Subclinical Hypothyroidism- An Undermined Aetiology for Uncontrolled Diabetes Mellitus Type II

M. Chauhan¹, M. Wahane², P. Tyagi³

¹Consultant, Department of General Medicine, Civil Hospital, Silvassa, Haveli. ²Assistant Professor, Department of General Medicine, Namo Medical College, Silvassa, Haveli. ³Assistant Professor, Department of General Medicine, Namo Medical College, Silvassa, Haveli.

ABSTRACT

BACKGROUND
Type 2 diabetes and thyroid disorders are the two most common endocrinopathies.¹ Several studies have demonstrated relationship between DM type 2 and thyroid dysfunction, but there are only a few studies done to evaluate the association between subclinical hypothyroidism and glycaemic control of the diabetic patients.

METHODS
It was a cross sectional case control study in 100 diabetic patients out of which 50 cases had poor glycaemic control and 50 controls were patients with good glycaemic control. Subclinical hypothyroidism was defined as elevated TSH (>4 mIU/L) with normal free T4 and in absence of any clinical features.

RESULTS
50 age and sex matched diabetics with HbA1c >6.5 were compared with diabetics with HbA1c <6.5 for thyroid abnormalities. 15% uncontrolled diabetic male and 30% of uncontrolled females had subclinical hypothyroidism compared to 0% male and 11% female with HbA1c <6.5. This when compared to hypothyroid frequency among case and control groups was found to be 5% males and 3.3% females compared to 0% and 3.7% in control group respectively. The frequency of hyperthyroidism was 5% and 6.7% in male and females of case group compared to 4.3% and 3.7% in male and female of control group.

CONCLUSIONS
The prevalence of subclinical hypothyroidism was more in the group with poor glycaemic control as compared to patients with HbA1c <6.5. Diabetics with poor control have an underlying subclinical hypothyroidism which may accentuate impaired glycaemic control and vice versa.

KEYWORDS
Subclinical Hypothyroidism, Type II Diabetics
Type 2 diabetes mellitus is associated with metabolic dysregulation which causes secondary pathophysiological changes of multiple organ systems leading to tremendous burden on individual health. One of such effect is seen on thyroid homeostasis. Thyroid and diabetes are two most common endocrinopathies encountered in practice. Both conditions frequently coexist and prevalence of thyroid dysfunction is higher in diabetic compared to normal. Subclinical hypothyroidism is defined as elevated level of serum TSH with normal level of serum freeT4. The overall prevalence of subclinical hypothyroidism is reported to range from 4-10% but may vary with gender and age.

In patient with Type 2 diabetes the prevalence of hypothyroidism and hyperthyroidism is similar in comparison to non-diabetics. However in the type 2 diabetics the presence of highly frequent subclinical forms of hypothyroidism should be ruled out since they may be associated with higher cardiovascular risk. It has long been recognised that thyroid hormone have marked effects on glucose homeostasis, glucose intolerance and associated with hypothyroid is characterised by insulin resistance. In order to review common pathological mechanisms between diabetes and thyroid dysregulation it has to be acknowledged that thyroid hormones exert profound effects in the regulation of glucose homeostasis which include modifications of the circulatory level of insulin and counter regulatory hormones, intestinal absorption, hepatic production and peripheral tissue uptake of glucose.

Hence, thyroid hormones have a profound effect in modifying glucose metabolism and as a proof of above said concept most diabetic have to adjust their insulin requirements, when overt thyrotoxicosis or hypothyroidism ensue. Prompt therapeutic intervention of thyroid dysfunction success in reverting metabolic decompensation. However, since diabetes has turned into an epidemic disease the focus is nowadays directed toward the possible interaction between thyroid disease and insulin resistance. The prevalence of subclinical hypothyroidism in previous studies in diabetics was 2.2% to 17% and some studies also discard such observation. Moreover little is known of subclinical hypothyroidism and diabetes type 2 association and this study was done to further evaluate in this direction.

