Prevalence of Thyroid Dysfunction in type 1 Diabetic Punjabi population

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Diabetes mellitus (DM) is a common endocrine metabolic disorder, characterized by hyperglycemia resulting from a variable interaction of hereditary and environmental factors. DM is commonly associated with thyroid dysfunction. The aim of the present study was to evaluate the frequency of thyroid dysfunction in subjects with type 1 diabetes. To meet the above objective blood sample was collected from 20 type 1 diabetic subjects and 100 healthy non diabetic subjects and investigated for total triiodothyronine (T3), total thyroxine (T4), free triiodothyronine (FT3), free thyroxine (FT4), thyroid stimulating hormone (TSH), plasma glucose fasting(FPG) and glycosylated hemoglobin (HbA1c). The level of T3, T4, FT3 and FT4 were significantly lower while the level of TSH was significantly higher in type 1 diabetics as compared to non-diabetics. The prevalence of thyroid dysfunction among type 1 diabetic Punjabi population is very high (25%) with primary hypothyroidism being more common. Failure to recognize the presence of abnormal thyroid hormone level in type 1 diabetes may be a primary cause of poor management often encountered in some treated type 1 diabetics. There is therefore need for the routine assay of thyroid hormones in type 1 diabetic, particularly in those patients whose conditions are difficult to manage.

Keywords — Diabetes, Hypothyroidism, FT3, FT4, T3,T4,TSH

I. INTRODUCTION

Type 1 diabetes is an autoimmune disease where the host immune system destroys the insulin producing β-cells in the pancreas. This type of diabetes accounts for 10-15% of all people with the disease. It can appear at any age, although commonly under 40 and is triggered by environmental factors such as viruses, diet or chemicals in people genetically predisposed. People with type 1 diabetes must be injected with insulin several times a day and follow careful diet and exercise plan [1].

Next to diabetes, thyroid disease is other common endocrine problem present in India. It is second only to diabetes as the most common condition to affect the endocrine system. Thyroid is a butterfly-shaped gland located in the neck just below the Adam’s Apple and above the collar-bone. It produces two hormones, thyroxin (T4) and triiodothyronine (T3) which enters the blood stream and affect the metabolism of the heart, liver, muscles and other organs. Thyroid gland operates as a part of feed back mechanism involving the hypothalamus and the pituitary gland which are located in the brain. The hypothalamus secretes thyrotropin-releasing hormone (TRH), which stimulates the anterior pituitary gland to secrete thyrotropin or thyroid stimulating hormone (TSH). TSH increases iodide uptake and oxidation that leads to organification and coupling in thyroid gland. These are necessary steps to produce the thyroid hormones T4 and T3. Of thyroid hormones secreted 90% is T4 and 9% is T3. T3 is derived from deiodination of T4; therefore 80% of circulating T3 is obtained from T4. Excessive T4 and to a small degree T3 circulating in the serum inhibits secretion of TSH and TRH, thereby completing the feedback cycle [2].

Thyroid hormones exert profound effect in the regulation of glucose homeostasis. These effects include modifications of circulating insulin levels and counter regulatory hormones, intestinal absorption, hepatic production and peripheral tissues (fat and muscle) uptake of glucose. It has long been known that thyroid hormones act differentially in liver, skeletal muscle and adipose tissue, the main targets of insulin action. While thyroid hormones oppose the action of insulin and stimulate hepatic gluconeogenesis and glycogenolysis [3] they up regulate the expression of genes such as GLUT-4 and phosphoglycerate kinase, involved in glucose transport and glycolysis respectively, thus acting synergistically with insulin [4] in facilitating glucose disposal and utilization in peripheral tissues.

