

## **Some Hormonal And Hematological Changes Accompanied With Type 2 Diabetes Mellitus**

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**Abstract.** The goal of this research to examine the alterations in a few and hormonal and hematological markers that took place in persons with type 2 diabetes Mellitus T2DM. The current research is being conducted at the Al-Hussein Hospital's diabetes and endocrinology center in the province of Al-Muthanna. There were 200 participants in the study: 100 were T2DM patients and 100 were controls. Patients and controls ranged in age from 24 to 50. In this study, spectrophotometry was used to assess fasting blood sugar (FBS) at 546 nm, the Sysmax-Kx-21 was used to measure hematological parameters (RBC, Hb, RDW, WBC, PLT, and MPV), and the ELSA technique was used to detect hormones (TSH, T3, and T4). The FBS of T2DM patients is considerably upper than that of control patients ( $P < 0.05$ ), according to the results. However, the findings indicate that patients with T2MD had meaningfully lower ranks of TSH, T3, and T4 when paralleled to the control grouping. Hematological parameter data indicate that patients with T2DM had significantly lower RBC and Hb when paralleled to the control grouping, but considerably upper RDW, WBC, PLT, and MPV ( $P < 0.05$ ) when paralleled to the control grouping.

### **Highlights:**

1. Higher FBS in T2DM patients compared to healthy controls.
2. Lower TSH, T3, T4 in T2DM group than controls.
3. Altered blood markers: Low RBC, Hb; high RDW, WBC, PLT, MPV.

**Keywords:** T2DM , Hormones , Blood parameters

## **Introduction**

Diabetes mellitus is a category of metabolic illnesses, have elevated blood sugar levels as a result of either insufficient insulin secreted by the pancreas or cells that are not sensitive to the insulin generated. There are several general kinds of diabetes mellitus, comprising kind 1, kind 2, gestational diabetes, and additional types(1). (T2DM) is a enduring metabolic disease caused by either an insulin secretary malfunction (deficits in insulin) or insulin resistance with insulin insufficiency(2).

Additional consequences could include diabetic foot, retinopathy, neuropathy, cardiovascular disease, chronic renal failure, poor wound healing, and erectile dysfunction (3) . The most predominant kind of diabetes, accountancy for 90–95% of entirely cases diagnosed, is type 2, which is linked to advanced age, obesity, impaired

glucose metabolism, and physical inactivity (4). Insulin resistance, a condition where cells do not use insulin as it should, is typically the primary sign of T2DM. The capability of the pancreas to decrease insulin steadily diminishes as the requirement for it increases (5). The thyroid gland conceals two main active hormones, thyroxine and triiodothyronine, which are also mentioned to as T4 and T3, separately. These hormones significantly raise the body's metabolic proportion. These hormones alter how human cells use energy-producing substances and control the metabolism of proteins, fats, and carbohydrates. Hyperthyroidism causes an aberrant reaction to glucose tolerance tests because glucose increases more quickly than usual and increases the breakdown of insulin (6). There has long been evidence that thyroid hormone (TH) influences glucose homeostasis. TH has been associated with the growth of pancreatic  $\beta$ -cells and the metabolism of glucose through the gastrointestinal tract, liver, pancreas, skeletal muscles, adipose tissue, and central nervous system (7). The formation and function of pancreatic  $\beta$ -cells have stood related to TH achievement in a number of studies. There are thyroid hormone receptors (THRs) on neonatal  $\beta$ -cells (8)(9).

It has been demonstrated that T2DM patients experience alterations in the hematological indices, such as platelet counts, white blood cell (WBC), and red blood cell (RBC) (10).

Reactive oxygen species (ROS) and glycation developments are increased in diabetes patients with persistent hyperglycemia, which alters hematological parameters (11)

## Methods

### -Subject and study location

Samples were taken from 200 participants, 100 of whom had type 2 diabetic mellitus (T2DM) and the other 100 were healthy, patients and controls ranging in age from 24 to 50, The study was conducted at the diabetes and endocrinology center of Al-Hussein Hospital in the province of Al-Muthanna

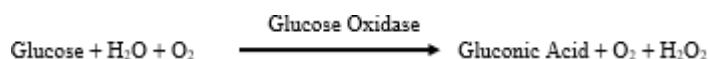
### -Blood sample

After a 12-hours fast, six milliliters of blood were extracted, The blood samples were separated into two portions. The first 2 milliliters were placed in an EDTA tube to estimate the hematological parameters. The second stayed left to coagulate at room temperature in a gel test tube. The serum stayed aspirated following centrifugation at

4000 cycles per minute for 5 minutes. Fasting blood sugar (FBS) was measured on the day of collection, and the serum stood then kept at -20°C until it was needed to estimate the hormonal parameters (TSH, T3, and T4).

