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Frequency of Thyroid Dysfunction Among Diabetes in Punjabi Population

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ABSTRACT : The aim of the present study was to examine the frequency of thyroid disease among diabetes in Punjabi population and to investigate the effect of *Diabetes mellitus* on thyroid hormone levels and other biochemical variables. The totals of 200 subjects including 100 diabetic (20 type 1 and 80 type 2) and 100 non diabetic controls subjects were included in the present study. Each patient was investigated for plasma glucose fasting (FPG), glycosylated hemoglobin (HbA1c), serum cholesterol, serum triglyceride, high density lipoproteins (HDL) low density lipoproteins (LDL), very low density lipoproteins (VLDL), blood urea, serum creatinine, SGOT, SGPT, total triiodthyronine (T3), total thyroxine (T4), free triidothyronine (FT3) free thyroxine (FT4) and thyroid stimulating hormone (TSH).Patients with diabetes showed significantly higher levels of TSH, FPG , HbA1c, serum cholesterol, serum triglyceride, LDL, VLDL, blood urea, creatinine, SGOT, SGPT and significantly lower levels of T3, T4, FT3, FT4 and HDL as compared to non-diabetics. Among the 100 diabetics patients studied 29% shows abnormal thyroid hormone levels (24% had hypothyroidism and 5% had hyperthyroidism) whereas in 100 non diabetics subjects only 4 % of the subjects were having abnormal thyroid dysfunction.

Keyword : Diabetes, Hypothyroidism, Hyperthyroidism, T3, T4, TSH, FT3 and FT4.

INTRODUCTION

Diabetes mellitus (DM) and thyroid diseases are two common endocrinopathies seen in general population. The association between diabetes and thyroid dysfunction had been recognized since 1979, (Feely *et al.*, 1979; Gray *et al.*, 1979). Since then most of the studies have reported the prevalence of thyroid dysfunction among diabetes patients to be between 2.2 to 17% (Perros *et al.*, 1995; Smithson, 1998). Fewer studies have observed very high prevalence of thyroid dysfunction in diabetes *i.e.* 31 % and 46.5% respectively (Celani *et al.*, 1994; Udiong *et al.*, 2007)

Thyroid hormones are insulin antagonists, both insulin and thyroid hormones are involved in cellular metabolism and excess and deficit of any one can result in functional derangement of the other (Sugure *el al.*, 1999).

Thyroid disease is a pathological state which adversely affects diabetic control and is commonly found in most forms of DM. It is generally associated with advanced age in type 2 diabetes and autoimmune diseases in type 1 diabetes (Shah, 2007). DM may affect thyroid function either at the level of hypothalamic control of TSH release or at the conversion of T4 to T3 in the peripheral tissue. It has been well documented that hyperglycemia leads to reversible reduction of the activity and hepatic concentration of T4-5-deiodinase, low serum concentration of T3 and low, normal, or high level of T4 (Shah, 2007).

In hyperthyroidism there is elevation in the rate of glucose absorption, production (and utilization) and glycogen synthesis (and degradation) leading to decreased glycogen level (Donckier, 2003) but insulin resistance, degradation and requirements are increased and there is increased secretion with exaggerated effects of glucagon and adrenaline on the liver, all these change may lead to diabetic ketoacidosis in state of insufficient insulin supply. For these reason the dosage of oral anti diabetic drugs and insulin should be increased in diabetic patients with thyroid disease.

In hypothyroidism there is reduction in the rate of glucose absorption, gluconeogenesis and glucose production (and utilization) and glycogen synthesis (and degradation) leading to increased glycogen level. Additionally, insulin half-life will be prolonged with increase in its level and reduction in insulin requirement. Glucose level will be stabilized during treatment of hypothyroidism but the risk of recurrent hypoglycemia will increase if insulin dose is not decreased (Mohn *et al.*, 2002).

Since thyroid hormone regulate metabolism and diabetes can alter metabolism of food stuff, the metabolism of organisms may be further affected by the combination of thyroid disease and diabetes.

The relationship between diabetes mellitus and thyroid dysfunction has not been demonstrated in Punjab although the prevalence of diabetes mellitus is very high and increasing. Due to the lack of adequate information about the two conditions, preventive management is difficult to plan and yet there could be many diabetic patients who

may have thyroid dysfunction which may greatly affect their glycemic control. Malfunctions like thyroid disease which can occurs in diabetes mellitus and that causes metabolic disturbances can further complicate management of patients and escalate the cost of diabetes mellitus treatments.

Keeping the above in view the aim of the present study was to examine the frequency of thyroid disease in patients with diabetes mellitus and study the effect of diabetes on other biochemical variables in Punjabi population.

