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Original Research

Study of Correlation of Glycosylated Haemoglobin and Thyroid Stimulating Hormone levels in Non-Diabetic Patients with Hypothyroidism

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ABSTRACT:
Background: Type 2 diabetes mellitus and hypothyroidism are the most prevalent metabolic disorders. Coexistence of thyroid disease and diabetes mellitus is a well-recognized positive association. The effect of thyroid dysfunction on glucose metabolism in non-diabetic patients is a thrust area of research. Present study was conducted to study the levels of glycosylated haemoglobin (HbA1c) in non-diabetic patients with hypothyroidism. **Material and methods**: This case-control study was conducted on 100 subjects. A total of 50 subjects with hypothyroidism and without diabetes were selected as cases and another 50 age and sex matched normal healthy individuals were selected as controls. An independent t-test was applied to find out the significance of the statistical difference amongst various parameters in the case and the control groups. Regression analysis was done for correlation between serum TSH, T3, T4 and HbA1c. **Results**: It was found that there was a positive correlation between the levels of serum TSH (µU/L) and HbA1c (%) in all the participants of the study by Pearson's correlation coefficient. **Conclusion**: HbA1c levels were increased in hypothyroid patients. The present study suggests that HbA1c levels should be interpreted with caution in hypothyroid patients.
Keywords: diabetes mellitus, HbA1c, hypothyroidism, TSH

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INTRODUCTION:
Glycosylated haemoglobin or HbA1c is a product of a ketoamine reaction between the N-terminal valine of both ß-chains of the haemoglobin and the glucose molecule. The major form of glycated haemoglobin is haemoglobin A1c (HbA1c).[1] HbA1c ≥6.5% is considered as diabetes and the American Diabetes Association has also suggested that the level of HbA1c between 5.7 to 6.4% is diagnostic of pre-diabetes.[2,3]
Thyroid dysfunction is not uncommon in the general population and is the second most common endocrine disease after diabetes mellitus. Decreased production of thyroid hormone is the key feature of hypothyroidism.[4]
The HbA1c levels depend not only on the prevailing glycaemia but also on the life span of the red blood cells. Thus the conditions which affect the red cell turnover or survival can lead to erroneous estimation of the HbA1c levels as false high or false low.[5]
Coexistence of thyroid disease and diabetes mellitus is a well-recognized positive association. The effect of thyroid dysfunction on glucose metabolism in non-diabetic patients is a thrust area of research. Present study was conducted to study the levels of glycosylated haemoglobin (HbA1c) in non-diabetic patients with hypothyroidism.

MATERIAL AND METHODS:
This case-control study was conducted on 100 subjects. A total of 50 subjects of hypothyroidism without diabetes were selected as cases and another 50 age and sex matched normal healthy individuals were selected as the control. Ethical committee clearance was obtained and all the candidates were informed about the

study. An informed consent in writing was taken from all the subjects.

Procedure:
Venous blood from the antecubital vein was drawn after a period of overnight fasting. A total of 4 ml of blood was withdrawn - 2 ml for thyroid function tests and the remaining 2 ml for the estimation of fasting blood sugar. T3, T4 and TSH were estimated by electrochemiluminiscence method. High performance liquid chromatography (HPLC) method was used for HbA1c estimation.

Inclusion criteria:
- Absence of chronic diseases
- Absence of acute illnesses for at least 7days
- Age between 20 – 60 years
- Willing to sign the consent

Exclusion criteria:
- Haematological disorders
- Chronic diseases
- Recent acute diseases
- Pregnancy
- Lactation and smoking

STATISTICAL ANALYSIS
All the data required for this study were collected and analysed statistically to determine the significance of different parameters by using SPSS software. All values were taken in the form of mean ± SD. Comparison between the case and the control groups were made using Student's t-test (unpaired), and the p-value of less than 0.05 was considered to be statistically significant. Regression analysis was done for correlation between serum TSH and HbA1c.

