Original Research Paper

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General Medicine

ASSOCIATION BETWEEN SUBCLINICAL HYPOTHYROIDISM AND RAISED CARDIOVASCULAR EVENTS AMONG TYPE 2 DIABETES MELLITUS

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ABSTRACT

BACKGROUND: Thyroid disorders are having direct association with cardiovascular system related disorders. Many studies reported the short-term impact of thyroid disorders on cardiovascular system, but their long-term impact is still not clear. Similarly, Type 2 Diabetes Mellitus (T2DM) has direct association with cardiovascular diseases. In this study long term effect of subclinical hypothyroidism over cardiovascular system among T2DM cases was assessed and it is also tried to understand that is there any synergistic effect of subclinical hypothyroidism with T2DM.

MATERIAL AND METHOD: a cross sectional case control study was planned to assess the any synergistic impact of subclinical hypothyroidism in T2DM cases. T2DM Patients attended the OPD and admitted the ward of medicine department were recruited in the study. Patients with subclinical hypothyroidism were selected as case and patients without subclinical hypothyroidism were selected as control. Total 100 cases and 100 matched controls were selected over a period of one year in present study. For selection of cases and control 4.7 mU/L TSH level was defined as a cut off range for subclinical hypothyroidism with normal T3 and T4 level.

RESULTS: baseline demographic profile of both cases and controls group were similar, no statistically significant difference between groups observed. Prevalence of existing Coronary artery disease, Peripheral vascular diseases, Cerebrovascular events, and ischemic colon other were almost similar in cases and control group similarly, new events and mortality due to these conditions were also statistically insignificant between groups.

CONCLUSION: subclinical hypothyroidism does not affect the cardiovascular outcome among T2DM cases. based on study findings management of subclinical hypothyroidism among T2DM cases is not recommended.

KEYWORDS : Sub Clinical Hypothyroidism (SCH), T2DM, Cardiovascular Diseases (CVD)

INTRODUCTION:

T2DM is a disease that affects every organ of human body because it is related to carbohydrate metabolism which is essential for all organs to get energy. Reduced serum insulin level and insulin resistance can be responsible for T2DM or raised blood glucose level. T2DM is most common type of diabetes mellitus in the world and its prevalence is higher in developing countries over developed countries. Prevalence of T2DM mellitus is increasing over a period of decades in India which may be due to improved health care service, screening, and management of T2DM cases. T2DM is a lifestyle related disease urbanization, reduced physical activity, high calorie diet and increased social, cultural, and behavioral changes are responsible for it. Based on the latest NFHS-5, 6.3% female population above 15 years of age were having raised blood sugar level and 7.2% of male were having raised blood sugar level in India[1]. Probability of cardiovascular disorders among T2DM is higher than normal population. Similarly, probability of other vascular disorders like stroke, peripheral arterial disease, and cardiomyopathy is also very high among T2DM patients.

Framingham heart study and other clinical trials have shown that chances of cardiovascular disease and premature deaths among T2DM cases is higher. In initial years of Framingham cohort prevalence of diabetes was 6% among women and 8% among men population. Incidences of cardiovascular events among diabetic males were 2 times higher than normal population and among diabetic females it was 3 times higher[2]. Similarly, Multiple Risk Factor Trial reported the three times higher chances of mortality due cardiovascular diseases among T2DM cases in comparison normal population[3]. Morality due to cardiovascular diseases among T2DM was similar in all ethnic groups and higher in all age group[3].

Diabetes Mellitus independently a risk factor for cardiovascular diseases, stroke, myocardial infraction, and congestive heart failure. Diabetic patients are having equal chances of getting cardiovascular events without history of event as non-diabetic patient with history of cardiovascular event. Diabetic women were having higher incidence rate of cardiovascular event in comparison to men[4].

As per definition of subclinical hypothyroidism serum T4 and T3 level should be within normal range and TSH level should be raised. Studies reported that raised level of TSH independently linked with higher chances of myocardial infraction and aortic atherosclerosis but few study reported no such association between subclinical hypothyroidism and cardiovascular disorders[5,6,7]. Prevalence of subclinical hypothyroidism among T2DM patients is comparatively higher than other disorder[8].

Hypothyroidism is a known risk factor for cardiovascular disorders but effect of subclinical hypothyroidism on cardiovascular disorders is still not very clear. In present study it is hypothesized that if subclinical hypothyroidism related with increase in cardiovascular risk, then, instinctively, it can be exaggerated in patients with type 2 diabetes which is already a high cardiovascular risk population. Present case control study was planned to understand cardiovascular outcomes among T2DM with Subclinical hypothyroidism.

SUBJECTS & METHODS:

A cross-sectional case control study was planned in BIMR Super Specialty Hospital of Gwalior Madhya Pradesh to assess the impact of subclinical hypothyroidism in T2DM cases. T2DM Patients attended the OPD and admitted the ward of medicine department were recruited in the study. Patients with subclinical hypothyroidism were selected as case and patients without subclinical hypothyroidism were selected as control. Total 100 cases and 100 matched controls were selected over a period of one year in present study. T2DM cases with a cut off raised TSH (>4.7 mU/L) level, normal serum free T4 and T3 level with clinical outcomes in last one year were selected as cases. Type 1 diabetes mellitus, overt hypothyroidism, patients on anti-thyroid medication were excluded. To identify the control group, a TSH range of 0.5-4.7.0 mU/L was used as the selection criteria. 100 types 2 diabetes patients with a TSH of 0.5-4.7 mU/L during the same period were selected as control. Control group patients was matched as per age, gender, and duration of T2DM. Demographic information personal history, clinical history and laboratory investigations were collected from all subjects. Sample size was calculated to detect difference in odds of 4 with 80% power and 5% of significance level[6].

