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Title: **Interpretations of Heamatological Parameters in COVID-19 Patients with Diabetic Mellitus Comorbidity**

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Interpretations of Heamatological Parameters in COVID-19 Patients with Diabetic Mellitus Comorbidity

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Abstract

Coronaviruses (CoVs) can infect a wide range of wild and domestic hosts including animals, avian, mammals, rodents, and human beings. COVID infection has already been reported in whales, bats, mice, birds, and giraffes,s and infection to domestic and life stock cause heavy losses to the economy. These viruses cause mild to severe respiratory, enteric, and systemic infections. Worldwide 525,268,297 (May 19, 2022) individuals have been infected since the first case of COVID-19 was reported in Wuhan China with 6,295,402 deaths (May 19, 2022). In Pakistan, a total of 1,529,560 cases of COVID-19 have been reported with 30,379 deaths (May 19, 2022). Province wise data reported 577,201 cases in Sindh, 219,616 in KPK, 506,865 in Punjab, 135,312 in Islamabad, 35,494 in Baluchistan, and 43,324/11,748 in AJK/GB. This study evaluated the hematological parameters in diabetic patients affected by COVID-19. This cross-sectional retrospective study was conducted at the Department of Pathology, Aziz Bhatti Shaheed Hospital, Gujrat, Pakistan. Data were collected from a total of 111 patients of COVID-19 with DM comorbidities and analyzed for the comparison of Leukocytes parameters, platelets count, Red Blood Cell (RBC) counts, and their indices Packed Cell Volume (PCV), Mean Corpuscular Volume (MCV), Mean Corpuscular Hemoglobin (MCH) and Mean Corpuscular Hemoglobin Concentration (MCHC)] with their reference values. The mean RBC count was 4.45 with SD (±0.84). The data also showed the mean of Hemoglobin (Hb) level as 12.45 g/dl (SD ±3.01), PCV as 36.06 (SD ±9.16), MCV as 81.86 (SD ±7.32), MCH as 29.05 (SD ±6.27), and MCHC as 32.61 (SD ±3.65). A comparison was also made between male and female COVID-19-enrolled patients for hematological associated changes in DM. The frequency distribution of leukocytes and

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thrombocytes showed lymphocytosis and thrombocytopenia. It was Concluded that hematological parameters are important in monitoring disease severity, progression, and management in COVID-19 patients with diabetes comorbidity.

Keywords: COVID-19, hematological parameters, Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Volume (MCV), Packed Cell Volume (PCV), Red Blood Cells (RBC)

Introduction

Coronaviruses (CoVs) can infect a wide range of wild and domestic hosts including animals, avian, mammals, rodents, and human beings [1, 2]. These viruses cause mild to severe respiratory, enteric, and systemic infections. They usually present infection with pneumonia or common cold like symptoms in human beings and other hosts. Before the emergence of COVID-19 in December 2019, six (6) coronavirus (CoVs) strains namely HCoV-OC43, HCoV-229E, HCoV-NL63, and HCoV HKU1 were causing mid-upper respiratory tract infection, particularly in immune compromised patients, such as children and aged people [3].

Worldwide 525,268,297 (May 19, 2022) individuals has been infected since the first case of COVID-19 was reported in Wuhan, China with 6,295,402 deaths to date. In Pakistan, a total of 1,529,560 cases of COVID-19 have been reported with 30,379 deaths. Province wise data reported 577,201 cases in Sindh, 219,616 in KPK, 506,865 in Punjab, 135,312 in Islamabad, 35,494 in Baluchistan, and 43,324/11,748 in AJK/GB. It is the span of about three years and the pandemic is still raging [4]. The greatest number of cases have been reported in the USA amounting to 84,692,706 cases along with the highest number of deaths, that is, 1,028,014. India ranks second with 43,129,563 cases and 524,303 deaths. Currently (May 19, 2022), the total active cases are 23,955,058. Among these, 99.8% patients are with mild conditions, while 0.02% patients remain critical (https://www.worldometers.info/coronavirus/). In Pakistan, a total of 1,529,560 cases have been reported with 30,379 deaths (https://covid.gov.pk/) [5].

It has been reported that Type 2 Diabetes Mellitus (T2DM) is associated with severe outcomes of COVID-19 [6]. High mortality and morbidity has been observed in terminal age patients with an underlying comorbidity like DM. The possible reason of severity may be that these patients are more

prone to infection in hyperglycemia and inflammation, which makes their condition more severe. It is a challenge for physicians to control hyperglacemia during COVID-19 infection in order to save the patients from serious disease outcomes [7, 8].

