

COVID-19 Patients from Duhok City, Iraq:

Serum Reactive Protein (CRP)

and D-dimer Level

Mohammed A. Khidhir¹,

Saad A. Alnuaimi²,

Shimal Zubair³,

Abdelhamid M. Yousif³,

Salah M. Jameel³, and Riyad F. Taha³.

1. Asist.Prof.Dr Al-Manara University, Missan, Iraq. Email: khidhirmaf@gmail.com

2. Asist.Prof.Dr, Assistant Professor Dr., Accounting Department, College of Business Administration, Al-Bayan University. Email: saad.ahmed@albayan.edu.iq

3. Cihan University-Duhok, Department of Medical Laboratory, Dohuk, Dohuk, Iraq. Students.

COVID-19 Patients from Duhok City, Iraq: Serum Reactive Protein (CRP) and D-dimer Level

Mohammed A. Khidhir¹, Saad A. Alnuaimi², Shimal Zubair³, Abdelhamid M. Yousif³, Salah M. Jameel³, and Riyadh F. Taha³.

1. Asist.Prof.Dr Al-Manara University, Missan, Iraq. Email: khidhirmaf@gmail.com

2. Asist.Prof.Dr, Assistant Professor Dr., Accounting Department, College of Business Administration, Al-Bayan University. Email: saad.ahmed@albayan.edu.iq

3. Cihan University-Duhok, Department of Medical Laboratory, Dohuk, Dohuk, Iraq. Students.

ABSTRACT

Due to rapid human-to-human transmission, coronavirus illness has become a global epidemic. It can lead to neurological, cardiovascular, and pulmonary conditions that range from moderate to fatal. To reduce mortality, the current study aimed to determine whether high levels of D-dimer and CRP indicate a poor prognosis in COVID-19 progression. This study aims to investigate the potential presence of distinct ranges for D-dimer and serum CRP levels in patients who are eligible for COVID-19 registration and to explore any differences between these ranges. This study aims to gain insight into how individuals with a positive COVID-19 diagnosis may exhibit varying levels of both D-dimer and serum CRP, and how these differences may differ across different age groups of males and females. (Fowler, S., 2014). This study included more than 100 patients with confirmed COVID-19 infections. According to our research, age and CRP showed a positive association with a significant p-value of 0.000. However, the association with CRP had a significant p-value of 0.02. CRP enjoyed a positive association, according to our research, with a substantial p-value of 0.000. However, with a p-value of 0.02, the data indicate an insignificant positive connection between age and D-dimer. (Fowler, S., 2014).

Gender has no impact on D-dimer readings in the study's samples, as demonstrated by a substantial inverse association between gender and D-dimer, indicating that sex has a minimal effect on CRP levels. (Fowler, S., 2014).

KEYWORDS: D-Dimer Level, Gender, Covid-19, C-reactive protein.

INTRODUCTION

A new coronavirus disease, COVID-19, emerged in late 2019 and triggered a global pandemic. (Rostami, M, Mansouritorghabeh, H, 2020), (Fowler, S. 2014). Some patients might develop multi-organ failure, severe breathing problems, or they might die suddenly because of the disease (Rostami, M, Mansouritorghabeh, H, 2020). (Fowler, S. 2014). The stimulation of the coagulation system and the inflammatory response is one of the distinctive features of COVID-19, and it may result in coagulation challenges and organ damage (WHO, 2019). D-

dimer and CRP constitute two markers that indicate these processes (Zhang, Yan, and Fan, 2020; Milowitz, Kunichoff, and Garshick, 2021).

