

ORIGINAL ARTICLE

STUDY OF COMPARISON OF SERUM LIPID PROFILE, ELECTROCARDIOGRAPHICAL & ECHOCARDIOGRAPHICAL CHANGES BETWEEN EUTHYROID DIABETIC & HYPOTHYROID DIABETIC PATIENTS IN A TERTIARY CARE HOSPITAL, KOLKATA

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ABSTRACT

Introduction: Insulin and thyroid hormone metabolism and functions are dependent on each other. But the presence of hypothyroidism in type 2 diabetes mellitus patients and its impact on cardiovascular system are a less explored area. **Aim:** To compare the serum lipid profile, Electrocardiography & Echocardiographical changes between Euthyroid diabetic & hypothyroid diabetic patient and to document the difference in cardiovascular complications between these two groups.

Methodology: A cross-sectional observational study conducted on 100 Type 2 Diabetes Mellitus patients who were divided into euthyroid and hypothyroid diabetic group and were subjected to tests for dyslipidemia (Total Cholesterol, Triglyceride, HDL-C and LDL – C) and cardiological dysfunction using ECG and Echocardiography and the results were compared.

Results: 31% diabetic patients were hypothyroid and their mean cholesterol, triglyceride, Low density lipoprotein were 239.03 mg/dl, 181.35 mg/dl and 171.74 mg/dl respectively and hence found to be significantly increased as compared to euthyroid diabetic patients. In ECG, hypothyroid diabetic patients showed sinus bradycardia (32.6%), low QRS voltage (19.35%) and increased QTc interval (16.13%). In Echocardiography, 9.68% and 58.06% hypothyroid diabetic patients had grade 2 and grade 1 diastolic dysfunction respectively with significant correlation.

Conclusion: Dyslipidemia with cardiological dysfunction is found to be more prevalent in hypothyroid (including subclinical hypothyroid) diabetes mellitus patients with significant association as compared to euthyroid diabetic patients.

Keywords: Type 2 Diabetes Mellitus, Hypothyroidism, Dyslipidemia, Diastolic dysfunction

INTRODUCTION

Diabetes and thyroid dysfunction are most common endocrinal disorders in adult population. Insulin & thyroid hormone metabolism can result in functional abnormalities of one-another. Hyperglycemia & hypothyroidism both act as an independent risk factor for ischaemic & non ischaemic cardiovascular diseases. Thyroid stimulating hormone (TSH) level is inversely related to Cell function. In subclinical hypothyroidism GLUT2 expression is reduced leading to insulin resistance i.e. further aggravating Type 2 diabetes mellitus (T2 DM) severity as well as complications. Hypothyroidism decreases inotropic & chronotropic effects thus reduces blood flow to tissue &

also causes left ventricular dysfunction. Hypothyroidism is consistently associated with elevation of total & Low Density Lipoprotein (LDL) Cholesterol and triglyceride. Electrocardiographical (ECG) changes include sinus bradycardia, increased PR interval, low amplitude of P wave & QRS complex, alteration of ST Segment, inverted T waves. T₂DM is associated with dyslipidemia which includes increased triglycerides, decreased High density Lipoprotein (HDL), increased LDL & increased apolipoprotein B. Myocardial Infarction(MI), stroke or non ischemic cardiovascular disease is the cause of death in upto 80% of patients with T₂DM. So the presence of hypothyroidism doubles the risk of cardiovascular

disease in T2DM patients.¹⁻⁴ This study intends to see the increased level of cardiovascular complications with this dual endocrinal disorder and to determine the prevalence of hypothyroidism in T₂DM patients.

METHODOLOGY

The present study was a cross-sectional study, conducted at Medical college & hospital, Kolkata from January 2015 to July 2016 on 100 T₂DM patients. T₂DM with hyperthyroidism, T₂DM patients with known structural heart disease, patients who were already taking hypolipidemic drugs, ACE inhibitors, anti anginal drugs, pregnant women, patients with infection, trauma, pre-existing liver/renal disease were excluded from the study group. In the study patients, thyroid status was found using clinical symptoms and signs, TSH and FT4 levels. The patients were then divided into euthyroid diabetic and hypothyroid diabetic group. They were subjected to tests pertaining to serum lipid profile, ECG and echocardiography. Dyslipidemia was considered to be present when the values of Serum cholesterol > 200 mg/dl, LDL > 100 mg/dl, Triglyceride > 150 mg/dl, HDL < 40 mg/dl (Men) and < 50 mg/dl (females). In echocardiography, parameters which were used were Ejection fraction, left ventricular internal diameter (diastolic & systolic), fractional shortening for systolic dysfunction. Mitral E & A velocity, ventricular E/A ratio, annular tissue motion (e'), isovolumetric relaxation time (IVRT), Deceleration time (DT) & left atrial diameter were used for assessing diastolic dysfunction and staging was done accordingly EF < 55% and FS < 25% were taken as significant.

