

**Study of thyroid dysfunction in type 2 diabetes mellitus patients of Agra city**Alok Mawar<sup>1\*</sup>, Pawan Kumar Kare<sup>2</sup>, Kamla Pati Mishra<sup>3</sup>, Raj Kumari Chahar<sup>1</sup><sup>1</sup>Department of Biochemistry, Sarojini Naidu Medical College, Agra, India<sup>2</sup>Department of Biochemistry, University College of Medical Sciences, Delhi, India<sup>3</sup>Department of Biochemistry, LLRM Medical College, Meerut, India**\*Correspondence Info:**

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E-mail: [mawaralok@yahoo.com](mailto:mawaralok@yahoo.com)**Abstract**

**Background:** Type 2 Diabetes Mellitus (Type 2 DM) and associated thyroid dysfunctions are very common in Indian population. Studies on the relationship between diabetes mellitus and thyroid dysfunction are very few in North Indian population. Due to the lack of adequate information about this relationship may be responsible for diabetic patients who may have developed thyroid dysfunction.

**Methods:** The objective of this study was to investigate the thyroid dysfunction in type 2 diabetes mellitus patients of Agra city. The study population consisted of (n = 100) subjects divided into two groups: diabetic group (n = 50) and non-diabetic (n = 50) as healthy control group. The biochemical parameters like; fasting plasma glucose, total triiodothyronine T<sub>3</sub>, total thyroxine T<sub>4</sub> and thyroid stimulating hormone (TSH) were measured for assessment of thyroid dysfunction.

**Results:** A significant increase in the level of fasting plasma glucose was observed in diabetic patients as compared to healthy controls. In our results, the level of T<sub>3</sub> and T<sub>4</sub> did not change significantly in diabetic subjects as compared to the control subjects. The serum TSH level was significantly higher in diabetic patients as compared to healthy control subjects.

**Conclusion:** The present study identified the patients at risk with subclinical hypothyroidism in type 2 diabetes. Therefore, the screening of thyroid dysfunction in type 2 DM patients is essential to reduce the severity of disease and endocrinal abnormalities in diabetic patients.

**Keywords:** Type 2 diabetes mellitus, Glycosylated haemoglobin, Thyroid hormone

**1. Introduction**

Diabetes mellitus (DM) is a leading cause of health related problems and death in different populations worldwide [1]. It is characterized by chronic hyperglycemia resulting from insulin resistance or defective secretion of insulin by pancreatic  $\beta$  - cells or both [2]. According to World Health Organization (WHO), the worldwide prevalence of diabetes in 2002 was 170 million, and the number projected to grow up to 366 million or more by 2030 [3]. Sedentary lifestyle, various diet patterns, ethnicity and a genetic predisposition are the major factors responsible for the causes of the epidemic [4].

Thyroid disorders are also common in the general population and it is the second most common condition to affect the endocrine system. As a result it is common for an individual to be affected by both thyroid disease and diabetes [5]. Various studies have reported the low prevalence of thyroid dysfunction in among diabetic patients between 2.2 to 17 % in their respective population [6, 7]. However, fewer studies have showed higher prevalence of thyroid dysfunction

in diabetes from 31 % to 46.5 % [8, 9]. Hypothyroidism is a clinical syndrome occurs from a deficiency of thyroid hormones. It is very common thyroid problem in diabetic patients [10].

Thyroid hormones and insulin are the antagonists and both are involved in cellular metabolism of carbohydrates, proteins, and lipids. The functional impairment occurs in thyroid hormone as well as insulin if their levels changed [11]. Thyroid disease is a pathological state that adversely affects diabetic control and is commonly found in most forms of DM which is associated with advanced age in type2 diabetes and autoimmune diseases in type 1 diabetes. DM appears to influence thyroid function in two sites; firstly at the level of hypothalamic control of TSH release and secondly at the conversion of T<sub>4</sub> to T<sub>3</sub> in the peripheral tissue. Increased hyperglycemia causes reversible reduction of the activity and hepatic concentration of T<sub>4</sub>-5-deiodinase, low serum T<sub>3</sub>, increase in reverse T<sub>3</sub> and also variation in the level of T<sub>4</sub> [12]. Failure to identify the

imbalance of thyroid hormones in patients with type 2 diabetes may be a major cause of poor management and diagnosis of diabetic patients. Therefore, there is need to consider the thyroid hormones in type 2 diabetic patients as routine investigations and serum T<sub>3</sub>, serum T<sub>4</sub> and serum TSH are more reliable and sensitive tests for thyroid dysfunction in the management of type 2 diabetic patients. Therefore, the present study is carried out for the assessment of thyroid dysfunction in type 2 diabetic patients of Agra city by measurement of serum T<sub>3</sub>, serum T<sub>4</sub> and serum TSH levels.

