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Relationship between Uric Acid with Thyroid Disorders of Diabetic Patients in Iraq

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***Abstract*—Uric acid is the product of purine metabolism. its raised can lead to complications associated with metabolic diseases. We seek to shed light on the association between thyroid disorders in diabetes and hyperuricemia. The aim of this study is to demonstrate the association of uric acid with diabetes and its chronic complications through aspects of pathogenesis and clinical research Anthropometric, clinical, and hormonal measurements. patients (140) were divided into three groups. Sixty T2DM with euthyroidism (G_1), fifty T2DM with hypothyroidism (G_2), and Thirty T2DM with hyperthyroidism (G_3). A high significant correlation ($P < 0.01$, $P= 1$) between uric acid Vs. G_1, G_2, and G_3 groups. Uric acid significantly differed at ($P< 0.05$) between (G_1 Vs. G_2), and (G_1 Vs. G_3) .A negative correlation between uric acid and thyroids hormones at G_1, G_2, and G_3 groups. The study showed the effect of uric acid through the correlation coefficient for both clinical and hormonal indicators in diabetic patients with thyroid dysfunction.**

***Keywords*— Diabetes mellitus, Thyroid function test, Uric acid, Hyperuricemia, Lipid profile.**

I. INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a complex disease with chronic metabolic symptoms. T2DM patients suffer from a commixture of genetic profiles and unhealthy lifestyle. The global prevalence is 9.1%, which equates to 415 million adults being affected by illness [1].

Risk factors for complications of hypothyroidism were identified through thyroid function tests even before symptoms were detected, so the subclinical diagnosis of thyroid dysfunction is clearer [2]. Naturally, uric acid is produced as a final component of purine metabolism within levels that are supposed to remain constant in the blood, while its elevation indicates an imbalance between its production and excretion [3]. Accordingly, uric acid has been indicated as an independent predictive factor for metabolic disorders such as metabolic syndrome, diabetes, and hyperlipidemia, in addition to chronic kidney disease and cardiovascular disease [4-7]. Hyperuricemia was becoming a significant medical problem worldwide, and its prevalence has increased dramatically in the past few decades [8-9]. Many epidemiological studies suggest that hyperuricemia is associated with hypertension, cardiovascular disease, diabetes, and dyslipidemia, so that; uric acid can be exert influence on thyroid hormones [10].
Endocrine disorders refer to large metabolic diseases, the most common of which are diabetes and thyroid dysfunction. In addition to publishing reports indicating the existence of an important correlation between thyroid diseases and diabetes, because the thyroid has a general role in maintaining glucose metabolism and insulin function. While diabetes can affect thyroid function, as evidence shows a decrease in the response of thyrotropin-releasing hormone, causing a decrease in T_3, on the other hand, it is noted that even a brief rise in T_3 can result in insulin resistance, which in turn can lead to the development of T2DM [10] .

Studies show uncontrolled deterioration status in patients with T2DM, which they have factors like variations in β-cell mass and a reduction in insulin secretion, increased rapid glucagon secretion, insulin resistance, and increased catecholamine levels that lead to hyperthyroidism [11- 12]. Lower TSH levels reduce thyroid hormone levels and reduce insulin antagonism. As TSH levels decrease, thyroid hormone levels increase and insulin antagonism increases. Increased insulin resistance is the most obvious feature in patients with hyperthyroidism, but the mechanism has not yet been clarified [13]. Recently, energy balance problems have been detected using a thyroid hormone sensitivity test (FT4 and TSH) as well as account their excessive elevation as a diagnostic guide to thyroid hormone syndrome [14].

The symptoms of hypothyroidism include decreased hepatic glucose synthesis, impaired glucose elimination, extended peripheral glucose buildup, gluconeogenesis, and decreased absorption of glucose from the gastrointestinal tract [15].

On the other hand, different effects of hypothyroidism on glucose metabolism in T2DM can occur. Insulin resistance can also result from subclinical hypothyroidism because of a slowed rate of insulin activation. GLUT 2 generation [16] translocation brought on by glucose.

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Furthermore, a study found that decreased kidney clearance of insulin in hypothyroidism resulted in a lower physiological need for the hormone. In hypothyroidism, anorexia may be a contributing factor to decreased insulin production. Moreover, several preclinical and clinical investigations have linked hypothyroidism to insulin resistance [17].

