

## Original Research Article

# Thyroid hormones, blood glucose and glycosylated hemoglobin in healthy Sudanese subjects

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## ABSTRACT

**Background:** Diabetes mellitus and thyroid diseases are the most prevalent metabolic disorders in Sudan. The value of HbA1c reflects the glycemic status over the last 2-3 months. So, in this study, an insight for thyroid hormone regulation of glucose metabolism is investigated. Is to study the association between thyroid hormones levels, fasting blood sugar (FBS) and HbA1c in healthy adults.

**Methods:** A cross sectional study was performed in a healthy Sudanese cohort in the period between September 2017 to November 2018, involving 610 healthy adult Sudanese aged 20 to 60 years. HbA1c, fasting blood sugar (FBS), T3, T4 and TSH were measured.

**Results:** The study results demonstrated a significant association between the median concentration of T3 and T4 with plasma level of HbA1c. A significant linear correlation between serum concentration of T3 and fasting blood sugar (FBS) was observed. Inverse correlation was detected between serum TSH and HbA1c, FBS in study population.

**Conclusions:** The present study concluded that FBS and HbA1c levels were increased with increasing of both T3 and T4. Based on this study all the thyroid patients' especially hyperthyroid patients should have regular checkup of their glucose levels.

**Keywords:** Blood glucose, Glycosylated haemoglobin, Thyroid hormones

## INTRODUCTION

The American Diabetes Association (ADA) and World Health Organization (WHO) have approved the use of HbA1c for the screening and the diagnosis of diabetes, both organizations have suggested that the level of

HbA1c  $\geq 6.5\%$  is considered as diabetes and the ADA has also suggested that the level of HbA1c between 5.7 to 6.4% is diagnostic of pre-diabetes.<sup>1-3</sup> The major form of the glycated haemoglobin is haemoglobin A1c (HbA1c).<sup>4</sup> The HbA1c concentration not only depends on prevailing glycaemia but also the life span of the erythrocytes and

therefore the conditions which affect the erythrocyte turnover or survival that lead to falsely high or low HbA1c levels.<sup>5</sup> A study conducted by Kim MK et al, showed that even in the absence of diabetes, there was spurious elevation of HbA1c in patients with hypothyroidism.<sup>6</sup>

In hypothyroidism, there is a reduction in glucose-induced insulin secretion by beta cells, and the response of beta cells to glucose or catecholamine is increased in hyperthyroidism due to increased beta cell mass. Moreover, insulin clearance is increased in thyrotoxicosis.<sup>7,8</sup> It was reported that HbA1c levels are increased in both hypothyroid and hyperthyroid patients.<sup>9</sup> In both disorders the increase in HbA1c might be due to different actions of thyroid hormones on liver, skeletal muscles and adipose tissue.<sup>10</sup> In hypothyroidism, the decreased absorption and conversely decreased utilization of glucose is also associated with hyper-insulinemia and insulin resistance, probably causing transient elevations in the glucose concentrations and thus contributing to glycation of serum proteins.<sup>11</sup> Insulin resistance is the cause of increased glucose levels in hypothyroid levels.<sup>12,13</sup>

The higher levels of FBS and HbA1c in hyperthyroid group compared to normal controls appeared as changes of carbohydrate metabolism.<sup>14-17</sup> A significant correlation between TSH and HbA1c serum levels has also been found.<sup>18</sup> Low RBC turnover, with a predominance of older cells are associated with a falsely elevated HbA1c. Proven examples include iron and vitamin B12 deficiencies and renal failure.<sup>19-21</sup> The elevated HbA1c levels in iron deficiency anaemia could be explained by the assumption that if the serum glucose remains constant, a decrease in the haemoglobin concentration might lead to an increase in the glycated fraction.<sup>22,23</sup>

## METHODS

A cross sectional study was performed in a healthy Sudanese cohort in the period between September 2017 to November 2018, involving 610 healthy adults aged 20 to 60 years (males=121, females=489) randomly selected from students, staff, and employees of governmental universities all over the country. Inclusion criteria include; absence of chronic diseases, absence of acute illnesses for at least 7days, age group of 20 – 60 years old and signing the consent. The exclusion criteria include; hematological disorders, chronic diseases, recent acute diseases, pregnancy, lactation and smoking. Ethical approval was issued by the ethical committee of the National Ribat University and from the Federal Ministry of Health. Written consent was obtained from the participants. Participants were interviewed and filled a questionnaire. 5ml of blood were obtained from each subject. HbA1c was measured by using modified ELISA reader known as COPAS Integra 800. Auto analyzer A 15 was used to measure Fasting Blood Sugar (FBS). Serum

was separated by centrifugation at 5000 rpm for 5 min. Sera were used to measure TSH, T4, and T3.

