Prospective Evaluation of Coexistence of Subclinical Hypothyroidism with Type 2 Diabetes Mellitus and Its Effect on Metabolic Profile

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ABSTRACT

BACKGROUND

Subclinical hypothyroidism is the term used to describe a condition where there is isolated elevated serum thyroid stimulating hormone level in the setting of normal serum free thyroxin levels in the absence or presence of symptoms. There is no uniformity in various studies regarding association between subclinical hypothyroidism and type 2 diabetes mellitus with regard to prevalence and change in metabolic profile.

METHODS

After enrolment of patients, a detailed relevant history of patients was taken and detailed clinical examination was done. All information obtained from patients was recorded in predesigned proforma. After 8 hours of fasting, serum levels of glucose, HbA1c, total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglycerides (TG) and low-density lipoprotein cholesterol (LDL-C) by fully automated clinical biochemistry analyser EM 200 were checked. Serum free T3, free T4 and thyroid stimulating hormone (TSH) were measured using standard assay.

RESULTS

Fasting glucose was significantly higher (P = .00001) in diabetes mellitus plus subclinical hypothyroidism group than patients with diabetes mellitus (DM) and euthyroid group (156.3 + 15.77 mg / dl vs. 128.1 + 21.44 mg / dl). Fasting insulin was significantly higher (P = .00001) in diabetes mellitus plus subclinical hypothyroidism group than patients with DM and euthyroid group (3.69 + 0.82 mu / L vs. 2.36 + 0.75 mu / L). There was no significant difference between two groups regarding HbA1c.

CONCLUSIONS

From our study we conclude that prevalence of subclinical hypothyroidism was higher in type 2 diabetes patients than normal population and there was female predominance. Body mass index was significantly higher in subclinical hypothyroidism group and there was no significant difference between the two groups regarding duration of diabetes mellitus. Patients with subclinical hypothyroidism have poor glycaemic control.

KEYWORDS

Subclinical Hypothyroidism, Diabetes Mellitus, Metabolic Profile

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BACKGROUND

Diabetes mellitus is a group of chronic metabolic disorders characterised by increased level of plasma glucose.[1] The metabolic dysregulation associated with it causes secondary "pathophysiological changes in multiple organ system which is responsible for tremendous burden on individual with diabetes mellitus."[2]

As per fact sheet World Health Organization, there is increasing trend in global prevalence of diabetes mellitus that is 4.7 % in 1980 to 8.5 % in 2014 and in low- and middle-income countries than in high-income countries.[3,4] Subclinical hypothyroidism is the term used to describe a condition where isolated elevated serum thyroid stimulating hormone level in the setting of normal serum free thyroxin levels in the absence or presence of symptoms.[5,6] Sub clinical hypothyroidism is a risk factor for future symptomatic thyroid disorder.[7] Thozhukat Sathyapalan et al. has reported from U.K. that subclinical hypothyroidism has protective effect on non-cardiovascular mortality in type 2 diabetes and has no additive cardiovascular risk factor [8]. Cho JH, Kim HJ, Lee JH, et al. have concluded that the prevalence of subclinical hypothyroidism was similar between type 2 diabetes mellitus patient and healthy population but associated with poor glycaemic control.[9] Han C, He X, Xia X, et al. has reported that type 2 diabetes patients are more likely to have subclinical diabetes mellitus than healthy patients and is associated with increased diabetic complications.[10] Ghada A. Mohamed Amira MElsayed et al. has concluded that subclinical hypothyroidism is a common endocrine disorder in patients with Type 2 diabetes and associated with a higher prevalence of vascular complications.[11]

From these literature survey, it is clear that the there is no uniformity regarding association between subclinical hypothyroidism and type 2 diabetes mellitus. Based on these finding we started our study with a hypothesis that there is no association between subclinical hypothyroidism and type 2 diabetes mellitus. So this study has been designed to study the prevalence of subclinical hypothyroidism in type 2 diabetes mellitus and comparison of metabolic parameters between patients with type 2 diabetes mellitus and subclinical hypothyroidism and patients with type 2 diabetes mellitus alone.

METHODS

This is a prospective observational study conducted in the Department of General Medicine and Endocrinology Konaseema Institute Medical Sciences, Amalapuram, Andhra Pradesh, India from April 2017 to January 2020.

Selection of Patients

During our study period we have enrolled 180 patients with diabetes mellitus and 180 normal healthy people for the evaluation of prevalence of subclinical hypothyroidism in general population and diabetes mellitus patient based on selection criteria. Out of these patients in diabetes group we have selected two group first DM + euthyroidism group and second DM + SCH (diabetes mellitus + subclinical hypothyroidism) group. Each group had 30 patients. Patients were selected based on the following inclusion and exclusion criteria. Patients of age more than 4 years of both sexes were included in the study.

