Thyroid Dysfunction in Patients with Type-2 Diabetes Mellitus in Eastern India

ABSTRACT

Context  To study the prevalence of thyroid dysfunction in type-2 diabetics and spectrum of thyroid dysfunction in view of importance of thyroid disorders on glycemic status and complications of diabetes mellitus (DM).

Aim  The aim of this study is to establish the relationship between the diabetes and thyroid dysfunction probably affected as a consequence to the autoimmune pathology.

Settings and Design  It was a case control study done in the Department of General Medicine, MKCG Medical College, a tertiary care hospital of southern Odisha.

Patients and Methods  A total of 50 cases (diagnosed case of type-2 DM) and 50 healthy controls were taken in consideration randomly. Thyroid function tests were done using chemiluminescence assay. Then it was analysed statistically after tabulation.

Statistical Analysis Used  Statistical analysis was done using Chi-square test for categorical variables. Student’s t-test was used for finding significance between the means. A ‘P’-value of <0.05 was considered significant.

Results  Thyroid dysfunction was found to be more in type-2 DM (16%) than in healthy controls (4%) which was significant. Among those diabetic patients with thyroid dysfunction, 6 (75%) out of 8 were females. The mean BMI was high in diabetic patients with thyroid dysfunction. The HbA1c levels in patients who had thyroid dysfunction were high. Those with thyroid dysfunction had a mean total cholesterol level higher than euthyroid diabetics and controls. Goitre was found to be present in 4% of cases of type-2 DM.

Conclusion  Type-2 DM and thyroid diseases have a significant association. Subclinical hypothyroidism and hypothyroidism (overt) were the commonest thyroid abnormality in type-2 DM. Thyroid dysfunction was associated with worsening dyslipidemia in type-2 DM.

KEYWORDS  Type-2 DM, thyroid dysfunction, latent autoimmune diabetes of adulthood

KEY MESSAGES  DM is a very common disease in eastern India. But, the association of DM with hypothyroidism is to be kept in mind. Early screening of hypothyroidism and hypertriglyceridemia in type-2 DM patients will help to diagnose these comorbidities prior to their clinical manifestations leading to timely management preventing mortality and morbidity.

INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors. The impact of this disease on the quality of life and on morbidity and mortality through the complications that affect the small and large vessels resulting in retinopathy, nephropathy, neuropathy and ischaemic heart disease, and large vessel obstruction have been emphasised by the findings of the national commission (USA) on diabetes and DCCT trial. Diabetes being the most common endocrine metabolic disorder, there was curiosity to understand and learn the association of this with another common endocrine gland function, i.e., the thyroid gland. The association between these two disorders has long been recognised, although the prevalence of thyroid dysfunction in diabetic population varies widely between studies. There are numerous lines of evidence to suggest that type-1 DM is an autoimmune disorder. These include the presence of insulinit, presence of antibodies and auto-reactive T-cell’s against islet antigens, an association with some other known organ specific autoimmune diseases (thyroid disorders and pernicious anaemia).
A number of reports have also indicated a higher than normal prevalence of thyroid disorders in type-2 diabetic patients, with hypothyroidism being the most common disorder.6 The aim of this study is to establish the relationship between the diabetes and thyroid dysfunction probably affected as a consequence to the autoimmune pathology. Thyroid dysfunction was associated with worsening dyslipidemia in type-2 DM. Increased thyroid dysfunction in latent autoimmune diabetes of adulthood (LADA) warrants islet cell antibody screening in type-2 DM to exclude autoimmune thyroid disorders.

**SUBJECTS AND METHODS**

It was a case–control study undertaken in the Department of Medicine, M.K.C.G Medical College Hospital, Berhampur, Orissa, during the period October 2013 to October 2015. This study included 50 diagnosed cases of type-2 DM and 50 age- and sex-matched healthy controls. Patients who are known cases of type-2 DM attending OPD and inpatients of M.K.C.G Medical College, Berhampur Type-2 DM cases, with age >35 years, who were on oral hypoglycemic agents for a period of at least 6 months were included. The diagnosis of type-2 DM was based on ADA criteria. The known patients with thyroid disease and subjects having coexistent conditions and factors who can influence the thyroid hormone levels were excluded like history of neck irradiation, pregnancy, febrile states, burns, trauma, cirrhosis liver, renal failure, advanced malignancies, myocardial infarction and drugs like OCP, salicylates, phenytoin, danazol, amiodarone, clofibrate, beta blockers, etc. Patients were diagnosed to have

1. Overt hypothyroidism, when TSH >6.02 μU/ml, free T4 <0.89 ng/dl and/or free T3 <1.4 pg/ml
2. Overt hyperthyroidism, when TSH <0.3 μU/ml, free T4 >1.76 ng/dl and/or free T3 >4.2 pg/ml
3. Subclinical hypothyroidism, when TSH >6.02 μU/ml with normal free T3 and free T4.
4. Subclinical hyperthyroidism, when TSH <0.3 μU/ml with normal free T3 and free T4.