Existing studies suggest that heamatological parameters comprise a good index for disease monitoring, progression, and mortality in case of COVID-19 due to their association with the disease. Neutrophil dysfunction, lymphopenia, and thrombocytopenia progress towards disseminated intravascular coagulation (DIC). Therefore, complete blood count (CBC) in COVID-19 is a good marker of the disease status. Previous studies also reported that neutropenia and high inflammatory response disturb the neutrophil vs lymphocytes ratio (NLR) in critically ill patients [9, 10]. These studies also showed that thrombocytopenia and disturbed mean platelets volume (MPV) lead to disturbed coagulation profile (PT, APTT, INR) [11, 12]. The increased monocytes count and decreased lymphocytes (LMR) number are associated with poor prognosis of disease and a high mortality rate. LMR ration is highly sensitive for patients with comorbidities, such as diabetes and cardiovascular diseases. The hypoxic condition may also be due to low RBC counts, Hb level, and red cell indices (HCT, MCH, and MCHC) [8].

The current study was designed to evaluate the heamatological parameters exclusively in patients with all forms of diabetes.

Material and Methods

This cross-sectional retrospective study was conducted at the Department of Pathology, Aziz Bhatti Shaheed Hospital, Gujrat, Pakistan. Ethical approval was granted by the Institutional Review Board of the University of Lahore, Gujrat Campus, Pakistan. The data of COVID-19 patients with DM was collected for the months January-May, 2022. All patients with DM in the age group 18-80 years presenting with COVID-19 were included in this study.

Samples were collected from individuals with symptoms such as fever, cough, dyspnea, and respiratory distress, after taking their informed consent. Both oropharyngeal and nasopharyngeal specimens using swab were collected from the suspected individuals. For further testing, CBC was performed on Sysmax Hematology Analyser (Sysmax, Canada). The

samples were collected in EDTA vial. The vials were labeled and tests were performed on CBC analyzer to check different hematological parameters.

Results

The data of a total of 111 patients of COVID-19 with DM comorbidity was analyzed for the comparison of RBC counts and their indices PCV, MCV, MCH and MCHC with their normal values. Table 1 showed the frequency distribution of differential Leukocytes Count with respect to gender. The mean of neutrophil count for male was observed as higher than female. However, lymphocytes, monocytes, and Eosinophils distribution was observed higher among female.

Table 2 shows the distribution of RBC counts and their indices. The mean RBC count observed was 4.45 with SD (±0.84). The data also yielded the mean Hb level of 12.45 g/dl (SD ±3.01), PCV level of 36.06 (SD ±9.16), MCV level of 81.86 (SD ±7.32), MCH level of 29.05 (SD ±6.27), and MCHC level of 32.61 (SD ±3.65). The data for RBC indices was equally distributed between both genders; therefore, it is not shown in a graphical or tabulated form. In the data, platelet count was observed as 214732, while SD ± 106428.21. The high difference SD indicated that data was not uniformly distributed in case of platelet count. The mean of Total Leukocytes Counts (TLC) was observed 10810/ul with SD ± 6284.80.

Discussion

CBC is included in the basic profile of diagnostic tests. It is an inexpensive and easily performed technique available in all clinical labs. CBC includes different counts and associated haematological values, such as white blood count (TLC) and differential leukocytes count (DLC) (neutrophils, monocytes, lymphocytes, eosinophils and basophils). RBC parameters include RBC counts, Hb level, and red cell indices (PCV, MCV, MCH, MCHC), as well as platelet count (PLT) and platelet indices (MPV). All these parameters are good predictors of disease prognosis, monitoring, and management. Neutrophils are important components of the inflammatory process in the immune system. They are mainly involved in phagocytosis and are also regulated by macrophages, epithelial cells, mast cells, and other inflammatory molecules. Similarly, the interaction of macrophages and lymphocytes produces antibodies and generates a specific type of immunity. RBCs play a vital role in oxygen delivery and buffering systems in the body. Furthermore, thrombocytes also regulate haemostasis and inflammation.

Therefore, haematological parameters are considered as good markers of inflammation, immune efficiency, hypoxic conditions, cellular stress, and haemostasis [13].

