

Evaluation of Thyroid Function Test in Sudanese Patients with Type 2 Diabetes Mellitus

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ABSTRACT

Diabetes mellitus (DM) is a very common endocrinological disorder with inappropriate hyperglycemia due to either an absolute deficiency of insulin secretion or a reduction in the biological effectiveness of insulin or both. The present study was carried out aiming to evaluate thyroid function in patients with type 2 DM. In this case-control study, a total of 90 subjects were recruited to participate, where 45 subjects were diagnosed as type 2 DM as the study group and other 45 subjects were apparently healthy as control group to evaluate the effect of DM on thyroid function. Thyroid dysfunction was evaluated by investigating the subjects for Total tri-iodothyronine (T3), Total thyroxine (T4) and thyroid stimulating hormone (TSH). All these parameters were measured by using ELISA technique, fasting plasma glucose (FPG), and glycated hemoglobin (HbA_{1c}) were measured spectrophotometrically. Statistical analysis was performed using software statistical package for social sciences (SPSS) version 21 using independent samples test, Pearson's correlation. Independent samples test analyses showed a significant decrease in mean level of T3, T4 ($p<0.05$) for both, while significant increase was observed in TSH level ($p<0.05$) when compared with the control group. Person's correlation reveals that there were insignificant positive correlation between FPG, HbA1c and duration of DM with the study parameters (T3 and T4) with $p> 0.05$ and insignificant negative correlation between FPG, HbA1c and duration of DM with the study parameter (TSH) with $p> 0.05$. Abnormal thyroid function was found to be higher in type 2 diabetes mellitus subjects when compared to non-diabetic subjects.

Key words: Diabetes mellitus, Hypothyroidism, T3, T4, TSH.

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INTRODUCTION

Diabetes mellitus (DM) a common endocrine metabolic disorder, is a leading cause of death worldwide (Faghilimnai et al., 2006). It is characterized by hyperglycemia resulting from a variable interaction of hereditary and environmental factors and is due to the combination insulin resistance (impairment in insulin-mediated glucose disposal) and defective secretion of insulin by pancreatic β -cells or both (World Health Organization, 1985). The WHO estimate of diabetes prevalence for all age groups world was 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030 (Wild et al., 2007). New addition to these complications is the thyroid dysfunction which is

indicated by the recent studies (Parpazafiropoulou et al., 2010; Swamy et al., 2012).

The first report showing the association between diabetes and thyroid dysfunction was published in 1979 (Feely and Isles, 1979; Gray et al., 1979). Since then a number of studies have estimated the prevalence of thyroid dysfunction among diabetes patients to be varying from 2.2 to 17%, the most common disorder being subclinical hypothyroidism (Perros et al., 1995; Smithson et al., 1998). However, few studies also estimated much higher prevalence of thyroid dysfunction in diabetes that is, 31 and 46.5%, respectively (Celani et al., 1994; Udoing et al., 2007). Thyroid hormones are insulin antagonists, both insulin and thyroid hormones are involved in cellular

Table 1. Descriptive summary for the study variables within diabetic and nondiabetic groups.

Variables	Type 2 DM (n=45) $\bar{x} \pm SD$	Non-diabetic (n=45) $\bar{x} \pm SD$
Age/years	48.73 \pm 2.57	45.01 \pm 3.64
Gender	F 23.51% M 22.59%	F 28.62% M 17.38%
Fasting blood glucose (mg/dl)	256.17 \pm 99.9	-
HbA1c (%)	9.7 \pm 1.86	-
Duration of DM (Years)	6.29 \pm 1.11	-

*Results expressed as Mean \pm SD and significant difference considered as p-value \leq 0.05.

metabolism and excess and deficit of any one can result in functional derangement of the other (Sugure et al., 1999). Thyroid disease is a pathological state that adversely affects diabetic control and is commonly found in most forms of DM. Diabetes mellitus appears to influence thyroid function in two sites; first at the level of hypothalamic control of TSH release and secondly at the conversion of T4 to T3 in the peripheral tissue. Marked hyperglycemia causes reversible reduction of the activity and hepatic concentration of T4-5-deiodinase, low serum concentration of T3, elevated levels of reverse T3 and low, normal or high level of T4 (Shah et al., 2007).

