www.jmscr.igmpublication.org *Impact Factor 1.1147*

ISSN (e)-2347-176x

IGM Publication Journal Of Medical Science And Clinical Research An Official Publication Of IGM Publication

A Study of Thyroid Function in Diabetes Mellitus

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Abstract

Diabetes Mellitus and Thyroid Disease are two common endocrinopathies seen in adult population of North Eastern region of India. Presence of thyroid dysfunction in Diabetic patients makes management of the disease more difficult. This is a hospital based study done to compare the prevalence and form of thyroid dysfunction in Diabetic patients and non-Diabetic controls. Thyroid Function (TSH, TT3, TT4, FT3, FT4) was studied in 100 cases of Diabetes Mellitus and 100 non-diabetic controls. There was significant difference in TSH levels in between Diabetics and Non-Diabetics (2.94±2.1mIU/Lvs2.18±1.5 mIU/L, p<0.05). TT4 and FT4 levels also showed significant difference in between the two groups,TT4(118.53±54.83nmol/L vs 95.5±26.12nmol/L, p=.0002), FT4 (10.42 ±22.91pmol/L, 14.54±5.28pmol/L, p<.0001). Thyroid dysfunction was found to be 43% in Diabetics as compared to 21 % in non-Diabetics. In Diabetics 35% were hypothyroid and 8% hyperthyroid. 37.29% of female diabetics were found to be hypothyroid as compared to 31.7% of male diabetics.

Keywords- *Diabetes Mellitus, Hyperthyroid, Hypothyroid, TSH (Thyroid Stimulating Hormone), TT4 (Total thyroxine), FT4 (Free Thyroxine), TT3 (Total Tri-iodothyronine), FT3 (free tri-iodothyronine).*

INTRODUCTION

Diabetes Mellitus and Thyroid Disease are the two common endocrinopathies seen in adult population [1]. The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000 and is estimated to be 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2002 to 366 million in 2030 [2].

With India having the highest number of diabetic patients in the world, the sugar disease is posing an enormous health problem in the country The International Diabetes Federation estimates that the number of diabetic patients in India more than doubled from 19 million in 1995 to 40.9 million in 2007. It is projected to increase to 69.9 million by 2025.

Thyroid related disorders are posing as the next diabetes to affect the nearly forty million Indians. The term "Thyroid Diabetes", was coined in the early literature to depict the influence of thyroid hormone excess in the deterioration of glucose control.[3] Diabetic patients have a higher prevalence of thyroid disorders compared with the general population, because patients with one organ specific autoimmune disease are at risk of developing other autoimmune disorders.[4,5] Thyroid disorders have been reported as 13.4%, with the highest in patients with Type1 Diabetes Mellitus(31.4%) and lowest in patients with type 2 Diabetes Mellitus(6.8%).[6] A number of reports have however indicated a higher than normal prevalence of thyroid disorders in type 2 diabetic patients, with hypothyroidism being the most common disorder.[7] In other studies the frequency of hypothyroidism in patients with diabetes mellitus has been reported as 0.7 % to 4 % and hyperthyroidism has varied from 3.2 % to 4.6 %.[8] The physiological and biochemical interrelationship between Insulin and iodothyronines and the influence of both insulin and iodothyronines on the metabolism of carbohydrates, proteins and lipids are recorded.[9,10] The presence of thyroid dysfunction may affect diabetes control.[4] Taking all these facts into consideration the aim of this study was

a) To compare the prevalence of thyroid dysfunction in Diabetic patients with age and sex matched Non-Diabetic control group.

b) To find out the form of thyroid dysfunction more commonly found in Diabetics.

c) To evaluate the pattern of thyroid dysfunction found in male and female diabetics.

2. MATERIALS & METHODS:

The present study population comprised of 100 diagnosed cases of Diabetes Mellitus and 100 non-diabetic controls.

All the data was collected from Central Clinical Laboratory, Gauhati Medical College and Hospital (GMCH) from July 2013 to December 2013.

2.1 Criteria for selection of Cases:

Inclusion Criteria : Diagnosed cases of diabetes receiving treatment with oral hypoglycaemic agents and/or insulin therapy and who had no previous history of thyroid dys-function.

Exclusion Criteria :The study excluded very ill-patients with complication of diabetes mellitus and also patients with previous history of thyroid dysfunction.

Age and sex matched non-diabetics with no history of thyroid disorder were taken as control subjects .

