Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2016; 4(8D):3031-3036 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI: 10.36347/sjams.2016.v04i08.057

Original Research Article

Does the glycemic control and duration of diabetes affect Thyroid Dysfunction? A cross-sectional study from a tertiary hospital in Central Gujarat

Dr. Keyur Brahme[1], Dr. Jaydeep Devaliya[2], Dr. Ishani Haldar[3], Dr. Mahendra Parmar[4], Dr Kalpita Shringarpure[5]

[1]Assistant Professor, [3]Resident, [4]Associate Professor, Dept. of Medicine, Baroda Medical College, Vadodara, Gujarat, India

[2,5]Tutor, Dept. of Community Medicine(PSM), Baroda Medical College, Vadodara, Gujarat, India

***Corresponding author**
Dr. Keyur Brahme
Email: keyurbrahme@gmail.com

Abstract: Diabetes Mellitus (DM); a chronic metabolic syndrome and thryoid dysfunctions (TD) are the commonest endocrine disorder leading to high morbidity. Few studies have shown the association between the two. Hence this study was undertaken to understand association of thyroid dysfunction with the duration of diabetes and the degree of glycemic control. A cross-sectional study on 212 diabetic individuals was conducted in Sir Sayajirao General Hospital. All the patients were subjected to a detailed clinical history and examination including Hemogram and biochemical parameters [Random blood sugar (RBS), Fasting blood sugar (FBS), Post-prandial blood sugar (PP2BS), HbA1C and Thyroid profile (fasting): S.TSH, Free T3, Free T4]. The outcome measure was thyroid dysfunction and input variables included the duration of DM and glycemic control. Data was entered in MS Excel and analysed using Epi Info V3.5.4. The total prevalence of thyroid dysfunction (TD) was 24.2% among all 212 DM patients. Prevalence of TD was more in the group with poor glycemic control (82.5 %), which was higher than the group with good glycemic control (65.15 %).Prevalence of TD was greater (57.15%) in the population which had a longer duration of DM compared to those who had a shorter duration of DM (8.75%). There is a significant association of TD with duration of DM and poor glycemic control. It is necessary to screen all DM cases for TD for secondary prevention and also for primary prevention(early diagnosis and treatment); as thyroid dysfunction along with diabetes mellitus carries varyingly high rates of morbidity.
Keywords: Thyroid dysfunction, Diabetes mellitus, association, glycemic control.

INTRODUCTION

Diabetes Mellitus (DM), a chronic metabolic syndrome[1]is characterized by chronic hyperglycemia. The deficiency in the secretion of insulin or due to the peripheral resistance at the cellular level, leads to hyperglycaemia[1,2]. It leads to disturbance in carbohydrate, fat and protein metabolism secondary to deficiency in insulin secretion or in its action[1,3,4].

Several pathogenic processes ranging from autoimmune destruction of the beta cells of the pancreas with consequent insulin deficiency to abnormalities that result in resistance to insulin action may lead to DM[1,5]. This pathophysiology leads to diabetic complications viz. diabetic foot, diabetic neuropathy and vasculopathy, diabetic nephropathy and retinopathy, musculoskeletopathies and endocrinopathies, adding to its morbidity and mortality[5,6].

Thyroid disorders are second to DM, which is the commonest endocrine disorder leading to death[4,5]. Over the last two decades, the worldwide prevalence of diabetes has increased from an estimated 30 million in 1980 to over 200 million in 2010[4,7], prevalence of DM in the worldwide population being over 260 million in 2015[2,8]. Current trends show that approximately 438 million people worldwide will have DM by the end of 2030[4,8,9].The prevalence of thyroid dysfunction (TD) ranges from6.6% to 13.4% in general population[6,8], while in diabetics, their prevalence is still higher ranging from 10% to 24%[6,8]. This association between diabetes and TD was first published in 1979 and later through different methods[3,4,9]. The pathophysiology of various endocrinopathies like TD in patients of DM is remains unclear[4,5].

Iodothyronines are insulin antagonist[5] with high levels being diabetogenic while absence of the hormone inhibits the development of diabetes[5,11]. Diabetes mellitus and hyperthyroidism are metabolic disorders that affect the carbohydrate, protein and lipid levels also. Diabetes affects thyroid function at two sites[10,11] first at hypothalamic level by controlling the TSH release and secondly at the peripheral level by converting T4 to T3. The development of thyroid dysfunction is dependent on age of onset and on the duration of DM[11]. Studies comparing the incidence of specific thyroid dysfunction between type 1 and type 2 diabetic patients show different inferences i.e. general consensus remains that TD among patients shows proportionate increment with age of onset, longer duration of diabetes, poorer glycaemic control and with patients having relatively higher abnormal body mass index and other co-morbid states like cardiovascular diseases namely hypertension, atherosclerosis and obesity[11-14]. Also just like in general population, in diabetics as well TD can occur either as SCH or hypothyroid or less commonly as hyperthyroid[8,9,15].