There are two main disorders of thyroid gland, hypothyroidism or an under active thyroid gland and hyperthyroidism or an overactive thyroid gland. It adversely affects diabetic control and is commonly found in most forms of Diabetes Mellitus (DM) which
Thyroid disorders are widely common amongst diabetic patients with variable prevalence among the different populations. The NHANES III observed an increased frequency of thyroid dysfunction with advancing age and prevalence of thyroid disease was higher in women as compared to men and was more frequent in diabetic subjects as compared to non diabetic [8]. Another study demonstrated prevalence of 13.4% of thyroid diseases in diabetics with highest prevalence in type 1 female diabetics (31.4%) and lowest prevalence in type 2 male diabetic (6.9%)[9]. A prevalence of 12.3% was reported among Greek diabetic patients [10]. In another study a prevalence of 16% was reported in Saudi patients with type 2 diabetic [11]. In Jordan, a study reported that thyroid dysfunction was present in 12.5% of type 2 patients [12]. However, thyroid disorders were found to be more common in subjects with type 1 diabetes compared to those with type 2 diabetes.

The relationship between type 1 diabetes and thyroid dysfunction has not been extensively studied in Punjab although the prevalence of diabetes mellitus is very high and increasing. It is possible that there are diabetic patients who might have thyroid dysfunction which may greatly affect their glycemic control. Due to the lack of adequate information about the two conditions, preventive management is difficult to plan. Keeping the above in view the objectives of the present study are to estimate & compare the levels of thyroid hormones (T3, T4, FT3, FT4 and TSH) in type 1 diabetics and non diabetics subjects and to evaluate the prevalence of thyroid dysfunctions in diabetic and non diabetic control subjects not previously diagnosed having thyroid dysfunction.

II. MATERIALS AND METHODS

The subjects were selected from the cases presenting with type 1 diabetes in the OPD and ward of department of medicine, in Civil Hospitals of Kapurthala, Jalandhar and Amritsar. An informed verbal consent was taken from each and every patient.

The study population consisted of 20 type 1 diabetic and 100 non diabetic subjects. The criteria for diagnosis of type 1 diabetes were the American Diabetic Association criteria; FPG of 110 mg/dl, random blood sugar of 200 mg/dl or taking hypoglycemic drugs and/or using insulin and did not have any episodes of ketosis in the past. All patients with diseases that may affect thyroid function were excluded.

The non diabetes volunteers without history of DM whose FPG were less than 110 mg /dl on two occasions were taken as the control samples. These volunteers included non-diabetic subjects who came in the hospitals for routine...
checkups as advised by their attending physicians. The controls were not taking any drugs.

Venous blood sample were withdrawn and assayed for thyroid function such as FT3, FT4, T3, T4, TSH and other biochemical investigation such as FPG and HbA1c. The serum levels of FT3 (normal range 1.5-4.2 pg/ml), FT4 (normal range 0.8-1.68 ng/dl), T3 (normal range 70-210 ng/dl), T4 (normal range 5.2-11.8 µg/dl) and TSH (normal range 0.2-5.2 µIU/ml) were determined by electrochemiluminous method on Elecsys 2010. FPG (normal range 70-110mg/dl) and HbA1c (normal range 4.2-6.2%) were determined on semi automated clinical chemistry analyzer. The following guidelines for detection of thyroid dysfunction were considered: 1) Normal – when FT3, FT4, T3, T4 and TSH were within the normal range. 2) Primary hypothyroidism – when TSH is more than 5.2 mIU/L and FT3, FT4, T3, T4 is less than the normal value. 3) Primary hyperthyroidism - when TSH is less than 0.2 mIU/L and FT3, FT4, T3, T4 is more than the normal values. 4) Subclinical hypothyroidism – when TSH is more than 5.2 mIU/L and FT3, FT4, T3, T4 is within the normal range. 5) Subclinical hyperthyroidism – when TSH is less than 0.2 mIU/L and FT3, FT4, T3, T4 are within the normal range.

Statistical Analysis
The results obtained from the above investigation were analysed and expressed as mean ± SD. The comparison was done by student t test on no. of variable of each parameter using SPSS version 10.