Diastolic dysfunction was staged as follows: **Stage 0 (Normal)** - E/A ratio between 1 and 2, $e' \geq 8-10$, EDT between 150 and 190ms, IVRT between 60 and 90ms, and left atrial diameter (<4.1 cm in men and <3.9 cm in women). **Stage 1 (Impaired Relaxation)** - E/A ratio < 1, $e' \leq 8-10$, $E/e' \leq 8$ **Stage 2 (Pseudonormal)** - E/A ratio between 1 and 1.5, $e' \leq 8-10$, $E/e' = 9-12$, IVRT > 90 ms Mild to moderate left atrial enlargement (4.1-5.1 cm in men and 3.9-4.6 cm in women). **Stages 3-4 (Restrictive)** - E/A ratio > 1.5, $e' \leq 8-10$, $E/e' \geq 13$ and At least two of the following: (a) EDT < 150ms (b) IVRT < 70 (c) severe left atrial enlargement (≥ 5.2 cm in men and ≥ 4.7 cm in women). The results of the tests were used to compare the serum lipid profile, ECG & Echocardiographical changes between euthyroid diabetic & hypothyroid diabetic patients and document the differences of cardiological dysfunction between these two groups and its association with hypothyroid state in Type 2 Diabetes Mellitus. Written informed consent was taken from patients and studied protocol was approved by institutional ethics committee for human research, Medical college Kolkata.

Statistical Analysis: Categorical variables were expressed as number of patients and percentage of patients and compared across the groups using Pearson's Chi Square test for Independence of Attributes. Continuous variables were expressed as Mean \pm Standard Deviation and compared across the 2 groups using unpaired t test. The statistical software SPSS version 20 was used for the analysis. An alpha level of 5% was taken, i.e. if any p value is less than 0.05 it was considered as significant.

RESULT

In the present study of 100 Type 2 Diabetes Mellitus patients 51 patients were female and 49 were male patients whereas 69 patients (69%) were found to be euthyroid and 31 patients (31%) were hypothyroid in which 17 patients had subclinical hypothyroidism. Out of the 31 hypothyroid diabetic patients, 20 patients (64.52%) were female and rest 11 patients (35.48%) were male. The mean age of euthyroid diabetic patients was found to be 44.96 years (± 2.79) whereas hypothyroid diabetic patients mean age was 49.87 (± 2.99) years. Analysing the lipid profile of patients, the mean total cholesterol level in hypothyroid diabetic patients was found to be 239.03 mg/dl which was significantly increased ($p < 0.05$) compared to 199.7 mg/dl in euthyroid diabetic patients. 32.26% hypothyroid diabetic patients had cholesterol level of ≥ 240 mg/dl (High level according to ATP III Classification of dyslipidemia) as compared to none being euthyroid diabetic. The mean LDL level of hypothyroid diabetic patients was found to be 171.74 mg/dl as compared to 125.54 mg/dl in euthyroid diabetic. 6.45% patients of hypothyroid diabetes had LDL levels of ≥ 190 whereas none in euthyroid diabetic. The mean HDL level in hypothyroid diabetic patients was 31.03 mg/dl as compared to 40.5 mg/dl in euthyroid diabetic patients. The triglyceride level of hypothyroid diabetic patients was found to be increased with mean value being 181.35 mg/dl as compared to 144.84 mg/dl in euthyroid diabetic patients. 45.16% patients of hypothyroid diabetes had triglyceride levels of ≥ 180 mg/dl.

ECG study of the hypothyroid diabetic patients revealed sinus bradycardia (32.26%), low QRS voltage (19.35%), increased QT interval (16.13%), and ventricular premature complexes (9.68%) which showed significant association ($p < 0.05$) comparing to the euthyroid diabetic patients. ST depression was found in 12.9% and T inversion was present in 9.68% of hypothyroid diabetes patients and no significant association ($p > 0.05$) was found between ST-T changes in ECG and Thyroid status in diabetes.