However it has been difficult to show a direct correlation between the metabolic control of DM and impairment in thyroid hormone metabolism. An improved understanding of the mechanisms through which diabetes alters the hormonal profile like thyroid should lead to better preventive and therapeutic interventions only because diabetic patients suffer disproportionately from these conditions in terms of increased prevalence, severity, and morbidity[8-10].

Investigation of the thyroid functions which in most cases refers to follicular cell function[4], includes measurement of secretions (hormones) of the gland such as iodothyronine, carrier protein levels, trophic hormone such as thyroid stimulating hormone (TSH) and thyroxin releasing hormone (TRH). The effects of iodothyronine on the various metabolic pathways are assessed by specific tests, such as free T4, free T3 and TSH[6,9,10].

Since the former is predominant of the two, usually TD should be checked in every patient of diabetes who are either newly detected or are already known cases of DM[6,8-10]. Few studies have concluded that because the prevalence of TD is higher in diabetics, their screening becomes necessary which not only helps in secondary but in some cases may help in primary prevention of the same[16-17].

Hence tests to determine the prevalence of clinical and subclinical thyroid diseases and other similar complications in the diabetic population becomes necessary. So, in this study, we aim to study the association of thyroid dysfunction with the duration of DM and the degree of glycemic control. This could help in early diagnosis of asymptomatic thyroid dysfunction in patients with DM.

MATERIAL AND METHODS

A cross-sectional study of 212 individuals was conducted in SSG Hospital, Vadodara, Gujarat, including all patients; both indoor and outdoor, coming to SSG hospital from 1st February 2015 to 31st September 2015. Taking a prevalence rate of 32%[17] among diabetics in India, power of the study as 80%, allowable error of 20% (relative error), the sample size was deduced at 212.

Patients of age more than 18 years and both sexes with diabetes mellitus types 1 and 2, either a newly detected case or an already known case, either on regular treatment inclusive of both injectable insulin and/or oral hypoglycemic drugs, diet therapy or those who were not on any treatment at all and willing to give consent were included in the study. Patients less than 18 years of age, unwilling to give consent, known cases of thyroid disorders, having DM secondary to pancreatitis, steroid therapy, old debilitated patients, patients presenting with Diabetic ketoacidosis and on drugs like like Amiodarone, Antithyroid, lithium etc which alter the thyroid function and profile were excluded from the study.

All the patients were subjected to a detailed clinical history and examination including Hemogram and biochemical parameters [Random blood sugar (RBS), Fasting blood sugar (FBS), Post-prandial blood sugar (PP2BS), HbA1C and Thyroid profile (fasting): S.TSH, Free T3, Free T4]

The outcome measure was thyroid dysfunction while input variables included the duration of DM and glycemic control.

Patients were considered as having DM if they had random blood glucose of more than 200mg/dl or fasting glucose more than 126mg/dl or 2-hour post-prandial glucose more than 200mg/dl or HbA1C value of more than 6.5 g/ml. Patients having onset of diabetes at an age of less than 35 years and with dependence on insulin therapy alone for complete control, were considered as diabetes type 1, rest others as type 2.

Thyroid dysfunction was considered as present if the patient had primary hypothyroidism i.e. when T3 and T4 were less than, and S.TSH levels were more than the normal range. Secondary hypothyroidism was considered ifT3 and T4 were more than, and S.TSH levels were less than the normal range. Subclinical Hypothyroidism was considered if T3 and T4 were normal and S.TSH was more than the normal range.

Statistical analysis

All data were collected from the target population and entered in Microsoft Excel sheet. The data was analyzed using Epi-info software V3.5.4 and expressed in categorical variables. Prevalence of thyroid dysfunction was expressed proportions and percentages, while association with the duration of DM and glycemic control was shown using chi-square test, at 95% confidence limits.

RESULTS

In this study, 212 patients with diabetes mellitus were enrolled, of which 16 (7.6%) had type 1 DM while 196 (92.4%) had type 2 DM.

