Clinical Severity of COVID-19 Infection in Relation to Peptide Procalcitonin Level and Other Factors in Diabetic Patients

Sadeq Sahib Sadeq[1], Jawad Kadhum Muraih[2]
[1, 2]Department of Chemistry, College of science, Al-Muthanna University, Iraq.
Email: jmuraih@mu.edu.iq
E-mail: Sadiqsaheb1@gmail.com

Abstract

Background: SARS (Severe Acute Respiratory Syndrome) is a type of acute respiratory syndrome. Coronavirus 2 is a new type of coronavirus that produces Coronavirus 2019 (COVID19), the twentieth century's most challenging pandemic

Aim: To learn more about the link between Diabetes Mellitus (DM) and COVID-19 prognosis.

Methods: The study included 132 patients divided into four groups, included 66 patients have Covid-19 with/without diabetes mellitus.

Results: The results of most measured parameters of patients with/without DM are appeared high such as Fast Blood Glucose (FBG), Procalcitonin (PCT), Urea, Creatinine, WBC, and Neutrophil. But low in Lymphocytes and Platelets.

Conclusion: COVID-19 individuals with diabetes mellitus may have the largest risk factor.

Keywords: COVID-19, PCT, Urea and Creatinine

1. Introduction

In 2002, the first lethal coronavirus, SARS-COV, was found in Guangdong Province, China. SARS-COV infected many people and caused SARS-related deaths (a 10% mortality rate) in 29 countries over the course of two years before disappearing. In 2012, In Saudi Arabia, the Middle East respiratory syndrome coronavirus (MERS-COV) was discovered. In 2015, South Korea experienced a similar pandemic, as did Saudi Arabia in 2018. There are 2,519 confirmed MERS cases and 866 deaths (a 35 percent mortality rate) in 27 countries as of January 2020. A novel coronavirus strain capable of causing severe respiratory sickness, in December of this year, it was discovered in Wuhan, China. The World Health Organization (WHO) has given this new virus the designations SARS-CoV-2 and Coronavirus Disease 2019 (COVID-19).

Virion particles attach to the ACE2 receptor and infect the host cell. The genome (ss RNA) of the parasite is subsequently linked to the ribosomes of the host, resulting in the translation of two co-terminal and massive polyproteins, which are then digested by proteolytic enzymes/proteolysis [1]. Coronavirus main protease (3CLpro) and papain-like protease mediate proteolysis (PLpro).

Diabetes mellitus (DM) is a metabolic disorder characterized by the presence of persistent hyperglycemia as well as abnormalities in carbohydrate, protein, and lipid metabolism to varying degrees. DM has a variety of causes and etiologies, but they all have the inevitability of alterations in insulin secretion or insulin hormone sensitivity, or both, at some point during its natural history.

The pancreas secrete Insulin and glucagon hormones. The beta (ß) cells secrete Insulin and the alpha (α) cells secrete glucagon, both are present in the islets cells of Langerhan's. Insulin decreases the blood glucose level by glycogenesis and transports glucose into the liver, muscles, and adipose tissue. whereas alpha (α) cells play an important role in controlling blood glucose via producing the glucagon which elevate the blood glucose level by accelerating the glycogenolysis.

Procalcitonin (PCT) is a biomarker for bacterial infection of the lower respiratory tract that guides antibiotic therapy in the intensive care unit (ICU). In hospitalized COVID-19 patients, bacterial co-infections account for fewer than 10% of cases, but they are more common in critically ill patients. In critically ill COVID-19 patients, bacterial respiratory infection was recently predicted to be between 14 and 28 percent. However, since the epidemic's beginning, antibiotic prescribing has grown, posing a global threat to antimicrobial resistance [2].

Using limited cubic splines, the relationship between PCT concentration and the risk of COVID-19 mortality is also investigated. PCT is a non-hormonal glycoprotein that is the precursor to calcitonin. PCT levels in the blood are generally undetectable or very low. Bacterial infections cause higher amounts of PCT, whereas viral infections cause lower levels. As a result, it's possible to distinguish between bacterial and viral illnesses [3]. COVID-19 patients had high PCT levels in the SG with severe symptoms may also be suffering from bacterial infections [4].

PCT was found to be greater in the severe cases than in the non-severe ones. The greater levels of PCT in DM patients with COVID-19 infection in the study group, as compared to non-severe DM patients, suggested elevated chances of systemic infection and sepsis [5].