In the echocardiographical evaluation of the patients of the study, it was found that the mean ejection

fraction in hypothyroid diabetic patients was 52.26% as compared to euthyroid diabetic patients where it was 59.1 %. The mean LVIDd(Left ventricular internal diameter end diastole) in hypothyroid diabetic patients was found to be 57.58 mm as compared to 54.26 mm euthyroid diabetic patients whereas the mean LVIDs (Left ventricular internal diameter end systole) in hypothyroid diabetic patients was found to be 42.42 mm as compared to euthyroid diabetic patients where it was 36.78 mm. The mean percentage of fractional shortening (FS) in hypothyroid diabetic patients (26.48 %) was found to be decreased as compared to euthyroid diabetic patients(31) , 3 patients(9.68%) had grade II diastolic dysfunction , where as 18 patients(58.06%) had grade I diastolic dysfunction with a significant association (p < 0.05)

. The mean Mitral ‘E’ velocity in hypothyroid diabetic patients (70.39) was found to be decreased in hypothyroid diabetic patients as compared to euthyroid diabetic (85.62) whereas the mean Mitral ‘A’ velocity in hypothyroid diabetic patients (81.55) was found to be increased as compared to euthyroid diabetic patients (74.29). A decreased mean E/A ratio (velocity of diastolic early filling wave/velocity of late filling wave) in hypothyroid diabetic patients(0.88) was seen as compared to mean E/A ratio in euthyroid diabetic patients(1.16) .The study also revealed decreased Annular tissue motion (e') in hypothyroid diabetic patients(9.96) as compared to euthyroid diabetic patients (13.82) and increased mean E/e' ratio in hypothyroid diabetic patients (7.36) as compared to euthyroid diabetic patients (5.97) .

Table 1: Comparison of different parameters between euthyroid diabetic patients and hypothyroid diabetic patients

Factors	Thyroid Status (Mean ± Std. Deviation)		p-Value
	Euthyroid diabetic(n = 69)	Hypothyroid diabetic(n = 31)	
Age(years)	44.96 ± 2.79	49.87 ± 2.99	-
Weight (kg)	65.57 ± 2.13	68.58 ± 2.6	-
Height(cms)	159.97 ± 4.45	153.61 ± 2.65	-
BMI (kg/sqm)	25.65 ± 1.12	29.09 ± 1.52	-
SBP(mmhg)	138 ± 2.55	133 ± 3.24	-
DBP(mmhg)	76 ± 3.6	94 ± 2.7	-
HbA1c(%)	6.74 ± 0.1	7.16 ± 0.31	<0.001
TC(mg/dl)	199.71 ± 9.61	239.03 ± 9.73	0.012
TG (mg/dl)	144.84 ± 7.5	181.35 ± 3.67	<0.001
HDL(mg/dl)	40.51 ± 2.5	31.03 ± 2.12	0.034
LDL(mg/dl)	125.54 ± 5.37	171.74 ± 10.18	<0.001
EF(%)	59.1 ± 3.58	52.26 ± 4.58	0.002
LVIDd(mm)	54.26 ± 1.84	57.58 ± 2.94	0.003
LVIDs(mm)	36.78 ± 2.53	42.42 ± 4.36	0.013
FS(%)	32.9 ± 2.67	26.48 ± 4.08	0.002
E wave(cm/s)	85.62 ± 6.4	70.39 ± 12.79	0.003
A wave(cm/s)	74.29 ± 2.76	81.55 ± 6.27	0.034
E/A	1.16 ± 0.12	0.88 ± 0.22	0.012
e '(cm/s)	13.82 ± 1.85	9.96 ± 3.38	0.001
E/ e'	5.97 ± 0.44	7.36 ± 1.37	0.002
DT(ms)	186.12 ± 10.55	208 ± 21.08	0.003
IVRT(ms)	83.54 ± 9.23	98.65 ± 14.57	0.02
LA diam(mm)	38.13 ± 3.94	39 ± 4.34	0.325

Table 2: Distribution of ECG changes among euthyroid and hypothyroid diabetic patients

ECG changes	Thyroid Status		Total	p Value
	Euthyroid diabetic(n = 69)	Hypothyroid diabetic(n = 31)		
Low volt	0(0)	6(19.35)	6(6)	<0.001
Normal	54(78.26)	0(0)	54(54)	
QTc inc	0(0)	5(16.13)	5(5)	
Sinus brady	0(0)	10(32.26)	10(10)	
VPC	0(0)	3(9.68)	3(3)	

The mean Deceleration time in hypothyroid diabetic patients was found to be 208 milliseconds as compared to euthyroid diabetic patients where it was 186.12 milliseconds whereas the mean Isovolumic

pared to euthyroid diabetic patients where it was 186.12 milliseconds whereas the mean Isovolumic

relaxation time (IVRT) in hypothyroid diabetic patients was 98.65 milliseconds as compared to 83.54 milliseconds in euthyroid diabetic patients showing an increased deceleration time and Isovolumic relaxation time (IVRT) in hypothyroid diabetic patients. The mean Left atrial diameter was not found to be significantly associated between this two groups.