Thyroid dysfunction and diabetes mellitus

The total prevalence of thyroid dysfunction (TD) was 52 (24.52%) among all 212 DM patients. Sub-clinical Hypothyroidism was the most common thyroid dysfunction (11.8%) followed by hypothyroidism with prevalence rate of 8.96%. Hyperthyroidism was the least common in the DM patients (3.77%) (Table 1).Prevalence of SCH amongst cases of TD in type 2 DM was 50% while it was 33.3% in type 1 DM. Prevalence of Hypothyroidism amongst cases of TD in type 2 DM was 34.78% which was less than that in type 1 DM (50%). Prevalence of hyperthyroidism amongst cases of TD was 15.21 % in type 2 DM patients, while it was less in type 1 DM (16.66%). Thus, the overall prevalence of thyroid dysfunction in type 2 DM was 23.46% compared to type 1 DM (37.5%), which was significantly different (*Chi square=0.042, p<0.05)* (Table 1)

Table 1: Prevalence of thyroid dysfunction in DM-1 and DM-2

Thyroid Function	DM-1 (N=16)	DM-2 (N= 196)	Total (N=212)
Euthyroid	10	150	160
Sub-clinical Hypothyroidism (SCH)	2	23	25
Hypothyroid	3	16	19
Hyperthyroid	1	7	8
Total	16	196	212
Chi square=0.042p<0.05			

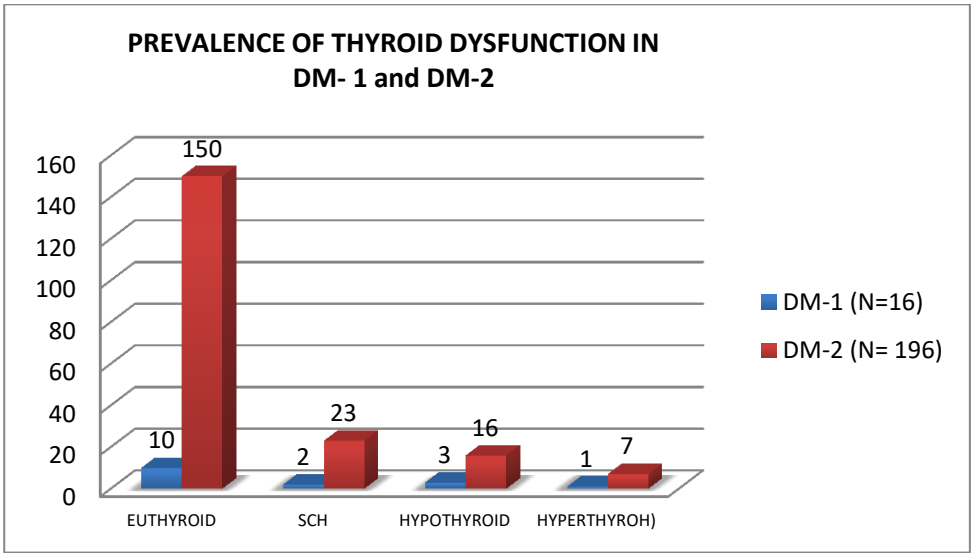

Figure 1: Prevalence of thyroid dysfunction in DM-1 and DM-2

Glycemic control and diabetes mellitus

Patients having HbA1C <10 were considered to have a good glycemic control while patients with HbA1C >10 were considered as having poor glycemic control.

There were total 16 patients with good glycemic control, of which 6 had type 1 DM (37.5%) and 10 had type 2 DM (62.5%), while in the second group with poor glycemic control, there were 196 patients; 126 having type 1 DM (64.29 %) and 70 having type 2 DM(35.71%).**(Table 2)**

Thus a better glycemic control was more prevalent in type 2 DM (62.5%) and a poorer glycemic control was more prevalent in type 1 DM (64.29%). However, this difference is not significant (*Chi square 3.45, p>0.05*) which thus proves that there is no

association between the type of DM and degree of glycaemic control.

Table 2 : Glycaemic control in different types of Diabetes Mellitus

Type	HbA1C<10	%	HbA1C>10	%	Total	%
I	6	37.5%	126	64.29%	132	62.27%
II	10	62.5%	70	35.71%	80	37.73%
Total	16	100%	196	100%	212	100%
Chi square = 3.45 p>0.05						

Thyroid dysfunction and glycemic control

In our study, the prevalence of euthyroid state was more in patients with a comparatively good glycemic control i.e. with HbA1C <10, the prevalence of which was 34.85 %. While in patients with a poorer glycemic control i.e. with HbA1C >10, the prevalence of euthyroid state was just 17.5% (Table 3).

Hence the prevalence of TD was more in the group with poor glycemic control ie 66 cases of 80 cases (82.5 %), which was higher than the group with good glycemic control i.e. 86 cases of 132(65.15 %) (Table 3). Thus it can be inferred that prevalence of TD proportionately increases with poorer glycemic index and hence there is a strong association between the two. Also in both the groups, amongst cases of TD, SCH had highest prevalence while hyperthyroid conditionwas the least prevalent.

