HEMATOLOGICAL CHARACTERISTICS OF DIABETIC PATIENTS WITH COVID 19 INFECTION

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Abstract –

Background - Diabetic patients have been severely affected by Covid 19 infection. It has been reported that the disease is more progressive leading to venous and arterial thromboembolism, due to multiple factors. This study was conducted to determine hematologic parameters including D-dimer in diabetic patients with Covid -19 infection in association with disease severity and treatment.

Method - This retrospective cohort study was conducted at King Fahad Medical City, Saudi Arabia after taking IRB approval, by collecting data regarding all hematological laboratory parameters, disease severity, and anticoagulant treatment ofCovid 19 diabetic patients (n=159) from medical records from March-December 2020.

Result - Mean value of White Blood Cells, Neutrophils, Monocytes, Eosinophils, Lymphocyte Monocyte Ratio, C reactive protein, Serum ferritin, and LDH levels was elevated in severe cases than mild cases with statistical significant increase in HbA1c (0.047),Serum fibrinogen (0.007), C reactive protein (0.005), Serumferritin (0.034), and serum LDH (0.015).Mortality was observed in 14 (8.8%) patients and all of thesehad severe covid-19 with Diabetes.In our study, treatment with low molecular weight heparin was not significantly related to severity.

Conclusion - The routine blood parameters if detected early will enable physicians to identify severe cases of Covid -19 patients with Diabetes for prompt treatment and save considerable time and resources.

Keywords - Covid-19, Diabetes, Haematology, Parameters

I. INTRODUCTION

The Covid-19 has already infected more than 524 million people and resulted in more than 6.29 million deaths globally [1].Covid -19 has varied clinical manifestations from trivial flu like symptoms to multiple system failure and death, especially due to significant impact on the hematopoietic system and hemostasis.

It has been reported that prevalence of diabetes was 20%. among Covid patients[2]. Disease severity and outcome in these patients are related to numerous markers like serum ferritin, C-reactive protein, interleukin-6, fibrinogen, serum LDH and D-dimer[3-5].In Diabetic patients with Covid -19 infection, the disease is more severeleading to venous and arterial thromboembolism, due to multiple factors such as inflammation, hypoxia, immobilization, diabetes and disseminated intravascular coagulationand is associated with increased morbidity [6].

Guozhen Li reported that the mortality rate for diabetic patients with COVID-19 was 14.5 % which is higher than non-diabetic patients (5.7%). This could be due to higher level of D-dimer, and low lymphocyte count at admittance. So, patients with COVID-19 and diabetes need extra attention[7].

Every patient with COVID-19 is required to be placed on prophylactic doses of anticoagulation, usually with low molecular weight heparin (LMWH), unless contraindicated[8].Hematological aberrations in COVID-19 are associated with disease progression, severity and mortality. Lymphopenia, thrombocytopenia, abnormal coagulation profile is very well reported in patients of Covid-19[9].

The leucocyte count, neutrophil count, neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), and ferritin level were significantly higher in the severe disease subgroup than those in the non-severe subgroup ($p<0.001$). The lymphocyte counts and lymphocyte to monocyte ratio (LMR) were significantly lower in the severe disease subgroup than those in the non-severe subgroup ($p<0.001$). NLR was positively correlated with the COVID-19 risk (adjusted OR 1.438, $p=0.012$) whereas the

association of PLR and LMR with COVID-19 risk was unclear[10].However, there are very few studies on specific information regarding hematological parameters of patients with diabetes and COVID-19.

These parameters if detected early can play a vital role in early prediction of disease severity and can provide a better guide for prompt management of patients, thus, can help in decreasing the disease morbidity and mortality.

II. OBJECTIVE

This study was conducted to determine hematologic parameters including D-dimer in diabetic patients with Covid -19 infection in association with disease severity and treatment.

III. METHOD

This retrospective cohort study was conducted at King Fahad Medical City, Saudi Arabia after taking IRB approval(IRB no:20:737), by collecting data regarding all hematological laboratory parameters, disease severity, and anticoagulant treatment of Covid 19 diabetic patients (n=159) from medical records from March-December 2020.All diabetic patients with covid-19 infection>18 years were included, whereas Non diabetic Covid-19 patients , and patients with incomplete records and prior hematological disorders were excluded.

Mild disease was demarcated for patients with symptoms of fever, sore throat, cough and no sign of pneumonia on X-rays. Patients with respiratory distress (respiratory rate >30 breath per min, O_2 saturation less than 93% and more than 50% lung infiltrate were classified as severe disease.