III. RESULTS
Among the 20 type 1 diabetic subjects, 12 were male and 8 were female and among the 100 non-diabetic subjects 48 were male and 52 were females. The levels and comparison of mean of FPG and HbA1c in type 1 diabetic and non-diabetic subjects are shown in Table 1. The mean FPG levels (151.4±12.55 mg/dl) in type 1 diabetic subjects was very significantly (p=<.0001) higher than the mean (88.52±6.72 mg/dl) value in non-diabetic subjects. Similarly mean value of HbA1c (7.01±0.46 %) in type 1 diabetic subjects was very significantly (p=<.0001) higher than non-diabetic subjects (5.0±2.22 %).

Thyroid related Tests
The levels and comparison of mean serum FT3, FT4, T3, T4 and TSH in type 1 diabetic and non-diabetic groups are shown in Table 2. The mean (2.01±0.45 pg/ml) serum free T3 levels in type 1 diabetic subjects was significantly (p=<.0001) lower than the mean (2.87±0.32 pg/ml) in non-diabetic subjects. The mean (0.97±0.19 ng/dl) serum free T4 in type 1 diabetic subjects was lower than mean (1.23±0.10 ng/dl) in non-diabetic subjects and this differences was statistically very significant (p=.0001). The mean serum T3 in type 1 diabetic and non-diabetic subjects was (108.1±25.28 ng/dl) and (144.68±12.94 ng/dl) respectively. Serum T3 value was significantly (p=<.0001) different when compared between two groups. The mean (6.37±1.03 µg/dl) serum T4 levels in type 1 diabetic subjects was significantly (p=<.0001) lower than the mean (8.07±.76 µg/dl) in non-diabetic subjects. There was very high significant (p=<.0001) difference between the mean (6.52±5.32µIU/ml) serum TSH levels in type 1 diabetic subjects compared with mean (2.29±1.60 µIU/ml) in non-diabetic subjects.

Prevalence of thyroid disorders in diabetes mellitus
In our study the frequency of thyroid dysfunction was 5 (25% ) in diabetic subjects as compared to 4 (4%) in non-diabetic subjects.
When the subjects were sub grouped on the basis of gender it was observed that prevalence of abnormal thyroid function was more in females as compare to males type 1 diabetic subjects (Table 3).

The subjects with thyroid dysfunction were further subgrouped into subclinical and primary thyroid diseases (Table 4). In type 1 diabetic subjects there were two cases of sub clinical hypothyroidism and three cases of primary hypothyroidism. In case of non-diabetic group four subjects were having sub clinical hypothyroidism. There was no case of subclinical and primary hyperthyroidism in both the groups.

### Table 3: Distribution of thyroid disorders according to gender in type 1 diabetes and non diabetic subjects

<table>
<thead>
<tr>
<th>Group</th>
<th>Type 1 diabetes mellitus (N = 20)</th>
<th>Non Diabetics (N = 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects having thyroid disorders in</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2 (10%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Female</td>
<td>3 (15%)</td>
<td>3 (3%)</td>
</tr>
<tr>
<td>Total</td>
<td>5 (25%)</td>
<td>4 (4%)</td>
</tr>
</tbody>
</table>

When both types of diabetes were studied, 25% had lower thyroid hormone level (Table 3). Our study is comparable with other studies [18,20,21,22] on thyroid disorder in diabetes showing the high prevalence of hypothyroidism. Among 20 diabetic subject studied, 25% had lower thyroid hormone level where as in non-diabetic subjects, only 4% had lower thyroid hormone level (Table 3). Our study is being supported by the other studies by[18,20,21,22]on thyroid disorder in diabetes showing the high prevalence of hypothyroidism. (both clinical and sub clinical hypothyroidism) as compared to hyperthyroidism. The presence of both raised and low levels of thyroid hormones in diabetes in this study may also be due to modified TRH synthesis and release [17] and may depend on the glycemic status of diabetics studied. Glycemic status is influenced by insulin which in known to modulate TRH and TSH.