Peripheral muscles in hypothyroid conditions exhibit reduced sensitivity to insulin, according to in vitro investigations [18]. Dysregulation of uric acid metabolism suggests a probable role for such disorders [19]. Moreover, numerous writers have demonstrated a clear connection between hypothyroidism and insulin resistance [20]. Nonetheless, certain investigators have noted incongruous results, underscoring the necessity for additional investigation in this domain.

The aim of this study: To demonstrate the association of Aspects of etiology and clinical research about uric acid and diabetes and its chronic consequences Clinical, anthropometric, and hormone.

II. PATHEINT AND METHODS

Patients: One hundred forty patients with a duration of illness exceeding 10 years participated in this study, divided into three groups. Sixty T2DM with euthyroidism (G_1), Fifty T2DMwith hypothyroidism (G_2), and Thirty T2DM with hyperthyroidism (G_3), age between (33-65) years. Weight, age, gender, and BMI were all recorded. The formula for calculating BMI was weight (in kilos) divided by height (in square meters). The participants were selected from the National Diabetic Centre -Mustansiriyah University during October and February 2023. Biochemical parameters: blood samples were obtained for laboratory analysis, which included measurement of fasting serum glucose (FSG), glycated haemoglobin (HbA1c), total cholesterol (TC), high-density lipoprotein (HDL), and low-density lipoprotein (LDL), triglycerides, as well as lipid profile, uric acid measured by cobas e111/Germany. Mini Vidas with Biometric Kits were measured serum total tri-iodothyronine (TT3), total thyroxin (TT4) and TSH.

A. STATISTICAL ANALYSIS

The data was displayed as Mean SD. The statistical analysis was conducted using the LSD method, with a significant threshold of P 0.05. Version 22 of the SPSS program (SPSS, Chicago, USA) was used.

III. RESULTS

The sequence parameters data were listed in Tables 1-6. A significant increase was seen between the groups ($P < 0.001$) G_1, G_2, and G_3 were obtained for age and body mass index (BMI). Regarding clinical parameters, a highly significant increase at ($P < 0.05$) were observed for FSG, HbA1c, and lipids profile except LDL it had insignificant at ($P > 0.05$), but a statistically high significant decrease at ($P < 0.05$) HDL see Table 1, and 2. Furthermore, the thyroids hormonal levels were shown a highly significant at ($P < 0.05$) among the study groups see Table 3, while uric acid levels had been recorded a highly difference significantly between Euothyroid Vs. Hypothyroid groups and Euothyroid Vs. Hyperthyroid groups at significant at ($P < 0.05$).

A statistically significant high correlation ($P < 0.01$, $P= 1$) was observed between the level of uric acid Vs. Euothyroid, Hypothyroid, and Hyperthyroid groups see Table 5. while as it is showed [Table 6] Uric acid levels and other parameters are negatively correlated with thyroids hormones at Euothyroid, Hypothyroid, and Hyperthyroid groups .

TABLE 1. ANTHROPOMETRIC MEASUREMENT AMONG STUDY GROUPS (EUTHYROID G_1, HYPOTHYROIDISM G_2, AND HYPERTHYROIDISM G_3)

	(G_1) (mean ±SD) (n=60)	**(G_2) (mean ±SD) (n=50)**	**(G_3) (mean ±SD) (n=30)**	**ANOVA (F value) (Tukey HSD Post Hoc test Significance)**
AGE (year)	43.383±9.72	51.200±7.06	49.933±7.09	F=13.5601*(a, b)
M/F ratio	1.0	1.0	1.0	
BMI (kg/m^2)	27.195±4.02	28.147±2.63	29.580±3.46	F = 4.7787*(b)

[a] Difference between Euothyroid Vs. Hypothyroid groups. The result is significant at $p < 0.05$.
[b] Difference between Euothyroid Vs. Hyperthyroid groups. The result is significant at $p < 0.05$.
* The p-value is < 0.00001. The result is highly significant at $p < 0.05$.
** The p-value is > 0.05. The result is insignificant at $p < 0.05$.

