1

Comparison of some hematological parameters between male and female patients infected with COVID-19

Hayder H. Abed[a,*], Ahmed Ghdhban Al-Ziaydi[b], Ihab Abbas Taher[a] and Ahmed K. Al Dulaimi[c]
[a]*Chemistry and Biochemistry Division, Faculty of Medicine, Al Muthanna University, Samawah, Iraq*
[b]*Department of Medical Chemistry, College of Medicine, University of Al-Qadisiyah, Qadisiyah, Iraq*
[c]*Laboratory Division, Al-Shafaa Hospital, Anbar Health Directorate, Ramadi, Iraq*

Abstract.
BACKGROUND: COVID-19 is a highly contagious virus that is rapidly spreading across the world. As the number of COVID-19 patients is quickly rising, and certain nations and areas, such as the third world countries, lack the medical resources, it is critical to track and monitor a patient's status using blood parameters on regular testing. The aim of this study is to compare the serum D-dimer levels, Ferritin, CRP, WBCs, Lymphocytes, and Neutrophils in male and female patients infected with COVID-19.
OBJECTIVE AND METHODS: The study procedure includes evaluating the D-dimer level, Ferritin, CRP, WBCs, lymphocytes, and neutrophils in 116 patients infected with COVID-19 (48 Females and 68 Males).
RESULT: The result of this study shows a significant increase in the D-dimer level in males 1618 ± 247.7 ng/ml compared to females 684.5 ± 53.69 ng/ml and a significant increase in Ferritin level in males 525.6 ± 69.55 μg/L compared to females 254.1 ± 33.73 μg/L. However, no other significant change is seen in the other parameters (CRP, LDH, and WBCs, L, and N) although all of these parameters are abnormal, compared to the normal reference values.
CONCLUSION: This study concludes that there is a significant increase in the D-dimer and Ferritin concentrations in male patients compared to female patients, who were infected with COVID-19. Also there are no significant differences in other parameters (CRP, LDH, WBCs, L, and N) between male and female patients.

Keywords: COVID-19, haematological parameters, D-dimer, ferritin

1. Introduction

In December of 2019, a new Coronavirus infectious disease (COVID-19) has been found in Wuhan, Hubei Province [1]. After evaluating the throat samples from patients, the "Chinese Center for Disease Control and Prevention" has confirmed that these cases are caused by a new kind of Coronavirus [2]. COVID-19 is a highly contagious virus that is rapidly spreading across the world, forcing the World Health Organization to de-

clare it as a 'Pandemic', as of March 12, 2020 [3]. The number of COVID-19 patients is quickly rising across the world, and certain nations and areas, such as the Third World countries, lack the medical resources to treat this pandemic. It is critical to track and monitor a patient's status using his/her blood parameters by regular testing [4]. Aside from the clinical symptoms and pulmonary computed tomography (CT) findings [5], a majority of verified COVID-19 patients have displayed laboratory changes in a variety of serological markers, including kidney and liver function tests, coagulation parameters, and inflammatory, biochemical, and hemocytometric parameters. For COVID-19 detection, complete blood count (CBC) is the most appropriate and effective during laboratory examination [6]. In certain

*Corresponding author: Hayder H. Abed, Chemistry and Biochemistry Division, Faculty of Medicine, Al Muthanna University, Samawah, Iraq. Tel.: +964 7805901007; E-mail: Hayderhussein862@mu.e.iq.

Table 1
Result analysis of parameters of patients

Type of test	Mean ± SEM of male	Mean ± SEM of female	Significantly different? ($P < 0.05$)
N	68	48	–
Age (years)	57.29 ± 2.013	58.38 ± 2.545	NS (0.7370)
D-Dimer (ng/ml)	1618 ± 247.7	684.5 ± 53.69	S** (0.0022)
Ferritin (μg/L)	525.6 ± 69.55	254.1 ± 33.73	S** (0.0024)
CRP (mg/L)	51.79 ± 4.250	41.81 ± 3.717	NS (0.0961)
LDH (U/L)	875.2 ± 78.49	782.3 ± 89.34	NS (0.4396)
WBCs * 10^3/mm^3	12.08 ± 0.8446	10.13 ± 1.111	NS (0.1570)
N * 10^3/mm^3	76.30 ± 2.072	79.38 ± 1.112	NS (0.2461)
L * 10^3/mm^3	19.66 ± 2.122	16.46 ± 0.957	NS (0.2299)

