Original Research Article

Thyroid Dysfunction and Diabetes: A Relationship That's Not Sweet

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Abstract

Background: The aim of the present study was to evaluate the clinical association of thyroid disorders in type 2 diabetes mellitus patients and to correlate the thyroid function tests with diabetic control, duration and its complications.

Materials and methods: A hospital based case control study was conducted at Department of Medicine of a tertiary care hospital. The study population included diagnosed cases of type 2 DM and their non-diabetic family members of similar age and gender as control. A detailed history was taken and examination was done as per the pre-tested, structured interview schedule. All patients in addition to hematological and routine urine work up underwent target organ evaluation for diabetes. All patients were evaluated for thyroid status and assessment of T3, T4 and TSH levels was carried out at our institution. Diabetic state of the patients was estimated by analyzing HbA1c and blood sugar indices (FBS/ PPBS). Data was analyzed using SPSS software ver. 21.

Results: Mean age of diabetics (T2DM) and non-diabetics was 55.09±10.99 years and 51.11±8.78 years respectively while in each group 57 (50%) males and 57 (50%) females were included. Among cases, 33 (29%) patients were detected with thyroid disorders of which 25 (22%) were hypothyroid and 8 (7%) were hyperthyroid. Among controls, 15 (13%) patients were detected with thyroid disorders of which 11 (9.6%) were hypothyroid and 4 (3.5%) were hyperthyroid. A significant association was observed between prevalence of thyroid disorder and diabetes ($p<0.05$). No association was observed between prevalence of thyroid disorder and control and duration of diabetes or presence of microvascular complications ($p>0.05$).

Conclusion: A high prevalence of Thyroid dysfunction was observed in type 2 Diabetes Mellitus patients as compared to non-diabetic population with Hypothyroidism and Clinical thyroid disorders being more common than hyperthyroidism and subclinical thyroid disease. Thus, one must have strong suspicion of thyroid dysfunction in patients with diabetes mellitus.

Key words

Diabetes Mellitus, Hypothyroidism, Hyperthyroidism, Thyroid Function Tests.

Introduction

Diabetes Mellitus (DM) and thyroid dysfunction (TD) are the two most common endocrine disorders in clinical practice [1]. The association between DM and TD is widely known, with the first studies published in 1979 [2]. Diabetes Mellitus is the commonest endocrine disorder and the leading cause of death worldwide [3]. The WHO estimated diabetes prevalence was 2.8% in 2000 and 4.4% in 2030. The total no. of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030 [4].

Thyroid dysfunction is a disorders of the thyroid gland which manifests either as hyper - or hypothyroidism and is reflected in the levels of thyroid stimulating hormone (TSH) [5]. Thyroid is the most common endocrine disorder in the general population after diabetes [6]. A number of studies estimated prevalence of thyroid dysfunction among diabetes patients ranging from 2.2-17% [7-9]. However, fewer studies have estimated higher prevalence of thyrodiabetics i.e. 31% and 46.5% respectively [10, 11]. These differences can be explained by different diagnostic criteria of TD, the degree of iodine intake among different regions, different sensitivities of the TSH assays and the large population diversity [12]. Defective insulin secretion leads to various metabolic aberrations in T2DM, spanning from hyperglycemia due to defective insulin-stimulated glucose uptake and up regulated hepatic glucose production, along with dyslipidaemia, which includes impaired homeostasis of fatty acids, triglycerides, and lipoproteins [13].

DM appears to influence thyroid function in two sites; firstly at the level of hypothalamic control of TSH release and secondly at peripheral tissue by converting T4 to T3. Hyperglycemia causes reduction in hepatic concentration of T4-5 deiodinase, low serum concentration of T3, raised levels of reverse T3 and low, normal, or high level of T4. Thyroid hormone regulate metabolism and diabetes can alter metabolism [14].

