters such as serum ferritin in Anbar Province.



Assessment the Correlation of D-dimer and Ferritin Level in Patients Infected with Covid-19 in Anbar Governorate of Iraq

Fig. 1. Prospective function of ferritin following COVID-19 infection during inflammation. Active development of ferritin by macrophages and cytokines can lead to high ferritin, which may in turn encourage the production of many (IL-1 β) and (IL-10)(Kernan and Carcillo, 2017).

MATERIALES AND METHODS

Collection of samples

Over the period from April 2020 to November 2020, 366 samples were collected from COVID-19 infected patients from the province of Al-Anbar. The qPCR technique and the covid 19 rapid test (bio-medomics) were done for all the samples. In this analysis, according to the ethics of scientific research, several variables such as gender, age, D-dimer and serum ferritin were taken into account.

Laboratory testing Determination of D- dimer and ferritin

Both of D-dimer and ferritin level are tested using automated Mini-Vidas system (Biomérieux, France). Reference range of less than 500 ng/ml for D-dimer and 28 -390 ng/ml for ferritin.

Statistical analysis

All the data was analyzed with descriptive statistical analysis using SPSS software, version 25.0. In order to compare the different classes, we used chi-squared tests between age and gender of patients, on the other hand we used paired-samples T- test between age or gender with D-dimer and ferritin. also, we used pearson correlation to know correlation between D-dimer and serum ferritin.

RESULTS

According to table 1, results showed a significant difference between gender and age of confirmed COVID-19 patients at χ^2 : 159.624, p- value: < 0.01. On the other hand, our results showed that the males are more affected to corona virus with (52.73%) than females with (47.27 %). Patients (less than 40) years were higher significant compared with the group more than 40 years with (43.99%) percentage.

Table 1: The relationship between gender and age of covid-19 patients.

		Total	gender	
			male	female
age	less than 40	205	193	173
	more than 40	161		
Total		366		
Chi: 159.624, P- value: <0.01				

Our results showed that mean of D-dimer (1216.9961 \pm 99.64764) for Covid-19 patients is higher significant from healthy control mean (162.6833 \pm 6.82347) , While mean of ferritin

(551.7026 \pm 194.59347) for Covid-19 patients is higher significant from healthy control mean (43.0116 \pm 1.69428). Table 2

Table 2: D-dimer and ferritin with healthy control.

	D-dimer	Control(dimer)	ferritin	control
Mean	1216.9961	162.6833	551.7026	43.0116
Std. Error of Mean	99.64764	6.82347	194.59347	1.69428

The study also found that Covid-19 virus infection had a major impact on the D-dimer level (p-value <0.001) and on both sexes as shown table 3.

Table 3: the relationship between Ferritin Level or D-dimer with COVID-19 patient's gender.

	gender	N	Mean	Std. Error Mean		p- value
D-dimer	male	193	652.3796	9.67336	6.239	<0.001
	female	173	1846.8863	200.22070		
Ferritin	male	193	369.8093	30.35552	0.987	0.324
	female	173	754.6241	410.36718		

The study also found that Covid-19 virus infection has a significant effect on the D-dimer level (p-value <0.001) and on both age groups.

Table 3: the relationship between Ferritin Level or D-dimer with COVID-19 patients age groups.

Assessment the Correlation of D-dimer and Ferritin Level in Patients Infected with Covid-19 in Anbar Governorate of Iraq

	age	N	Mean	Std. Error Mean	T	P-value
D-dimer	less than 40	205	638.8166	6.67778	6.960	<0.001
	more than 40	161	1953.1875	213.01311		
Ferritin	less than 40	205	362.2896	28.35898	1.099	0.273
	more than 40	161	792.8808	440.93037		

The Current findings have shown that coronavirus infection has triggered a substantial increasing in infected people's D-dimer level (p-value<0.01) relative to ferritin. table 4

Table 4: Relationship between

Statistics				
	D-dimer	Ferritin	p- value	Pearson cor.
Mean	1216.9961	551.7026	<0.01	0.210
Std. Error of Mean	99.64764	194.59347		

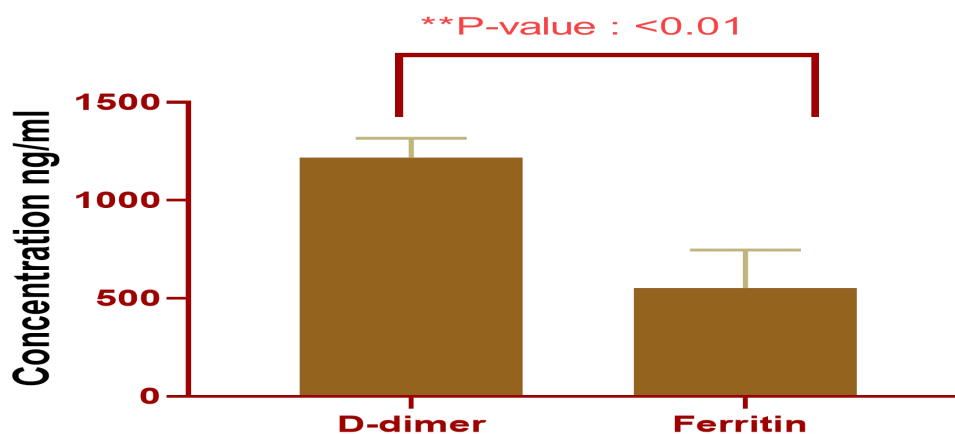


Figure 2: Relationship between D-dimer and ferritin levels with COVID-19 patients.