Significance of association between Subclinical hypothyroidism and cardiovascular disorders was assessed by using unpaired t test and chi square test. Data was compiled in MS excel and analyzed by using SPSS 22 statistical computer package.

RESULTS:

Total 100 patients with type 2 diabetes having Subclinical Hypothyroidism and 100 patients with type 2 diabetes without Subclinical Hypothyroidism were enrolled in the study. Table one is showing demographic parameters of both groups. The mean age of case group patients was 53.1 years compared to 52.4 years in control group patients. Serum TSH level is significantly higher in cases than control group. Gender, smoking and BMI of participants in groups was statistically insignificant. Baseline characteristics of cases and control group patients were appropriately matched and there was no statistical difference between groups. In table 2 prevalence vascular disorders independently and in combination were presented, difference in prevalence of vascular disorders between groups was also statistically insignificant.

Table 3 is showing the incidences rate of vascular disorders. New incidences of coronary artery diseases among cases 27 (27%) and control 26 (26%) group were almost similar while cerebrovascular events were higher among control group, but the difference was statistically insignificant. Incidence of peripheral vascular diseases and Subclinical Hypothyroidism Ischemic colon were also found statistically insignificant between groups.

Mortality from Cardiovascular diseases and other causes in the two groups is summarized in Table 4. Mortality due to cardiovascular disease was higher among cases (12%) than control group (9%) but this difference was statistically insignificant. Mortality due to cerebrovascular disease was higher among control (6%) than control group (2%). Similarly, mortality due to other causes and overall mortality was higher among control group however, the difference between group is statistically insignificant. In cases average duration of Subclinical hypothyroidism to baseline of the study was 3.7 years.

Table 1: Demographic parameters of study participants (Mean ± SEM)

Parameters		Cases (n=100)	Controls (n=100)	P Value
Age (Years)		53.1 ± 0.57	52.4 ± 0.45	0.336
Sex	Male	48	42	0.394
	Female	52	58	
Smokers % (n)		55 (55%)	62 (62%)	0.315
BMI (kg/m2)		30.1 ± 0.40	29.5 ± 0.33	0.249
TSH (mU/L)		7.1 ± 0.12	1.4 ± 0.17	<0.001
SBP		142 ± 1.7	144 ± 1.4	0.365
DBP		78 ± 0.8	80 ± 0.69	0.060
Total Cholesterol (mmol/L)		5.5 ± 0.1	5.4 ± 0.2	0.655
HbA1c (%)		8.4 ± 0.1	8.7 ± 0.1	0.159

Table 2: Prevalence of vascular disorders

Vascular Disorder	Cases (n=100)	Controls (n=100)	P Value
CAD	23 (23%)	22 (22%)	0.865
CVD	3 (3 %)	2 (2%)	0.651
PVD	5 (5%)	6 (6%)	0.756
CAD and CVD	2 (2%)	3 (3%)	0.651
CAD and PVD	5 (5%)	4 (4%)	0.733

Table 3: incidence rate of vascular events

New Vascular disorder	Cases (n=100)	Controls (n=100)	P Value
CAD	27(27%)	26 (26%)	0.873
CVD	12(12%)	15 (15%)	0.535
PVD	6 (6%)	7 (7%)	0.774
Ischemic colon	2 (2%)	1 (1%)	0.561

Table 4: Mortality due to vascular events and other causes in the two groups

Mortality due to vascular events	Cases (n=100)	Controls (n=100)	P Value
CAD	12 (12%)	9 (9%)	0.489
CVD	2 (2%)	6 (6%)	0.149
Other causes	12 (12%)	22 (22%)	0.060
Total	26 (26%)	37 (37%)	0.094

DISCUSSION AND CONCLUSION:

In present study statistically significant difference in mortality due to vascular disorder among patients with T2DM and subclinical hypothyroidism compared to patients of T2DM without Subclinical hypothyroidism was not observed. Prevalence of coronary artery disease, peripheral vascular disease, cerebrovascular disease, and combination of these disorders were also found similar among cases and control group. Similarly, difference in incidence rate of vascular disorders in cases and control group was also statistically insignificant. Present study findings are showing the concordance with Whickham cohort study which is a 20 year long follow up study to estimate thyroid disorder incidence rate and natural course of thyroid disorder. Whickham cohort study reported that Subclinical hypothyroidism was not associated with any cause of death and cardiovascular causes[5]. Similarly, Cardiovascular Health Study reported no significant association between subclinical hypothyroidism and mortality due to vascular disorders among type 3 diabetes mellitus patients[7]. Rotterdam Cohort Study[6] shows the divergence from the Whickham and Cardiovascular Health study. According to Rotterdam Cohort Study[6] subclinical hypothyroidism is significantly associated with cardiovascular event and risk factor for cardiovascular event like atherosclerosis. However, Rotterdam Cohort Study reported higher prevalence of subclinical hypothyroidism (11.8%) in comparison to Whickham and Cardiovascular Health study.

Case fatality due to coronary artery disease and cerebrovascular diseases are two to four times higher among T2DM cases[8]. In present study, subclinical hypothyroidism does not affect mortality in cases group due to vascular disorders like CAD, CVD and PVD even mortality was higher in control group but difference was statistically insignificant.

Based on present study fining it might be concluded that Subclinical Hypothyroidism among T2DM patients is not a matter of concern and it will not affect long term vascular outcome in T2DM patients. Routine use of thyroxine is not recommended for management of subclinical hypothyroidism, trial of thyroxine among symptomatic patients can be initiated based on clinical judgement of clinician.

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