Thus the relationship between TD and DM is characterized by a complex interaction of interdependence. Screening of TD, especially the subclinical dysfunction, in patients with DM is justified because most patients can be asymptomatic. Determining the prevalence of clinical and subclinical thyroid disease in diabetic patients in our country and its implications in the course of diabetes and known factors for cardiovascular risk is necessary. The present study was thus conducted to evaluate the clinical association of thyroid dysfunction in type 2 diabetes mellitus patients.

Materials and methods

A hospital based, case control study was conducted at Yenepoya Medical College Department of Medicine of a tertiary care hospital for duration of 2 years. The study population included diagnosed cases of type 2 DM with age > 30 years. Their non-diabetic family members of similar age and gender were selected as control.

Exclusion criteria

- Age </= 30 yrs.
- Non-Indian origin.
- Pregnant female.
- Critically ill patients.
- Known cases of thyroid disorders.
- Patients on Glucocorticoids, Valproate, Carbamazepine, Amiodarone.

Sample Size calculation

In a study conducted by Saha, et al. [15], the occurrence of thyroid abnormalities in patients with type 2 DM was 25% and in non-diabetics is 9%. Taking the expected frequency of thyroid abnormalities to be 25% in diabetics and 9% in non-diabetics and the type 1 error to be 5% and

power of the study to be 90%, the sample size at 95% confidence interval was 114 in each group (calculated by software G*Power ver. 3.1.7). So the final total sample size was 228.

Methodology

A detailed history was taken and examination was done as per the pre-tested, structured interview schedule. All patients in addition to hematological and routine urine work up underwent target organ evaluation for diabetes. All patients were evaluated for thyroid status and assessment of T3, T4 and TSH levels was carried out at our institution. The laboratory evaluation of thyroid functions was done by estimation of serum T3, T4 and TSH levels by chemilumiscence assay method. Two ml of blood was drawn and centrifuged and serum (500 microml) collected from that and incubated with the reagent (separate for T3, T4 and TSH) for about 1 hour at room temperature. Later the readings were taken from the instrument COBAS 6000.

The normal readings are:

T3 – 0.7-2.0 ng/ml
T4 – 4.5-11.0 microg/dl
TSH- 0.4-5.0 microIU/ml

Diabetic states of the patients were estimated by analyzing HbA1c and blood sugar indices (FBS/ PPBS) by glucose oxides wherein 1 ml of blood was drawn and centrifuged to collect the serum, 10 mu of serum is incubated with 1 ml of reagent at room temperature for 15 min. Later the reading was taken from the instrument. Patients were diagnosed based on the ADA criteria for diabetes [16]:

- Symptoms of diabetes plus random blood glucose concentration of 11.1 mmol/L (200 mg/dL); or
- Fasting plasma glucose of 7.0 mmol/L (126 mg/dL); or
- Two-hour plasma glucose of 11.1 mmol/ L (200 mg/dL) during an oral glucose tolerance test; or
- HbA1C >/= 6.5%

Data Analysis

Data was analyzed using SPSS 21.0 (SPSS Inc., Chicago, IL, USA) using appropriate statistical tests.

Results

The present study included a total of 228 subjects with 114 Cases (type 2 diabetics) and 114 controls (non-diabetics). Mean age of diabetics (T2DM) and non-diabetics was 55.09±10.99 years and 51.11±8.78 years respectively while in each group 57 (50%) males and 57 (50%) females were included. Both the groups were evenly matched with respect to age and gender distribution. Among cases, 33 (29%) patients were detected with thyroid disorders of which 25 (22%) were hypothyroid and 8 (7%) were hyperthyroid. Among controls, 15 (13%) patients were detected with thyroid disorders of which 11 (9.6%) were hypothyroid and 4 (3.5%) were hyperthyroid (**Table - 1**). A significant association was observed between prevalence of thyroid disorder and diabetes ($p<0.05$). Out of all the cases with thyroid disorders, about three fourth showed clinical features in both the groups while remaining was subclinical (non-tabulated). No association was observed between prevalence of thyroid disorder and control and duration of diabetes or presence of microvascular complications ($p>0.05$) (**Table – 2 to 4**).