Table 3: Thyroid dysfunction in groups with different glycemic control

Type	HbA1C <10	%	HbA1C >10	%	Total	%
Euthyroid	46	34.85 %	14	17.5 %	60	28.30 %
Subclinical Hypothyroidism	48	36.36 %	46	57.5 %	94	44.34 %
Hypothyroid	36	27.28 %	17	21.25 %	53	25 %
Hyperthyroid	2	1.51 %	3	3.75 %	5	2.35 %
Total	132	100 %	80	100 %	212	100 %
Chi square=0.019 p<0.05						

Thyroid function and duration of diabetes mellitus

In this study, out of 212 patients, 142 had a DM since less than 5 years. Among them, 130 (91.45%) cases were euthyroid and only 12 (8.55%) cases had TD.

Similarly out of the total study population, 70 patients had a longer duration of DM i.e. more than 5 years. Of these, only 30 (42.85%) cases were euthyroid while 40 (57.15%) cases had TD. Thus it was concluded that the prevalence of TD is greater in the population which had a longer duration of DM while the prevalence of the euthyroid state was higher in the other group which had a shorter duration of DM, with significant association between duration of DM and TD (Table 4).

Table 4 :Thyroid dysfunction based on duration of Diabetes Mellitus

Type	Duration of DM less than 5 Years (N/%)	Duration of DM more than 5 Years (N/%)	Total (N/%)
Euthyroid	130 (91.45)	30 (42.85%)	160 (75.47)
Thyroid dysfunction	12 (8.55)	40 (57.15%)	52 (24.43)
TOTAL	142	70	212
Chi square=0.037 p<0.05			

DISCUSSION

Thyroid dysfunction (TD) and DM are the two most common endocrinopathies. Diabetics have higher prevalence of thyroid dysfunction compared to general population.

In the present study, we found that the proportion of thyroid dysfunction among diabetics was a total of 52 out of 212 cases i.e. 24.52%. Of these TD cases, 11.79% were SCH which was thus the most common type of thyroid dysfunction, followed by hypothyroid and hyperthyroid condtions (8.96% and 3.77% respectively). SCH was more common in type 2 DM and both hypothyroidism and hyperthyroidism was more common in type 1 DM. Overall prevalence of thyroid dysfunction was less in type 2 DM compared to

type 1 DM. These results are consistent with the results of similar study done Catia C *et al*[18]. However in many other studies it has been proven that the overall prevalence of TD was higher in type 2 DM with respect to type 1 DM and this was attributed to a greater duration of exposure to diabetes in type 2 and younger age group of patients falling under type 1. However since prevalence of poorer glycemic control (denoted by HbA1C results more than 10) was higher in type 1 DM population (almost two-thirds) as compared to type 2 DM population (one thirds) this can explain the overall higher prevalence of TD in type 1 DM which is the inference of our study.

Some previous studies have shown that the risk of thyroid dysfunction proportionately increases with age[19,20]i.e. it is important to emphasize that the patients with longer duration of DM, could be older compared to those with lesser duration of DM. This hypothesis could be tested in future research. These findings may be more favorable to the subclinical abnormalities that could explain the higher frequencies found in DM population and hence the benefit of screening for thyroid dysfunction in them. There is a significant association of TD with the duration of DM and with a poorer glycaemic control. Similarly duration of DM also was associated with TD.

Proportion of TD patients with DM less than 5 years were lesser compared to those with DM more than 5 years. Euthyroid state was higher in the other group which had a shorter duration of DM. These results are consistent with a studies done by Vikhe VB *et al*[16] and another one done by Catia C[18]. Similar conclusion was derived in the study conducted in Manipur[18], in which amongst the population having a longer duration of diabetes more than 5 years, prevalence of thyroid dysfunction was 52% and prevalence of euthyroid in the same was 48%, both results being consistent to the inferences of our study.

CONCLUSION AND RECOMMENDATIONS

In this cross-sectional study of 212 DM patients, it was seen that thyroid dysfunction rises proportionally to the existence of DM in terms of years. There is a significant association of TD with duration of DM and poor glycemic control.

Thus, it is necessary to screen all DM cases for TD not only for their secondary prevention but at times also for primary prevention and early diagnosis and treatment; asthyroid dysfunction along with diabetes mellitus carries varyingly high rates of morbidity and mortality. This study has been conducted in a tertiary care hospital, wherein, a large number of DM and TD cases are seen. Since it was time bound, not all cases may have been included in the study. Hence, a long term follow up of the same patients could enable us to know the changes in TD based on glycemic control. Similar studies in other settings could be the way forward.