The abnormal thyroid hormone level may be out came of various medication the diabetes were receiving for example it is known that insulin 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 phenythioureas are known to suppress the level of FT₄ and T₃ while causing diabetes is attributed to the presence of thyroid hormones binding inhibitor (THBI), an inhibitor of extra thyroidal conversion enzyme (5'-deiodinase) of T₄ to T₃ and dysfunction of the hypothalamus-pituitary-thyroid axis [17]. These situations way prevail in diabetics & would be aggravated in poorly controlled diabetics. Stress, which is associated with diabetes, may also cause changes in the hypothalamus anterior pituitary axis in these diabetics. It appears that the presence of subclinical hypothyroidism and hypothyroidism may results from hypothalamus-hypophyseal- thyroid-axis disorders as suggested by [18].

There are few studies on the prevalence of thyroid dysfunction in diabetes. Some studies have targeted only type 1 diabetes, while other only type 2 diabetes. The prevalence of thyroid dysfunction varies among different population. The present study concluded 25% of diabetic subjects had thyroid dysfunction (Table 3). When we compared our study with different studies from different parts of the world the prevalence of thyroid dysfunction among patients varies. [19] reported prevalence of 10.8% thyroid dysfunction in DM patient while [20]reported that 46.5% of diabetic patient have thyroid disorder but all these studies showed high incidence of thyroid dysfunction among diabetic as compared to control population.

The prevalence of thyroid dysfunction were more in female as compared to male in our study (Table 3). These observations are consistent with the other studies [19,21]. This finding is probably associated with the higher prevalence of obesity recorded in female diabetics. Insulin, which is used in treating diabetes and is produced in normal quantities or in excess, has been associated with increased anabolic activity.

### IV. DISCUSSION

The mean serum FT₃, FT₄, T₃, T₄ were significantly lower (P=<.0001) in diabetic compared to non-diabetic control subjects, while the mean TSH level were significantly higher in diabetic compared to non-diabetic subjects (Table 2). These are in agreement with the number of reports on TSH level in type 1 and type 2 diabetes mellitus and many of them have recorded elevated TSH level [9,13,14]. The overall prevalence of thyroid disease in Scotland was found to be 13.4%, with prevalence of 31.4% in type 1 diabetic females, and lowest in type 2 diabetic males (6.9%)][9]. The Explanation for this finding is that the thyroid hormones, triiodothyroine and tetraiodothyroine are insulin antagonists that also potentiate the action of insulin indirectly [15]. In diabetic patients, the nocturnal TSH peak is blunted and TSH response to TRH is impaired [16] which is responsible for the occurrence of low thyroid hormones level in diabetics. The abnormal thyroid hormones levels found in

### Table 4: Type of thyroid disorders according to gender in type 1 diabetic and non diabetic subjects

<table>
<thead>
<tr>
<th>Types of diabetes along with the gender</th>
<th>Types of thyroid disorders*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Subclinical Hypothyroidism</td>
</tr>
<tr>
<td>Type 1 diabetic (N=20)</td>
<td>Male</td>
</tr>
<tr>
<td></td>
<td>Female</td>
</tr>
<tr>
<td>Non-diabetic (N=100)</td>
<td>Male</td>
</tr>
<tr>
<td></td>
<td>Female</td>
</tr>
</tbody>
</table>

*No case of Subclinical and Primary Hyperthyroidism
raised level of TSH [17]. These situations may explain the finding of low or raised thyroid hormones status in diabetic subjects. Nevertheless the situations in these diabetics does not seen to follow the pattern previously recorded in other non thyroid diseases such as liver diseases and Cushing syndrome where low thyroid hormone level were recorded. The thyroid hormones, triiodothyronine and tetraiodothyronine are insulin antagonists that also potentiate the action of insulin indirectly. These factors could be responsible for the occurrence of low thyroid hormones level in some diabetics.

V. REFERENCES


