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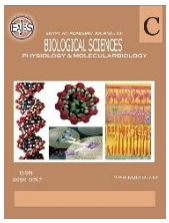

Effects of Some Physiology Factors on Type 1 Diabetes Mellitus Patients in Iraq

Hadeel M. Abbas[1], Maha M. Ali[1] and Noor M. Jassim[2]

[1]Department of Medical Lab Technique, Imam Jaafar Al-Sadiq University, IRAQ.
[2]Department of Medical Laboratories, College of Health and Medical Technology, Sawa University, Almuthana, IRAQ.

***E-mail:** hadeelmohsen514@gmail.com ; maha.moshreq@sadiq.edu.iq ; noor.m@sawauniversity.edu.iq

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ABSTRACT

Background: The autoimmune-mediated chronic condition known as type 1 diabetes mellitus (T1DM) is typified by the degeneration of the pancreatic β cells that produce insulin.**Method**: The study included 75 T1DM patients and 25 healthy subjects.**Results:** Hematological tests which included WBC, RBC, Hb, HCT, MCV, platelets and differential for patients and controls showed significant differences ($p<0.05$) found in WBC, platelets, neutrophils in patients as compared with the control group, while no significant differences($p>0.05$) were found in the results of RBC, Hb, HCT, MCV, lymphocytes between the groups of patients and controls. The erythrocyte sedimentation rate in patients and the healthy groups, where the results of the study showed a significant increase in ESR ($p<0.05$) of the patients (25.14±1.59mm/hr) compared with the healthy group (23.83±1.704mm/hr).**Biochemical Tests:** The results of estimation of the biochemical parameters values showed Significant increases were found in the results of blood sugar in patients as compared with the control group, while no significant differences ($p>0.05$) were found in the results of creatinine and urea between the patients and controls.**Conclusions:** According to the current study, compared to the control group, diabetes patients had significantly higher levels ($p<0.05$) of many inflammatory indicators, including WBC, platelets, neutrophils, and ESR.

INTRODUCTION

A person with diabetes mellitus, which encompasses various forms of T1DM and T2DM, has hyperglycemia. The most prevalent kind of diabetes mellitus, known as type 1 diabetes, is characterized by a total absence of insulin as a result of pancreatic beta-cell death (Alam *et al*., 2014).

Adults with type 1 diabetes may develop the disease later in life and may not exhibit the typical symptoms that are seen in children. Despite being classified as juvenile-onset according to traditional definitions, T1DM can strike anyone at any age, with up to 50% of cases occurring in adulthood(Thomas *et al*., 2018). Up to 50% of adults with type 1 diabetes (Hope *et al*., 2016).

When a person has symptoms and a random blood glucose concentration above 11.1 mmol/L (200 mg/dL) or above 70 mmol/L (126 mg/dL), they are diagnosed with diabetes; an abnormal oral glucose tolerance test result is also considered (Chawla et al., 2020). Atypical glycemia needs to occur twice in order to be symptomless. An additional basis for diagnosing diabetes is a glycated hemoglobin (HbA1c) concentration greater than 48 mmol/mol (65%).

HbA1c is less sensitive for diagnosis than fasting or stimulated blood glucose tests, though, because dysglycemia progression can occur quickly in T1DM patients (Hare &Topliss, 2022).

White blood cell count (WBC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), which are produced in a variety of tissues such as adipocytes, the liver, and the vasculature, are examples of inflammatory markers. Assays for WBC, ESR, and CRP are frequently available in clinical pathology labs (Pepys & Hirschfield, 2003).

Guo *et al*. (2015) revealed that the rate and severity of diabetes were correlated, independently, with the ESR. As a result, ESR can also be used as a gauge to assess how well diabetes patients are doing.

MATERIALS AND METHODS

a) Study group: There were 75 patients in this study. These samples were taken from the Najaf Center for Diabetes and Endocrine at Al-Sadr Teaching Hospital's laboratory. T1DM was present in every patient chosen for this study (blood samples were taken as standard clinical procedure). Patient's age and gender were among the epidemiological data gathered from hospital patient data sheets.

b) Control group: 25 individuals in good health who did not exhibit any clinical signs of illness or inflammatory conditions made up this group.

Blood Samples:

Five milliliters of venous blood—a sample drawn from both the control group and the patients were used for the tests.

1. Fresh 0.5 ml of the serum was utilized for the blood sugar, urea, and creatinine assays, following the collection of two milliliters in gel tubes and a five-minute centrifugation at 5000 rpm.
2. A milliliter was obtained in tubes containing the anticoagulant EDTA; one milliliter was utilized for hematology tests and one milliliter for PCR tests.
3. To perform the erythrocyte sedimentation rate (ESR) test, 1.6 ml was collected in tubes containing sodium citrate anticoagulant.