2.2 Data Collection : Samples which reached Central Laboratory-Biochemistry Section, GMCH and had tests request for both blood glucose and thyroid profile were set aside to be part of the study. After analysis the samples which had high blood glucose,(fasting glucose>126mg/dl,or Post-prandial glucose>200mg/dl) were taken as Diabetic cases and samples in which blood glucose was found to be normal (Fasting glucose<110mg/dl, Post-prandial glucose<140mg/dl), were taken as controls. Both cases and controls were followed up in the wards and selection of diabetic cases and nondiabetic controls was confirmed after taking their detailed medical history. Informed consent of the patients were taken and general health characteristics such as age , sex, dietary habits,menopausal status in women, drug history, were recorded. The thyroid profile data of diagnosed diabetic and non-diabetic controls available in Central Laboratory was collected and analysed.

2.3 Estimation of Thyroid Profile :

Thyroid Profile**:** Thyroid hormones T4, FT4,T3,FT3 and TSH was measured by chemiluminescent assay on Vitros 5600 using Vitros reagent packs.

2.4 Statistical analysis:

Statistical analysis was performed using SPSS 13 for Windows. Data were presented as mean ± SD. Two unrelated samples were compared by student T-test. Variation of grouped data was assessed by two-way analysis of variance.

2.5 Classification of the study participants into hyperthyroid, hypothyroid and euthyroid was based on the following criteria*:*

Hyperthyroid : FT4 values>28.2 pmol/L or TSH<0.465 mIU/L or both.

Hypothyroid : FT4 < 10pmol/L or TSH >4.68mIU/L or both.

Euthyroid : FT4 and TSH values within the range 10 – 28.2pmol/L and 0.465 – 4.68mIU/L respectively.

3. Results & Observations:

The present study was carried out with 100 diabetic cases and 100 non-diabetic controls.The maximum number of diabetic cases (38) and non-diabetic controls (40), were in the age group of 46-55 years.59% of diabetic cases were female and 41% were male.

TSH, TT4, FT4 levels were statistically higher in Diabetic case group than in non-diabetic controls. As shown in Table 3 there was no significant difference in the levels of TSH, T4, T3, and FT4 among the different age groups in diabetics. But FT3 showed significant difference, ($p<0.05$); among the different age groups.In non-diabetic controls there was significant difference in the levels of T4, T3 among the different age groups, while FT4, FT3, and TSH levels did not differ significantly.

Analyses of thyroid hormone levels according to sex in the diabetic cases showed significant difference in the FT3 values between male and female diabetics with females having a lower FT3 value (p-value 0.0028). TSH level was significantly higher in females than males, (2.23± 1.08mIU/L,1.60± 0.87mIU/L, p-value 0.0017). In non-diabetic control group there was significant difference in T4 and T3 levels , with females showing higher levels, p-value 0.0254 and 0.0088 respectively

P > .05 was considered not significant.

P < .05 was considered significant.

P < .01 was considered highly significant.

P < .001 was considered very highly significant.

Subjects grouped as hyperthyroid had FT4 values>28.2 pmol/L or TSH<0.465 mIU/L or both.

Those classified as being hypothyroid had FT4 < 10pmol/L or TSH >4.68mIU/L or both. Subjects grouped as Euthyroid had FT4 and TSH values within the range 10 – 28.2pmol/L and 0.465 – 4.68mIU/L respectively.

Table 1 : Thyroid dysfunction in diabetics and non-diabetics

Subjects	*Diabetics*			*Non-diabetics*		
	Male	*Female*	*Total*	*Male*	*Female*	*Total*
Total	*41*	*59*	*100*	*49*	*51*	*100*
Hypothyroid	*13*	*22*	*35*	*7*	*13*	*20*
Hyperthyroid	*3*	*5*	*8*	*0*	*1*	*1*
Euthyroid	*25*	*32*	*57*	*42*	*37*	*79*

Table 2:Level of TSH and thyroid hormones in diabetics and controls.