Discussion

Diabetes mellitus is an important health problem affecting major populations worldwide. The influence of endocrine and non-endocrine organs other than the pancreas on diabetes mellitus is documented. Occasionally, other endocrine disorders such as abnormal thyroid hormone levels are found in diabetes. The major alterations in thyroid [7] hormone system are a reduction in the TSH stimulation of the thyroid gland, probably caused by central hypothyroidism, and in the peripheral generation of T3 from T4. The present case control study was conducted with aim of studying the spectrum of thyroid dysfunction in diabetes mellitus patients.

Table – 1: Comparison of Thyroid dysfunction among Cases and Controls.

Thyroid Status	**Group**		**Total**
	Diabetics	**Non Diabetics**	
Normal	81	99	180
	71.1%	86.8%	78.9%
Hypothyroid	25	11	36
	21.9%	9.6%	15.8%
Hyperthyroid	8	4	12
	7.0%	3.5%	5.3%
Total	114	114	228
p- value	**0.0137**		

Table – 2: Association of Thyroid Dysfunction with Duration of Diabetes.

Thyroid Status	**Duration of DM**		**Total**
	</= 10 years	**> 10 years**	
Normal	69	12	81
	69.0%	85.7%	71.1%
Hypothyroid	24	1	25
	24.0%	7.1%	21.9%
Hyperthyroid	7	1	8
	7.0%	7.1%	7.0%
Total	100	14	114
p- value	**0.35**		

Table – 3: Association of Thyroid Dysfunction with Diabetic Microvascular Complications.

Thyroid Status	**Diabetic Complications**		**Total**
	No	**Yes**	
Normal	41	40	81
	69.5%	72.7%	71.1%
Hypothyroid	14	11	25
	23.7%	20.0%	21.9%
Hyperthyroid	4	4	8
	6.8%	7.3%	7.0%
Total	59	55	114
p- value	**0.89**		

In present study, a significant association was observed between prevalence of thyroid disorder and diabetes ($p<0.05$). Among cases, 29% patients were detected with thyroid disorders (22% hypothyroid and 7% hyperthyroid) while among controls only 13% patients had thyroid disorders (9.6% hypothyroid and 3.5% hyperthyroid).

Several reports documented a higher than normal prevalence of thyroid dysfunction in the diabetic population. Perros, et al. demonstrated an overall prevalence of 13.4% of thyroid diseases in diabetics [7]. Recently, a prevalence of 12.3% was reported among Greek diabetic patients [2] and 16% of Saudi patients with type 2 diabetes were found to have thyroid dysfunction [17]. In Jordan, a study reported that thyroid dysfunction was present in 12.5% of type 2 diabetic patients

[18]. Recently Pasupathi et al. [19] in their study found that prevalence of thyroid disorder was 45% among type 2 diabetics. Hypothyroidism was present in 28% and 17% had hyperthyroidism. Udiong, et al. [20] in his study from Nigeria found that prevalence of thyroid disorder was 46.5%. Hypothyroidism was present in 26.6% and 19.9% had hyperthyroidism. In a study by Ravishankar, et al., a total of 100 Type 2 DM patients were included. Thyroid disorders were present in 29%, Hypothyroidism in 1, hyperthyroid in 13 and subclinical hypothyroidism in 15 cases [21].

Table – 4: Association of Thyroid Dysfunction with Control of Diabetes.