Biochemical Tests:

Urea, creatinine, and blood sugar tests were done by using kits, which are products of BIOLABO REAGENT (Maizy, France).

Hematological Tests:

The automated hematology analyzer was used to calculate the following hematological parameters from blood samples for each patient: hemoglobin concentration (Hb), total red blood cell (RBC), white blood cell (WBC), hematocrit (HCT), mean corpuscular volume (MCV), platelet count, neutrophils, and lymphocytes.

The rate at which erythrocyte cells deposit is known as the erythrocyte sedimentation rate or ESR. According to Alende-Castro et al. (2019), the ESR is still frequently utilized as part of acute-phase response screening and monitoring tests for autoimmune, cancer, and infection.

The steps below were used to complete the ESR test:

1. Venous blood was drawn according to the protocol and placed in a 9 x 120 mm ESR vacuum tube with sodium citrate.
2. To prevent hemolysis, clotting, or bubbles, the tube was immediately inverted at 180 degrees six to eight times to ensure thorough mixing.
3. After the blood sample ESR tube is positioned vertically onto the detector at room temperature (about 20°C), the starting time and pertinent numbers are noted. After 30 minutes of holding the detector motionless, the millimeter of erythrocyte sedimentation was read.
4. Detailed reading technique: it aligned the plasma concave in ESR tubes to the zero scares of the ESR fast detector after remaining stable for 30 minutes. The upper surface of the erythrocyte was then lined up with the detector's scale to read the data.

RESULTS AND DISCUSSION

1. Hematological Tests:

Table 1, displays the results of hematological tests, including WBC, RBC, Hb, HCT, MCV, platelets, and differential, for both patients and controls. WBC,

platelets, and neutrophils showed significant differences ($p<0.05$) between the patient and control groups, but results for RBC, Hb, HCT, MCV, and lymphocytes showed no significant differences ($p>0.05$) between the patient and control groups.

The study's findings revealed a significant difference ($p<0.05$) in the erythrocyte sedimentation rate (ESR) between the patient group (25.14±1.59mm/hr) and the healthy group (23.83±1.704mm/hr).

Table 1: Hematological tests (WBC, RBC, HB, HCT, MCV, PLT, Differential White blood cell and ESR) for T1DM patients and controls.

Parameter	Diabetes mellitus type 1 patients (n=75)	Control (n=25)	P-values
RBC (cell×10^6/µL)	4.967±0.07864	4.736±0.1471	0.1525
WBC (cell×10^3/µL)	7.859±0.2586*	6.496±0.4408	0.0095
Hb (g/dL)	13.75±0.3183	12.92±0.3739	0.1614
HCT %	37.35±0.4971	36.81±0.9993	0.6015
MCV (fL)	76.24±0.7994	79.09±1.540	0.0862
PLT(cell×10^3/µL)	297.8±9.142*	213.1±8.728	0.0001
ESR (mm/hr)	25.14±1.59*	23.83±1.704	0.002
Differential white blood cell count			
Neutrophils (cell×10^3/µL)	54.14±1.397*	59.66±1.114	0.0302
Lymphocytes (cell×10^3/µL)	35.16±1.209	34.13±1.559	0.6529

Results values were expressed as mean± SE, *: $p< 0.05$ or significant differences between mean values. Abbreviations: RBC = Red blood cell, WBC = White blood cell, Hb= Hemoglobin, HCT = Hematocrit, MCV= Mean corpuscular volume, PLT=platelets, ESR=Erythrocytic Sedimentation Rate).

According to the current study, there was no discernible difference in the RBC and Hb levels between the patient and control groups ($p>0.05$). These findings corroborated a study by Ohara et al. (2016) that found no evidence of a significant difference ($p>0.05$) in RBC levels between the control group and the patient group.

These findings conflicted with a study by Kothari & Bokariya (2012), which found that when T1DM patients were compared to the control group, there was an increase in RBC and HB.It has been demonstrated that DM is directly linked to a number of hematological alterations that impact RBCs. The sustained elevation of glycosylated Hgb, which is linked to osmotic disruption, cytoplasmic viscosity, and structural and functional alterations in the Hgb molecule, is facilitated by hyperglycemia. All of these modifications may have a significant impact on the RBC indices, which comprise the mean cell hemoglobin (MCH), Hct, MCV, and RBC count (Alamri et al., 2019).