### RESULTS

50 age and sex matched diabetics with HbA1c >6.5 were compared to diabetics with HbA1c <6.5 for thyroid abnormalities. The p value for sex distribution was 0.5 and for age was 0.15 which was insignificant. This data suggests that both group have equal incidence of thyroid abnormality irrespective of their age or gender. It was observed that out of 50 patients in Diabetes Group, 30(60%) were females and 20(40%) were males. It was observed that out of 50 patients in Control Group, 27(54%) were females and 23(46%) were males. The p value for the sex distribution in both the groups is 0.545.

### METHODS

This study is case control study conducted in outpatient department of Civil Hospital Silvassa from duration of February 2019 to June 2019. The cases were diabetics with poor diabetic control (HbA1c >6.5) in age group of 30-60 compared to matched diabetics with good glycaemic control (HbA1c <6.5) as control. Both groups were screened for glycaemic status i.e. FBS PPBS and HbA1c. The diagnosis of DM was based on ADA criteria for Type 2 DM with duration of diabetes >1 year but less than <10 years. Patients with known history of liver, renal or cardiac disease, known thyroid disease, patients on medication which can alter sugar or thyroid levels like oral contraceptives, amiodarone, glucocorticoids, propranolol, rifampicin etc. Type 1 diabetics and adults under intensive care were excluded from study. The data was analysed by SPSS version 20.0. The comparison of normally distributed continuous variable between the group was performed using student’s t test. Nominal categorical data between the groups were compared using chi square test or fisher exact test as appropriate. For all statistical test a p value <0.05 was taken to indicate significant result.
It was observed that the HbA1c levels among the case was between (6.5-11.2) with the mean being 7.63. The HbA1c among the Control Group was between (4.5-9.8) with the mean being 5.16. Out of 50 patients in case Group the thyroid status for 33 patients (66%) were normal whereas out of 50 patients in control group 44 (88%) were normal and p value of this correlation is significant. The number of subclinical hypothyroidism cases in the uncontrolled Diabetic Group was 12(24%) and in the control group was 3(6%) and p value of this correlation is significant. The number of hypothyroidism patients in case was 4% and in the control group was 6% the p value of this correlation is in significant. The number of hyperthyroidism patients in the case was 4% and the control was 2% which again is insignificant. The number of subclinical hypothyroidism patients in the Males was 3(15%) in the diabetic group whereas none in the control group and in the females was 9(30%) in the uncontrolled diabetic group as compared to 3(11%) in the control group.

DISCUSSION

The association between DM and thyroid disorders is widely known, with the first studies published in 1979. Since then several studies in different countries were conducted to estimate the prevalence of Thyroid disorders in diabetic population. There is a great variability in the prevalence of Td in general population, ranging from 6.6% to 13.4%. 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 shall be an advantage in the management of type 2 DM. In conclusion, the results of our study showed a high prevalence of TD in the diabetic population which indicates that screening for thyroid disease among patients with diabetes should be routinely performed. The possible aggravation of classical risk factors such as hypertension and dyslipidaemia, arising from an undiagnosed thyroid dysfunction can lead to an increased cardiovascular risk in these patients. However, we reinforce that prospective studies with more patients are necessary to clarify the impact of thyroid disease in diabetic patient.

As observed by Udiong et al the T3 levels were comparatively higher in study group than the control group with values being (1.12±0.88 vs. 1.12±0.88). In the study conducted by Pasupathi et al the T3 levels were found to be higher in the study group than the control group with values being (1.00+.58 vs. 0.95+.35).

<table>
<thead>
<tr>
<th>Study</th>
<th>Diabetics</th>
<th>Control</th>
<th>p</th>
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<tbody>
<tr>
<td>Gurjjet al</td>
<td>46.95 ± 11.2</td>
<td>41.09 ± 11.01</td>
<td>NS</td>
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<tr>
<td>Ishay et al</td>
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<td>Pasupathi et al</td>
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<td>Anila et al</td>
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<td>Present Study</td>
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Table 7. Comparison of Age in Various Studies

In our study FT3 was significantly abnormal lower I diabetes group in comparison with control group (2.44-3.155 vs. 2.50-3.80) with significant p value 0.048. The same was not observed with other studies. The difference in mean T4 is significant in the study of Pashupati et al with values being higher in the study group as compared to control group (10.56 + 4.76 vs. 8.21+ 2.10), similar observation were by Udiong CE, et al however it is not so in our study. According to the study done by Chubb et al the group with type 2 DM poor glycaemic control was related with higher prevalence of SCH and that was more prominent in older females.