Thyroid Status	**Diabetes Control (HbA1c)**		**Total**
	</= 6.5%	**> 6.5%**	
Normal	10	71	81
	76.9%	70.3%	71.1%
Hypothyroid	3	22	25
	23.1%	21.8%	21.9%
Hyperthyroid	0	8	8
	0.0%	7.9%	7.0%
Total	13	101	114
p- value	**0.57**		

In present study we found that out of all the patients with thyroid disorders, about three fourth showed at least some kind of clinical features while remaining one fourth were subclinical. Shah et al. conducted study on 100 patients of diabetes mellitus in which 38 were males and 62 were female. Out of 31 diabetics with thyroid dysfunction, 23 patients were already diagnosed, on treatment and well controlled. Remaining 8 patients (out of 31), clinical features of abnormal thyroid function such as weight gain (37%), facial puffiness (12.5%) were found in 4 patients while 4 patients did not show any clinical evidence [22].

Bazrafshan, et al. observed a significant positive correlation between hemoglobin (HbA1c) concentration and TSH in their study [23]. In another similar study by Ghafari, et al. [24], duration of diabetes of more than 10 years has a relative risk of 1.66 (95% CI, 1.06–2.61; p-0.02). They concluded that diabetes duration of more is an important risk factor for thyroid disorders. Similar association with control and duration of DM was observed in few other studies in different ethnic groups [25-28]. But in present study, no association was observed between the prevalence of thyroid disorder and control and duration of diabetes or presence of microvascular complications (p>0.05).

Conclusion

A high prevalence of Thyroid dysfunction was observed in type 2 Diabetes Mellitus patients as compared to non-diabetic population with Hypothyroidism and Clinical thyroid disorders being more common than hyperthyroidism and subclinical thyroid disease. Thus, one must have strong suspicion of thyroid dysfunction in patients with diabetes mellitus. An aggressive and early screening of type 2 diabetics may prevent thyroid and diabetes related complications in such patients. However more such studies on larger scale are needed to know the complete spectrum of thyroid dysfunction in diabetes.

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References

1. Hage M, Zantout MSM, Azar ST. Tyroid disorders and diabetes mellitus. J Thyroid Res., 2011; 2011: 439463.
2. Papazafiropoulou A, Sotiropoulos A, Kokoloki A, Kardara M, Stamataki P, e Pappas S. Prevalence of thyroid dysfunction among greek type 2 diabetic patients attending an outpatient clinic. J Clin Med Res., 2010; 2: 75-78.
3. Faghilimnai S., Hashemipour M., Kelishadi B. Lipid profile of children with type 1 diabetes compared to controls. ARYA J., 2006; 2(1): 36 -38.
4. Wild S., Roglic G., Green A., Sicree R., King H. Global prevalence of diabetes. Diabetes Care, 2004; 27: 1047- 1053.
5. Tunbridge WMG, Evered DC, Hall R, Appleton D, Brewis M, Clarke F, et al. The spectrum of thyroid disease in a community: The Whickham survey. Clin Endocrinol., 1977; 7: 481- 493.
6. Gray R.S., Irvine W.J., Clarke B.F. Screening for thyroid dysfunction in diabetics. Br Med J., 1979; 2(6202): 1439.
7. Perros P, McCrimmon RJ, Shaw G, Frier BM. Frequency of thyroid dysfunction in diabetic patients: value of annual screening. Diabet Med., 1995; 12(7): 622-627.
8. Smithson MJ. Screening for thyroid dysfunction in a community population of diabetic patients. Diabet Med., 1998; 15(2): 148-150.
9. Radaideh AR, Ajlouni KM. Thyroid dysfunction in patients with type 2 diabetes mellitus in Jordan. National Center of Diabetes, Endocrinology and Genetics, Jordan University of Science and Technology, School of Medicine, Irbid, Jordan. Saudi Medical Journal, 2004; 25(8): 1046-1050.
10. Celani M.F., Bonati M.E., Stucci N. Prevalence of abnormal thyrotropin concentrations measured by a sensitive as- say in patients with Type 2 diabetes mellitus. Diabete Res., 1994; 27(1): 15-25.
11. Udoing C.E.J.A., Udoh E., Etukudoh M.E. Evaluation of thyroid function in diabetes mellitus in Calabar, Nigeria. Indian J Clin. Biochem., 2007; 22: 74-78.
12. Chen G, Juan W, Yinghua L, et al. Associations between cardiovascular risk, insulin resistance, β- cell function and thyroid dysfunction: A cross-sectional study in the ethnic minority group of Fujian Province in China. Euro J Endocrinol., 2010, 163: 775-782.
13. J.D. Baxter, P. Webb. Thyroid hormone mimetics: potential applications in atherosclerosis, obesity and type 2 diabetes. Nature Reviews Drug Discovery, 2009; 8(4): 308–320.
14. Shah SN. Thyroid disease in diabetes mellitus. J Assoc Physicians India, 2007; 32(12): 1057- 1059.
15. Saha HR, Khan H, Sarkar BC, Khan SA, Sana NK, Sugawara A, Choudhury S. A comparative study of thyroid hormone and lipid status of patient with and without diabetes in adults. Open Journal of Endocrine and Metabolic Diseases, 2013 May 23; 3(02): 113.
16. American Diabetes Association. 2. Classification and diagnosis of diabetes. Diabetes care, 2015 Jan 1; 38(Supplement 1): S8-16.
17. D. H. Akbar, M. M. Ahmed, J. Al-Mughales. Thyroid dysfunction and thyroid autoimmunity in Saudi type 2 diabetics. Acta Diabetologica, 2006; 43(1): 14–18.
18. A R. M. Radaideh, M. K. Nusier, F. L. Amari, et al. Thyroid dysfunction in patients with type 2 diabetes mellitus in Jordan. Saudi Medical Journal, 2004; 25(8): 1046–1050.