Data was transferred to excel and analyzed in SPSS version 22, Illinois, USA. Descriptive statistics were calculated for hematologic parameters and Pearson correlationto correlate these parameters with the severity of the disease. Laboratory parameters were compared between mild and severe cases using independent t tests. Quantitative variables such as Hemoglobin, white blood count (WBC), Differential white blood count including neutrophil to lymphocyte ratio (NLR), Lymphocyte to monocyte ratio(LMR), Platelet to Lymphocyte ratio (PLR), Prothrombin time PT, activated partial thromboplastin time APTT, Ferritin, D-dimer, lactate dehydrogenase (LDH), C-reactive protein (CRP) were analyzed. P-value equal or less than 0.05 was considered significant.

IV. RESULTS

Demographic features and hematological parameters of patients with Covid -19 infection and diabetes mellitus(n=159) at the time of admission who later developed mild or severe illness are depicted in Table 1,2, and 3.

Out of 159 patients,94.3% of patients were more than 40years, and Covid -19 with Diabetes was predominant in males91(57.2%),than females68(42.8%).Severe cases were 107(67.3%) and mild cases were 51(32.1%). (Table 1)

General Characteristics	N(%)
Ethnicity Saudi Non Saudi	106(66.7%) 53(33.3%)
Gender Male Female	91(57.2%) 68(42.8%)
Age	<40 =9(5.7%) >40 =150 (94.3%)
Covid -19 severity Mild Severe	51(32.1%) 107(67.3%)
Mortality Yes No	14(8.8%) 145(91.2%)
Length of hospital stay <3 weeks >3 weeks	 134(84.3%) 25(15.7%)
ICU admission Yes No	41(25.8%) 118(74.2%)
LMWH given Yes No	147(92.5%) 5(3.1%)
Comorbidities Yes No	 137(86.2%) 22(13.8%)
Complications during hospitalization Yes No	12(7.5%) 147(92.5%)

Table 1. Demographic features of patients with Covid -19 infection and diabetes mellitus at the time of admission who later developed mild or severe illness.(n=159)

Hematological Parameter	All Patients Mean ±SD	Normal value
HbA1C at admission	5.56(4.999)	4-5.6%
Hemoglobin g/dl	12.94(2.251)	>13 in males >12 in females
WBC 10^9 cells/L	8.71(7.676)	4.5-11
Neutrophil count10^9 cells/L	71.58(15.096)	2.0-8.0
Lymphocyte count10^9 cells/L	19.41(11.779)	1.0-4.8
Monocyte count10^9 cells/L	7.72(12.515)	0.30-0.90
Eosinophil count10^9 cells/L	0.78(1.93)	0-0.5
Basophil count10^9 cells/L	.30(.282)	0.02-0.05
LMR	3.63(5.965)	2.97-4.83
PLR	21.86(2.251)	36.63-172.68
NLR	6.38(7.970)	0.3-2.1
Platelet count10^9 cells/L	259.50(97.366)	150-400
Activated PTT secs	31.52(4.349)	30-40
PT secs	13.62(2.285)	11-13.5
Fibrinogen g/L	1.86(3.710)	2.0-4.0
D-Dimer mg/L	2.73(8.940)	<0.50
C Reactive protein mg/L	81.67(87.06)	<10
Serum ferritin µg/L	954.70(162.72)	12-300
LDH units/L	481.13(221.946	140-280

Table 2:Hematological parameters of patients with Covid -19 infection and diabetes mellitus at the time of admission. (n=101)
LMR: Lymphocyte/Monocyte ratio; PLR:Platelet/Lymphocyte ratio; NLR: Neutrophil/lymphocyte ratio

Mean value of White Blood Cells, Neutrophils, Monocytes, Eosinophils, Lymphocyte Monocyte Ratio, C reactive protein, Serum ferritin, and LDH levels was elevated in severe cases than mild cases with statistical significant increase in HbA1c (0.047), Serum fibrinogen (0.007), C reactive protein (0.005), Serum ferritin (0.034), and serum LDH (0.015).(Table 3, (Fig 1)