The most prevalent signs of a COVID-19 patient's CBC being abnormal are decreased lymphocytes and moderate thrombocytopenia. Overall, these data demonstrated that In COVID-19, the lymphocyte count is clinically and biologically relevant, and lymphopenia is a serious hematological condition with a poor prognosis. In COVID-19 patients, lymphopenia is induced by a number

doi.org/10.31838/hiv22.02.309 Received: 07.04.22, Revised: 08.05.22, Accepted: 11.08.22

of primary mechanisms, including infections of lymphatic organs, direct infections, cytokine storm, and negative impacts of certain metabolic products, bone marrow suppression, and epigenetic alterations. The neutrophil to lymphocyte ratio (NLR) is a crucial indication of systemic inflammation that is frequently used to predict the outcome of bacterial infections, particularly in pneumonia patients. WBCs are shifting away from lymphocytes and towards neutrophils is thought to occur in severe cases of COVID-19, and calculation of NLR may help clinicians treat patients effectively [6].

Kidneys are also susceptible to direct or indirect injury by coronavirus COVID-19 as evidenced by elevation in renal function tests (RFT) (serum Creatinine and Blood Urea). A considerable number of patients with the coronavirus COVID-19 experienced alterations in biochemical indicators related to renal function. According to a recent study, The Spike protein of coronavirus 2 interacts with human angiotensin-converting enzyme II (ACE2) molecules. The expression of ACE2 receptors has been found in kidneys as well as the lungs and heart. Among the researches reviewed, sepsis, which induced cytokine storm syndrome due to the virus, was indicated as a possible mechanism [6, 7].

One of the diagnostic criteria for a suspected COVID-19 case is a normal or low WBC and a low lymphocyte count. However, new research has discovered that a portion of COVID-19 individuals have a high white blood cell count in their peripheral blood. There have been investigations on the general epidemiological results, clinical and clinical outcome aspects of COVID-19 patients. However, detailed information about COVID-19 patients with a high leukocyte count is still unavailable [8].

Peripheral lymphocyte counts and blood leukocytes are normal or slightly decreased throughout the incubation period, it usually lasts 1-14 days and occurs in the early stages of the disease, when non-specific symptoms are present. SARS-CoV-2 primarily affects tissues that express high levels of ACE2, such as the heart, lungs, and gastrointestinal tract, after viremia [9].

COVID-19 individuals have shown signs of neutrophilia and lymphopenia, which are thought to be linked to the severity of the illness. The majority of investigations found that severe cases of COVID-19 pneumonia were associated with neutrophilia (absolute neutrophil count above the normal range; 3–7.5 109/L) and/or lymphocytopenia (lymphocyte count less than 1.5 109/L). In the early stages of SARS, The neutrophil to lymphocyte ratio (NLR) has also been shown to predict the severity of CoV-2 virus infection [10].

The NLR has been recommended as a predictive biomarker for COVID-19 patients with poor results since high WBC, neutrophil counts, and reduced lymphocyte counts have been repeatedly reported in COVID-19 patients with bad outcomes.

T lymphocytes and other immune cells were activated, resulting in the so-called hyper inflammatory response. Uncontrolled inflammation is assumed to be the main cause of illness severity and death during COVID-19 infection. Atypical thrombotic events and coagulation leading to vascular occlusion have also been identified as key causes to the increased death rate [11].

Additionally, baseline lymphocyte and platelet counts were not related to in-hospital mortality both in unadjusted or fully adjusted models [12].

2. Materials and Methods

The study comprised 132 patients divided into four groups: 33 patients with diabetic Covid-19, 33 patients with type 2 diabetes mellitus, 33 patients with Covid-19 without diabetic, and 33 patients as a reference group. Male or female (40-75) years old. The research was conducted between September 2021 and February 2022.

3. Results

This study showed a significant variance in FBG parameters means among four study groups (Covid and control, DM with Covid+DM), where p value was <0.0001. The results showed a significant difference when compared between (COVID+DM) group with control and DM groups, where p value was 0.001 and <0.0001 for WBC mean, respectively. Also significant differences among Covid when compared with DM and Control groups, where p value was 0.007 and 0.008, respectively. This agreed with the study carried by.

The results showed significant difference among (COVID+DM) group when compared with control and DM groups, where p value was 0.006 for Platelets means. Also it was found significant difference of Platelets means among COVID group when compared with control and DM groups, where p value was 0.008 and 0.009 respectively, which is identical to the finding in the study done [13], except between DM and control. Also discovered in individuals with COVID-19, a low platelet count has been related to a higher risk of serious disease and death.