The study's findings revealed that T1DM patients had a significantly higher WBC count ($p<0.05$) than the control group.The leukocyte count was significantly higher in T1DM patients as compared to the control group ($p <0.05$), which is in line with the findings of Uko *et al.* (2013).

According to Farhan's (2019) study, T1DM patients had higher WBC counts than controls.

The study conducted by Fang *et al.* (2018) revealed a decrease in total WBC counts. The study also found that the decrease was caused by a decrease of 10.96% in neutrophils and a decrease of 21.74% in monocytes. According to their findings, these results were different.

The increase in neutrophils relative to the healthy control group may be the cause of the elevated white blood cell count in T1DM patients.

White blood cell count is a fundamental measure of the degree of inflammation. On the other hand, data point to the neutrophil-lymphocyte ratio (NLR) as a more accurate risk factor for predicting unfavorable outcomes in a range of medical conditions. Patients with diabetes mellitus and impaired glucose tolerance showed higher NLRs than healthy individuals (Shiny *et al.,* 2014).

According to the current study, PLT levels in T1DM patients were significantly higher ($p<0.05$) than in the control group.As is the case in certain chronic inflammatory disorders, the size of platelets in the circulation is correlated with the degree of inflammation (Gunluoglu *et al.,* 2014).The current investigation was carried out in conjunction with the Kodiatte et al. (2012) study, which demonstrated that individuals with diabetes had higher mean platelet volumes than non-diabetics.

These findings aligned with a study by Sabor et al. (2012) that noted a rise in PLT count and that platelets from diabetic patients are hyperreactive and play a critical role in atherothrombosis. There is mounting evidence that these patients have larger, hyperreactive platelets that adhere and aggregate more readily and produce more platelet-dependent thrombin.

These results differed with studied Venkatesh *et al*. (2018) which found PLT was considerably lower in T1DM cases compared to controls. Korkmaz (2019) found no significant change in PLT between T1DM patients and controls ($p>0.05$). T1DM patients had significantly higher neutrophil counts ($p<0.05$) than the control group.These findings and their justification were in line with a 2016 study by Salman and Qasim, which found that T1DM patients had higher neutrophil counts than the healthy control group.

Huang *et al*. (2016) found that T1DM patients had higher neutrophil counts than the control group and that higher neutrophil counts were associated with an increased risk of vascular disease. These results corroborated that study.

The study conducted by Battaglia (2014) found that the decrease in neutrophils in circulation in type 1 diabetes may be due to the cells being recruited into the tissues, or it could be the result of a persistent viral infection. These findings were at odds with the latter study.

The development and maintenance of aberrant immune responses and organ damage may be significantly influenced by neutrophils. Patients with T1DM had reduced neutrophil functions, including phagocytosis, lysosomal enzyme release, and microbicidal activities (Kaplan, 2013; Lodge *et al.,* 2020).

The present study showed there were no significant ($p>0.05$) elevated lymphocytes in the patient group when compared to the control group.A 2004 study by Otton et al. found that although there was a higher percentage of diabetic lymphocytes in the patient group compared to the control group, the difference was not statistically significant.

The process of lymphocyte apoptosis is crucial for a healthy immune system operation. It controls the magnitude and duration of immune responses and eliminates developing lymphocytes that do not express an antigen receptor. Apoptotic cells may disappear if the timing of their death is off. Apoptosis problems can have disastrous consequences, including the possibility of stroke damage to the organism. However, abnormalities in the process of apoptosis can cause autoimmune diseases and play a role in the etiology of type 1 diabetes (Colucci *et al.,* 1997).

The current investigation revealed that there was no statistically significant ($p>0.05$) difference in the mean cell volume (MCV) between the control and patient groups, nor a significant difference in the hematocrit (HCT) between the patient and control groups.According to Adane and colleagues' 2020 study, DM patients had significantly lower HCT ($p <0.001$) and MCV ($p <0.001$) when compared to controls.

These findings were at odds with research by Davidson *et al.* (1981) that found that the MCV count of T1DM patients was significantly higher ($p<0.005$) than that of the control group.There was a noticeable correlation between diabetes and the erythrocyte sedimentation rate (ESR). According to the hazard ratio, men with an erythrocyte sedimentation rate in the lowest quartile may have had a lower risk of developing diabetes than men with an ESR in the top quartile. This finding lends support to the theory that inflammation plays a significant role in the etiology of diabetes (Zlonis, 1993). To diagnose ailments and monitor disease activity, the erythrocyte sedimentation rate has been extensively utilized as a nonspecific indicator of inflammation. Particularly in the context of infections and rheumatic conditions, its usefulness has frequently been contrasted with that of other acute-phase reactants, such as C-reactive protein (Gillum &Sempos, 1997).