Thyroid function tests were done using chemiluminescence assay. The statistical analysis was done using Chi-square test for categorical variables. Student’s t-test was used for finding significance between the means. A ‘P-value <0.05’ was considered significant.

**RESULTS**

A total of 50 cases of type-2 DM aged >35 years who presented to the hospital were included in the study and controls were taken with same age and sex. The mean age of the diabetic group was 51.38 ± 7.42 years and that of control group was 50 ± 7.55 years.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Thyroid dysfunction in type-2 DM and controls.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid dysfunction</td>
<td>Type-2 DM</td>
</tr>
<tr>
<td>Subclinical hypothyroidism</td>
<td>5</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>3</td>
</tr>
<tr>
<td>Subclinical hyperthyroidism</td>
<td>0</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>8 (16%)</td>
</tr>
</tbody>
</table>

The mean duration of diabetes was 6.06 ± 3.25 years. After the clinical and laboratory assessment, the results were analysed. Subclinical hypothyroidism and hypothyroidism were the commonest thyroid dysfunction in both cases and controls (Table 1). Thyroid dysfunction was found to be more in type-2 DM (16%) than in healthy controls (4%), which was statistically significant.

As seen in Table 2, hypothyroidism and subclinical hypothyroidism is more evident in the elderly age groups (55–65 years). Among those diabetic patients with thyroid dysfunction (subclinical hypothyroidism and hypothyroidism), 6 (75%) out of 8 were females.

**Comparison of body mass index between cases and controls**

The mean BMI of diabetic patients with thyroid dysfunction (subclinical and overt hypothyroidism) was 29.03 ± 1.54 while that of euthyroid diabetics was 26.04 ± 2.38 and that in healthy controls was 21.32 ± 2.76 kg/m².

**Comparison of TSH levels between cases and controls**

The mean TSH levels in diabetics with thyroid dysfunction was 11.88 ± 5.62 while that in euthyroid diabetics was 2.66 ± 1.04 and in controls was 2.56 ± 2.12.

**Mean HbA1c levels in cases**

The HbA1c levels which reflect the glycemic control in patients who had thyroid dysfunction was found to be 10.33 ± 2.37 while that of euthyroid diabetics was 7.16 ± 1.04 and that of control population being in the range of 4–6%.

**Lipid profile variations in diabetics and controls total cholesterol level distribution**

Out of the 50 diabetic patients studied, 7 were found to have thyroid dysfunction. Those with thyroid dysfunction had a mean total cholesterol level of 257.87 mg/dl with a standard deviation of 28.68 while that of the euthyroid diabetics found to be 204.11 ± 11.35 mg/dl and controls was 180 ± 15.96 mg/dl.
Thyroid anomaly in diabetes

of Nobre et al. (2002) on 298 cases of type-2 DM, who found an overall prevalence of thyroid dysfunction in 12.7% with cases of subclinical hypothyroidism predominating (68.7%) the picture. 2% cases of hyperthyroidism were also detected. There were no cases of hyperthyroidism, subclinical or overt, detected in the present sample of diabetic population studied. This could be related mainly to the smaller sample size taken and partly to the old age group of sample studied, as there is increased prevalence of thyroid hyper function than hyper function as age advances. Recently, there has been an increase in reports which confirm a higher incidence of autoimmune thyroid diseases even in type-2 DM (Krejci et al. (2004)). A possible source of error could be the accidental inclusion of LADA (up to 20% of type-2 DM) in whom there is an increased prevalence of autoimmune thyroid disorders (42%) especially in thyroid hypo function than type-2 DM patients which has been only addressed to a minor extent by including diabetics who were on OHA for quite some time. A correct exclusion of such cases could have been possible only by detection of antibodies (GAD65, ICA512).

Also the percentage of thyroid profile abnormality detected in the general population was 4% which is lower with the data of Whickham survey by Tunbridge et al. (1997), which found it to be 6.6%. The variation can be due to many factors like the smaller sample size, difference in the sensitivity of estimation method and variability in the prevalence of autoimmune factors in different populations. The study by Smithson (1998) in a larger population of 206 cases of type-2 DM also showed a higher female ratio with the prevalence in female diabetics as 10.9% and males as 6.9%, whereas, in this study, that was 12 and 4%, respectively. A possible confounding factor could be an increase in female (27/50) samples, but not amounting to this high a difference which definitely shows a higher prevalence in thyroid disease in females (Table 3).

**Table 2** Age distribution of thyroid dysfunction in diabetics.

<table>
<thead>
<tr>
<th>Age group in years</th>
<th>Type-2 DM</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hypothyroid</td>
<td>Subclinical hypothyroidism</td>
</tr>
<tr>
<td>35–45</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>45–55</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>55–65</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

**Table 3** Sex distribution of thyroid dysfunction.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Type-2 DM</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hypothyroid</td>
<td>Subclinical hypothyroidism</td>
</tr>
<tr>
<td>Male</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Female</td>
<td>2</td>
<td>4</td>
</tr>
</tbody>
</table>

**Triglyceride level distribution**

A total of 7 out of 50 diabetic patients had a mean triglyceride level of 196.62 ± 19.63 mg/dl and that of euthyroid diabetics was 162.26 ± 20.49 mg/dl; the mean level in the controls was 140.18 ± 17.12 mg/dl.