MATERIALS AND METHODS

This descriptive analytical case-control study carried out in Khartoum State during December 2015 to March 2016 from the Diabetic and Endocrinol Hospital and abdalmonem diabetic center. Ninety subjects were enrolled in this study, classified as 45 diagnosed T2DM and 45 apparently healthy subjects as control. All diabetic patients were diagnosed with Diabetes mellitus based on the American Diabetes Association Criteria for type 2 Diabetes Mellitus:

1. Fasting plasma glucose level higher than 126 mg/ dl
2. Plasma Glucose level exceeding 200 mg/ dl at 2 h in the 75 g oral glucose tolerance test.
3. Symptoms of Diabetes and Random plasma glucose >200 mg/ dl.
4. HbA1C $> 6.5\%$.

Patients taking drugs that influence the thyroid function, post partum women, subjects with acute illness that affects thyroid hormones status, and patients who present with complain of fever, neck pain and viral infection were excluded from this study. Both cases and controls were non-alcoholic, non-smoker and non-hypertensive. The study has been approved by the local ethics committee of Al-Neelain University. All participants in the study were given their written informed consent considering the aims of the study and sample and clinical information's were used anonymously. A 5 ml of venous blood specimens were collected from all subjects. 2.5 ml was added to a container that contains fluoride oxalate as

anticoagulant for estimation of plasma glucose and HbA1c, and another 2.5 ml of blood were allowed to clot at room temperature for 1 h, and then subjected to centrifugation for 3 min at 4000 rpm. Then serums were stored at -20°C until assay.

Laboratory Analysis

Plasma glucose and HbA_{1C} were measured using semi automated clinical chemistry analyzer. The serum levels of tT3, tT4 (competitive enzyme immunoassay) and TSH (sandwich enzyme immunoassay) were measured by enzyme immunoassay analyzer URIT-660.

Statistical Analysis

Statistical analysis was performed using software statistical package for social sciences (SPSS) version 21, quantitative results were analyzed statistically using independent samples test, Pearson's correlation was used to correlate between study parameter and study variables. P- value less than 0.05 was considered as statistically significant at 95% confidence intervals.

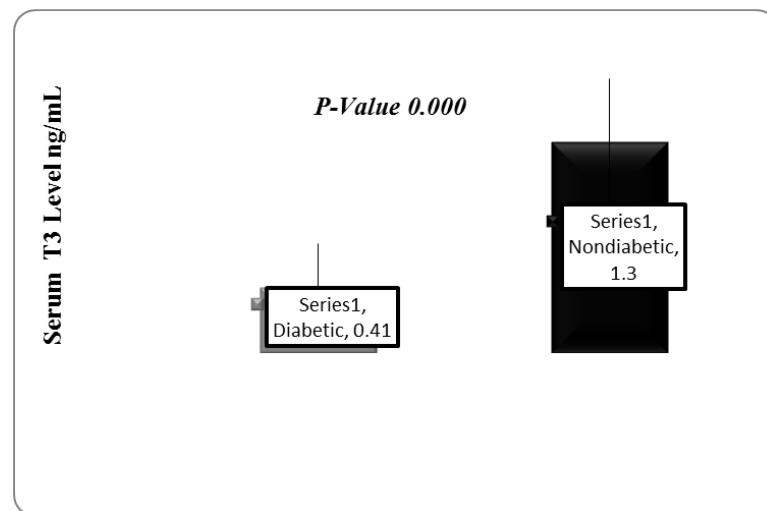
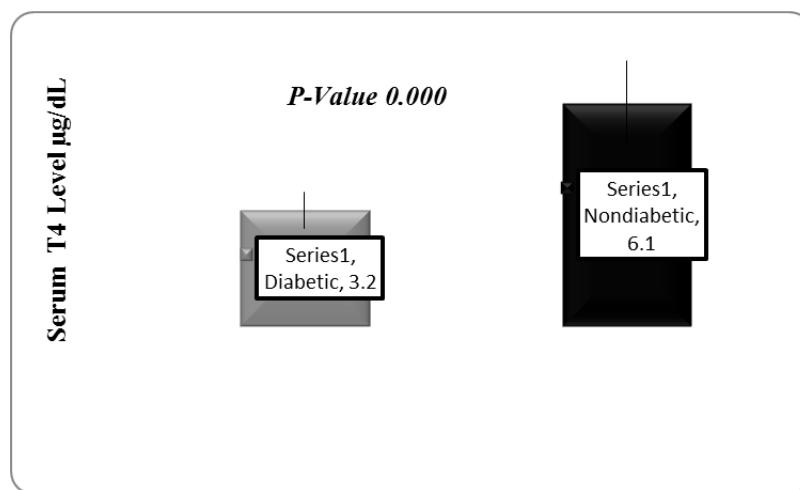
RESULTS