MATERIAL AND METHODS

The subjects were selected from the cases presenting with diabetes mellitus 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 100 Diabetic (20 type 1 and 80 type 2) and 100 non diabetic subjects. The criteria to diagnose diabetes mellitus was based on FPG level of 110mg/dl or higher, at more than two occasions and were receiving treatments such as insulin, oral hypoglycemic drugs and or physical exercise for diabetics mellitus. The initial criteria used for separating type 1 and type 2 subjects were the physician classification based on age of onset of diabetes and dependence on Insulin Therapy alone to achieve normal plasma concentration.

The non diabetes volunteers without history of diabetics mellitus whose FPG was less than 110 mg /dl on two occasions were 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.

The study excluded subjects suffering from rheumatoid arthritis, tuberculosis, collagen disorders, liver diseases, renal diseases, cardiac failure and gout.

Blood samples were collected from all the 200 subjects. They were kept on over night fast at least for 10 hrs before blood collection. 5 ml of venous blood was taken in dry disposable syringe under aseptic conditions in sterile, dry vial for biochemical analysis.

The serum levels of T3, T4, FT3, FT4 and TSH were estimated by electrochemiluminous method on Elcysis 2010. FPG, HbA1c, cholesterol, triglycerides, HDL, LDL, VLDL, blood urea, serum creatinine, SGOT and SGPT, were determined on semi automated clinical chemistry analyzer.

Statistical Analysis

The result were expressed as mean + SD of each variable. The comparison between means was performed by student t test using SPSS version 10. P-value of 0.05 or less was interpreted as significant for the analysis.

RESULTS AND DISCUSSION

Table 1 presents the sex and age distribution of diabetic and non-diabetic subjects. In diabetic subjects 47 (47%) were males and 53 (53%) were females while in non diabetic subjects 48 (48%) were male and 52 (52%) were females. Mean age of diabetic subjects was 40.95 ± 11.2 and that of Non-diabetic subjects was 41.09 ± 11.1.

Table 1: Sex and age distribution of diabetic and non-diabetic subjects.

Group	*Sex*	*No*	*Mean age in years*
Diabetic subjects	Male	47	
(N = 100)	Female	53	40.95 ± 11.2
Non-diabetic subjects	Male	48	
(N = 100)	Female	52	41.09 ± 11.1

Table 2 shows the levels of various biochemical parameters in diabetic and non-diabetic subjects. FPG, HbA1c, serum cholesterol, serum triglycerides, serum LDL, serum VLDL, SGOT, SGPT, blood urea and serum creatinine were significantly higher while serum HDL was significantly lower in diabetic as compare to non-diabetic subjects.

In the present study a very high significant elevation in serum cholesterol, serum triglycerides, serum LDL and serum VLDL and low level of serum HDL was observed in diabetic as compare to non-diabetic subject. This may be accounted for by decrease in basal metabolic rate (BMR) in diabetic patients due to untreated hypothyroidism that commonly occurs may causes serious illness and further complicate lipid disturbances (Erin Mccanlies *et al.*, 1998). Gray *et al.*, (1981) had reported elevated total cholesterol and triglyceride in diabetics with increased level of TSH and dyslipidaemia is dependent on glycemic control. In the case of subclinical hypothyroidism (increased TSH), elevated total cholesterol, triglycerides and LDL-C with compareable HDL-C have been reported by Nadia *et al.*, 2002 . The abnormally high concentration of serum lipids in diabetes is mainly a result of the increase in mobilization of free fatty acids from peripheral depots. This happens because reduced insulin levels increase the activity of the hormone-sensitive lipase. On the other hand, glucagons, catecholamines, and other hormones enhance lipolysis. The marked hyperlipemia that characterizes the diabetic state may therefore be regarded as a consequence of the uninhibited actions of lipolytic hormones on fat depots (Suryawanshi *et al.*, 2006).

In the present study increased blood urea production in diabetes may be accounted for by enhanced catabolism of both liver and plasma proteins (Prakasam *et al.*, 2004). Diabetic hyperglycemia induces elevation of the plasma level of urea and creatinine, which are considered significant markers of renal dysfunction.

Table 2: Comparison of various biochemical parameters in diabetic and non-diabetic subjects

Parameters	*Diabetic subjects (N = 100)*	*Non-diabetic subjects (N = 100)*	*P value*
FPG (mg/dl)	157.45±14.41	88.52±6.72	<0.0001
HbA1c (% age)	7.18±0.73	5.01±0.22	<0.0001
Serum Cholesterol (mg/dl)	191.89±22.02	166.21±9.67	<0.0001
Serum Triglycerides (mg/dl)	158.27±30.62	123.69±15.87	<0.0001
Serum HDL (mg/dl)	42.80±2.79	44.70±1.49	<0.0001
Serum LDL(mg/dl)	116.90±15.90	96.8±7.86	<0.0001
Serum VLDL(mg/dl)	31.47±6.44	24.78±3.15	<0.0001
Serum SGOT (U/L)	33.18±8.14	30.11±3.65	<0.0007
Serum SGPT (U/L)	35.65±8.50	32.38±3.61	<0.0001
Blood Urea (mg/dl)	33.58±6.97	29.72±2.69	<0.0001
Serum Creatinine (mg/dl)	1.13±0.23	1.00±0.09	<0.0001

*Values are given as mean ± SD.