D-dimer is the result of the disintegration of connected fibrin, which is produced during blood coagulation. Thus, increased D-dimer levels were indicative of increased thrombin and fibrinolysis production, leading to an increased probability of arterial and venous embolism (Hai-Han Yu et al., 2020). Based on multiple studies, D-dimer levels are correlated with disease severity and mortality in individuals with COVID-19, and these levels are higher in these patients than in those with other viral infections or in healthy controls (Rostami and Mansouritorghabeh 2020). According to Lippi and Mattiuzzi (2020), Tang, N.; Li, D.; Wang, X.; Sun, Z. (2014). 17 studies were put together into a meta-analysis that discovered the combined sensitivity and specificity of D-dimer to predict deaths in COV-19 patients were between 85% and 67%, respectively (Lippi and Mattiuzzi 2020A level above 0.5 g/ml was usually suggestive of a poor outcome (Zhang, Yan, and Fan 2020; Hai-Han Yu 1, Chuan Qin 1, Man Chen 1, Wei Wang 1, Dai-Shi Tian 2020; Fien, von, and Sebastian 2021); however, Depending on the study's results, multiple limits were applied to determine the greatest effective D-dimer separating value. (Olson et al. 2013).

In response to a disease or irritation, the liver produces CRP, a protein associated with the acute phase (Smilowitz, Kunichoff, and Garshick, 2021; Stringer, Braude, and Myint, 2021). CRP contains the capacity to control immune cell production of cytokines, connect to pathogens and help in their clearance, and activate the system known as complement (Smilowitz, Kunichoff, and Garshick, 2021; Stringer D, Braude, and Myint PK, 2021; Fowler, S., 2014). A higher risk of heart disease, also that diseases, and mortality have been linked to elevated levels of CRP, which indicate systemic inflammation (Nathaniel R Smilowitz, Dennis Kunichoff, Michael Garshick, Binita Shah, Michael Pillinger, Judith S Hochman, Jeffrey S Berger. Jun 2021), (Liu F, Li L, Xu M, et al. 2020). According to other studies, CRP levels correspond with illness duration and death in COV-19 patients and are higher in healthy controls and patients with other viral infections (Smilowitz, Kunichoff, & Garshick., 2021), (Li Y, Wang M, Zhou Y, et al. 2020), (Sharma R, Agarwal M, Gupta M, Somendra S, Saxena SK. Published 2020 Apr 30.).

Several contradictory studies were published on the blood group relation with COVID-19 (Roediger, H., Nestojko, J., Smith, N., 2019), (Fowler, S., 2014). They found that those with blood type O are less vulnerable to COVID-19 infection than those with non-O blood group (Roediger, H., Nestojko, J., Smith, N., 2019; Fowler, S., 2014).

In the present study, we investigated the possibility that higher D-dimer and CRP levels may serve as predictive signals for the progression of COVID-19 toward more severe outcomes. Furthermore, we attempted to examine the differences in these levels between males and females (Vahidy et al., 2021) and between age groups (Zhang et al., 2020; Fowler, 2014). We aim to contribute to the development of effective methods for reducing COVID-19-related fatalities by understanding the relationship between these biomarkers and the progression of the illness (Fowler, S., 2014).

To achieve these goals, we utilized a sample of over one hundred patients who tested positive for COVID-19 to conduct a comprehensive analysis. To provide light on the purpose

of these biomarkers in the course of disease, we sought any noteworthy correlations between D-dimer and CRP levels and age. Furthermore, to examine any differences in COVID-19 disease between genders, we analyzed gender-based differences in these biomarker levels.

The relationship between age, D-dimer, and disease progression in COVID-19 patients could assist doctors and nurses in making informed decisions regarding patient care and treatment. Additionally, it may provide valuable insights into the underlying causes of the disease and suggest potential therapeutic options. 2014; Fowler, S.

METHODS AND MATERIALS

All patients who were admitted to the hospital for COVID-19 (CRP) and D-dimer level checks were included in this study. (Fowler, S., 2014). The following software was used to analyze these data: SPSS version 26.0, Microsoft Excel for 2019, and an analysis of variance (ANOVA) table. (Ali, Y., et al., 2022). The study design and participants were based at the Vin Hospital & Medical Complex in Duhok City, which served as the site of this retrospective investigation. Patients with the COVID-19 infection ranged in age from 7 to 89 years old. Following the WHO's interim recommendations, they underwent testing at an on-site clinical laboratory, where RNA detection using SARS-CoV-2 was employed to verify the results. Everyone who was brought to the hospital for admission to have their COVID-19, C-reactive proteins, and D-dimer levels checked participated in this study between February 4th, 2020, and July 24th, 2020, five days later, and an official result (dead or discharged) (Fowler, S. 2014). 107 patients remain after patients with data that was missing were excluded. The Vin Hospital, as well as the Medical Complex's Scientific Ethics Commission, provided approval for the study and waived the requirement for informed consent.