NS: Non-significant, S** high Significant, N: Neutrophils, L: Lymphocytes.

people, severe pulmonary disorder and extra-pulmonary disease can become life-threatening events, as also respiratory failure. The D-dimer levels seem to have increased in almost half the number of patients, and abnormal D-dimer levels are associated with a poor prognosis [7]. A simple blood test that provides information on the inflammatory process, such as leucocyte count and other features, such as, lymphocyte predominance, neutrophil, the neutrophil-lymphocyte ratio (N/L ratio), C-reactive protein (CRP) as an inflammatory marker, collateral organ damage (acute liver failure, acute renal failure), and disease severity, can be useful in the diagnosis and monitoring of disease conditions [8]. The purpose of this study is to compare the D-dimer levels, Ferritin, CRP, WBCs, N, and L, in male and female COVID-19 patients.

2. Material and methods

2.1. Subject

This cross-sectional study was carried out in the Department of Health, Alshifa Hospital, Al-Anbar, Iraq, from June 2021 to January 2022. The present study included 116 patients (48 Females and 68 Males), who were infected with COVID-19 from two to four days. The consent form was signed by all the human volunteers None of the patients were vaccinated against COVID-19. SARS Cov-2 Qualitative Real Time-Polymerase Chain Reaction was used to confirm COVID-19 infection in patients (RT-PCR). This study excluded patients who did not have SARS-CoV-2 or had tested negative for it, Also patients with chronic disease were excluded.

2.2. Data collection and laboratory tests

Blood was collected from patients and used directly in routine lab tests. WBCs, lymphocytes (L) and neutrophils (N) were analyzed using the CBC Horiba ABX Micros 60 instrument (Japan), D-Dimer, CRP, and Ferritin using the SPX200 chemical analyzer instrument (Japan).

2.3. Statistical analysis

All Curves, Tables, and results were analyzed using the Graph Pad prism Program (Version 6), which utilized the independent T test.

3. Results

This study included 116 patients, who consisted of 68 males and 48 females, who were in the mean age of (57.29 ± 2.013) and (58.38 ± 2.545) years, for males and females, respectively. There was no significant age difference between them and the p-value was equal to 0.7370, as shown in Table 1.

The results show a significant change in the D-dimer values between males and females, with values of 1618 $\pm$ 247.7 ng/ml and 684.5 $\pm$ 53.69 ng/ml, respectively, whereas, the p-value is equal to 0.0022, as shown in Table 1. The results of the Ferritin show a significant difference, 525.6 $\pm$ 69.55 μg/L and 254.1 $\pm$ 33.73 μg/L, in males and females, respectively, and a p-value equal to 0.0024, as shown in Table 1. There are no significant differences in C-reactive protein between males and females, with values equal to 51.79 $\pm$ 4.250 mg/L and 41.81 $\pm$ 3.717 mg/L, respectively, with a p-value of 0.4396, as shown in Table 1. Lactate dehydrogenase (LDH) results show no significant difference in the values in males and females, 875.2 $\pm$ 78.49 U/L and 782.3 $\pm$ 89.34 U/L, respectively, whereas, p-value is 0.4396, as shown in Table 1. As a result, it can be seen that there is no significant difference in WBCs between males

and females, $(12.08 \pm 0.8446)10^3/mm^3$ and (10.13 ± 1.111) $10^3/mm^3$, respectively, as shown in Table 1. The results also show no significant difference in neutrophils (N), with values of (76.30 ± 2.072) $10^3/mm^3$ and (79.38 ± 1.112) $10^3/mm^3$, and a p-value of 0.2461, as shown in Table 1, whereas, Lymphocytes (L) show a non-significant difference in male and female patients, with values of (19.66 ± 2.122) $10^3/mm^3$ and (16.46 ± 0.9575) $10^3/mm^3$, respectively, and a p-value of 0.2299, as shown in Table 1.