DISCUSSION

In the present study which comprised of 100 type 2 diabetes mellitus patients the prevalence of hypothyroid diabetic patients was found to be 31% (including 17 % subclinical hypothyroidism). The mean BMI in hypothyroid diabetic patients was found to be increased (29.09+1.52 kg/sq m) than euthyroid diabetic patients(25.65+1.12 kg/sq m). In hypothyroid diabetic patients the mean DBP (Diastolic blood pressure) was 94+2.7 mmhg whereas it was 76+3.5 in euthyroid diabetic patients. The Mean HbA1c levels in hypothyroid diabetic patients (7.16 +0.31%) was found to be increased than euthyroid diabetic patients (6.74 +0.1%) similar to the studies done by M. Anita Devi et al and Pasupathi et al.. Hence there is a presence of poor glycemic control in patients having both hypothyroid and diabetes in comparison to patients of diabetes mellitus alone. In hypothyroid diabetic patients mean cholesterol (239.03mg/dl), mean LDL (171.74) & mean triglyceride (181.35) was found to be significantly increased & mean HDL (31.03mg/dl) was found significantly decreased than euthyroid diabetic patients. A study by Prasanna K. Satpathy et al showed mean Total cholesterol as 240.38 mg/dl, LDL as 144.13 mg /dl, HDL as 37.72 mg/dl and Triglycerides as 174.4mg/dl, and significant association with hypothyroid diabetes patients similar to the present study. ECG study of the hypothyroid diabetic patients revealed sinus bradycardia (32.26%), low QRS voltage (19.35%), increased QT interval (16.13%), and ventricular premature complexes (9.68%) which showed significant association ($p < 0.05$) comparing to the euthyroid diabetic patients. The study by Prasanna K. Satpathy et al, there was presence of sinus bradycardia (27.27 %), low voltage complexes (18.18 %), ventricular premature complexes (4.5 %), ST depression and T inversion (34 %) in patients of hypothyroidism. In echocardiographical study, the mean ejection fraction in hypothyroid diabetic patients was 52.26% whereas 59.1% in euthyroid diabetic patients. The mean percentage of fractional shortening (FS) in hypothyroid diabetic patients (26.48 %) was found to be decreased with a significant association ($p < 0.05$) as compared to mean FS in euthyroid diabetic patients (32.9%). Study by Prasanna K. Satpathy et al, the mean ejection fraction was found to be 55 %, mean LVIDD was 41.93 mm, mean LDIDs was 30.16 mm and mean percentage of fractional shortening was found

to be 28.53 %.^{5,6} Hence the systolic dysfunction in the present study involving hypothyroid diabetic patients was found to be increasingly evident as compared to the above mentioned study. In hypothyroid diabetic patients (31), 3 patients(9.68%) had grade II diastolic dysfunction, whereas 18 patients(58.06%) had grade I diastolic dysfunction with a significant association ($p < 0.05$). A decreased mean E/A ratio in hypothyroid diabetic patients(0.88) was seen with a significant association ($p < 0.05$) as compared to mean E/A ratio in euthyroid diabetic patients(1.16). There was also significantly decreased annular tissue motion(e'), increased E/ e' ratio, increased isovolumetric & deceleration time in hypothyroid diabetic patients as compared with euthyroid diabetic patient. A study by Prahlad Karki et al showed Diastolic dysfunction in 37.5% patients (15 patients out of total 40 patients). Of the patients of diastolic dysfunction, one had grade 2 diastolic dysfunction and the rest had grade 1 diastolic dysfunctions. Pericardial effusion in hypothyroid diabetic patients was 12.9% as compared to euthyroid diabetic patients (0%) whereas in the study by Prahlad Karki et al, pericardial effusion was observed in 5 (12.5%) cases of hypothyroidism. It was seen that the dyslipidemia and cardiological dysfunction (Electrocardiological, systolic and diastolic dysfunction) is more prevalent in hypothyroid diabetes mellitus patients with significant association comparing with euthyroid diabetes mellitus patients.⁶⁻⁹

CONCLUSION

Hence as per the present study results thyroid dysfunction in Type 2 Diabetes Mellitus patients should be carried out annually with a systematic approach as per ADA guideline so that early intervention will reduce long term cardiovascular morbidity and mortality in these patients.

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