## 2. Material and Methods

### 2.1 Study Design

This study was carried out in the Department of Biochemistry, Sarojini Naidu Medical College and Hospital, Agra, India, between 1<sup>st</sup> January 2012 to 31<sup>st</sup> August 2012. Total (n = 100) subjects were recruited and divided into two groups. Group I included (n = 50) diagnosed cases with type 2 DM and (n = 50) age and sex matched healthy controls. The subjects were in the age group of 35 to 65 years of both sexes. Clinical examination and personal history of both groups were recorded by physician in the OPD of Department of Medicine and biochemical investigations were conducted in the Biochemistry Laboratory, Sarojini Naidu Medical College and Hospital, Agra. The diagnosis of type 2 DM was according to the World Health Organization (WHO) definition: those having fasting plasma glucose >7.0 mmol/L (126 mg/dL) or taking anti-diabetic medications. The study was approved by the Institutional Ethical Committee of Sarojini Naidu Medical College and Hospital, Agra, U.P. and patients were recruited for the study after taking their written consent.

### 2.2 Biochemical parameters estimation

Blood samples were drawn in sodium fluoride (NaF) and plain tubes from the antecubital vein in the morning after an overnight fast. Serum was separated from blood by centrifugation at 3000 rpm for 10 minutes. Fasting blood glucose was estimated by Glucose oxidase-peroxidase (GOD-POD) enzymatic method by using spectrophotometer (Systonics). Glycosylated haemoglobin (HbA1c) was measured by resin ion exchange method. Estimation of total T<sub>3</sub> (serum triiodothyronine), total T<sub>4</sub> and total TSH (serum thyroid stimulating hormone) were done by commercial available ELISA kit.

### 2.3 Statistical analysis

Statistical analysis was performed with the SPSS 16.0 software. All the values were expressed as Mean±SD Student's t-test was used to assess the statistical significance of the results. p value ≤0.05 was used as a threshold of significance.

## 3. Results

The demographic characteristics of the study subjects are presented in [Table 1]. Total (n = 100) subjects

were selected in the present study. Out of one hundred subjects, n = 50 volunteers (n = 30 males and n = 20 females) were in healthy control group, in which fifteen belonged to rural area and thirty five belonged to urban area. Total (n = 50) subjects out of which 28 males and 22 females were in diabetic group, out of these, thirty five subjects belonged to urban area and only fifteen subjects from rural area. The mean of age in control subjects was 48 ± 9.0 years while in diabetic patients it was 53 ± 9.3 years. The mean value of BMI in diabetic patients was 25 ± 3.2kg/m<sup>2</sup> not significantly increased as compared to the control subjects (23 ± 0.9 kg/m<sup>2</sup>). Mean duration of diabetes in the present study was 5.8 ± 2.2 years.

The values of fasting blood glucose, serum T<sub>3</sub>, serum T<sub>4</sub> and serum TSH levels are listed in [Table 2]. In healthy control group, mean fasting blood glucose, serum T<sub>3</sub>, serum T<sub>4</sub> and serum TSH levels were 80± 7.0 mg/ dl (range 70 - 97 mg/ dl), 133 ± 28.3 ng/dl (range 96-181ng/dl), 7.64 ± 1.38ng/dl (range 4.6 - 10.1ng/dl) and 1.54 ± 1.11µIU/ml (range 0.6 - 4.3µIU/ml) respectively. In diabetic group, fasting blood glucose, serum T<sub>3</sub>, serum T<sub>4</sub> and serum TSH levels were 154 ± 67.4 mg/ dl (range 73 - 297 mg/ dl), 137 ± 12.6 ng/dl (range 110 - 180 ng/dl), 8.02 ± 1.18 ng/dl (range 5.17 - 9.54 ng/dl) and 5.34 ± 3.58 µIU/ml (range 1.09-18.62µIU/ml) respectively. The levels of fasting blood glucose and serum TSH were significantly increased in diabetic patients as compared to the healthy controls. However, no significant change was observed for serum T<sub>3</sub> and T<sub>4</sub> in these two groups.