The results for Lymphocytes means showed there was a significant difference among (COVID+DM) group when compared with control and DM groups, where p value was <0.0001. Also it was found a significant difference among COVID group when compared with control and DM groups, where p value was <0.0001, as seen in the study [12], who was found in COVID-19 patients that lymphocytes and lymphocyte subsets, particularly T cells, were significantly reduced, especially in those with diabetes mellitus.

This study's findings revealed that there was a significant difference in Neutrophilia level among (COVID+DM) group when compared with control and DM groups, where p value was <0.0001 for Neutrophilia means. Also it was found a significant difference among Covid group when compared with control and DM groups, where p value was 0.001 for Neutrophilia means, which is similar to the results found [14] that COVID-19 patients have a higher Neutrophilia count linked to an elevated risk of severe disease and death.

This study showed a significant variance in PCT parameters means among study groups (Covid and control, DM with Covid+DM), where p value was <0.0001. These results in this study showed a significant difference in PCT levels among (COVID+DM) group with control and DM groups, where the p-value was <0.0001 for PCT

means. Also, it was found a significant difference among the COVID group when compared with control and DM groups, where the p-value was <0.0001 for PCT means, as seen in the study carried out [3], who was found that PCT was increased with diabetes.

The results of this study showed a considerable difference in Urea levels among the (COVID+DM) group, DM and control groups, where the p-value was <0.0001. Also, it was found a significant difference among the COVID group when compared with control and DM groups, where the p-value was 0.001 and <0.0001, respectively. The results in this study showed a considerable difference in Creatinine levels among the (COVID+DM) group, DM and control groups, where the p-value was <0.0001. Also, when compared to DM, there was a significant difference with COVID groups, since a p value was 0.05. The control group, on the other hand, showed no discernible differences, since the p-value was 0.08.

4. Discussion

The increased severity of COVID 19 infection could be attributable to uncontrolled diabetes, as high blood glucose is linked to a faulty immunological response, as well as an increased risk of secondary infection and delayed healing. However, many of other DM patients are well controlled on oral antidiabetic medications and insulin, there is no significant difference in blood glucose levels between individuals with DM alone and people with COVID 19 with no DM.

WBC count including lymphocytes, neutrophils, and platelet count differed in comparison between groups in this study which appeared to be a normal in some patients and an elevated or low in others which indicate differences in severity and clinical outcome of the infection. Many studies confirmed that low lymphocytes, platelets, and high neutrophils count at presentation are associated with a poor outcome. This may be done to that low lymphocytes which indicate a defective immune response, low platelets increase risk of hemorrhage and high neutrophils that indicate an underlying secondary bacterial infection [15].

Procalcitonin is a proenzyme that is used as a sign of bacterial infection that is elevated when there is bacteria reaching the bloodstream, and its elevation is a marker of severity as its points to sepsis [16]. Increasing levels of creatinine and urea in Covid-19 patients were recorded in some trials, indicating a renal changes. Covid-19 allows for direct infection of kidney tubular cells, which have ACE2 receptors on their surface. This result agreed with a data that studied by. There is a significant differences in creatinine level between patients who have DM and others have no DM. This is related to the fact that the presence of DM per se is enough to cause elevating creatinine level due to the toxic effect of glucose on the renal system.

5. Conclusion

COVID-19 individuals with diabetes mellitus may have the largest risk factor, increasing mortality and raising inflammatory indicators in addition to the effect on Kidney (Urea and Creatinine).

Acknowledgments

The authors of this study offer their grateful thanks to the laboratory staff of Youssef Najm center for their cooperation and assistance throughout my stay with them, at Al-Hussein Teaching Hospital.

Conflicts of interest

No conflict of interest from authors regarding the publication of this manuscript.

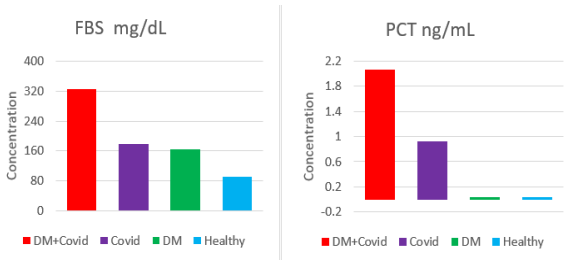
Table 1: comparison between patient groups based on the means of different biochemical parameters.