TABLE 2. BIOCHEMICAL PARAMETERS AMONG GROUPS OF STUDY (EUOTHYROID G_1, HYPOTHYROID G_2 , AND HYPERTHYROID G_3)

	(G_1) (mean ±SD) (n=60)	**(G_2) (mean ±SD) (n=50)**	**(G_3) (mean ±SD) (n=30)**	**ANOVA (F value) (Tukey HSD Post Hoc test Significance)**
FSG (mg/dl)	95.017±9.02	191.500±69.22	184.067±72.658	F=52.6808*(a, b)
HbA1c (%)	5.158±0.481	8.428±2.113	8.833±2.259	F=72.8435*(a, b)
TG(mg/dl)	106.717±25.81	168.420±77.509	174.500±80.485	F=18.5263*(a, b)
TC(mg/dl)	176.150±34.813	218.280±48.656	217.767±47.250	F=16.3762*(a, b)
LDL (mg/dl)	106.643±32.239	113.753±39.022	107.770±36.808	F= 0.4941**
HDL (mg/dl)	49.283±6.977	45.620±6.324	45.367±8.845	F=4.6825*(a, b)

TABLE 3. HORMONAL PARAMETERS AMONG GROUPS OF STUDY (EUOTHYROID G_1, HYPOTHYROID G_2 AND HYPERTHYROID G_3)

	(G_1) (mean ±SD) (n=60)	**(G_2) (mean ±SD) (n=50)**	**(G_3) (mean ±SD) (n=30)**	**ANOVA (F value) (Tukey HSD Post Hoc test Significance)**
TSH (µU/ml)	1.727±0.844	16.264±7.630	0.047±0.010	F=174.6998*(a, c)
TT_4 (µmol/l)	92.317±24.325	56.680±10.267	185.767±47.745	F=205.1646*(a, b, c)
TT_3 (µmol/l)	1.862±0.496	0.825±0.241	4.507±1.698	F=175.1934*(a, b, c)

TABLE 4. URIC ACID LEVELS AMONG GROUPS OF STUDY (EUOTHYROID G_1, HYPOTHYROID G_2 AND HYPERTHYROID G_3)

	(G_1) (mean ±SD) (n=60)	(G_2) (mean ±SD) (n=50)	(G_3) (mean ±SD) (n=30)	ANOVA (F value) (Tukey HSD Post Hoc test Significance)
S. Uric acid (mg/dl)	4.075±0.65	5.848±1.47	5.433±0.89	F=40.9499*(a, b)

TABLE 5. COEFFICIENT OF CORRELATIONS (R) OF URIC ACID AMONG THE STUDY GROUPS

	S. Uric acid euothyroid (r)	S. Uric acid hypothyroid (r)	S. Uric acid hyperthyroid (r)
S. Uric acid (r) euothyroid	**1**	**0.070**	**-0.293**
S. Uric acid (r) hypothroid	**0.070**	**1**	**-0.215**
S. Uric acid (r) hyperthroid	**-0.293**	**-0.215**	**1**

TABLE 6. COEFFICTNT OF CORRELATION (r) OF URIC ACID WITH T3, T4, AND TSH AMONGE THE STUDY GROUPS.

	Euothyroid (Uric acid (mg/dl) (r)	Hypothyroid (Uric acid (mg/dl) (r)	Hyperthyroid (Uric acid (mg/dl) (r)
T_3 (µmol/l)	-0.151	-0.143	0.202
T_4 (µmol/l)	-0.118	0.077	0.101
TSH (µU/ml)	-0.132	0.140	0.206

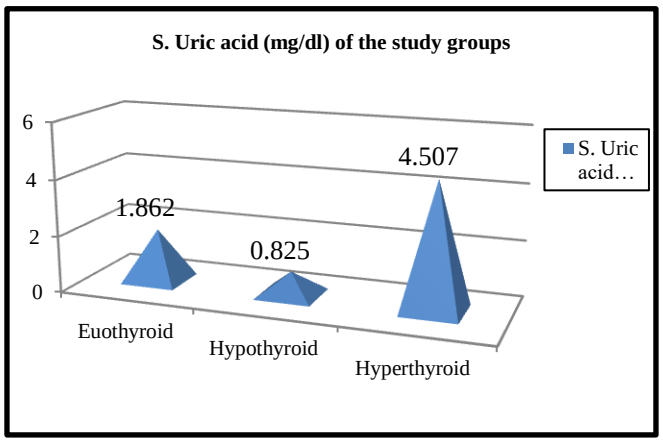

Figure 1. Uric acid levels among groups of study (Euothyroid, Hypothyroid and Hyperthyroid)

