

## Correlation Between Thyroid Profile and Glycated Haemoglobin (HbA1c) in Type 2 Diabetes Mellitus Patients

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**Abstract:** Diabetes mellitus is a global health problem affecting major populations worldwide. It is a group of metabolic disorders characterized by absolute or relative deficiencies in insulin secretion with chronic hyperglycaemia and disturbances of carbohydrate, lipid, and protein metabolism. Thyroid hormones are secreted from thyroid gland. Thyroid hormone replacement is associated with a decrease in Glycated Hemoglobin (HbA1c) level. The present study was undertaken to study correlation between thyroid profile and glycated Haemoglobin (HbA1c) in Type 2 Diabetes Mellitus patients. A hospital based case control study was carried out in Dept. of Biochemistry, North Bengal Medical College, Sirajganj, Bangladesh from July to December 2022. 100 participants were in the study group and 100 participants in control groups were enrolled by following procedure. Patients aged 30 years or more who came to routine health check-up were taken for the study. Basic information, clinical history was taken from the record files. 50 cases of Type 2 Diabetes mellitus and 50 healthy controls were taken. Blood samples were collected and analyzed for thyroid profile, HbA1c, Fasting Blood Sugar and Renal Function Test. We found that there was a positive correlation between TSH (Thyroid stimulating hormone) and HbA1c levels, and a negative correlation between Thyroid hormones [Triiodothyronine (T<sub>3</sub>) & Thyroxine (T<sub>4</sub>)] and Glycated Haemoglobin (HbA1c) in cases of type 2 Diabetes Mellitus. There is a significant decrease in TT<sub>3</sub> (Total Triiodothyronine) and TT<sub>4</sub> (Total Thyroxine) and significantly increased TSH in cases of Diabetes mellitus as compare to healthy Controls. We found that out of 50 cases of type 2 Diabetes Mellitus, 31% patients showed thyroid disorders. There is a high prevalence of thyroid disorders in Diabetic patients. If not diagnosed early, it could negatively affect diabetes and its complications. Therefore, routine screening of thyroid profile in diabetic patients is advisable to improve quality of life and reduce morbidity rate.

**Keywords:** Thyroid profile, Glycated Hemoglobin (HbA1c), Type 2 Diabetes Mellitus.

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## INTRODUCTION

Diabetes mellitus is a global health problem affecting major populations worldwide. It is a group of metabolic disorders characterized by absolute or relative deficiencies in insulin secretion with chronic hyperglycaemia and disturbances of carbohydrate, lipid, and protein metabolism [1]. Thyroid hormones are secreted from thyroid gland. Upon stimulation by thyroid stimulating hormone (TSH), the thyroid gland responds by producing and releasing two thyroid hormones [2]. Insulin and thyroid hormones are intimately involved in

cellular metabolism and thus excess or deficit of either of these hormones result in the functional derangement of the other. The report showing the association between diabetes and thyroid dysfunction were first published in 1979 [3], stating that prevalence of thyroid dysfunction varied from 2.2%– 17% in diabetics. Diabetic women are more frequently affected than men and hypothyroidism is more common than thyrotoxicosis [4]. One of the important function of thyroid hormones is the regulation of carbohydrate metabolism and pancreatic function and on the other hand, diabetes affects thyroid function tests to variable extents so diabetes and thyroid disorders have

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been shown to mutually influence each other and association between both conditions have been reported [5, 6]. Thyroid hormone abnormalities are frequently associated with diabetes and unidentified thyroid dysfunction could negatively impact diabetes and its complications [7]. Thyroid hormone replacement is associated with a decrease in glycated hemoglobin (HbA1c) level, which is influenced by increased erythropoiesis rather than by changes in glucose level [8, 9]. Glycemic control in diabetic patients is usually monitored by determination of HbA1c levels (glycated haemoglobin) which is now the gold standard, and gives an estimate of the amount of glucose in the blood over the previous three months. Therefore, this study is undertaken to provide a comprehensive and comparative study of TT<sub>3</sub> and TT<sub>4</sub>, TSH and glycemic control parameter Glycated Haemoglobin [HbA1c] in patients of Type 2 DM.

## MATERIALS AND METHODS

A hospital based case control study was carried out in Dept. of Biochemistry, North Bengal Medical College, Sirajganj, Bangladesh from July to December 2022. 100 participants were in the study group and 100 participants in control groups were enrolled by following procedure. Patients aged 30 years or more who came to routine health check-up were taken for the study. Basic information, clinical history was taken from the record files.