4. Discussion

The virus's extended incubation time and high contagiousness, together with modern worldwide air travel, are some of the primary factors that have aided the fast spread of SARS-CoV-2 [9]. In our linked and globalized society, this has had an enormous influence on the health systems and global economies.

Some limitations, such as, a lack of reliable data on the prevalence a certain gender, by age or comorbidities by age and gender, or the assumption of risk factor independence, are expected to have little impact on the findings. Finally, given the age range, gender, and comorbidities associated with COVID-19, the equation provided here may be used to forecast even a single patient's risk of dying from COVID-19.

Increased incidence of SARS-CoV-2 infection among younger adults is expected to contribute to COVID-19 community transmission, especially to people who are at increased risk of severe disease, such as the elderly [10]. Targeted mitigation methods, such as, age-appropriate messaging on the 'preventive measures to be taken', via social media, must be prioritized, to minimize infection and transmission among younger individuals. There is no significant age difference between males and females in this research.

One of the tests used to diagnose thrombosis in patients was the D-dimer level. According to research, increased fibrinogen and D-dimer concentrations were associated with a poor prognosis in the early stages of COVID-19 sickness; and approximately a three- to four-time increase in D-dimer levels was associated with a poor prognosis [11,12]. Furthermore, underlying conditions such as cancer, diabetes, stroke, and female pregnancy could cause the D-dimer levels to rise in COVID-19 patients [13]. Measuring the amount of D-dimer concentrations and coagulation parameters from the start of the COVID-19 illness could help regulate and manage the condition [14].

The D-dimer concentration measurement is a laboratory test that is used to assess COVID-19 patients. As thrombosis can develop in multiple organs, leading to organ failure in severe COVID-19 cases, D-dimer monitoring will be a useful method that can be utilized in clinical practice to detect COVID-19 infection [15]. A COVID-19 patient's problems also increase when the D-Dimer levels rise. To avoid complications and reduce interventions, it is necessary to continuously monitor the D-dimer levels and label 'anticoagulation' as a management tool for COVID-19 disease. The findings of this study show that the D-dimer level increases twice as fast in male patients than in female COVID-19 patients, in the early stages [16].

Ferritin is an important modulator of immunological dysregulation, particularly in severe hyperferritinemia, and it contributes to the cytokine storm through direct immunosuppressive and pro-inflammatory activities [17]. In recent times, serum ferritin has been discovered to be one of the indicators of mortality in COVID-19 patients [18]. Serum ferritin may be a simple and effective laboratory test, which can serve as a marker of SARS-CoV2 infection for diagnosing and monitoring the inflammatory process in COVID-19 patients [19]. The results indicate a considerable rise in ferritin in COVID 19 patients. It increases twice as much in male patients as compared to female patients.

CRP is a helpful inflammatory marker and indication that is involved in host resistance to invading infections as well as inflammation [20]. In individuals infected with 2019-nCoV, CRP is strongly linked with acute lung damage [21]. The findings revealed an increase in CRP in both male and female groups, with no significant differences between them. CRP levels of greater than 40 mg/L have previously been found to be predictive indicators for the progression of pneumonia to respiratory failure in MERS-CoV-infected people [22].

The lactate dehydrogenase enzyme (LDH) is an intracellular enzyme that converts pyruvate to lactate during anaerobic glycolysis [23]. Serum lactate dehydrogenase is routinely tested in a range of illnesses, including cancer, and inflammation and high LDH levels in the blood have been related to a poor prognosis. Although studies have indicated that those with severe COVID-19 have higher blood LDH levels, no research has looked into how this influences the severity and mortality of COVID-19 [24]. The findings of this study corroborated with a prior research on LDH elevation in COVID-19 patients, indicating that there was no significant difference in LDH elevation in male and female COVID-19 patients.

According to several studies, severe COVID-19 is linked to an increase in the quantity of white blood cells [25]. One in every four COVID-19 positive individuals, on the other hand, may develop some type of leukopenia, with lymphopenia, accounting for a majority (63.0%) [26]. Although some data suggest that thrombocytopenia, neutropenia, and lymphopenia have a predictive significance in the SARS-CoV-2 infection, further research is needed [27].

