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Original Research Article

Glycosylated hemoglobin – A prediction marker for the development of CVD in hypothyroid patients

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ARTICLE INFO	A B S T R A C T
Article history: Received 26-08-2020 Accepted 04-09-2020 Available online 28-09-2020	Background: Thyroid hormones & TSH are associated with the etiology of type 2 diabetes (T2DM) and probably contribute to the development of the various complications of T2DM. The association of thyroid hormones & TSH with cardiovascular diseases in confirmed hypothyroid patients is still not clear. Aim & Objectives: The aim of our study is to determine the correlation of HbA1c with thyrotropin (TSH) and thyroid hormones in the development of cardiovascular diseases (CVD) in known patients of
Keywords: Glycosylated hemoglobin Hypothyroid TSH CVD	 hypothyroidism. Materials and Methods: This was a case control observational study carried out among total of 172 patients (100 patients and 72 controls). They were divided into in to two groups cases which are hypothyroid patient and control group. Blood sample (3 ml) was collected and Fasting blood sugar, complete lipid profile were assayed on Vitros 250 auto analyzer Johnson and Johnson USA. The circulating thyroid hormones assayed for T3, T4 and TSH by enzyme linked florescent assay (ELFA) technique using Vidas auto-analyzer. Glycosylated hemoglobin measured by kit based method where anticoagulated whole blood used as sample. Body weight and height were measured for body mass index (BMI) (kg/m²). Results: Our study demonstrate that Mean of BMI, W.C, FBS, HbA1c, TC, TG, LDL and VLDL were higher in cases as compared to HDL which is higher in control group as compared to case group, Our study also shows that serum T3 values correlates positively and significantly with waist circumference, fasting sugar level, triglycerides and LDL-C while correlates only positively with, HbA1c and HDL-C, whereas TSH correlates positively only with LDL and HDL Levels. Conclusion: Our study concludes that the cumulative quantification of indicators like TSH & HbA1c will function as a biomarker for hypothyroid patients who are at risk to develop CVD in their later stages of life.
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1. Introduction

Glycosylated Hemoglobin (HbA1c), a form of hemoglobin (Hb) is formed by the glycation of the amino acid value of β -chain of Hemoglobin and it reflects the degree of control of of type 2 diabetes mellitus over a specific period of time.¹

Recently, the American Diabetes Association (ADA) has proposed the HbA1c values for prediabetics and diabetic patient. Values between 5.7% and 6.5% represents

In type 2 DM, values more than $\geq 6.5\%$, indicate poor control of the levels of blood glucose and are firmly associated with the long-term risk of complications, such as cardiovascular disease, neuropathy, nephropathy and retinopathy.^{3–5} So, the role HbA1c may be used as an index of cumulative glycemic exposure in type 2 diabetes mellitus and assessment of cardiovascular risk.^{6,7}

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prediabetes and if the values are $\geq 6.5\%$ it is considered as diabetes mellitus.²

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Thyroid dysfunctions are one in every foremost common types of endocrine disorder in our country. It has an impression on numerous systems of our body. The disorder manifests during a broad spectrum of clinical and biochemical diseases from undiagnosed disorder to myxedema.⁸

Action of thyroid hormones has long been identified as an important determinant of glucose regulation.⁹

In hypothyroidism, there is a reduction in insulin secretion by pancreatic beta cells and It was documented that the levels of HbA1c are increased in patients of hypothyroidism.¹⁰ In hypothyroidism, decreased utilization of glucose contrarily due to decreased absorption is also associated with hyper-insulinemia and insulin resistance, apparently leads to transient increase in the glucose levels and thus contributing to serum proteins glycation.¹¹

A positive correlation between thyroid disorder and diabetes mellitus patient is well established but to find out the effect of thyroid disorders on glucose metabolism in non diabetic thyroid patients is an area for comprehensive study.

Present study was planned to assess cumulative effect of thyroid disorders and diabetes in the development of CVD and to find out if there is any possible prognostic association exists between levels of HbA1c and the CVD events in the patients of hypothyroidism.

2. Materials and Methods

Present study a hospital based study conducted in collaboration with Department of Medicine and Department of Biochemistry, Subharti Medical College, its associated Chatrapati Shivaji Subharti (CSS) Hospital Meerut, A total of 172 patients (100 patients and 72 controls) who were willing to take part were chosen for the study.

2.1. Study design

This was a Case-Control Observational study.

2.2. Study period and duration

The present study of 18 months was from January 2015 to August 2016.

2.3. Source of data

The patients who referred from Medicine OPD of Subharti CSS Hospital, having signs and symptoms of thyroid disorders were included.

2.4. Inclusion criteria

All patients attending Medicine OPD having signs and symptoms of thyroid disorders were selected aged between 20-60 yrs, who were permanent resident of study area.

2.5. Exclusion criteria

Patients with non significant history of thyroid profile.

Patients with incomplete thyroid profile.

Patients with H/O drugs intake 1 month prior to sampling effecting CHD and thyroid profile & also patients on steroids Patients with Chronic Renal Failure (CRF).