DATA ANALYSIS

Participation in this study was open to all patients hospitalized for testing for COVID-19, C-reactive protein, and D-dimer. For data analysis, we use the software Excel 2019, ANOVA tables, and SPSS version 26.0. (Ali, Y., et al., 2022).

RESULTS

Increasing levels of CRP have been correlated with nosocomial illnesses in COVID-19 patients who did not fully recover, according to reports. (Li Y, Wang M, Zhou Y, et al., 2020). Elevated levels of CRP, possibly a diagnostic for inflammation and a strong indicator of the severity of illness in COVID-19 infections (Zhang, Yan, & Fan, 2020) There have also been reports of elevated CRP levels in older people. (Roediger, H., Nestojko, J., Smith, N. S. , 2019).

The data analysis reveals how D-Dimer and CRP, two independent factors, affect the dependent variable, age. Additionally, as shown in Tables 1 and 2, the analysis using ANOVA reveals that these variables account for 14.4% of the variation in age, with an R-squared value of 0.144. However, the data in Table 3 demonstrates the relationship between each of the variables. (Ali, Y., et al., 2022) (Fowler, S., 2014).. The association between CRP and age was

shown to have a p-value of 0.000 and a statistically significant coefficient of 0.377. The result demonstrates a significant relationship between the amount of CRP and age.. Additionally, the association between age and D-dimer levels is shown in Table 4. The correlational analysis yielded a significant correlation coefficient of 0.293 and a Pearson's correlation coefficient of 0.002. (Fowler, S., 2014). This suggests that age and D-Dimer levels have a moderate relationship. The correlation analysis has found a p-value of 0.002, and a statistically significant correlation coefficient of 0.293 was highlighted, while these associations were statistically significant at the strong level (0.01) for (2-tailed).

Table 1: Model Summary

Model Summary ^b

| Model | R | R Square | Adjusted R Square | Std. Error of the Estimate | Durbin-Watson |
|-------|-------------------|----------|-------------------|----------------------------|---------------|
| 1 | .379 ^a | .144 | .127 | 17.864 | 2.123 |

a. Predictors: (Constant), D-Dimer, C-Reactive Protein

b. Dependent Variable: Age

Table (2)- ANOVA

| Model | | Sum of Squares | Df | Mean Square | F | Sig. |
|-------|------------|----------------|-----|-------------|-------|-------------------|
| 1 | Regression | 5510.052 | 2 | 2755.026 | 8.633 | .000 ^b |
| | Residual | 32870.826 | 103 | 319.134 | | |
| | Total | 38380.877 | 105 | | | |



Table3. Correlation between variables

Correlations

| | | C-Reactive | |
|--------------------|---------------------|--------------------|--------------------|
| | | Age | Protien |
| Age | Pearson Correlation | 1 | .377 ^{**} |
| | Sig. (2-tailed) | | .000 |
| | N | 106 | 106 |
| C-Reactive Protien | Pearson Correlation | .377 ^{**} | 1 |
| | Sig. (2-tailed) | .000 | |
| | N | 106 | 106 |