This study has found a significant increase in WBCs in both male and female groups. This increase is associated with an increase in neutrophil cells, which is consistent with other researches that confirm the use of parameter tests that confirmed an increase in neutrophils, for detecting infection with COVID19 patients [28].

5. Conclusion

This study concludes that there is a significantly higher level of increase in D-dimer and Ferritin concentrations in male patients compared to female patients infected with COVID-19. No significant differences in other parameters (CRP, LDH, WBCs, N, and L) are seen, although all of these parameters are abnormal, compared to the normal reference values.

Conflict of interest

The authors declare that they have no conflict of interest.

References

[1] Y. Yang, W. Shang and X. Rao, Facing the COVID-19 outbreak: What should we know and what could we do? J Med Virol, 2020.

[2] P. Liu, M. Yang, X. Zhao, Y. Guo, L. Wang, J. Zhang, W. Lei, W. Han, F. Jiang and W.J. Liu, Cold-chain transportation in the frozen food industry may have caused a recurrence of COVID-19 cases in destination: Successful isolation of SARS-CoV-2 virus from the imported frozen cod package surface, *Biosafety and Health* **2** (2020), 199–201.

[3] D. Cucinotta and M. Vanelli, WHO declares COVID-19 a pandemic, *Acta Bio Medica: Atenei Parmensis* **91** (2020), 157.

[4] J. Zhou, S. Lee, X. Wang, Y. Li, W.K.K. Wu, T. Liu, Z. Cao, D.D. Zeng, K.S.K. Leung and A.K.C. Wai, Development of a multivariable prediction model for severe COVID-19 disease: A population-based study from Hong Kong, *NPJ Digit Med* **4** (2021), 1–9.

[5] J. Wu, X. Wu, W. Zeng, D. Guo, Z. Fang, L. Chen, H. Huang and C. Li, Chest CT findings in patients with coronavirus disease 2019 and its relationship with clinical features, *Invest Radiol* **55** (2020), 257.

[6] H.C. Çubukçu, D.İ. Topcu, N. Bayraktar, M. Gülşen, N. Sarı and A.H. Arslan, Detection of COVID-19 by Machine Learning Using Routine Laboratory Tests, Am J Clin Pathol, 2021.

[7] L. Townsend, H. Fogarty, A. Dyer, I. Martin-Loeches, C. Bannan, P. Nadarajan, C. Bergin, C. O'Farrelly, N. Conlon and N.M. Bourke, Prolonged elevation of D-dimer levels in convalescent COVID-19 patients is independent of the acute phase response, *Journal of Thrombosis and Haemostasis* **19** (2021), 1064–1070.

[8] D.B. Dubey, S. Mishra, H.D. Reddy, A. Rizvi and W. Ali, Hematological and serum biochemistry parameters as a prognostic indicator of severally ill versus mild Covid-19 patients: A study from tertiary hospital in North India, *Clin Epidemiol Glob Health* **12** (2021), 100806.

[9] M.G. Manoj, M.K.S. Kumar, K.T. Valsaraj, C. Sivan and S.K. Vijayan, Potential link between compromised air quality and transmission of the novel corona virus (SARS-CoV-2) in affected areas, *Environ Res* **190** (2020), 110001.

[10] J.W. Cabore, H.C. Karamagi, H. Kipruto, J.A. Asamani, B. Droti, A.B.W. Seydi, R. Titi-Ofei, B. Impouma, M. Yao and Z. Yoti, The potential effects of widespread community transmission of SARS-CoV-2 infection in the World Health Organization African Region: A predictive model, *BMJ Glob Health* **5** (2020), e002647.

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

[12] L. Naymagon, N. Zubizarreta, J. Feld, M. van Gerwen, M. Alsen, S. Thibaud, A. Kessler, S. Venugopal, I. Makki and Q. Qin, Admission D-dimer levels, D-dimer trends, and outcomes in COVID-19, *Thromb Res* **196** (2020), 99–105.

[13] X. He, F. Yao, J. Chen, Y. Wang, X. Fang, X. Lin, H. Long, Q. Wang and Q. Wu, The poor prognosis and influencing factors of high D-dimer levels for COVID-19 patients, *Sci Rep* **11** (2021), 1–7.