DISCUSSION

A major general health threat that needs rapid intervention is the COVID-19 pandemic. Despite the intense efforts to discover novel SARS-CoV2 drugs, this technique is repetitive with little progress to date. Medicine repurposing has also been known as the best way to locate COVID-19 restorative specialists to cope with the desperation of the case[9]. One of the fragments formed when plasmin cleaves fibrin is D-dimers. The tests are routinely used to rule out the diagnosis of thrombosis as part of a diagnostic algorithm. However, plasma D-dimer levels are often increased by any pathological or non-pathological process that increases the development or breakdown of fibrin[10].

The results were showed that COVID-19 patients with slightly higher levels of D-dimer, highlighting the likelihood of more apparent coagulation system activation. Although the levels of D-dimer were associated with inflammatory markers and appeared to normalize in most patients in the convalescent stage, an irregular increase can imply successful anticoagulant therapy. As we say, this is the first study on the

relationship between COVID-19 levels of D-dimer and ferritin and other parameters such as gender and age, as well as the variance during infection period.

Coronavirus infection affects the body's biomarker, as the amount of Ferritin. In this study, the patients with COVID-19, suffer from increasing the Ferritin level in their serum. This excess may cause secondary bacterial infection and intensify COVID-19 infection. Another study, the levels of ferritin in the patient's serum COVID-19 were hgher than healthy control [11].

Many factors have been reported that influence with spreading of coronavirus infection, the most notable being sex and the patient's age. Many studies reported relationship between gender and COVID-19 infection [12]. Compared to women, the response of antibodies in plasma of convalescent from men is impressive considering that women typically have more immune response than men[13]. The outcome of the current study indicates the infection of male is more than women. This can be explained by the nature of men's working and they meet many people daily and they exposure to infected patients compared with women that stay most of the time

Assessment the Correlation of D-dimer and Ferritin Level in Patients Infected with Covid-19 in Anbar Governorate of Iraq

at home according to their traditions and habits in Al Anbar city of Iraq. which influence the strength of the immune system in addition to the hormonal disparity.

CONCLUSION

The age and gender factor play an important role in the prevalence of corona virus infection in the present research, and that Covid-19 infection causes both D-dimer and the blood ferritin level to increase, so it can be relied on in the early diagnosis of COVID-19 infection.

REFERENCES

1. M. İ. Hayiroğlu, T. Çınar, and A. İ. Tekkeşin, "Fibrinogen and D-dimer variances and anticoagulation recommendations in Covid-19: current literature review," *Rev. Assoc. Med. Bras.*, vol. 66, no. 6, pp. 842–848, 2020.
2. B. Henry *et al.*, "Lymphopenia and neutrophilia at admission predicts severity and mortality in patients with COVID-19: a meta-analysis," *Acta Biomed*, vol. 7, p. 91, 2020.
3. F. Tita-Nwa, A. Bos, A. Adjei, W. B. Ershler, D. L. Longo, and L. Ferrucci, "Correlates of D-dimer in older persons," *Aging Clin. Exp. Res.*, vol. 22, no. 1, pp. 20–23, 2010.
4. J. J. Michiels, G. Palareti, and P. de Moerloose, "Fibrin D-dimer testing for venous and arterial thrombotic disease," in *Seminars in vascular medicine*, 2005, vol. 5, no. 04, pp. 311–314.
5. X.-J. Zhang *et al.*, "In-hospital use of statins is associated with a reduced risk of mortality among individuals with COVID-19," *Cell Metab.*, vol. 32, no. 2, pp. 176–187, 2020.
6. C. Huang *et al.*, "Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China," *Lancet*, vol. 395, no. 10223, pp. 497–506, 2020.
7. T. Matsubara *et al.*, "Significance of plasma fibrinogen level and antithrombin activity in sepsis: a multicenter cohort study using a cubic spline model," *Thromb. Res.*, vol. 181, pp. 17–23, 2019.
8. C. Rosário, G. Zandman-Goddard, E. G. Meyron-Holtz, D. P. D'Cruz, and Y. Shoenfeld, "The hyperferritinemic syndrome: macrophage activation syndrome, Still's disease, septic shock and catastrophic antiphospholipid syndrome," *BMC Med.*, vol. 11, no. 1, p. 185, 2013.
9. A. B. Durojaiye, J.-R. D. Clarke, G. A. Stamatiades, and C. Wang, "Repurposing cefuroxime for treatment of COVID-19: a scoping review of in silico studies," *J. Biomol. Struct. Dyn.*, pp. 1–8, 2020.
10. L. Linkins and S. Takach Lapner, "Review of D-dimer testing: Good, Bad, and Ugly," *Int. J. Lab. Hematol.*, vol. 39, pp. 98–103, 2017.
11. B. Zhou, J. She, Y. Wang, and X. Ma, "Utility of ferritin, procalcitonin, and C-reactive protein in severe patients with 2019 novel coronavirus disease," 2020.
12. E. P. Scully, J. Haverfield, R. L. Ursin, C. Tannenbaum, and S. L. Klein, "Considering how biological sex impacts immune responses and COVID-19 outcomes," *Nat. Rev. Immunol.*, pp. 1–6, 2020.
13. A. L. AL-Furat, "study the relationship between CRP and Ferritin in people infection with COVID-19 in AL-Najaf Governorate, Iraq."
14. K. F. Kernan and J. A. Carcillo, "Hyperferritinemia and inflammation," *Int. Immunol.*, vol. 29, no. 9, pp. 401–409, 2017.