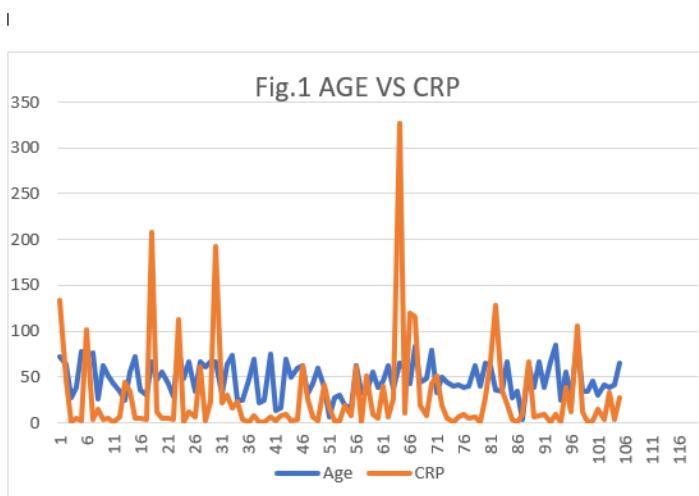
**. Correlation is significant at the 0.01 level (2-tailed).

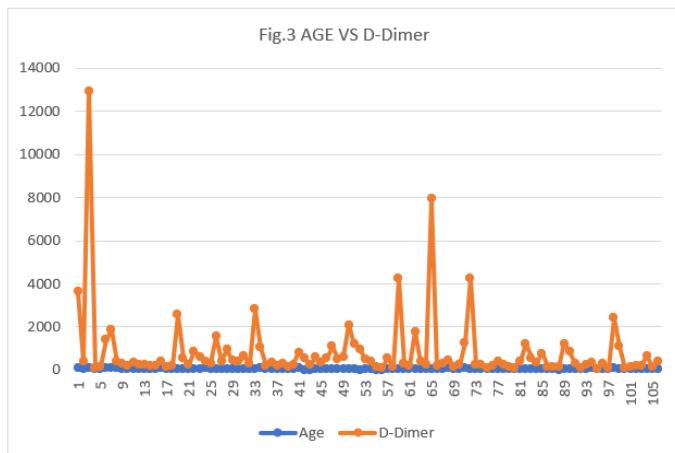
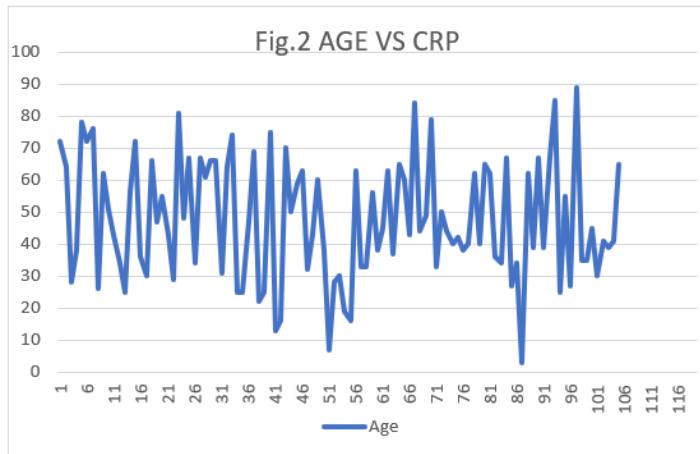
Table 4. Relation between D-Dimer value and age of the patients

| | | Correlations | |
|---------|---------------------|--------------|---------|
| | | Age | D-Dimer |
| Age | Pearson Correlation | 1 | .293** |
| | Sig. (2-tailed) | | .002 |
| | N | 106 | 106 |
| D-Dimer | Pearson Correlation | .293** | 1 |
| | Sig. (2-tailed) | .002 | |
| | N | 106 | 106 |

**. Correlation is significant at the 0.01 level (2-tailed).

Also, Figures (1) and (2) probably provide the graphical representations of the age correlations of D-Dimer and CRP, respectively. These graphs could offer a visual representation of the connections identified in the data.





These results indicate strong correlations among age, D-Dimer, and CRP, suggesting that these biomarkers may be related to the aging process or diseases associated with aging.