Exclusion Criteria

Known case of thyroid disorder
Hepatic and renal disorder
Cardiovascular diseases
Malignancy

Sample Size

Considering the prevalence of subclinical hypothyroidism to be 11 % based on previous study of Sahu MT, Das V, Mittal S, Agarwal A, Sahu M et al. and Deshmukh V, Behl A et al., and prevalence of diabetes mellitus to be 11.8 %, precision of 5 %, confidence interval of 95 % and population of Amalapuram, India 141000, sample size was calculated for prevalence of subclinical hypothyroidism to be 160. Considering 10 % dropout, sample size was taken to be 180.[12,13,14] For calculation of sample size we used calculator for sample size for a prevalence survey, with finite population correction.[15]

Ethics

Present study is approved by the institutional ethics committee. Written informed consent was obtained from all patients or relatives of patients before enrolling them for study.

After enrolment of patients, a detailed relevant history of patients was taken and detailed clinical examination was done. All information obtained from patients was recorded in predesigned proforma. After 8 hours of fasting, serum levels of glucose, HbA1C, total cholesterol, HDL-C, triglycerides (TG) and LDL-C by fully automated clinical biochemistry analyser EM 200 were checked. Serum free T3 free T4 and TSH were measured using standard assay. Subclinical hypothyroidism was defined as an elevated TSH level (> 4.2 mIU / L) and a normal plasma T3 and T4 level. Plasma insulin was determined by using enzyme linked immunosorbent assay. Homeostasis model assessment-insulin resistance (HOMA-IR) was calculated by using the following formula [16]

$$(FPI\ (Fasting\ Plasma\ Insulin) \times FPG\ (Fasting\ Plasma\ Glucose)\ /\ 22.5.$$

Statistical Analysis

Data was recorded in excel sheet and statistical analysis was done with software Statistical Package for the Social Sciences (SPSS)-14 version. Qualitative data was calculated as percentage and proportions and were analysed by chi-square test. Quantitative data was expressed as mean ± SD

and these data was analysed by unpaired student t test. The P value less than 0.05 was taken as significant.

RESULTS

As per selection criteria 180 healthy population and 180 diabetes mellitus patients were enrolled in this study for evaluation of prevalence of subclinical hypothyroidism.

Variable		With DM	Without DM	P Value
Subclinical hypothyroidism	Absent	148 (82.2 %)	164 (91.12 %)	0.013 Chi square statistic 6.1538
	Present	32 (17.78 %)	16 (8.89 %)	

Table 1. Frequency of SCH in General Population and DM Patients

As per Table 1, out of 180 diabetes mellitus patients 148 (82.2 %) were euthyroid and 32 (17.78 %) patients had subclinical hypothyroidism and out of 180 healthy people 164 (91.12 %) were euthyroid and 16 (8.89 %) patients had subclinical hypothyroidism which is significantly lower than diabetic populations.

Variables		DM + Euthyroidism Group (N = 30)	DM+ SCH Group (N = 30)	P Value
Sex	Age	55.86 + 6.41	54.73 + 5.57	.23
Male	42	18 (60 %)	10 (33.33 %)	.03
Female	38	12 (40 %)	20 (66.67 %)	
BMI (kg / m2)		25.23 + 1.94	27.09 + 2.38	0.000
Duration of diabetes		3.21 + 1.60	3.51 + 1.52	.23

Table 2. Demography of Patients in DM Group and DM + SCH Group

There was no significant difference between mean age of patients in DM + euthyroidism and DM + SCH group (55.86 + 6.41 vs. 54.73 +5.57). There was male predominance in euthyroidism (18 (60 %) vs. 12 (40 %)) group but there was female predominance in diabetes mellitus and subclinical hypothyroidism group (10 (33.33 %) vs. 20 (66.67 %). This finding was significant statistically. Body mass index was significantly higher in subclinical hypothyroidism group and there was no significant difference between two groups regarding duration of diabetes mellitus.