Certain heamatological parameters show variations during the course of COVID-19. These parameters indicate disease severity in the case of T2DM patients with COVID-19. The current study included N=111 subjects with confirm COVID-19 infection and diabetes. Gender distribution was kept uniform across both groups to exclude the subject bias. The RBC data showed the mean of Hb levels and RBC counts as within normal limits. This is contradictory to studies which reported the prevalence of anaemia in case of uncontrolled diabetes [12]. Since data on diabetes control is not available; therefore, the results of these studies cannot be rejected. A large scale similar study can validate our finding related to COVID associated DM.

COVID-19 infection causes autoimmune haemolytic anaemia in diabetic patients. Other anaemic factors may include medical treatment, bone marrow infiltrating anaemia, nutritional deficiencies, and blood loss (acute/chronic) [14]. PCV and other red cell indices were also reported within normal limits in the current study. A study from Bangladesh correlated RBC counts and PCV, positively. It supported the narrative of low RBC counts and related parameters but also found some parameters to be within the normal range. The studies which observed anaemia in diabetic patients also showed a low number of red cell indices and vice versa [15].

TLC was reported as high in our study but within the normal range. Gender distribution of white cell parameters was not found to be significant. Previous studies related the levels of WBC parameters with the severity/non-severity of the disease. Ramesh [9] related TLC with mortality. The study narrated that the level of TLC above 8950 cells/cmm may increase mortality, even though it is considered within the normal range for patients with other diseases [9]. These findings act as simple parameters to predict disease severity, clinical decision-making and patient management for a clinician dealing with COVID-19 patients, particularly those with a comorbidity like diabetes [16].

Table 1. Frequency Distribution of Differential Leukocytes Count

		Neutrophils (%)	Lymphocytes (%)	Monocytes (%)	Eosinophils (%)
Male	Frequency (n)	57	57	57	57
	Mean	44.32	53.23	1.37	1.07
	Std. deviation	23.32	24.43	1.26	1.03
Female	Frequency (n)	54	54	54	54
	Mean	41.87	55.02	1.76	1.19
	Std. deviation	23.52	24.23	1.10	1.18

Table 2. Frequency Distribution of RBC Count, Indices and Platelets Counts

	RBC 10^{12}/L	Hemoglobin g/dl	PCV %	MCV fl	MCHpg/ cell	MCHCg/ dl	TLC/ cmm	Platelets /ul
Frequency	111	111	111	111	111	111	111	111
Mean	4.45	12.45	36.06	81.86	29.05	32.61	214732	10810
Std.deviation	0.84	3.01	9.16	7.32	6.27	3.65	106428.21	6284.80

COVID-19 infection starts with an inflammatory cascade and recruitment of immune cells, which proceed to cytotoxic storm and ultimately, death. Severity of disease induces ARDS, acute pneumonia, and multi-organ failure (MOF), if management fails with a poor response. Disease may lead to severity in comorbidities [7]. Neutrophil dysfunction, lymphocytopenia, and thrombocytopenia progress to DIC. Therefore, CBC is a good marker of the disease status in COVID-19 patients. Previous studies reported that neutropenia and high inflammatory response disturb the neutrophil vs lymphocytes ratio (NLR) in critically ill patients.

Thrombocytopenia was observed in severe COVID-19 patients and their severe condition was related to mortality. Thrombocytosis was also related to poor prognosis in other studies. However, comorbidities were not the cause of changes in platelet count and indices. RDW is an excellent discriminating parameter between survivors and non-surviving patients [17, 18]. Hypercoagulability is also due to cytokine storm and plasmin activation. This causes elevated levels of D-dimer, fibrinogen, and also cause DIC, which is more severe in hyperglycaemia [11,]. It is also suggested that men are more prone to this disease as compared to women and they present the disease in a severe form. Although, our study did not show gender difference for any parameter except eosinophil count.

It is recommended that haematological parameters are good predictors for measuring disease progression, patient management, and mortality index during COVID-19; therefore, they should be monitored daily in diabetic COVID-19 patients. A comprehensive monogram should be established for the early management of the disease. Current vaccination and its efficacy must also be evaluated and monitored using haematological parameters. Comorbidities, such as diabetes are contributory factors in increasing the severity of COVID-19 infection in patients. Therefore, these high-risk patients should monitor their haematological profile on a daily basis on the advice of their clinician.

References

1. Decaro N, Lorusso A. Novel human coronavirus (SARS-CoV-2): A lesson from animal coronaviruses. *Vet Microbiol*. 2020;244:e108693. https://doi.org/10.1016/j.vetmic.2020.108693

2. Abdel-Moneim AS, Abdelwhab EM. Evidence for SARS-CoV-2 infection of animal hosts. *Pathogens*. 2020;9(7):e529. https://doi.org/10.3390/pathogens9070529

3. Giwa A, Desai A. Novel coronavirus COVID-19: An overview for emergency clinicians. *Emerg Med Pract*. 2020;22(2 Suppl 2):1-21.