DISCUSSION

The goal of this study is to determine whether elevated levels of CRP and D-dimer can be used to predict the progression of COVID-19. We aimed to provide insights that could help reduce disease-related deaths by examining the relationships between these indicators and age and gender. The outcomes of this study can contribute to the growing body of knowledge about the pathogenesis of COVID-19. (Sharma R, Agarwal M, Gupta M, Somendra S, Saxena SK., Published 2020 Apr 30.) And support the creation of focused interventions intended to minimize its effects. Our findings underscore the significance of monitoring CRP and D-Dimer levels in COVID-19 patients. The study found that gender had no influence on D-dimer or CRP measurements in the samples used. (Vahidy FS, Pan AP, Ahnstedt H, et al., 2021) This means that, regardless of gender, such biomarkers may be helpful predictors of disease progression and treatment success.

Amplified CRP levels have been connected with severe illness and unfavorable outcomes in COVID-19 patients. We can also say that it is an indication of inflammation

(Smilowitz, Kunichoff, & Garshick., 2021). Conversely, increased D-Dimer levels may suggest a heightened risk of coagulation or blood clots, which are frequent COV-19 consequences (Stringer D, Braude , & Myint PK, , 2021).

Although D-dimer and CRP levels are not unique to COVID-19 and may increase in other cases, monitoring these biomarkers can nevertheless yield significant insights into the disease's development and treatment efficacy. Continuously monitoring these signs can help healthcare providers make informed decisions about patient care and management.

ACKNOWLEDGMENT

The Duhok hospitals were a great help in providing the information needed for this project, and the author is grateful to them in advance for their assistance.

Declaration: There aren't any apparent contradictions between the authors' interests. We certify that the work is original and not currently under consideration for publication elsewhere.

REFERENCES

Ali, Y., et al.,. (2022). A stepwise multiple regression model to predict Fusarium wilt in lentil—Wiley *Online Library*, 29(4), p. e2088.

Chen Y, K. S. (2021). In COVID-19: Vulnerability, immunity and intervention. *Ageing Res Rev.*, 101-205.

Fien , A., von , M., & Sebastian , H. j. (2021). "2 *Maria Magnusson*,3-5 *Nigel Mackman*,6 *Charlotte Thalin*,2,* and *Ton Lisman*1,**Sustained prothrombotic changes in COVID-19 patients 4 months after hospital discharge*. 2021. London.

Fowler, S. (2014). *Influence of free and reduced lunch student population on state test scores and the ACT*. (Doctoral dissertation, Northwest Missouri State University).Missouri State University.

Hai-Han Yu 1, Chuan Qin 1, Man Chen 1, Wei Wang 1, Dai-Shi Tian. . (2020, Nov). D-dimer level is associated with the severity of COVID-19. *j Thromb Res*, 195, 219-225 doi: 10.1016/j.thromres.2020.07.047 .

Li Y, Wang M, Zhou Y, et al. (2020). Acute phase proteins and their role in COVID-19 infection. 2020;100:483-488. *Int J Infect Dis.*, 100, 483-488.

Lippi, G., & Mattiuzzi, C. (2020). D-dimer is Associated With Severity of Coronavirus Disease 2019: A Pooled Analysis. *J Thromb Haemost. 2020;120(5):876-878. J Thromb Haemost., 120(5), 876-878.*

Liu F, Li L, Xu M, et al. (2020). Prognostic value of interleukin-6, C-reactive protein, and procalcitonin in patients with COVID-19. *J Clin Virol. 2020;127:104370. J Clin Virol. , 127:104370.*

Nathaniel R Smilowitz , Dennis Kunichoff , Michael Garshick , Binita Shah , Michael Pillinger , Judith S Hochman , Jeffrey S Berger. . (jun 2021). C-reactive protein and clinical outcomes in patients with COVID-19. *Eur Heart J, 42(23), 2270-2279.*

Olson , G., Cunningham , M., Higgins , R., & Eby , C. (2013). "D-dimer: simple test, tough problems". *Archives of Pathology & Laboratory Medicine. . Brandt JT, 137(8), 1030-1038. doi:Olson JD, Cunningham MT, Higgins RA, Eby CS, Brandt JT (August 2013). "D-dimer: simple test, tough problems". A10.5858/arpa.2012-0296-CP. PMID 23899057.*