In our study the TSH was significantly abnormal (high and low) in diabetics with poor control than in diabetics with good control (3.65+3.73; p=0.028). Though the difference was greater for the high level TSH (hypothyroid) than for the low levels, both are not significantly strong enough (p=0.2). Among the 50 cases investigated 30% had low TSH while 4% had high TSH. In the control group 10% had low TSH and 2% had high TSH. These findings show a high incidence of abnormal TSH (both low and high) in patient with poor glycaemic control. Although these are not statistically significant which might be due to sample size. Similar results were reported by Udiong and co-worker and Pasupathi et al and Anita Devi et al.

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<tr>
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<td>Pasupathi et al</td>
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<td>Present Study</td>
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Table 6. Glycated Haemoglobin

As observed by Pashupati et al the prevalence of thyroid disorders in type 2 DM patients was found to be 45% out of which 28% had hypothyroidism and only 17% had hyperthyroidism. As observed by Celani et al the prevalence of the thyroid disorders in type 2 DM patients was found to be 31.4% out of which 48.3% had subclinical hypothyroidism and 23.1% had hypothyroidism and only 4.4% had hyperthyroidism. As observed by Gurjjet Singh et al the prevalence of thyroid disorders in type 2 DM patients was found to be as high as 48.3% had subclinical hypothyroidism and 23.1% had hypothyroidism and only 4.4% had hyperthyroidism. It was observed in our study that the prevalence of thyroid disorders in type 2 DM patients with poor control was found to be 34% out of which 24% had subclinical hypothyroidism and 6% had hypothyroidism and only 4% had hyperthyroidism. In the study done by Cho et al it was observed SCH risk increased in patient with poor glycaemic control specially HbA1c >9%.

<table>
<thead>
<tr>
<th>Studies</th>
<th>Prevalence of TD in T2DM</th>
<th>Subclinical Hypothyroidism</th>
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<tr>
<td>Pasupathi et al</td>
<td>45%</td>
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<tr>
<td>Celani et al</td>
<td>31.4%</td>
<td>48.3%</td>
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<tr>
<td>Udiong et al</td>
<td>-</td>
<td>26.8%</td>
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<tr>
<td>Gurjjet et al</td>
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<td>27.7%</td>
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<tr>
<td>Present Study</td>
<td>34%</td>
<td>24%</td>
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Table 9. Showing Prevalence of Thyroid Disorders in Type 2 Diabetics
In the present study although biochemically we found 15 cases with hypothyroidism only 3 had some of the symptoms. It appears that the presence of subclinical hypothyroidism and hyperthyroidism may result from hypothalamus-hypophyseal-thyroid axis disorders as suggested by Celani et al.\textsuperscript{12} failure to recognise the presence of abnormal thyroid hormone levels in diabetes may be a primary cause of poor management often encountered in some treated diabetics. There is therefore need for the routine assay of thyroid hormones in diabetics, particularly those whose sugar levels are difficult to manage. Such association of SCH with poor glycaemic control can be secondary to insulin resistance. Fasting insulinemia was reported in patient with SCH\textsuperscript{17} moreover Matejkova et al\textsuperscript{21} demonstrated that patient with SCH have insulin resistance compared to that of patient with hypothyroidism. This was investigated and impaired translocation of GLUT4 on cell surface was also proposed as a probable aetiology. Although insulin resistance indexes such as Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) it can be speculated that insulin resistance would be elevated in poor glycaemic control group. All previous work indicated that HOMA-IR was higher in diabetic with SCH than in those with normal thyroid function.\textsuperscript{20} Radaideh et al\textsuperscript{22} also revealed positive correlation between TSH and HOMA-IR. Interestingly opposite results are also reported by some investigators who suggest that SCH could be a reflection of physiological adaptation against damage brought by Diabetes.\textsuperscript{19,21} Such controversy warrants further studies to be done in this field.

CONCLUSIONS

The prevalence of subclinical hypothyroidism was more in the group with poor glycaemic control as compared to patients with HbA1c <6.5. Diabetics with poor control have an underlying subclinical hypothyroidism which may accentuate impaired glycaemic control and vice versa.

REFERENCES