All subjects were age matched ranged from (50 to 60) years old. Samples were analyzed to measure the level thyroid function test, and the results were analyzed statistically and data were represented as mean \pm SD. Table 1 shows a descriptive summary for the study variables within diabetic and non-diabetic groups. Comparison of thyroid hormone levels between DM and non-diabetic subjects was presented in Table 2 and Figure 1 there were a highly significant decrease in the levels of serum T3 in a comparison to the control group ($p < 0.05$) where the mean level of T3 0.4 ± 0.3 (ng / ml) for test group and 1.3 ± 0.4 (ng / ml) for control group. Table 2, Figure 2 also demonstrated a highly significant decrease in the levels of serum T4 in a comparison to the control group ($p < 0.05$) where the mean level of T4 3.2 ± 0.5 (μ g / dl) for test group and 6.1 ± 1.2 (μ g / dl) for control group. Table 2 and Figure 3 illustrate that there were a highly significant increase in the levels of serum

Table 2. Comparison for mean level of thyroid hormones levels between diabetic and non-diabetic subjects.

Variables	Patient Mean \pm SD N=45	Control Mean \pm SD N=45	p-value
T3(ng/ml)	0.4 \pm 0.3	1.3 \pm 0.4	0.002
T4 (μ g/dl)	3.2 \pm 0.5	6.1 \pm 1.2	0.02
TSH (μ IU/ml)	10.7 \pm 2.8	1.1 \pm 1.2	0.001

*Results expressed as Mean \pm SD and significant difference considered as p-value \leq 0.05.

**Figure 1.** Comparison of serum T3 level between T2DM and non-diabetic subjects.**Figure 2.** Comparison of serum T4 level between T2DM and non-diabetic subjects.

TSH in a comparison to the control group ($p < 0.05$) where the mean level of TSH 10.7 ± 2.8 (μ IU /ml) for test group and 1.1 ± 1.2 (μ IU /ml) for control group. Table 3 Shows the Correlation between study parameters and variables in Diabetic patients.

DISCUSSION

The thyroid hormones are insulin antagonists that also

potentiate the action of insulin indirectly. TRH synthesis decreases in diabetes mellitus. These facts could be responsible for the occurrences of low thyroid hormone levels in some diabetics. The level of TSH in our study was significantly higher in type 2 diabetes mellitus subjects than in non-diabetics healthy subjects ($p < 0.05$). Results obtained from present study have shown that in type 2 diabetes mellitus, hypothyroidism is frequently observed. The results of present study were in