The values of fasting blood glucose, serum T<sub>3</sub>, serum T<sub>4</sub> and serum TSH levels in male group are presented in [Table 3]. In healthy control male group (n = 30), fasting blood glucose, serum T<sub>3</sub>, serum T<sub>4</sub> and serum TSH levels were 79 ± 6.35 mg/dl (range 70 - 95 mg/dl), 138 ± 19.4 ng/dl (range 111- 181ng/dl), 7.63 ± 1.21 ng/dl (range 5.35 - 9.95ng/dl) and 1.54 ± 1.1µIU/ml (range 0.6 - 3.52 µIU/ml) respectively, while in diabetic male (n = 23), the values for fasting blood glucose, serum T<sub>3</sub>, serum T<sub>4</sub> and serum TSH levels were 148.4 ± 69.7 mg/dl (range 73 - 282.7 mg/dl), 135 ± 12.25 ng/dl (range 110 - 170 ng/dl), 8.11 ± 1.2ng/dl (range 5.17- 9.54 ng/dl) and 5.0 ± 3.86 µIU/ml (range 1.09 - 18.62µIU/ml) respectively. The levels of fasting blood glucose and serum TSH were significantly higher (p < 0.001) in diabetic male patients as compared to healthy male controls.

The fasting blood glucose, serum T<sub>3</sub>, serum T<sub>4</sub> and serum TSH levels in female group are listed in [Table 4]. In healthy control female group (n = 20), fasting blood glucose, serum T<sub>3</sub>, serum T<sub>4</sub> and serum TSH levels were 81.8 ± 7.6 mg/dl (range 70 - 97 mg/dl), 135 ± 23ng/dl (range 96 - 181 ng/dl), 7.66 ± 1.66 (range 4.6 - 10.1ng/dl) and 1.53 ± 1.18 µIU/ml (range 0.6 - 4.3µIU/ml) respectively while in diabetic female patients (n = 17), values for fasting blood glucose, serum T<sub>3</sub>, serum T<sub>4</sub> and serum TSH levels were 160.8 ± 65.7

mg/dl (range 82.7 - 297 mg/dl),  $139 \pm 13.18$  ng/dl (range 121-180 ng/dl),  $7.9 \pm 1.19$  ng/dl (range 6 - 9.21 ng/dl) and  $5.8 \pm 2.54$   $\mu$ IU/ml (range 1.2 - 9.56  $\mu$ IU/ml) respectively. The levels of fasting blood glucose and serum TSH were significantly increased ( $p < 0.001$ ) in diabetic female patients as compared to the healthy female control while the level of

serum T<sub>3</sub>, serum T<sub>4</sub> in diabetic female did not change significantly. In the present study, there were no significant change ( $p > 0.05$ ) in fasting blood glucose, serum T<sub>3</sub>, serum T<sub>4</sub> levels and a significantly change ( $p < 0.001$ ) in the serum TSH level was found between male diabetic patients and female diabetics patients are listed in [Table 5].

**Table 1: Demographic data of study subjects**

	Controls (n = 50)	Cases (n = 50)
Male	n = 30	n = 28
Female	n = 20	n = 22
Rural	n = 15	n = 10
Urban	n = 35	n = 40
Age (30 - 65 years)	$48 \pm 9.0$	$53 \pm 9.3$
Weight (kg)	$64 \pm 9.5$	$62 \pm 8.8$
Height (cm)	$165.9 \pm 10.6$	$163.8 \pm 9.9$
BMI (kg/m <sup>2</sup> )	$23 \pm 0.9$	$25 \pm 3.2$
Duration of diabetes (years)	-	$5.8 \pm 2.2$

Data are presented as mean  $\pm$  SD

**Table 2: Fasting blood glucose, serum T<sub>3</sub>, serum T<sub>4</sub> and serum TSH levels in healthy controls and type 2 diabetic patients**

Parameters	Control group (n = 50)	Diabetic group (n = 50)	p value
FBG (mg/dl)	$80 \pm 7.01$	$154 \pm 67.44$	$p < 0.001$
T3 (ng/dl)	$133 \pm 28.3$	$137 \pm 12.6$	$p > 0.05$
T4 (ng/dl)	$7.64 \pm 1.38$	$8.02 \pm 1.18$	$p > 0.05$
TSH ( $\mu$ IU/ml)	$1.54 \pm 1.11$	$5.34 \pm 3.58$	$p < 0.001$