**LDL cholesterol distribution**

The diabetic patients with thyroid dysfunction had a mean LDL cholesterol level of 159.37 ± 16.18 mg/dl and that of euthyroid diabetics was 105.83 ± 12.96 mg/dl while that of controls was 92.18 ± 18.23 mg/dl.

**Prevalence of thyroid swelling among cases and controls**

Goitre was found to be present in 4% of cases of type-2 DM patients with patients having thyroid dysfunction predominating (12.5%). Goitre was detected in 4% of controls amongst whom 1 out of 2 were having thyroid hypothyroidism.

**DISCUSSION**

Out of the 50 cases, 8 (16%) patients were found to have thyroid dysfunction with 5 of them having subclinical hypothyroidism and 3 patients with overt hypothyroidism while in the control population 2 (4%) were found to have thyroid dysfunction of which one with subclinical hypothyroidism and other with overt hypothyroidism. The association of type-2 DM and thyroid disease was significant. This result goes in hand with the study of Akbar et al. (2005) on type-2 DM patients who had reported an overall prevalence of 16% cases of thyroid dysfunction and 42% in cases of LADA. The most common thyroid abnormality detected was subclinical hypothyroidism (5 out of 8 cases) followed by overt hypothyroidism (3 out of 8 cases). This report also tallies with the study of Nobre et al. (2002) on 298 cases of type-2 DM, who found an overall prevalence of thyroid dysfunction in 12.7% with cases of subclinical hypothyroidism predominating (68.7%) the picture. 2% cases of hyperthyroidism were also detected. There were no cases of hyperthyroidism, subclinical or overt, detected in the present sample of diabetic population studied. This could be related mainly to the smaller sample size taken and partly to the old age group of sample studied, as there is increased prevalence of thyroid hyper function than hyper function as age advances. Recently, there has been an increase in reports which confirm a higher incidence of autoimmune thyroid diseases even in type-2 DM (Krejci et al. (2004)). A possible source of error could be the accidental inclusion of LADA (up to 20% of type-2 DM) in whom there is an increased prevalence of autoimmune thyroid disorders (42%) especially in thyroid hypo function than type-2 DM patients which has been only addressed to a minor extent by including diabetics who were on OHA for quite some time. A correct exclusion of such cases could have been possible only by detection of antibodies (GAD65, ICA512).

Also the percentage of thyroid profile abnormality detected in the general population was 4% which is lower with the data of Whickham survey by Tunbridge et al. (1997), which found it to be 6.6%. The variation can be due to many factors like the smaller sample size, difference in the sensitivity of estimation method and variability in the prevalence of autoimmune factors in different populations. The study by Smithson (1998) in a larger population of 206 cases of type-2 DM also showed a higher female ratio with the prevalence in female diabetics as 10.9% and males as 6.9%, whereas, in this study, that was 12 and 4%, respectively. A possible confounding factor could be an increase in female (27/50) samples, but not amounting to this high a difference which definitely shows a higher prevalence in thyroid disease in females (Table 3).
The mean body mass index in diabetic patients was 29.03 ± 1.54 kg/m², which was higher than that amongst controls (21.32 ± 2.76 kg/m²) and euthyroid diabetics (26.04 ± 2.38 kg/m²). This observation attained significance as like the study by Kenigsberg et al. (1976) who reports large number of obese patients in diabetes, possibly due to obesity associated insulin resistance.

The mean HbA1c level in diabetics with thyroid dysfunction was (10.33 ± 2.37) higher than those of euthyroid ones (7.16 ± 1.04). The study by Schleinger et al. (1982) shows a poor glycemic control inducing a ‘low T3 state’ in patients with both type-1 and type-2 DM, However, it should be emphasised that a low T3 syndrome may occur diseases characterised by increased catabolism. The lipid level variations in diabetics show higher than normal values of total cholesterol, triglycerides and LDL cholesterol in diabetic patients with thyroid dysfunction when compared to control population and even higher levels than of euthyroid diabetic individuals. Thus, thyroid disease coexisting with diabetes adds on to the natural dyslipidemia seen in DM. This is in accordance with the Fremantle diabetic study by Davis et al. (2005), who suggested that thyroid dysfunction may cause dyslipidemia through altered insulin sensitivity.

**CONCLUSION**

- Type-2 DM and thyroid diseases have a significant association (P-value of 0.045).
- Subclinical hypothyroidism and hypothyroidism (overt) were the commonest thyroid abnormality in type-2 DM.
- Thyroid dysfunction was more prevalent in female diabetic patients than in males.
- Thyroid dysfunction was associated with worsening dyslipidemia in type-2 DM.
- Increased thyroid dysfunction in LADA warrants islet cell antibody screening in type-2 DM to exclude autoimmune thyroid disorders.

**REFERENCES**