Metabolic Parameter	DM + Euthyroidism Group	DM + SCH Group	P Value
Fasting glucose (mg / dl)	128.1 + 21.44	156.3 + 15.77	0.00
Fasting insulin mu / L	2.36 + 0.75	3.69 + 0.82	0.00
HbA1C	6.62 + 0.82	6.98 + 1.12	1.35
TG (mg / dl)	173.4 + 30.27	159.1 + 17.99	0.33
HDL cholesterol (mg / dl)	44.85 + 6.26	48.52 + 3.08	0.01
LDL cholesterol (mg / dl)	112.31 + 25.36	117.85 + 8.90	0.184
plasma free T3 (nmol / L)	1.29 + 0.99	1.37 + 0.48	0.25
plasma free T4	1.31 + .25	1.34 + 0.36	0.44
Plasma TSH	1.79 + .24	4.58 + 1.3	0.0001

Table 3. Comparison of Metabolic Parameters between Patients in DM Group and DM+ SCH Group

Regarding comparison of metabolic parameters in two groups, fasting glucose was significantly higher (P = .00001) in diabetes mellitus plus subclinical hypothyroidism group than patients with DM and euthyroid group (156.3 + 15.77 mg / dl vs. 128.1 + 21.44 mg / dl). Fasting insulin was significantly higher (P = .00001) in diabetes mellitus plus subclinical hypothyroidism group than patients with DM and euthyroid group (3.69 + 0.82 mu / L vs. 2.36 + 0.75 mu / L). There was no significant difference between two group regarding HbA1c. The mean concentration of triglyceride was higher in DM and euthyroid group than patients with diabetes mellitus plus subclinical hypothyroidism but without statistical significance. Serum HDL-C was significantly higher in diabetes mellitus plus subclinical hypothyroidism group than patients with DM and euthyroid group (48.52 + 3.08 vs 44.85 + 6.26). There was no significant difference between two groups regarding serum LDL concentration. There was no significant difference between two groups with respect to plasma free T3 and T4 concentration but plasma TSH was significantly higher in diabetes mellitus plus subclinical hypothyroidism group.

DISCUSSION

Subclinical hypothyroidism is a condition characterised by elevated TSH concentration with change in plasma T3 and T4 concentration. Prevalence of subclinical hypothyroidism is varying between 9 and 11.4 % in general population.[12,13] In present study, we have observed that 17.78 % type 2 diabetes mellitus patients have subclinical hypothyroidism in comparison to 8.89 % in normal healthy population which is significantly higher. Han C, He X, Xia X, et al. prevalence of subclinical hypothyroidism in type 2 diabetes mellitus patient ranged from 4.69 % to 18.86 % this finding corroborates with our study[10]. There was no significant association between the groups with regard to age. Study of Gopinath B, et al. supports our study.[17] There was significant female predominance in subclinical hypothyroidism, this finding corroborates with the finding of Ghada A. Mohamed et al.[11] Body mass index was significantly higher in subclinical hypothyroidism group which corroborates with the finding of Cho JH, Kim HJ, Lee JH, et al.[10] Manjunath Sc et al. has reported that the mean of BMI was higher in subclinical hypothyroidism group but was not significant statistically.[18]

Regarding comparison of metabolic parameters in both groups, one of the important findings in our study was fasting plasma glucose and fasting insulin concentration was higher in subclinical hypothyroidism group but there was no significant difference in glycosylated haemoglobin percentage. "Maratou E, Hadjidakis DJ, Kollias A and Khan SH, Fazal N have concluded that subclinical hypothyroidism is associated with increased risk of insulin resistance and so poor glycaemic control in diabetes mellitus patients which corroborates with our finding.[19,20] From the present study, we have observed that mean of TG concentration was statistically similar in both groups but HDL-C was significantly higher in subclinical hypothyroidism. Gray RS, Smith AF, Clarke BF have concluded that subclinical hypothyroidism along with type 2 DM is associated with increased risk of ischemic heart disease but there is no difference between TG concentration in both groups this supports our finding.[21] Hueston WJ, Pearson WS et al. has concluded that subclinical hypothyroidism along with type 2 DM is not associated with abnormalities in serum cholesterol or triglyceride levels.[22] Cho JH, Kim HJ, Lee JH, et al. has concluded that subclinical hypothyroidism patients has better HDL-C profiles than those with normal thyroid function which corroborates with our finding.[10] In present

study, we have observed that the mean concentration of LDL was similar in both groups which is supported by the work of Díez JJ, Iglesias P et al.[23]

CONCLUSIONS

From our study we conclude that prevalence of subclinical hypothyroidism was higher in type 2 diabetes patients than normal population and there was female predominance. Body mass index was significantly higher in subclinical hypothyroidism group and there was no significant difference between the two groups regarding duration of diabetes mellitus. Patients with subclinical hypothyroidism have poor glycemic control. The lipid parameters were comparable in both groups but serum HDL-C was significantly higher in diabetes mellitus plus subclinical hypothyroidism group than in patients with DM and euthyroid group.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
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