Values are given in mean  $\pm$  SD,  $p < 0.05$ ; significance level

**Table 3: Comparison of fasting blood glucose, T<sub>3</sub> and T<sub>4</sub> levels in healthy control male group and diabetic male group**

Parameters	Control male group (n = 30)	Diabetic male group (n = 23)	p value
FBG (mg/dl)	$79 \pm 6.35$	$148 \pm 69.66$	$p < 0.001$
T3 (ng/dl)	$138 \pm 19.4$	$135 \pm 12.25$	$p > 0.05$
T4 (ng/dl)	$7.63 \pm 1.21$	$8.11 \pm 1.2$	$p > 0.05$
TSH ( $\mu$ IU/ml)	$1.54 \pm 1.1$	$5.0 \pm 3.86$	$p < 0.001$

Values are given in mean  $\pm$  SD,  $p < 0.05$ ; significance level

**Table 4: Comparison of fasting blood glucose, T<sub>3</sub> and T<sub>4</sub> levels in healthy control female group and diabetic female group**

Parameters	Control female group (n = 20)	Diabetic female group (n = 17)	p value
FBG (mg/dl)	$81 \pm 7.6$	$160 \pm 65.72$	$P < 0.001$
T3 (ng/dl)	$135 \pm 23$	$139 \pm 13.18$	$P > 0.05$
T4 (ng/dl)	$7.66 \pm 1.66$	$7.9 \pm 1.19$	$P > 0.05$
TSH ( $\mu$ IU/ml)	$1.53 \pm 1.18$	$5.8 \pm 2.54$	$P < 0.001$

Values are given in mean  $\pm$  SD,  $p < 0.05$ ; significance level

**Table 5: Comparison of fasting blood glucose, T<sub>3</sub>, T<sub>4</sub> and TSH levels in diabetic male and diabetic female**

Parameters	Diabetic Male (n = 23)	Diabetic Female (n = 17)	p value
FBS (mg/dl)	$148 \pm 69.66$	$160 \pm 65.72$	$p > 0.05$
T3 (ng/dl)	$135 \pm 12.25$	$139 \pm 13.18$	$p > 0.05$
T4 (ng/dl)	$8.11 \pm 1.2$	$7.9 \pm 1.19$	$p > 0.05$
TSH ( $\mu$ IU/ml)	$5.0 \pm 3.86$	$5.8 \pm 2.54$	$p > 0.05$

Values are given in mean  $\pm$  SD,  $p < 0.05$ ; significance level

#### 4. Discussion

In the present study, the fasting blood glucose level was significantly higher ( $p < 0.001$ ) in diabetic subjects as compared to healthy controls, establishing a clear hyperglycemia condition. However, the blood glucose level was not significantly higher in diabetic females as compared to diabetic males. In support to our results similar observations were found in various studies. Hyperglycemia in diabetic patients have associated with vascular damage, impairment in functions of various organs like; eyes, kidneys, nerves, heart and also with endocrine organs.

In our results, the level of  $T_3$  did not change significantly in diabetic subjects as compared to the control subjects. The  $T_3$  levels did not differ significantly between healthy males and diabetic males. Similarly, there was no significant change in  $T_3$  levels in healthy females and diabetic females. Our observation was similar with earlier study of Swamy et al [13]. Serum  $T_4$  level did not change significantly in diabetic patients as compared to control subjects. The  $T_4$  level also did not change significantly in diabetic male subjects as compared to healthy control male subjects. Similarly, there was no significant difference in  $T_4$  levels between healthy females and diabetic females. This finding was similar with the findings of some other studies [14].

The serum TSH level was significantly higher in diabetic subjects as compared to healthy control subjects. The TSH level was significantly higher in diabetic males as compared to healthy control males. Similarly, there was a significant increase in TSH level in diabetic females as compared to healthy control females ( $p < 0.001$ ). The TSH level did not differ between diabetic males and diabetic females. Similar observations have been reported by the earlier studies [14, 15]. The TSH levels in diabetic males were significantly lower than the diabetic females. The results indicating subclinical hypothyroidism found in diabetic females as compare to diabetic males in Agra population. This may be related with the higher prevalence of obesity found in female's diabetic patients as compared to males in Agra population.

#### 4. Conclusion

The present study identified the patients at risk with subclinical hypothyroidism in diabetic patients of Agra city. Therefore, the screening of thyroid dysfunction in type 2 DM patients is necessary to reduce the vascular complications and management of diabetes and also reduce the risk of thyroid hormone dysfunction.

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