REFERENCES:

1. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2014; 37(Suppl. 1):S81-S90.
2. Syed MA, Mitchell BE, Pietropaolo SL, Zhang YJ, Henderson TS, Kelley DE *et al*. Is type 2 diabetes a chronic inflammatory/autoimmune disease? Diabetes Nutr Metab. 2002; 15(2):68-83.
3. Sridhar GR, Nagamani G. Clinical association of autoimmune diseases with DM. Ann N Y Acad Sci. 2002; 958: 390-2.
4. Fauci A, Braunwald E, Kasper D, Hauser S, Longo D, Jameson J, Loscalzo J; Harrison's Principles of Internal Medicine. 18th Edition,McGraw-Hill Companies, New york, 2011.
5. Feely J, Isles TE. Screening for thyroid dysfunction in diabetics. Br Med J 1979; 1(6179): 1678.
6. Palma CCSSV, Pavesi M, Nogueira VG, *et al*. Prevalence of thyroid dysfunction in patients with diabetes mellitus. Diabetology & Metabolic Syndrome. 2013;5:58.
7. Baxter JD, Webb P, Thyroid hormone mimetics: potential applications in atherosclerosis, obesity and type 2 diabetes. Nature Reviews Drug Discovery, 2009; 8(4):308-320.
8. Umpierrez GE, Latif KA, Murphy MB, Lambeth HC, Stentz F, Bush A *et al*: Thyroid dysfunction in patients with type 1 diabetes. Diabetes Care 2003, 26:1181-1185.
9. Chen G, Juan W, Yinghua L. *et al*. Associations between cardiovascular risk, insulin resistence, β-cell function and thyroid dysfunction : a cross-sectionsl study in She ethnic minority group of Fujian Province in China. Euro J Endocrinol. 2010;163:775–782.
10. Celani MF, Bonati ME, Stucci N. Prevalence of abnormal thyrotropin concentrations measured by a sensitive assay in patients with Type 2 diabetes mellitus. Diabete Res. 1994; 27(l):15-25.
11. Udiong CEJ, Udoh AE, Etukudoh ME. Evaluation of thyroid function in diabetes mellitus in Calabar, Nigeria. .. Indian J Clin. Biochem.. 2007;22(2):74-78.
12. Shah SN; Thyroid disease in diabetes mellitus. J Assoc Physicians India, 2007; 32: 1057-1059.
13. International Expert Committee. International Expert Committee report on the role of the A1C assay in the diagnosis of diabetes. Diabetes Care 2009;32: 1327-1334.
14. Kumar PR, Bhansali A, Ravikiran M, Bhansali S, Dutta P, Thakur JS. The Utility of glycated hemoglobin in diagnosing type 2 diabetes mellitus: a community-based study. J Clin Endocrinol Metab 2010;95:2832-2835.

15. Gharib H, Tuttle RM, Baskin HJ, Fish LH, Singer PA, McDermott MT. Consensus statement. Subclinical thyroid dysfunction: a joint statement on management from the American Association of Clinical Endocrinologists, the Thyroid Association and The Endocrine Society. J Clin Endocrinol Metab 2005, 90:581-585.
16. Vikhe VB, Kanitkar SA, Tamakuwala KK, Gaikwad AN, Kalyan M, Agarwal RR. Thyroid Dysfunction in Patients with Type 2 Diabetes Mellitus at Tertiary Care Centre. Natl J Med Res. 2013; 3(4): 377-380.
17. Demitrost L, Ranabir S. Thyroid dysfunction in type 2 diabetes mellitus: A retrospective study. Indian J Endocrinol Metab. 2012;16(Suppl 2):S334-S335.
18. Palma CCSSV, Pavesi M, Nogueira VG, *et al*. Prevalence of thyroid dysfunction in patients with diabetes mellitus. Diabetology & Metabolic Syndrome. 2013;5:58.
19. Chubb SA, Davis WA, Inman Z, Davis TM: Prevalence and progression of subclinical hypothyroidism in women with type 2 diabetes: the Fremantle Diabetes Study. Clin Endocrinol (Oxf) 2005, 62(4):480-486.20. Chen HS, Wu TE, Jap TS, Lu RA, Wang ML, Chen RL *et al*. Subclinical hypothyroidism is a risk factor for nephropathy and cardiovascular diseases in Type 2 diabetic patients. Diabet Med 2007, 24(12):1336-1344.