### **Calculating the concentration of fasting blood sugar (FBS)**

By using an enzymatic colorimetric test, plasma glucose was determined. The glucose level was assessed according to (12)(13). It uses hydrogen peroxide to liberate glucose oxidase, which enzymatically oxidizes glucose to gluconate. Then, peroxide reacts with phenol to generate quinonimine, which is measured spectrophotometrically at 546 nm using the following equations.



### **Assessment the levels of Thyroid stimulating hormones , Triiodothyronine and Tetraiodothyronine)**

Using a specialized kit supplied by Monobind Inc., USA, the Enzyme Linked Immune Sorbent Assay (ELSA) process stood used to quantify the levels of triiodothyronine (T3), thyroid stimulating hormones (TSH), and tetraiodothyronine (T4) in human serum or plasma, The wavelength (450 nm) at which the absorbance was measured (14)(15). The fundamental components required for solid stage enzyme immunoassay are , enzyme-antigen conjugate, native antigen and substrate and immobilized antibody. when an enzyme-antigen conjugate, immobilized antibody, and serum comprising native antigen are combined. For a restricted amount of antibody binding sites, a competitive process occurs among the enzyme-antigen conjugate and the natural antigen.

### **Evaluation of Hematological Parameters**

Samples of blood were put in an EDTA tube and then gently mixed using a blood mixer, Following that, Sysmax-Kx-21 was used to assess all complete blood cell counts (CBC), which comprise RBC, Hb, RDW, WBC, PLT, and MPV(16). Statistical analysis

This study used a completely randomized design (CRD) and employed the independent t-test, one-way ANOVA, and the least important differentiation at the ( $P < 0.05$ ) flat of import to parallel treatment means. The statistical program social science (SPSS 22) stood used to process and investigate the information, and the results were presented as Mean  $\pm$  SD (17).

## Result and Discussion

The results demonstrated that sick with T2DM had upper fasting blood sugar (FBS) ranks than those in the controlling group ( $P > 0.05$ ), whereas the TSH, T3, and T4 of the patients showed considerably decrease than those of the control grouping ( $P > 0.05$ ), as table (1).

Table(1) FBS and Hormonal factors in patients with T2DM and control

<b>Parameters</b>	<b>Control Mean<math>\pm</math>SD</b>	<b>patients with T2DM Mean<math>\pm</math>SD</b>
<b>FBS mg/dL</b>	82.11 $\pm$ 9.32	239.57 $\pm$ 26.16*
<b>TSH (<math>\mu</math>IU/ml)</b>	3.62 $\pm$ 0.57	1.59 $\pm$ 0.63 *
<b>T3 (ng/dl)</b>	2.15 $\pm$ 0.38	0.7 3 $\pm$ 0.19 *
<b>T4 (<math>\mu</math>g/dl)</b>	4.86 $\pm$ 0.79	2.10 $\pm$ 0.96 *

\*represent significant difference between T2DM patients and control subjects

According to the results of hematological parameters, sick with T2DM had significantly lower ranks of hemoglobin (Hb) and red blood cells (RBC) than the controlling group ( $P < 0.05$ ). However, the current findings indicate that sick with T2DM had meaningfully higher ranks of RBCs distribution width (RDW), (WBC), (PLT), and mean platelet volume (MPV) than control subjects ( $P < 0.05$ ), as table(2).

Table (2) Hematological parameters in patients with T2DM and control

<b>Hematological factors</b>	<b>Control Mean±SD</b>	<b>patients with T2DM Mean±SD</b>
<b>RBC</b> <b>10<sup>6</sup> /μL</b>	5.91± 1.02	3.24 ± 0.96*
<b>RDW (%)</b>	12.69±073	16.07±1.25*
<b>Hb</b> <b>g/dl</b>	13.26±1.30	9.43±1.62*
<b>WBC</b> <b>10<sup>3</sup> /μL</b>	5.32 ± 0.79	10.73 ±1.12 *
<b>PLT</b> <b>10<sup>3</sup> /μL</b>	231.22± 28.12	275.87±.33.90*
<b>MPV</b> <b>Fl</b>	6.97 ±0.33	9.69 ±0.15*

\*represent significant difference between T2DM patients and control subjects .

## Discussion

Excessive blood glucose ranks are a hallmark of diabetes mellitus.(T1DM) is triggered through a partial or whole lack of insulin excretion by the pancreas, while (T2DM) is triggered through insufficient insulin use by body cells, demonstrating how it affects the metabolism of proteins, lipids, and carbohydrates(18)(19). (T2DM) is brought on by insulin's incapacity to improve glucose absorption and consumption in peripheral tissues (muscle, liver, and adipose tissue), insulin fighting, and a progressive decline in beta cell insulin production, which raise blood sugar levels(20) .The thyroid gland influences the body's metabolism in addition to the pancreas. The thyroid gland secretes hormones that control insulin secretion and the metabolism of carbohydrates. There is a strong relationship between these two hormones. Therefore, any alteration in one hormone's level may have an impact on the efficacy of another hormone (18). TSH, T3, and T4 levels in persons with T2DM were significantly lower in the current study. This finding may be because thyroid disorders and diabetes mellitus have a strong underlying link. Diabetes can change thyroid function, and thyroid hormone is involved in regulating