parameter	Covid+DM Mean±SD	Covid Mean±SD	DM Mean±SD	Control Mean±SD	P-value
FBG	323.45±72	180.52±49.1	163±33.2	89.9±8.04	<0.0001
WBC	11.46 ±4.5	9.68 ± 6.3	7.95 ± 1.3	7.91 ± 1.7	0.001
PLT	238 ± 53.6	240 ± 50.9	247 ± 78	250 ± 78.9	0.003
lymph	0.70 ± 0.30	0.82 ± 0.39	2.30 ± 0.61	2.40 ± 0.69	<0.0001
Neutr	10.52 ± 4.4	8.63 ± 6.2	5.42 ± 1.3	5.28 ± 1.7	<0.0001
PCT	2.23 ± 1.9	0.97 ± 0.6	0.02 ± 0.01	0.03 ± 0.03	<0.0001
Creatinine	1.23 ± 0.54	0.81 ± 0.24	0.65 ± 0.20	0.67 ± 0.20	<0.0001
urea	82.4 ± 36.7	46.4 ± 18.02	34.7 ± 9.1	25.4 ± 7.4	<0.0001

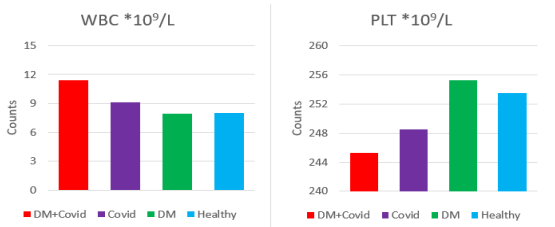
Table 2: represents p-values of two different comparisons. First, different biochemical measurements between diabetic patients infected by Covid-19 compared with diabetic and the second represent the comparison between the Covid-19 patients with healthy people.

parameter	DM Mean±SD	Covid+DM Mean±SD	P-value	Control Mean±SD	Covid Mean±SD	P-value
FBG	163± 33.2	323.45 ±72	<0.0001	89.9 ±8.04	180.52±49.1	<0.0001
PCT	0.02 ± 0.01	2.23 ± 1.9	<0.0001	0.03 ±0.03	0.97 ± 0.6	<0.0001
WBC	7.95 ± 1.3	11.46 ±4.5	0.001	7.91 ± 1.7	9.68 ± 6.3	0.007
PLT	247 ± 78	238 ± 53.6	0.006	250 ± 78.9	240 ± 50.9	0.009
Lymph	2.30 ± 0.61	0.70 ± 0.30	<0.0001	2.40 ±0.69	0.82 ± 0.39	<0.0001
Neutro	5.42 ± 1.3	10.52 ± 4.4	<0.0001	5.28 ± 1.7	8.63 ± 6.2	0.001
Urea	34.7 ± 9.1	82.4 ± 36.7	<0.0001	25.4 ± 7.4	46.4 ±18.02	<0.0001
Creatinine	0.65 ± 0.20	1.23 ± 0.54	<0.0001	0.67 ±0.20	0.81 ± 0.24	0.08

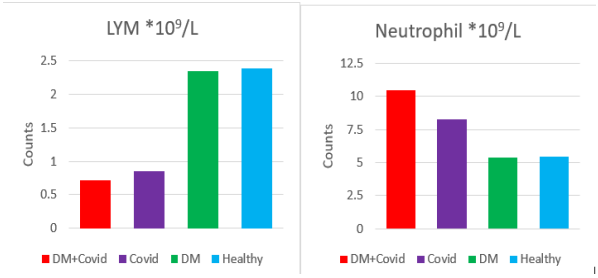
(A) FBG (B) PCT



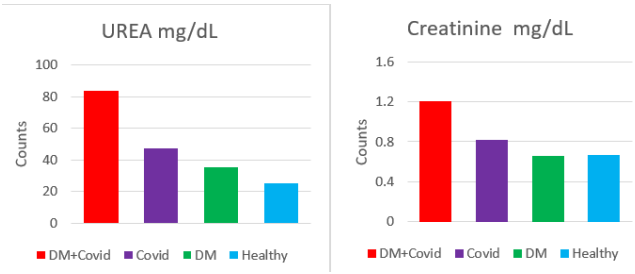
(C) WBC (D) PLT



(E) LYM (F) NEUTRO



(G) UREA (H) CREATININE



Figures: Comparison means of laboratory tests among four study groups

(1) Control: Healthy persons, Blue color, (2) DM: Diabetes mellitus, Green color (3) COVID: COVID without diabetes, Purple color (4) COVID+DM: COVID with Diabetes, red color. Data are appeared for (A) FBS: fasting blood sugar, (B) PCT: Procalcitonin, (C) WBC: White Blood Cells, (D) PLT, Platelets, (E) LYM: Lymphocytes, (F) Neutrophil, (G) Urea, and (H) Creatinine.