19. Palanisamy Pasupathi. Screening for Thyroid Dysfunction in the Diabetic/Non-Diabetic Population. Thyroid Science, 2008; 3(8): 1-6.
20. C.E.J. Udiong, A.E. Udoh, M. E. Etukudoh. Evaluation of thyroid function in diabetes mellitus in Calabar, Nigeria. Indian Journal of Clinical Biochemistry, 2007; 22(2): 74-78.
21. Ravishankar S. N. A prospective study of thyroid-dysfunction in patients with Type 2 diabetes in general population. Clinical Practice, 2013; 5(1): 17-27.
22. Shah T, Rathod T, Nayak H. Study of Thyroid Disorder in Patients of Diabetes Mellitus (100 Cases). Ind J Res., 2015 Sept; 4(9): 41-42.
23. Bazrafsham HR, Ramezani A, Salehu A, et al. Thyroid dysfunction and its relation with diabetes mellitus (NIDDM). J GorganUni Med Sci., 2002; 2: 5-11.
24. Al-Geffari M, Ahmad NA, Al-Sharqawi AH, Youssef AM, AlNaqeb D, Al-Rubeaan K. Risk factors for thyroid dysfunction among type 2 diabetic patients in a highly diabetes mellitus prevalent society. International journal of endocrinology, 2013; 23(1): 1-6.
25. Díez JJ, Sánchez P, Iglesias P. Prevalence of thyroid dysfunction in patients with type 2 diabetes. Experimental and Clinical Endocrinology and Diabetes, 2011; 119(4): 201–207.
26. Yang J-K, Liu W, Shi J, Li Y-B. An association between subclinical hypothyroidism and sight-threatening diabetic retinopathy in type 2 diabetic patients. Diabetes Care, 2010; 33(5): 1018–1020.
27. R Satish, V Mohan. Diabetes and Thyroid Diseases-Review. Int. J. Diab. Dev. Countries, 2003; 23: 120-123.
28. A. Shashi, Upasana, Devi, S. Singla. Association Between Hypothyroidism And Metabolic Syndrome In Type 2 Diabetic Patients: A Cross Sectional Study. International Journal of Basic and Applied Medical, 2013; 3(1): 98-109.