	Diabetics Range	Mean±SD	Control Range	Mean±SD	p-value
TSH(mIU/L)	<0.015-20.86	2.94±2.1	0.42-11.49	2.18±1.5	<0.05
T4(nmol/L)	55.34-167.31	118.53±54.83	57.53-153.02	95.50±26.12	0.0002
T3(nmol/L)	1.11-2.89	1.69±1.09	1.04-2.46	1.83±0.65	0.2769
FT4(pmol/L)	10.42-22.91	20.33±9.01	9.40-20.59	14.54±5.28	<.0001
FT3(pmol/L)	2.55-6.57	4.44±1.29	2.69-5.99	4.16±1.09	0.1034

Table 3:Comparision of the Levels of thyroid hormones in diabetics and non-diabetic controls in different age groups:

	DIABETIC CASES					NON-DIABETIC CONTROLS				
Age (years)	TSH (mIU/L) Mean ± SD	T4 (nmol/L) Mean ± SD	T3 (nmol/L) Mean ± SD	FT4 (pmol/L) Mean ± SD	FT3 (pmol/L) Mean ± SD	TSH (mIU/L) Mean ± SD	T4 (nmol/L) Mean ± SD	T3 (nmol/L) Mean ± SD	FT4 (pmol/L) Mean ± SD	FT3 (pmol/L) Mean ± SD
<35	2.10±1.31	115.06±45.56	1.74±0.92	15.06±27.03	3.81±1.20	2.08± 1.32	102.32±27.67	1.67±0.72	16.47 ±5.02	3.95±1.72
36-45	1.92±1.47	88.93±46.46	1.35±0.78	15.44±14.67	3.98±1.41	2.19± 1.09	101.54±17.37	1.97±0.80	16.86±5.41	4.06±1.4
46-55	2.16±1.53	112.74±50.84	1.69±1.17	17.24±20.59	4.15±0.94	2.01± 1.19	98.71±25.87	1.55± 0.32	14.29±6.56	3.56± 1.29
56-65	2.05±1.60	107.98±44.66	2.20±1.35	22.91±19.56	4.62±1.61	1.64± 1.23	126.90± 14.54	2.18±0.46	12.74±4.5	3.26±1.2
>65	1.97±1.81	139.12±115.9	1.60±1.40	14.8±11.45	3.18±1.44	1.98± 1.02	127.67±15.70	1.92±0.95	11.84±2.32	3.15± 1.57
P-value	>0.05	>0.05	>0.05	>0.05	<0.05	>0.05	<0.0001	0.0003	>0.05	>0.05

Table 4:Study of thyroid hormones according to sex in diabetic and non-diabetic controls:

	Diabetic cases			Non-diabetic controls		
	Males	Females	P-value	Males	Females	P-value
TSH(mIU/L)	1.60± 0.87	2.23± 1.08	0.0017	2.67± 1.23	2.31± 1.11	0.1282
T4(nmol/L)	124.45±50.06	113.38±54.44	0.2971	95.11±24.58	113.64±52.25	0.0254
T3(nmol/L)	1.97± 1.20	1.69±1.0	0.2287	1.8±0.54	2.06±0.43	0.0088
FT4(pmol/L)	20.72±6.82	19.05±9.14	0.2974	15.32±4.50	16.47±5.28	0.2401
FT3(pmol/L)	4.79±1.18	3.95±1.57	0.0028	3.09±1.27	3.46± 1.74	0.2280

In the present study 43% of diabetics had thyroid dysfunction, 35% of them were hypothyroid and 8% were hyperthyroid. When compared with non-diabetics thyroid dysfunction was found in only 21%, 20 non-diabetics being hypothyroid and 1 person hyperthyroid.

The maximum number of hypothyroid diabetics, 37.13% were in the age group of 46-55 years and also the maximum number of hyperthyroid diabetics 50% were in this age group.

4. DISCUSSION

Diabetes Mellitus is an important health problem that is affecting major population worldwide. It is characterized by absolute or relative deficiencies in insulin secretion and/or insulin action and is manifested as hyperglycemia. The influence of endocrine and non-endocrine organs other than the pancreas on Diabetes Mellius is well documented.[11,12,13] Occasionally other endocrine disorders such as abnormal thyroid hormone levels are found in Diabetes Mellitus.[14,9].

In this study the majority of diabetic cases were in the age group 46-55 years, i.e. 58 cases. This goes with the finding of a study by H. King et al.[2] titled " Global burden of Diabetes" , where it was found that majority of diabetics are in the 45-64 years age range in the developing countries.

TSH level was found to be significantly higher in Diabetic cases than in non-diabetic controls. Studies by Celani,[15] and Smithson,[16] recorded higher TSH levels in Diabetics while P. Pasupathi et al[17], and C.E.J.Udiong et al[18], recorded lower TSH levels in Diabetics. TSH level was found to be significantly higher in female diabetics as compared to male diabetics, a finding consistent with the findings of P.Pasupathi and C.E.J.Udiong.