IV. DISCUSSION

The factors that lead to T2DM are often complex genetic or epidemiological, causing chronic complications for patients, and a problem of great concern around the world [21]. The effect of Hyperuricemia has been confirmed through in vivo experiments. Several studies are consistent with our results on BMI, glucose tests, and lipid profiles [22], since that T2DM patient with thyroidsium have higher insulin resistance than T2DM controls. Moreother, people with hyperuricemia showed a greater increase in insulin resistance compared with people had normal uric acid level in T2DM patients with thyroid disorders [23].

The relationship between uric acid, diabetic macroangiopathy, and atherosclerosis has been studied in many studies [24- 26]. The results showed that the groups had significantly higher levels of blood uric acid [27- 28] consistent with the results of the current study. Researchers have found that among hospitalized T2DM patients, hyperuricemia is associated with a higher prevalence of atrial fibrillation [29-30]. Disease-onset atrial fibrillation, which is four times more likely to be caused by hyperuricemia and is associated with cardiovascular disease and death [24], is the result of hyperuricemia.

Metabolic disorders diseases occur as a result of raising blood acidity permanently [31- 33], as in hyperuricemia case where insulin signals are directly affecting or blocking the receptor-level recruitment of ectonucleotide pyrophosphatase/ phosphodiesterase 1 (ENPP1) [34]. Accordingly, there are overlapping factors affecting on glucose metabolism and insulin sensitivity [24]. In addition, the liver's contribution play a main role in hyperglycemia, developing acquiring hyperinsulinemia, glucose intolerance, and peripheral insulin resistance [35]. Glucose intolerance in thyrotoxicosis is caused by increased hepatic glucose production and accelerated glycogenolysis [36].

The most significant connection between hypothyroidism, thyroid dysfunction, and type 2 diabetes is insulin resistance among the aforementioned variables. Rather than hepatic insulin resistance, hyperinsulinemia is caused by excessive glucose production. Furthermore, in T2DM patients receiving insulin, increasing fasting plasma glucose (FPG) concentrations have been demonstrated to be significantly regulated by increased hepatic glucose production [37].

Furthermore, absorption efficiency decreases when insulin resistance increases, leading to an increase in muscle glucose, as well as, an increased glucose liver production causes an exacerbation of the problem. In this respect, it is important to note that hyperinsulinemia can arise in hypothyroidism as well as hyperthyroidism. Recent research suggests that lipid metabolism may be reduced by insulin resistance [38]. Thus, it seems that thyroid dysfunction and diabetes type 2 may be related to insulin resistance. Similarly, another study found a negative correlation between TSH and insulin resistance as well as \-cell malfunction. This relationship may be explained by the thyroid hormones' insulin-antagonistic characteristics in conjunction with increased TSH. Reduced TSH levels are frequently the consequence of elevated blood T3 and T4 levels via a negative feedback mechanism [39].

Today, it is common knowledge that thyroid hormones play as clinical entities exceedingly associated with metabolic health. Previous studies have reported a cross-sectional association between thyroid hormone sensitivity and diabetes, but the relationship is not yet clear. We aimed to study the relationship about hyperuricemia in diabetic patients with thyroid hormone dysfunction [40- 41].

V. CONCLUSIONS

Our study revealed that insulin resistance mediates the relationship between impaired sensitivity to thyroid

hormones and hyperuricemia in the euthyroid group. TG, FBG, and HbA1c levels were lower in subjects with normal uric acid levels in type 2 diabetic patients with thyroid disease, as indicated by higher TC, LDL-C, and HbA1c levels and lower HDL-C levels. There was a significant increase in these results might offer helpful hints for comprehending how reduced thyroid hormone sensitivity and hyperuricemia interact in patients with hypothyroidism, and weight loss may contribute remedy thyroid hormones sensitivity that suggest clinical significance.

CONFLICT OF INTEREST

Authors declare that they have no conflict of interest

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