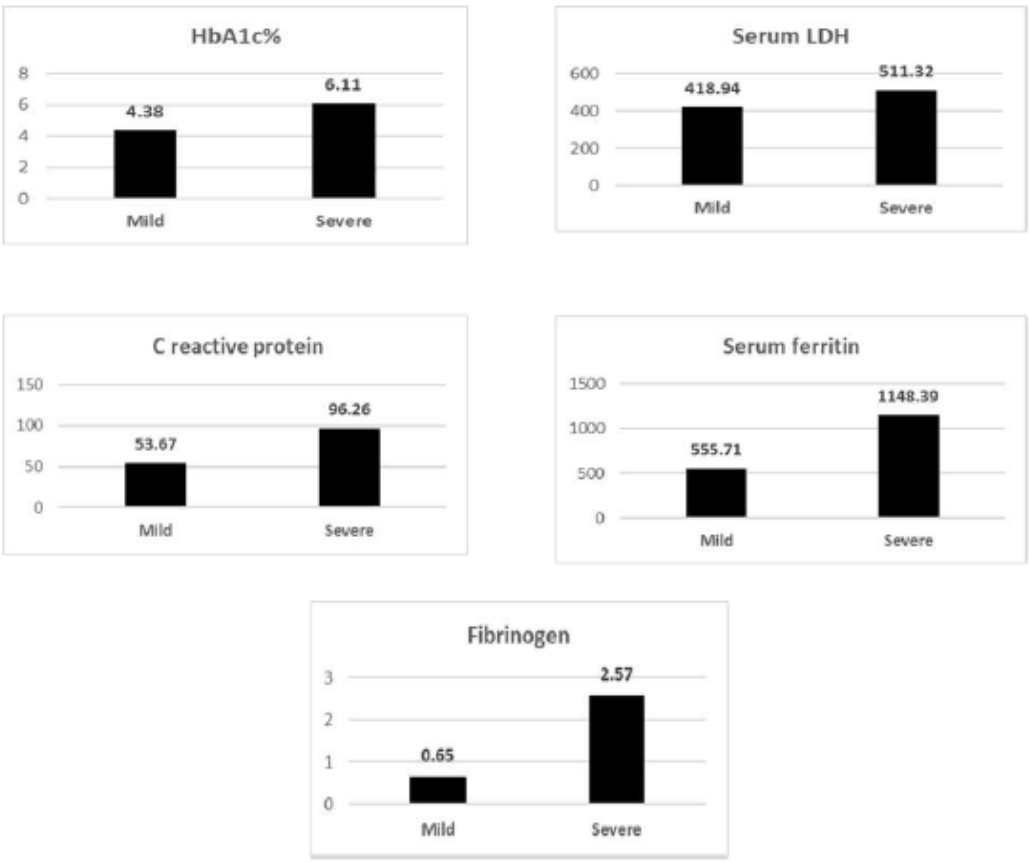

Fig 1Corelation between Covid -19 severity and Lab Paramaters with clinical significance <0.05.

Mortality was observed in 14 (8.8%) patientsand all of these had severe covid-19 with Diabetes. LMWH was started in 92.5(%) of all cases.

V. DISCUSSION

Variations in hematological characteristics in patients with COVID-19 are evolving as imperative features of Covid -19 infection that triggers coagulation activation, inflammatory reactions, hypercoagulability induction and cytokine storms that ultimately indicate disease severity. The patient deterioration condition will lead to admission to intensive care unit and death [11].An analysis by Varikasuvu et al showed that diabetic COVID-19 patients are highly vulnerable to coagulation abnormalities and inflammation than the non-diabetic COVID-19 cases. The levels of serum ferritin (standardized mean difference-SMD: 0.47), C-reactive protein (SMD = 0.53), interleukin-6 (SMD = 0.3), fibrinogen (SMD = 0.31), and D-dimers (SMD = 0.54), were increased in diabetic COVID-19 cases compared to non-diabetic COVID-19 patients, signifying coagulation irregularities and inflammatory storm [12]. In our study severe cases of Covid -19 diabetic cases were 107(67.3%) and mild cases were 51(32.1%).Mean value of White Blood Cells, Neutrophils, Monocytes, Eosinophils, Lymphocyte Monocyte Ratio, C reactive protein, Serum ferritin, and LDH levels was elevated in severe cases than mild cases with statistical significant increase in HbA1c (0.047), Serum fibrinogen (0.007), C reactive protein (0.005), Serum ferritin (0.034), and serum LDH (0.015). (Table 3).