The ESR values exhibit sensitivity to inflammation due to their influence from a variety of inflammatory factors. The inflammatory response test (ESR) has been utilized to diagnose tuberculosis since 1921. ESR is a frequently used predictive biomarker for a number of chronic conditions, including systemic inflammatory response syndrome and anti-neutrophil cytoplasmic antibody-associated vasculitis. In patients with diabetes mellitus, it can also be an independent predictor of chronic inflammation, which may lead to a recurrence of osteomyelitis (Lin *et al.,* 2016).

Similarly, Assayag et al. (2008) found that ESR counts were higher in T1DM patients than in the control group.The study by Januszewski et al. (2016), which demonstrated that T1DM patients had higher ESR counts than those without the condition, was consistent with these results.

These results disagreed with a study by Ford (2002) which recorded that the erythrocyte sedimentation rate was not significantly associated with diabetes mellitus incidence.

Biochemical Tests:

Table 2, shows the results of estimating the biochemical parameter values. Blood sugar levels increased significantly in patients when compared to the control group, while creatinine and urea levels did not change significantly ($p>0.05$) between the two groups.

Table 2: Biochemical tests (serum urea, creatinine, and blood sugar) of T1DM patients and controls.

Parameter	Diabetes mellitus type 1 Patients	Controls	*p*-values
Urea (mg/dl)	25.25± 1.155	22.68±1.300	0.2320
Creatinine (mg/dl)	0.76 ± 0.039	0.70± 0.041	0.4449
blood sugar(mg/dl)	231.93 ± 1.594 *	98.32 ± 2.721	0.00012

Results values were expressed as mean± SE, *: $p< 0.05$ or significant differences between values of parameters.

The present study showed there is a slight increase in urea and creatinine in patients compared to the control group (though not statistically significant), while blood sugar had a significant increase($p<0.05$) in the patient group compared to the control group.

Serum levels of urea, creatinine, and glucose are known to rise in uncontrolled diabetics when their blood sugar levels rise, which is typically linked to severe kidney damage. For this purpose, serum creatinine and urea measurements are readily accessible and can aid in the early detection of diabetic kidney disease and prevent it from progressing to end-stage renal disease. The breakdown product of creatinine phosphate, which is continuously released from skeletal muscle, is creatinine (Larsen & Kronenberg, 2011).

Conversely, as people aged, their kidney nephrons grew older and more worn

out, which led to an increase in urea and creatinine (Grimaldi *et al.*, 2002; Goyal *et al.*, 2012).

Biomarkers for diabetic nephropathy, such as serum urea and creatinine, are known to be elevated in uncontrolled diabetics with hyperglycemia and typically correspond with the degree of kidney damage. Serum urea and creatinine measurements are readily available tests for this purpose that can help limit the progression of end-stage renal disease (ESRD) and help detect and prevent diabetic kidney disease at an early stage. Males were more likely than females to have high serum creatinine levels, which may be related to the aforementioned fact that men have higher muscle mass than females and that creatinine is stored in muscle mass as a waste product (Kamal, 2014).

According to Zimmet *et al.* (2001), skeletal muscle releases creatinine, the breakdown product of creatinine phosphate, at a constant rate.The blood sugar level and detected increase in urea level reported by Shrestha et al. (2008) are comparable to the results of this study.The study conducted by Bamanikar *et al.* (2016) revealed that diabetics had significantly higher levels of urea and creatinine when compared to the non-diabetic control group. These findings were in line with the study's findings.

These outcomes agreed with Chutani & Pande's findings. (2017) showed an increase in levels of both serum creatinine and urea in the patient group as compared to control group and an increase in BS levels in patients as compared to control group.

A study conducted in 2016 by Hussein et al. revealed that the mean blood urea and S. creatinine levels in the diabetes subjects were significantly higher ($p \leq 0.05$) than in the non-diabetic control group. Various studies showed that blood urea levels increased proportionally to the increase in serum creatinine.

Conclusions:

The present study suggested that significant increases ($p<0.05$) were found in some inflammatory markers like WBC, platelets, neutrophils, and ESR in diabetes patients as compared with the control group.

Declarations:

Ethical Approval: It is not applicable.

Conflict of interests: The authors declare no conflict of interest.

Authors Contributions: I hereby verify that all authors mentioned on the title page have made substantial contributions to the conception and design of the study, have thoroughly reviewed the manuscript, confirm the accuracy and authenticity of the data and its interpretation, and consent to its submission.

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Availability of Data and Materials: All datasets analysed and described during the present study are available from the corresponding author upon reasonable request.

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