Roediger, H., Nestojko, J., Smith, N. S. . (2019). *Strategies to Improve Learning and Retention During Training. In book: London: Human Performance Optimization.*

Rostami, M., & Mansouritorghabeh, H. (2020). D-dimer level in COVID-19 infection: a systematic review. *Expert Rev Hematol, 13(11), 1265-1275.*

Rostami, M, & Mansouritorghabeh, H. (2020). D-dimer level in COVID-19 infection: a systematic review. *Expert Rev Hemato, 13(11), 1265-1275.*

Sharma R, Agarwal M, Gupta M, Somendra S, Saxena SK. (Published 2020 Apr 30.). Clinical Characteristics and Differential Clinical Diagnosis of Novel Coronavirus Disease 2019 (COVID-19). *Sharma R, Agarwal M, Gupta M, Somendra S, Saxena SK. Clinical Characteristics and Differential Clinical Diagnosis of Novel Coronavirus Disease 2019 (COVID-19). , 55-70 doi:10.1007/978-981-15-.*

Smilowitz, N., Kunichoff, D., & Garshick, M. A. (2021). C-reactive protein and clinical outcomes in patients with COVID-19. *Eur Heart J, 42(23), 2270-2279.*

Stringer D, D., Braude, P., & Myint PK, P. (2021). The role of C-reactive protein as a prognostic marker in COVID-19. *Int J Epidemiol.. Thromb Res.* 2020 Nov;195:219-225., 50(2), 420-429.

Tang ,N; Li ,D; Wang ,X;Sun ,Z. (2020). Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost.,* 18(4), 844-847.

Vahidy FS, Pan AP, Ahnstedt H, et al. (2021). *Sex differences in susceptibility, severity, and outcomes of coronavirus disease 2019: Cross-sectional analysis from a diverse US metropolitan area.* PLoS One. 2021;16(1):e0245556. Published 2021 Jan 13. doi:10.1371/jo.

WHO (2019). *WHO Reports (2019).* New York: WHO.

Zhang, L., Yan, X., & Fan, Q. e. (2020). D-dimer levels on admission to predict in-hospital mortality in patients with COVID-19. *Journal of Thrombosis and Haemostasis,* 18(6), 1324-1329.

APPENDIX

Table (3)

| Descriptive Statistics | | | |
|------------------------|--------|----------------|-----|
| | Mean | Std. Deviation | N |
| Age | 47.86 | 19.119 | 106 |
| C-Reactive Protein | 30.408 | 52.9233 | 106 |

| Table (4)

Correlations

| | | D-Dimer | Gender |
|---------|---------------------|---------|--------|
| D-Dimer | Pearson Correlation | 1 | -.026 |
| | Sig. (2-tailed) | | .794 |
| Gender | N | 106 | 106 |
| | Pearson Correlation | -.026 | 1 |
| Gender | Sig. (2-tailed) | .794 | |
| | N | 106 | 106 |

Table (5)

Descriptive Statistics

| | Mean | Std. Deviation | N |
|---------|--------|----------------|-----|
| Age | 47.86 | 19.119 | 106 |
| D-Dimer | 769.58 | 1591.523 | 106 |

**TABLE -6- Coefficients**

| Model | Unstandardized Coefficients | | Standardized Coefficients | | |
|--------------------|-----------------------------|------------|---------------------------|--------|------|
| | B | Std. Error | Beta | t | Sig. |
| 1 (Constant) | 43.634 | 2.013 | | 21.675 | .000 |
| C-Reactive Protein | .122 | .046 | .338 | 2.638 | .010 |
| D-Dimer | .001 | .002 | .055 | .432 | .667 |

a. Dependent Variable: Age



Table (7)

Descriptive Statistics

| | Mean | Std. Deviation | N |
|--------------------|--------|----------------|-----|
| Age | 47.86 | 19.119 | 106 |
| C-Reactive Protein | 30.408 | 52.9233 | 106 |

Chart (1)