Hematological Parameter	Normal value	Mild cases	Severe cases	P value
HbA1C at admission	4-5.6%	4.38(5.043)	6.11(4.929)	0.047 *
Hemoglobin g/dl	>13 in males >12 in females	12.74(2.352)	13.06(2.195)	0.399
WBC 10^9 cells/L	4.5-11	8.66(5.677)	8.75(8.518)	0.944
Neutrophil count10^9 cells/L	2.0-8.0	70.66(15.717)	72.02(14.848)	0.604
Lymphocyte count10^9 cells/L	1.0-4.8	20.25(12.932)	19.00(11.225)	0.540
Monocyte count10^9 cells/L	0.30-0.90	7.16(4.237)	8.00(14.963)	0.699
Eosinophil count10^9 cells/L	0-0.5	.55(1.053)	.90(2.229)	0.306
Basophil count10^9 cells/L	0.02-0.05	.33(.321)	.29(.262)	0.364
LMR	2.97-4.83	3.35(2.846)	3.80(7.002)	0.659
PLR	36.63-172.68	25.20(34.648)	20.47(24.956)	0.330
NLR	0.3-2.1	7.02(8.712)	6.13(7.631)	0.513
Platelet count10^9 cells/L	150-400	266.53(105.14)	255.83(94.164)	0.521
Activated PTT secs	30-40	31.26(4.159)	31.61(4.462)	0.639
PT secs	11-13.5	13.42(1.855)	13.71(2.475)	0.446
Fibrinogen g/L	2.0-4.0	.65(1.621)	2.57(4.358)	0.007*
D-Dimer mg/L	<0.50	3.28(10.687)	2.45(7.959)	0.593
C Reactive protein mg/L	<10	53.67(68.892)	96.26(92.177)	0.005*
Serum ferritin µg/L	12-300	555.71(716.488)	1148.39(1885.9)	0.034*
LDH units/L	140-280	418.94(251.46)	511.32(200.538)	0.015

Table 3: Hematological parameters of patients with Covid -19 infection and diabetes mellitus at the time of admission who later developed non severe or severe illness. (n=101) * P value <0.05

In a retrospective cohort study of 380 patients, the numbers of lymphocytes and eosinophils were considerably lower in patients with critical disease than those with severe or moderate disease (p<0·0001), and prothrombin time, D-dimer, and fibrin degradation products considerably increased in severe cases (p<0·0001). Thrombotic and hemorrhagic events played a major role in patient's death. (19 [35%] of 55) [13].

Bansal A et al., showed significant association of D-Dimers with the severity of the COVID -19 disease. Patients with acute lung injury and severe infection will have disseminated intravascular coagulation (DIC) secondary to sepsis [14]. Ayusha et al reported that 1.5 µg/ml is the optimal cutoff value of admission D-dimer for predicting mortality in COVID-19 patients, with good sensitivity and specificity [15]. In our study it was more than 2.5mg/L in both mild and severe cases. Laboratory interpreters of clinical decline can aid in intensifying the care of the patients with this infection and support in suitable triaging and resource deployment.

A local study also reported that diabetic covid -19 patients have a higher mortality rate than their non-

diabetic counterparts, and patients with uncontrolled diabetic (HbA1C > 7%) on admittance often ends up in intensive care [16]. In our study mortality was observed in 14 (8.8%) patients and all of these had severe covid-19 with Diabetes.

In our study LMWH was started in 92.5% of all cases. Terpos et al in a Chinese study, reported that LMWH administration among patients with markedly elevated D-dimers or in those meeting the criteria for sepsis-induced DIC was significantly associated with improved 28-day overall survival, p=0.017 and p=0.029 among two patient groups, users versus non-users, respectively [17].

The anti-inflammatory properties of LMWH may be beneficial in COVID 19 patients and should be integrated with other antithrombotic treatments such as antithrombin, and recombinant thrombomodulin to hinder the complex 'immunothrombosis' process. [8] In our study treatment with low molecular weight heparin was not significantly related to severity.

VI. CONCLUSION

In conclusion, Covid-19 disease has a devastating effect on the hematopoietic system in Covid -19 patients with diabetes leading to major complications and untimely death. Baseline evaluation of hematological lab parameters, D-dimer and HB A1c followed by periodic assessment will enable physicians to provide tailored treatment and anticipate complications. Further, optimal anticoagulation regimen with or without adjunct antithrombotic therapies such as LMWH, may be useful in patients with COVID-19.

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DECLARATION OF INTEREST

The authors report no conflict of interest.

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