References

1. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, Schiergens T, Herrler G, Wu N. H., Nitsche A., Müller MA, Drosten C., Pöhlmann S. Cell. 2020;181:271.

2. Vanhomwegen C, Veliziotis I, Malinverni S, Konopnicki D, Dechamps P, Claus M, Roman A, Cotton F, Dauby N. Procalcitonin accurately predicts mortality but not bacterial infection in COVID-19 patients admitted to intensive care unit. Irish Journal of Medical Science (1971-). 2021;190(4):1649-52. https://doi.org/10.1007/s11845-020-02485-z

3. Yu C, Lei Q, Li W, Wang X, Liu W, Fan X, Li W. Clinical characteristics, associated factors, and predicting COVID-19 mortality risk: a retrospective study in Wuhan, China. American journal of preventive medicine. 2020;59(2):168-75. https://doi.org/10.1016/j.amepre.2020.05.002

4. Rodríguez A, Reyes L, Monclou J, Suberviola B, Bodí M, Sirgo G, Solé-Violán J, Guardiola J, Barahona D, Díaz E. Relationship between acute kidney injury and serum procalcitonin (PCT) concentration in critically ill patients with influenza infection. Medicina intensiva. 2018;42(7):399-408. https://doi.org/10.1016/j.medin.2017.12.004

5. Schuetz P, Christ-Crain M, Müller B. Biomarkers to improve diagnostic and prognostic accuracy in systemic infections. Current opinion in critical care. 2007;13(5):578-85. https://doi.org/10.1097/MCC.0b013e3282c9ac2a

6. Mahmoudi H, Alikhani MY, Taheri NM, Behzadi A. Assessment of changes in blood urea and creatinine levels in patients with coronavirus disease 2019 (COVID-19). 2020. https://doi.org/10.21203/rs.3.rs-25164/v1

7. Athari SZ, Mohajeri D, Nourazar MA, Doustar Y. Updates on coronavirus (COVID-19) and kidney. Journal of Nephropathology. 2020;9(4).

8. Zhao K, Li R, Wu X, Zhao Y, Wang T, Zheng Z, Zeng S, Ding X, Nie H. Clinical features in 52 patients with COVID-19 who have increased leukocyte count: a retrospective analysis. European Journal of Clinical Microbiology & Infectious Diseases. 2020;39(12):2279-87. https://doi.org/10.1007/s10096-020-03976-8

9. Terpos E, Ntanasis-Stathopoulos I, Elalamy I, Kastritis E, Sergentanis TN, Politou M, Psaltopoulou T, Gerotziafas G, Dimopoulos MA. Hematological findings and complications of COVID-19. American journal of hematology. 2020;95(7):834-47. https://doi.org/10.1002/ajh.25829

10. Selim S. Leukocyte count in COVID-19: an important consideration. The Egyptian Journal of Bronchology. 2020;14(1):1-2. https://doi.org/10.1186/s43168-020-00045-8

11. Kubánková M, Hohberger B, Hoffmanns J, Fürst J, Herrmann M, Guck J, Kräter M. Physical phenotype of blood cells is altered in COVID-19. Biophysical journal. 2021;120(14):2838-47. https://doi.org/10.1016/j.bpj.2021.05.025

12. Liu D, Wang Y, Zhao B, Lan L, Liu Y, Bao L, Chen H, Yang M, Li Q, Zeng Y. Overall reduced lymphocyte especially T and B subsets closely related to the poor prognosis and the disease severity in severe patients with COVID-19 and diabetes mellitus. Diabetology & Metabolic Syndrome. 2021;13(1):1-12. https://doi.org/10.1186/s13098-020-00622-3

13. Lippi G, Plebani M, Henry BM. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: a meta-analysis. Clinica chimica acta. 2020;506:145-8. https://doi.org/10.1016/j.cca.2020.03.022

14. Palladino M. Complete blood count alterations in COVID-19 patients: A narrative review. Biochemia medica. 2021;31(3):0-.

https://doi.org/10.11613/BM.2021.030501

15. Tong X, Cheng A, Yuan X, Zhong X, Wang H, Zhou W, Xu X, Li Y. Characteristics of peripheral white blood cells in COVID-19 patients revealed by a retrospective cohort study. BMC Infectious Diseases. 2021;21(1):1-10. https://doi.org/10.1186/s12879-021-06899-7

16. Gilbert DN. Procalcitonin as a biomarker in respiratory tract infection. Clinical Infectious Diseases. 2011;52(suppl_4):S346-S50. https://doi.org/10.1093/cid/cir050