RESULTS:
Male to female ratio in our study for cases was 1:2.7

Table 1: **Comparison of parameters in the cases and controls**

Parameters	Case (Mean±SD)	Control (Mean±SD)	p-value*
Age (Year)	51.55 ± 12.89	49.12 ± 12.00	0.33
FBS (mg/dl)	95.4 ± 5.13	94.75 ± 4.56	0.50
S. T3 (nmol/L)	1.94 ± 0.45	1.97± 0.42	0.73
S. T4 (nmol/L)	107.44 ± 15.76	108.53 ± 15.23	0.72
S. TSH (mU/L)	6.5 ± 1.24	2.87± 0.75	0.0001
HbA1c (%)	5.67± 0.29	5.19 ± 0.24	0.0001

Table 2: **HbA1c correlation with T3, T4, and TSH**

Parameter	Correlation Coefficient R	P value
S. T3 (nmol/L)	0.23	0.9
S. T4 (nmol/L)	0.22	0.12
S. TSH (mU/L)	0.32	0.02

A positive correlation between HbA1c and TSH was noted and it achieved statistical significance. A positive correlation between HbA1c and T3, T4 was also found but it was statistically insignificant.

DISCUSSION:
It is important to study the effects of thyroid hormones on HbA1c, so as to help us in better interpretation of its levels in patients with thyroid dysfunction. Taking into account the myriad other non-glycaemic factors that can affect HbA1c levels, the inclusion and exclusion criterion were devised.[6]
There is an obvious gender predilection for thyroid dysfunction, which is not the same as in any other metabolic abnormality. Various forms of thyroid dysfunction and Hashimoto's thyroiditis are more common in women, and the overall incidence increases with age in both sexes (TSH distributional shift with age), especially in women.[7]
In the present study, the mean age of cases was 51.55 years and the mean age of controls was 49.12 years. Male to female ratio in our study for cases was 1:2.7.
On comparison of case group which consists of subjects of hypothyroidism with the control group comprising of normal healthy individuals, the levels of serum TSH were significantly higher in the case group and this difference was statistically significant. The mean HbA1c levels in the case group were increased in case group on comparison with the control group.
There was no statistically significant difference between the case group and the control group for the age, FBS, serum T3 and serum T4 levels. The only difference in the case and the control groups was, in their levels of serum TSH. A statistically significant positive correlation was found between HbA1c and TSH levels. The correlations between HbA1c with T3 and T4 were statistically insignificant. These findings in our study are supported with other studies discussed below, which showed that the level of HbA1c is elevated in hyperthyroidism.
Billic-Komarica E et al[8] also reported that the correlation between the level of serum TSH and HbA1c was positive and significant. Subclinical hypothyroidism is an independent risk factor for insulin resistance through its effects on the adipose tissue and muscle. There seems to exist a correlation between hyperinsulinemia, insulin resistance and subclinical hypothyroidism. Subclinical hypothyroidism and insulin resistance are involved in compromising the glycemic control via numerous underlying mechanisms. There is a blunting in the glucose-induced insulin secretion by beta cells in hypothyroidism while hyperthyroidism results in an increased response of the beta cells to glucose or catecholamine due to increased beta cell mass. Moreover, insulin clearance is increased in thyrotoxicosis.[9,10]
Al-Sayed A et al[11] investigated the correlation between insulin resistance and subclinical hypothyroidism in Kuwaiti women and found that the insulin levels were significantly higher in the subclinical hypothyroid group compared to the normal control.

Kim MK et al[12] in their study found that there was a spurious elevation of HbA1c in patients with hypothyroidism even in the absence of diabetes mellitus.

The above findings by our study and other studies mentioned above might be explained by the fact that, thyroid hormones facilitate the glycogenolytic and gluconeogenic effects of epinephrine and glucagon and stimulate hepatic gluconeogenic enzymes (phosphoenolpyruvate 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.[10] On the other hand, reduced thyroid hormone levels might cause hypoglycemia.[13]

CONCLUSION:

HbA1c levels are increased in hypothyroid patients. The present study suggests that HbA1c levels need to be interpreted with this caution in patients with hypothyroidism. Further studies can be done on larger cohort to understand more precisely the nature and mechanism of such an association.

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