pancreas and glucose metabolism. Diabetes reduces TSH's reaction to thyrotropin-releasing hormone (TRH), which lowers T3 and T4 hormone levels and causes hypothyroidism (21). Lower T3 levels in T2DM are caused by a decline in the alteration of T3 from T4, and hyperglycemia causes a reversible drop in the concentration of hepatic thyroxine and deiodinase activity. 5' adenosine monophosphate-activated protein kinase (AMPK) may be the primary goal for modifying insulin sensitivity regulation and thyroid hormone feedback, which are connected to hunger and energy expenditure (22). The release of insulin is directly impacted by thyroid hormones. Changes in thyroid hormones raise the hazard of T2DM and can cause problems or exacerbate symptoms of the disease. Low thyroid hormones cause beta cells to produce less insulin (23). weakened glucose absorption from the peripheral glucose buildup, gastrointestinal tract, and impaired glucose clearance are the hallmarks of hypothyroidism, or low thyroid hormones (24). Thyroid hormone decline can have a variety of effects on type 2 diabetes's glucose metabolism. For example, a translocation of the GLUT 2 gene may source a lowered amount of insulin-stimulated glucose transport in subclinical hypothyroidism, which can prime to insulin resistance. Furthermore, anorectic conditions may also be a factor in hypothyroidism's decreased insulin production (25), where it was found that when hypothyroid, peripheral muscles lose their sensitivity to insulin (26). The research conducted by (27) discovered a direct connection between hypothyroidism and insulin resistance. RBC count and Hb concentration stood meaningfully lower in T2DM sick than in controls in the existing training, which is inconsistent with findings from studies by (28) and (29), which found that T2DM patients had higher RBC counts and Hb concentrations than controls. The decline in RBC and Hb in this study could be due to nonenzymatic glycosylation of Hb and RBC membrane proteins and increased production of ROS caused by prolonged hyperglycemia, which accelerates the aging of RBCs (30)(31)(32). Type 2 Diabetes mellitus -related chronic inflammation is typified by raised ranks of inflammatory cytokines, counting (IL-6) and (IL-1), these pro-inflammatory cytokines change the susceptibility of erythroid progenitors to erythropoietin, support immature RBC apoptosis, and decrease the quantity of circulating RBCs, which leads to anemia of inflammation (33).

According to the current study, T2DM patients had considerably higher RDW values than control groups. This result is consistent with (34). A higher RDW indicates

that there is heterogeneity among the circulating red blood cells, which is linked to erythropoiesis dysfunction and RBC deterioration(35). T2DM is frequently related with long-lasting inflammation and elevated oxidative stress, both of which are known to lower RBC survival, causing variations in RBC size and a decline in RBC count (36). In relation to WBC indices, the current research displayed that individuals with T2DM had higher total WBC counts. These findings are consistent with (37). An elevated WBC count could be the result of persistent hyperglycemia in diabetes, which raises the formation of (ROS) and glycation developments, altering hematological parameters. Additionally, elevated ROS production and glycation developments in persons with T2DM result in oxidative stress that is connected to tissue destruction and hematological deviations, for instance erythrocyte dysregulation, activated WBC, raised WBC counts, and PLT hyperactivity (37)(11). The study conducts by (38) there is no discernible difference in the RBC, WBC, and platelet counts of diabetic sick and well controls. The existing training's findings showed that T2DM patients had considerably greater MPV and platelet counts than the controls, which is consistent with research by (39). These findings could be caused by platelet and MPV, which are markers of thrombotic possible and the hazard of vascular problems in people with diabetes. The relief of S100A8/A9 via neutrophils may inductions IL-6 creation and thrombopoietin production from hepatocytes. this exciting bone marrow to produce more reticulated platelets, which stay linked to atheroprogession and atherothrombosis (40), The additional causes could be because platelet size and function are connected, and higher MPV, a measure of average size and platelet activity, is indicative of larger circulating platelets (41).Type 2 diabetic mellitus platelets stay lager , It have denser granules and stay more enzymatically and functionally overactive than smaller platelets, they create extra prothrombotic parameters for example thromboxane A<sub>2</sub>, serotonin, P-selectin, and platelet factor 4, which increases the risk of thrombotic events(42). Numerous variables, such as inflammation, endothelial dysfunction, oxidative stress, ,hyperglycemia and insulin resistance are also linked to platelet over activity in sick with T2DM (43)(44).

## Conclusion

We conclude from this research that there are significant alteration in concentration of some hormones ( TSH, T<sub>3</sub> , T<sub>4</sub>) and blood parameters(RBC, Hb, RDW, WBC, PLT, and MPV) for in sick with T2DM.



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