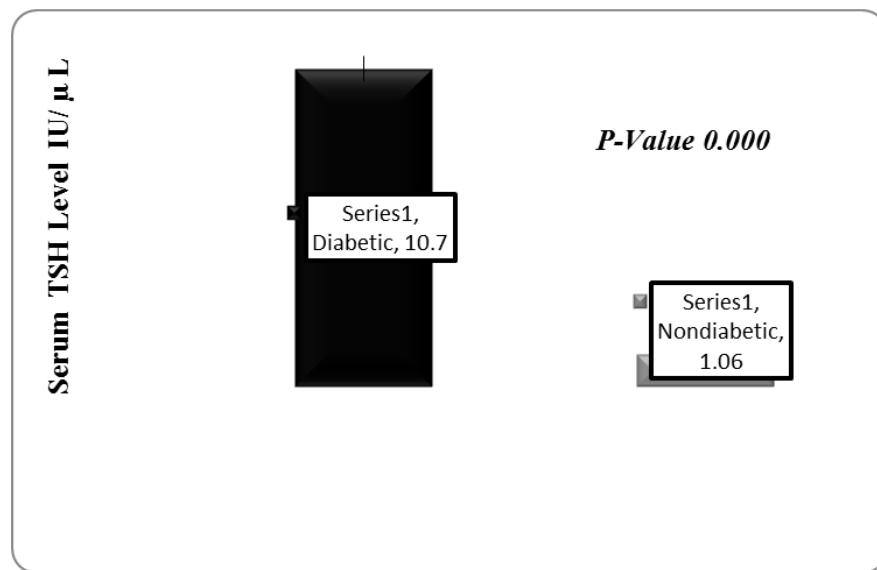


Figure 3. Comparison of serum TSH level between T2DM and non-diabetic subjects.

Table 3. Correlation between study parameters and variables in Diabetic patients.

	FBG	HBA₁C	Duration	T3	T4	TSH
FBG <i>R</i> -value		0.941	-0.068	0.045	0.003	-0.073
<i>p</i> -value		<0.001	0.656	0.769	0.983	0.635
HBA ₁ C <i>R</i> -value	0.941 ⁺⁺		0.005	0.104	0.074	-0.015
<i>p</i> -value	<0.001		0.972	0.495	0.629	0.920
Duration <i>R</i> -value	-0.068	0.005		0.240	0.190	-0.039
<i>p</i> -value	0.656	0.972		0.113	0.212	0.797

R indicates positive or negative correlation, P-value indicates strength of correlation.* Mean significant correlation. ** Mean highly significant correlation. *Results expressed as Mean \pm SD and significant difference considered as *p*-value ≤ 0.05 .

accordance with the reports of (Vinu et al., 2012. Singh et al., 1994, Swamy et al 2012, Suzuki et al., 1994, Celani et al., 1994, Demitrost et al., 2012 and Witting et al., 2014). The findings of this study are in line with what found by who recommended that thyroid screening is essential among diabetics to detect subclinical or clinical hypothyroidism (Aziz, 2015). The abnormal thyroid hormone level may be the outcome of various medications was receiving. For example, it is known that insulin (Boehringer, 1984), an anabolic hormone enhances the level of FT4 while it suppresses the level of T3 by inhibiting hepatic conversion of T4 to T3. On the other hand some of the oral hypoglycemic agents such as the phenylthioureas are known to suppress the level of FT4 and T3, while causing raised level of TSH (Smith et al., 1998; Whitley, 1984). Some of the type 2 diabetic was on oral hypoglycemic agents alone and some were on both insulin injection and oral hypoglycemic agents. These situations may explain the finding of abnormal thyroid hormones levels in diabetics in this study (*p*<0.05) may also be due to modified thyroid releasing hormone

(TRH)s synthesis and release (De- Greef, 1992) and may depend on the glycaemic status of the diabetics studied. Glycaemic status is influenced by insulin, which is known to modulate TRH and TSH levels (Reusch and Tomsa, 1996). Attributed the abnormal thyroid hormone levels found in diabetes to the presence of thyroid hormone binding inhibitor (THBI), an inhibitor of the extra thyroidal conversion enzyme (5'-deiodinase) of T4 to T3 and dysfunction of the hypothalamo – pituitary–thyroidaxis. These situations may prevail in diabetes and aggravated in poorly controlled diabetics.

CONCLUSION

Thus this study revealed a higher incidence of abnormal thyroid hormone level among type 2 diabetic subjects. The serum levels of total T3 and total T4 were significantly low, while serum TSH levels were higher in type 2 diabetes mellitus subjects as compared to the non-diabetic healthy subjects.

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