TT4 and FT4 levels also were significantly higher in Diabetic cases, while no significant differ ence was observed in the levels of TT3 and FT3. This is consistent with the finding of P.Pasupathi et al.[17]No significant difference was observed in thyroid hormone levels in different age groups, except FT3(P value <.05). FT3 level was also found to be significantly higher in males than females.

The abnormal thyroid hormone levels found in the diabetics may be the outcome of the various medications the diabetics were receiving and may depend on the glycemic status. Many investigators have reported that treatment of diabetes with sulfonylureas led to an increased incidence of hypothyroidism. It is known to suppress the levels of FT4 and T4 while causing raised levels of TSH.[19,20] Insulin, an anabolic hormone enhances the level of FT4 while it suppresses the levels of T3 by inhibiting hepatic conversion of T4 to T3.[21] Suzuki et al[22] attributed the abnormal thyroid hormone levels found in diabetes to the presence of Thyroid Hormone Binding Inhibitor (THBI), an inhibitor of extra thyroidal conversion enzyme of T4 to T3 and dysfunction of hypothalamus – hypophyseal thyroid axis. These situations may prevail in diabetics and would be aggravated in poorly controlled diabetics. Stress which is associated with diabetes mellitus may also cause changes in the hypothalamus anterior pituitary axis in these diabetics. The diet of

the people of North Eastern Region of India may also influence the thyroid hormone levels. Diet here is rich in green leafy vegetables and may exhibit goitrogenous effect on the thyroid. This however requires further research.

In this study, thyroid dysfunction was found to be more among the Diabetic cases compared to controls(43% vs 21%). This finding is in agreement with the findings of C.E.J.Udiong and P.Pasupathi et al. In the diabetic group 35% were hypothyroid and 8% were hyperthyroid while in controls, 20% were hypothyroid and 1% were hyperthyroid. Gender wise break-up of thyroid function abnormality showed the incidence of hypothyroidism to be more in females than males. 37.29% of the female diabetics were hypothyroid as compared to 31.70% of

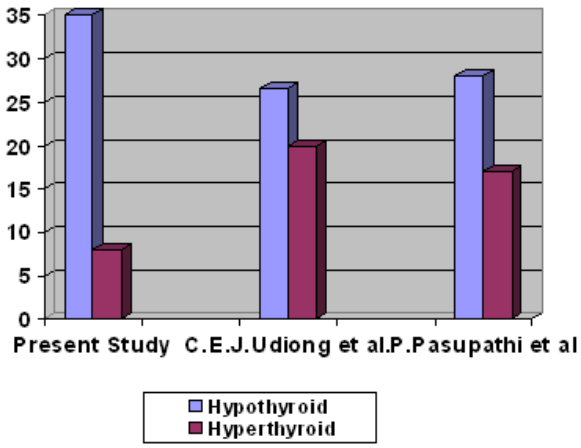

Fig 1 : Comparison of Thyroid dysfunction found in the present study with the findings of C.E.J.Udiong et al and P.Pasupathi et al.

males. Similar observations were made by Radetti et al(1994), Sacks et al,[23] Celani et al,[15] and P.Pasupathi et al. Hyperthyroidism was also found to be higher in females (8.47%) than males(7.32%).

Studying the age-wise distribution of thyroid dysfunction in diabetic cases, the maximum number of thyroid dysfunction was found in the age-groupn of 46-55 years. In a study by Mohd. A. Ardekani[24] the prevalence of thyroid dysfunction was highest between the ages 45-55 years with another spike between 56-65 years.So general screening for thyroid dysfunction should be done earlier (below 50 years) in our population than recommended in other populations.

5. CONCLUSION

Diabetes Mellitus and thyroid diseases are the two common endocrinopathies seen in the adult population. With insulin and thyroid hormones being intimately involved in cellular metabolism ,excess or deficit of either of these hormones could result in the functional derangement of the other. Diabetes in itself, or medications taken by diabetics coupled with the diet of the people may play an important role in determining the thyroid status in case of Diabetics. Presence of thyroid dysfunction in diabetics however makes management of the disease more difficult. So early diagnosis and management of thyroid dysfunction in case of Diabetics will surely go a long way in its proper management and prevention of complications. So routine assessment of thyroid hormone levels in diabetics, particularly the difficult to manage cases is recommended.

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