As shown in table 3 the serum levels of free T3, free T4, T3 and T4 were significantly lower while level of TSH was significantly increased in diabetic subjects as compare to non-diabetic subjects.

Table 3: Levels of serum thyroid hormones in diabetic and non-diabetic subjects.

Parameters	*Diabetic subjects (N = 100)*	*Non-diabetic subjects (N = 100)*	*P value*
Serum Free T3 (pg/ml)	2.19±0.81	2.87±0.32	<0.0001
Serum Free T4 (ng/dl)	1.05±0.39	1.23±0.10	<0.0001
Serum T3 (ng/dl)	117.37±39.56	144.68±12.94	<0.0001
Serum T4 (µg/dl)	6.94±2.07	8.07±0.76	<0.0001
Serum TSH (µIU/ml)	5.95±5.54	2.29±1.60	<0.0001

Values are given as mean ± SD.

The distribution of thyroid dysfunction according to the gender in diabetes mellitus (type 1, type 2) and control subjects are listed in table 4. The incidence of hypothyroidism is more in females as compare to males in both type 1 and type 2 diabetes.

Table 4: Type of thyroid disorders according to gender in Diabetes mellitus (Type 1, Type 2) and control group.

			Types of Thyroid disorders		
Types of Diabetes mellitus along with the gender	*Subclinical Hypothyroidism*		*Primary Hypothyroidism*	*Subclinical Hyperthyroidism*	*Primary Hyperthyroidism*
Type 1 (N = 20)	Male	1	1	0	0
	Female	1	2	0	0
Type 2 (N = 80)	Male	4	2	0	2
	Female	8	5	0	3
Non-Diabetic (N = 100)	Male	1	0	0	0
	Female	3	0	0	0

Out of 100 diabetic subjects studied, 29% shows abnormal thyroid functions with 24% having low thyroid hormone level and 5% having high thyroid hormone level) and 71% shows normal thyroid hormone level as shown in Fig. 1.

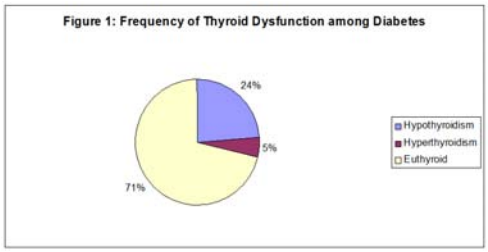

Fig. 1.

Thyroid is an important endocrine gland of human body and plays vital role in the normal functioning of the body. It has important effect on glucose metabolism along with lipids and proteins and conversely can be affected by abnormal glucose metabolism. Among the 100 diabetic subjects investigated, 24% had lower levels of thyroid hormones with 14% having subclinical hypothyroidism and 10% having primary hypothyroidism while 5% had higher thyroid hormones levels, all being cases of primary hyperthyroidism. Among the non diabetic subject 4% had lower levels of thyroid hormones. These findings indicate a high incidence of abnormal thyroid hormone levels in diabetics subject as compared to non-diabetic subjects. Our observations are in agreement with the earlier reports where altered thyroid hormone levels of different magnitudes have been reported in diabetic subjects (Celani *et al.*, 1994; Smithson, 1998; Suzuki *et al.*, 1994; Udiong *et al.*, 2007).

Some of the type 2 diabetic were on oral hypoglycemic agents alone and some were on both insulin injections and oral hypoglycemic agents while the type 1 subjects were treated with insulin injections alone. The abnormal thyroid hormones levels may be the outcome of the difference in drug therapies among diabetics. For example,

it is known that insulin, an anabolic hormone enhances the level of FT4 while it suppress the level of T3 by inhibiting hepatic conversion of T4 to T3 (Boehringer Mannheim, 1984). On the other hand some of the oral hypoglycemic agents such as the phenylthioureas are known to suppress the level of FT4 and T4, and raise the levels of TSH (Smith *et al.*, 1998; Whitley, 1984). These situations may explain the finding of low or raised thyroid hormones levels in the diabetics. The presence of both raised and low levels of thyroid hormones levels in diabetics in this study may also be due to modified thyroid releasing hormone (TRH) synthesis and release (de-Greef *et al.*, 1992) and may depend on the glycemic status of the diabetics studied. Glycemic status is influenced by insulin, which is known to modulate TRH and TSH levels (Reusch *et al.*, 1999).

CONCLUSIONS

This study shows a very high incidence (29%) of thyroid dysfunction among diabetic patients. Failure to recognize the presence of abnormal thyroid hormone levels may be a primary cause of poor management often encountered in some of the treated diabetics. There is therefore need for the routine assay of thyroid hormones in diabetic, particularly in those patients whose conditions are difficult to manage.

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