## Statistical analysis

Normality of continuous variable data was determined by using the Shapiro-Wilk test and normal Q-Q Plot, parametric continuous variables were presented as a mean±SD, while non-parametric continuous variables were presented as a median (interquartile range) and analyzed by Mann-Whitney U test. P value <0.05 was used for significance. The reference intervals were calculated by using lower and upper percentile limits with the 0.95 confidence intervals as the following; lower percentile limit is setted to the 2.5<sup>th</sup> percentile. Upper percentile limit is setted to the 97.5<sup>th</sup> statistical package for social science (SPSS) was used for analysis.

## RESULTS

Table 1 showed that the median level of HbA1c is 4.8% while the ranges of T3, T4 and TSH were 0.73-1.54 ng/ml, 4.1-10.6 ng/dl and 0.44-3.72µIU/ml respectively.

**Table 1: HbA1c correlation with T3, T4, and TSH.**

Parameters	n	Median + Range.	P value
HbA1c %	573	4.8	
T3ng/ml	610	1.1(0.73-1.54)	.004
T4ug/dl	610	7(4.1-10.6)	<0.001
TSH µIU/ml	610	1.32(0.44-3.72)	.217

A significantly positive correlation between HbA1c and T3, T4 was found (P=0.004) and (P=0.001) respectively, while the correlation between HbA1c and TSH was statistically insignificant (P= 0.217) (Table 1).

**Table 2: FBS correlation with T3, T4, and TSH.**

Parameters	n	Median + Range.	P value
FBS mg/dl	409	75	
T3 ng/ml	610	1.1(0.73-1.54)	.011
T4 ug/dl	610	7(4.1-10.6)	.309
TSH µIU/ml	610	1.32(0.44-3.72)	.371

Table 2 showed that the median of fasting blood glucose (FBG) is 75 mg/dL, while the ranges of T3, T4 and TSH were 0.73-1.54 ng/ml, 4.1-10.6 ng/dl and 0.44-3.72µIU/ml respectively. It showed linear significant correlation of median fasting blood glucose with the median concentration of T3 (P=0.011). The correlation of fasting blood glucose with T4 and TSH was found to be insignificant, P=0.309 and P=0.371 respectively.

## DISCUSSION

The metabolic disturbances associated with diabetes, cause pathophysiological changes in multiple organ

systems, that impose a heavy burden of morbidity and mortality from macro and microvascular complications.<sup>24</sup>

In the present study a positive linear significant correlation was observed between the serum levels of T3, T4 and HbA1c. These findings are supported with other studies, showing that the level of HbA1c is elevated in hyperthyroidism p.<sup>10,17</sup> This result might be explained by the fact that, thyroid hormones facilitate the glycogenolytic and gluconeogenic effects of epinephrine and glucagon and stimulate hepatic gluconeogenic enzymes (phosphoenol pyruvate carboxykinase) increasing blood glucose level and so does HbA1c. Another explanation of the hyperglycemic effect of thyroid hormones could be their anti-insulin actions in different organs.<sup>8</sup> On the other hand, reduced thyroid hormones level might cause hypoglycemia.<sup>25</sup> It is also known that insulin is an anabolic hormone which inhibits the hepatic conversion of T4 to T3, enhances the levels of FT4 while it suppresses the levels of T3.<sup>26,27</sup>

In this study, there was no significant association between TSH and glycemic control. While in other studies, TSH level was inversely associated with the plasma level of FBS and HbA1c, this might be because, hyperglycemia impairs TSH response for TRH.<sup>28</sup>

## CONCLUSION

From the present study we concluded that FBS and HbA1c levels are increased significantly with increasing levels of both T3 and T4. This may indicate that increase in thyroid hormonal level is strongly associated with the chronic hyperglycemia of adult Sudanese and so type-II diabetes mellitus.

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