### Inclusion Criteria

100 type II Diabetes Mellitus patients diagnosed as per American Diabetes Association (ADA) [10] having FPG >126 mg/dl, HbA1c > 6.5%, Serum Urea < 40 mg/dl, Serum Creatinine < 1.3mg/dl were included in the study as cases.

### Exclusion Criteria

Non Diabetic individuals, individuals having history of thyroid diseases and taking medicines that

affect thyroid function and individuals with Liver or kidney diseases were excluded from the study.

### Selection of Control Group:

#### Inclusion Criteria

Age and sex matched normal healthy individuals with FPG <110 mg/dl, HbA1c < 6.5%, Serum Urea < 40 mg/dl, Serum Creatinine <1.3mg/dl were included in the study as controls.

#### Exclusion Criteria

Individuals having history of thyroid diseases and individuals with liver or kidney diseases were excluded from the study.

### Blood Sample Collection and Processing

Samples were collected with an aseptic blood collection technique. Three vacutainers: Plain tube for Renal function tests, TSH, TT<sub>3</sub> and TT<sub>4</sub>. Sodium fluoride tube for Fasting plasma glucose and EDTA tube for HbA1c were taken. These blood samples were processed and analysed in the biochemistry laboratory for the estimation of FPG, HbA1c, TSH, TT<sub>3</sub> and TT<sub>4</sub>.

### Statistical Analysis

Data were entered and analysed through Excel 2007. Categorical variables were expressed through percentages while continuous variables were expressed as mean and standard deviation. Pearson correlation coefficient were calculated to know correlation between thyroid profile [Triiodothyronine (T<sub>3</sub>), Thyroxine (T<sub>4</sub>), Thyroid Stimulating Hormone (TSH)] and Glycated haemoglobin in cases of Type 2 Diabetes Mellitus.

## RESULTS

Table-1 shows that mean age among control groups was lower than the mean age of the case group. Fasting plasma glucose and Glycated haemoglobin were significantly higher (p value <0.05 in both). Mean TSH level were significantly higher in cases while serum Total T3 and Total T4 levels were significantly decreased in cases when compared to controls.

**Table 1: Comparison of Variables between Cases and Controls (N=100)**

Variables	Cases (n=50) (Mean + SD)	Controls (n=50) (Mean + SD)	p value
Age (Years)	55.09 ± 11.03	52.54 ± 9.06	0.06
Gender			
Female	21 (46.67%)	24(53.33%)	0.48
Male	29 (52.73%)	26(47.27%)	
Fasting Plasma Glucose (FPG) (mg/dl)	165.92 ± 45.86	94.63 ± 9.20	<0.0001**
Glycated haemoglobin (HbA1c) (%)	8.00 ± 1.58	5.65 ± 0.53	<0.05*
Thyroid Stimulating Hormone (TSH) (micro unit/ml)	4.36±2.45	3.32±2.10	<0.05*
Total Triiodothyronine (TT3) (nano mol/litre)	1.65±0.52	2±0.62	<0.05*
Total Thyroxine (TT4) (nano mol/litre)	99.77±30.49	114±31.47	<0.05*

\*p value less than 0.05 indicates significant value, \*\*p value less than 0.001 indicates highly significant value

**Table 2: Distribution of Diabetic Subjects with Abnormal Thyroid Profile (N=100)**

Thyroid Disorders	Cases		Controls
	HbA1c <7.5%	HbA1c >7.5%	
Hypothyroidism (Primary)	2	4	2
Hypothyroidism (Subclinical)	3	7	2
Hyperthyroidism (Primary)	0	1	0
Hyperthyroidism (Subclinical)	0	1	1
<b>Total</b>	<b>05</b>	<b>13</b>	<b>5</b>

Table 2 show that Categorical comparison of thyroid Diseases among type 2 Diabetes Mellitus having HbA1c < 7.5 %, HbA1c > 7.5 % and Healthy controls.