4. Hasoksuz M, Kilic S, Sarac F. Coronaviruses and SARS-COV-2. *Turk J Medical Sci*. 2020;50(9):549-556. https://doi.org/10.3906/sag-2004-127

5. Mahmood S. Exploring COVID-19 incidence hotspot in Metropolitan area of Pakistan using geo-statistical approach: A study of Lahore city. *Spat Inf Res*. 2022;30(4):469-476. https://doi.org/10.1007/s41324-021-00423-4

6. Nassar M, Daoud A, Nso N, et al. Diabetes mellitus and COVID-19: Review article. *Diab Metabo Synd*. 2021;15(6):e102268. https://doi.org/10.1016/j.dsx.2021.102268

7. Palaiodimos L, Chamorro-Pareja N, Karamanis D, et al. Diabetes is associated with increased risk for in-hospital mortality in patients with COVID-19: A systematic review and meta-analysis comprising 18,506 patients. *Hormones*. 2021;20(2):305-314. https://doi.org/10.1007/s42000-020-00246-2

8. Xiao F, Zhou Y-C, Zhang M-B, et al. Hyperglycemia and blood glucose deterioration are risk factors for severe COVID-19 with diabetes: A two-center cohort study. *J Med Virol*. 2022;94(5):1967-1975. https://doi.org/10.1002/jmv.27556

9. Ramesh J, Reddy SLS, Rajesh M, Varghese J. Evaluation of simple and cost-effective immuno- haematological markers to predict outcome in hospitalized severe COVID-19 patients, with a focus on diabetes mellitus - A retrospective study in Andhra Pradesh, India. *Diabetes Metab Syndr*. 2021;15(3):739-745. https://doi.org/10.1016/j.dsx.2021.03.025

10. Sun Y, Zhao R, Hu Z, et al. Differences in the clinical and hematological characteristics of COVID-19 patients with and without type 2 diabetes. 2020;2020:e1038585. https://doi.org/10.1155/2020/1038585

11. Varikasuvu SR, Varshney S, Dutt N. Markers of coagulation dysfunction and inflammation in diabetic and non-diabetic COVID-19. *J Thromb Thrombolysis*. 2021;51(4):941-946. https://doi.org/10.1007/s11239-020-02270-w

12. Varma A, Dergaa I, Abubaker M, et al. Covid-19 and diabetes in primary care - How do hematological parameters present in this cohort? 2021;16(3):147-153. https://doi.org/10.1080/17446651.2021.1909472

13. Usul E, Şan İ, Bekgöz B, Şahin A. Role of hematological parameters in COVID-19 patients in the emergency room. *Biomark Med*. 2020;14(13):1207-1215. https://doi.org/10.2217/bmm-2020-0317

14. Wu D, Gao S. Analysis of the lymphocyte count in type 2 diabetic patients with coronavirus disease (COVID-19): A retrospective study in a centralized treatment center. *Diabetes Res Clin Pract*. 2020;166:e108340. https://doi.org/10.1016/j.diabres.2020.108340

15. Rahman MA, Shanjana Y, Tushar MI, et al. Hematological abnormalities and comorbidities are associated with COVID-19 severity among hospitalized patients: Experience from Bangladesh. *PLOS ONE*. 2021;16(7):e0255379. https://doi.org/10.1371/journal.pone.0255379

16. Wu Y, Hou B, Liu J, Chen Y, Zhong P. Risk factors associated with long-term hospitalization in patients with COVID-19: A single-centered, retrospective study. *Front Med*. 2020:e315. https://doi.org/10.3389/fmed.2020.00315

17. Yang A-P, Liu J-p, Tao W-q, Li H-m. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. *Int Immunopharmacol*. 2020;84:e106504. https://doi.org/10.1016/j.intimp.2020.106504

18. Nafakhi H, Alareedh M, Al-Buthabhak K, Shaghee F, Nafakhi A, Kasim S. Predictors of adverse in-hospital outcome and recovery in patients with diabetes mellitus and COVID-19 pneumonia in Iraq. *Diabetes Metab Syndr*. 2021;15(1):33-38. https://doi.org/10.1016/j.dsx.2020.12.014Get