[14] Y. Yao, J. Cao, Q. Wang, Q. Shi, K. Liu, Z. Luo, X. Chen, S. Chen, K. Yu and Z. Huang, D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: A case control study, *J Intensive Care* **8** (2020), 1–11.

[15] S.R. Mucha, S. Dugar, K. McCrae, D.E. Joseph, J. Bartholomew, G. Sacha and M. Militello, Coagulopathy in COVID-19, *Cleve Clin J Med* **87** (2020), 461–468.

[16] S. Vidali, D. Morosetti, E. Cossu, M.L.E. Luisi, S. Pancani, V. Semeraro and G. Consales, D-dimer as an indicator of prognosis in SARS-CoV-2 infection: A systematic review, *ERJ Open Res* **6** (2020).

[17] M. Vargas-Vargas and C. Cortés-Rojo, Ferritin levels and COVID-19, *Revista Panamericana de Salud Pública* **44** (2020), e72.

[18] F. Banchini, G.M. Cattaneo and P. Capelli, Serum ferritin levels in inflammation: A retrospective comparative analysis between COVID-19 and emergency surgical non-COVID-19 patients, *World Journal of Emergency Surgery* **16** (2021), 1–7.

[19] G. Ponti, M. Maccaferri, C. Ruini, A. Tomasi and T. Ozben, Biomarkers associated with COVID-19 disease progression, *Crit Rev Clin Lab Sci* **57** (2020), 389–399.

[20] Y. Wu, L.A. Potempa, D. el Kebir and J.G. Filep, C-reactive protein and inflammation: Conformational changes affect function, *Biol Chem* **396** (2015), 1181–1197.

[21] Y. Liu, Y. Yang, C. Zhang, F. Huang, F. Wang, J. Yuan, Z. Wang, J. Li, J. Li and C. Feng, Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury, *Science China Life Sciences* **63** (2020), 364–374.

[22] W. Shang, J. Dong, Y. Ren, M. Tian, W. Li, J. Hu and Y. Li, The value of clinical parameters in predicting the severity of COVID-19, *J Med Virol* **92** (2020), 2188–2192.

[23] C. Granchi, S. Bertini, M. Macchia and F. Minutolo, Inhibitors of lactate dehydrogenase isoforms and their therapeutic potentials, *Curr Med Chem* **17** (2010), 672–697.

[24] C. Li, J. Ye, Q. Chen, W. Hu, L. Wang, Y. Fan, Z. Lu, J. Chen, Z. Chen and S. Chen, Elevated lactate dehydrogenase (LDH) level as an independent risk factor for the severity and mortality of COVID-19, *Aging (Albany NY)* **12** (2020), 15670.

[25] A. Anurag, P.K. Jha and A. Kumar, Differential white blood cell count in the COVID-19: A cross-sectional study of 148 patients, *Diabetes & Metabolic Syndrome: Clinical Research & Reviews* **14** (2020), 2099–2102.

[26] A. Pirsalehi, S. Salari, A. Baghestani, G. Sanadgol, D. Shirini, M.M. Baerz, S. Abdi, M.E. Akbari and D. Bashash, Differential alteration trend of white blood cells (WBCs) and monocytes count in severe and non-severe COVID-19 patients within a 7-day follow-up, *Iranian Journal of Microbiology* **13** (2021), 8.

[27] D. Wang, Y. Yin, C. Hu, X. Liu, X. Zhang, S. Zhou, M. Jian, H. Xu, J. Prowle and B. Hu, Clinical course and outcome of 107 patients infected with the novel coronavirus, SARS-CoV-2, discharged from two hospitals in Wuhan, China, *Crit Care* **24** (2020), 1–9.

[28] M.E. Ibrahim, O.S. Al-Aklobi, M.M. Abomughaid and M.A. Al-Ghamdi, Epidemiological, clinical, and laboratory findings for patients of different age groups with confirmed coronavirus disease 2019 (COVID-19) in a hospital in Saudi Arabia, *Plos One* **16** (2021), e0250955.