**Table 3: Correlation of Thyroid Profile with HbA1c (N=100)**

Parameters	Correlation Coefficient	p value
HbA1c – Thyroid Stimulating Hormone (TSH)	0.64	<0.001**
HbA1c – Total Triiodothyronine (TT <sub>3</sub> )	-0.38	<0.001**
HbA1c –Total Thyroxine (TT <sub>4</sub> )	-0.33	<0.001**

\*\*p value less than 0.001 indicates highly significant value

We found that there was a positive correlation between TSH (Thyroid stimulating hormone) and HbA1c levels, and a negative correlation between Thyroid hormones [Triiodothyronine (T<sub>3</sub>) & Thyroxine (T<sub>4</sub>)] and Glycated Haemoglobin (HbA1c) in cases of type 2 Diabetes Mellitus. There is a significant decrease in TT<sub>3</sub> (Total Triiodothyronine) and TT<sub>4</sub> (Total Thyroxine) and significantly increased TSH in cases of Diabetes mellitus as compare to healthy Controls. We found that out of 50 cases of type 2 Diabetes Mellitus, 31% patients showed thyroid disorders.

## DISCUSSION

Previous studies reported that DM type 2 do not affect T4, therefor observed normal level of T4 in diabetic patients when compared with reference range, hypothesize that medication of DM type 2 may influence the thyroid hormone profile thus observed normal results of T4 [9]. 50 cases of Type 2 Diabetes Mellitus and 50 healthy controls were included in the study. The results of our study showed that the levels of Total T3, Total T4 were significantly lower in diabetic patients as compare to controls and serum TSH was significantly higher in diabetics as compared to controls [Table-1]. This is in accordance with the studies of Vikram BV *et al.*, [10], Gurjeet S *et al.*, [11], and Shekhar CY *et al.*, [12]. In diabetic patients, the nocturnal TSH peak is blunted or abolished, and Response of TSH to TRH is also decreased [13]. Production of T3, T4 and iodide uptake by thyroid gland is diminished. In addition to these, deiodination of T4 to T3 is decreased which explains reduction in T3 and T4 level in serum [14]. In our study among the 100 diabetic subjects, investigated 12 % i.e.12 had hypothyroidism, 17% i.e.17 had subclinical hypothyroidism, 1% i.e.,1 had subclinical hyperthyroidism so total of 31% patients showed thyroid disorder. We also found that 5 % i.e. 5 of the healthy control subjects had abnormal thyroid status [See Table-2]. In Table-2, also suggests that HbA1c levels more than 7.5 % have the tallest bar representing Thyroid disorders

These findings suggest a high prevalence of thyroid disorders in diabetic population specially in uncontrolled Diabetes which is supported by the studies of Celani *et al.*, (Prevalence rate -31.4%) [15], Smithson (Prevalence rate -10.4%) [16]. Radaideh *et al.*, (Prevalence rate -12.5%) [17], Pimenta *et al.*, (Prevalence rate -51.6%) [18], Udiong *et al.*, (Prevalence rate -46.5%) [19]. In cases of type 2 Diabetes Mellitus, there was a positive correlation between TSH (correlation coefficient is 0.64, p value is < 0.001) and HbA1c. There was a negative or inverse correlation between HbA1c level and Total Triiodothyronine (Total T<sub>3</sub>) (correlation coefficient is -0.38, p value is < 0.001), there was also negative or inverse correlation between HbA1c level Total Thyroxine (Total T<sub>4</sub>) (correlation coefficient is -0.33, p value is < 0.001) [Table-3]. The observation of negative correlation between T3 and HbA1c is supported by the studies of Schlienger JL *et al.*, Bagchi N, [20, 21]. It has recently been reported that T3 has an anti-apoptotic and protective effect on the pancreatic beta cells [11]. T3 activates the PI-3 kinase pathway via thyroid hormone receptor on the beta cell, and stimulates insulin secretion. This may be related to an association between low Total T3 levels, and increased HbA1c [22, 23]. The observation of positive correlation between TSH and HbA1c is supported by the studies of Velija- Asimi *et al.*, [24]. They examined the effects of treatment of subclinical hypothyroidism and concluded that the correlation between TSH and HbA1c were positive and significant.

## CONCLUSION

The present study revealed that patients with Type 2 Diabetes Mellitus have higher prevalence of thyroid disorders. The most common thyroid disorder found in type 2 Diabetes Mellitus is hypothyroidism. In thyroid disorders, early signs and symptoms of underlying disease remain hidden. Also, most of the times undiagnosed thyroid disorders could negatively affect Diabetes and its complications. Therefore, routine

screening of thyroid profile in diabetic patients is beneficial and advisable to improve quality of life and reduce morbidity rates and its complications.

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