2.6. Sample collection

Blood sample of around (5ml) after overnight fasting was collected. Serum was separated by centrifuging blood sample at 3000 rpm for 10 min, Fasting blood sugar and complete lipid profile were assayed on Vitros 250 auto analyzer Johnson and Johnson USA by using Biored quality control.

The circulating thyroid hormones assayed for T3, T4 and TSH by enzyme linked florescent assay (ELFA) technique using Vidas auto-analyzer. The reference range for T3, T4 and TSH for our laboratory as: T3: 1.23–3.23 nmol/L, T4: 59–135 nmol/L & TSH: 0.4–4.2 mIU/L respectively.¹²

The patients were categorized into two groups. Those having T3, T4, and TSH levels within the reference range were categorized into the euthyroid group; patients having low T3, T4 and high TSH were in the hypothyroid group. Glycosylated hemoglobin measured by kit based method ¹³ where anticoagulated whole blood used as sample.

Participants recruited in this study received a general physical examination. Body weight and height were measured for body mass index (BMI) calculation $(kg/m^2,$ weight divided by squared height). Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice consecutively, and the average was calculated.

2.7. Statistical analysis

Statistical analysis was carried out with SPSS 16. ANOVA software package used in evaluation of significance between the mean of the two groups. Data were presented as mean \pm SD (standard deviation). Intergroup differences were tested by independent sample test (two groups). P-value < 0.05 was taken as statistical significant.

3. Result

The case control observational study was conducted among 172 subjects (100 cases and 72 control), The patients who presented with clinical symptoms of hypothyroidism and subclinical hypothyroidism were followed up and were subsequently screened for presence of CVD risk factors.

Out of which Male is 37% & Female is 63%, the F: M ratio is 1.7:1. (Table 1).

Present study showed the age of the total study subjects were ranged from 20 to 60 years. In the control group mean age of subjects was 41.66 ± 9.32 years whereas in case group mean age of subjects was 42.96 ± 8.08 years respectively.

Thyroid		Total				
dysfunction	20-30	31-40	41-50	51-60	Total	
Hypothyroid	4 (66%)	23 (82.1%)	41 (91.1%)	19 (90.4%)	87 (87%)	
Subclinical	2 (33%)	5 (17.9%)	4 (8.9%)	2 (9.6%)	13 (13%)	
Hypothyroid						
Total	6 (6%)	28 (28%)	45 (45%)	21 (21%)	100 (100%)	

Table 1: Age wise distribution of hypothyroid cases

Table 2: Distribution of study subjects (cases & control groups) according to the presence of different variables contributing to the CVD risk factors

Parameters	Cases(Mean± SD) (n=100)	Control(Mean± SD) (n=72)	P Value	95%CI	t value
Age(in years)	$42.96 {\pm} 8.08$	41.66±9.32	P <0.05	-3.99-1.39	0.95
BMI(kg/m ²)	32.01±7.15	$29.19{\pm}8.07$	P <0.05	-5.12-0.52	2.42
W.C(Inches)	$102.89 {\pm} 9.33$	$90.47 {\pm} 8.64$	P <0.05	-15.14-9.68	8.98
HbA1c (%)	6.21±2.33	4.43 ± 1.10	P <0.05	-2.36-1.18	5.97
FBG (mg/dl)	$142.44{\pm}20.84$	100.37 ± 12.31	P <0.05	-51.88-32.24	8.45
T.C (mg/dl)	$205.61 {\pm} 32.80$	142.7 ± 17.4	P >0.05	-14.99-3.66	8.8
TG (mg/dl)	$209.58 {\pm} 49.73$	$180.4{\pm}28.6$	P <0.05	-41.04-17.31	4.85
LDL-C (mg/dl)	130.05 ± 31.20	83.4.±23.4	P <0.05	-54.87-38.43	11.20
VLDL-C (mg/dl)	$41.8 {\pm} 9.98$	37.61±7.96	P <0.05	-6.89-1.48	3.05
HDL-C (mg/dl)	33.12 ± 5.43	$43.45 {\pm} 4.97$	P <0.05	8.75-11.90	12.93

Value <0 05 considered Statistically Significant

Table 3: Correlation betweenCardiovascular risk factors with levels of T3, T4& TSH

			57 1				
Parameters	T3		T4		TSH		
	r	Р	r	Р	r	Р	
W.C (in inch)	0.13	0.17	0.58	0.56	-0.21	0.02	
BMI (ht/wt ²)	0.01	0.90ns	-0.00	0.96	0.01	0.01	
HbA1c (%)	-0.06	0.54	-0.03	0.74	-0.13	0.19	
FBS (mg/dl)	-0.06	0.52	0.01	0.86	-0.09	0.33	
TG(mg/dl)	0.15	0.12	0.08	0.37	-0.00	0.99	
HDL-C(mg/dl)	-0.06	0.54	-0.06	0.55	0.04	0.64	
LDL-C(mg/dl)	-0.09	0.35	0.04	0.68	0.04	0.67	
Systolic BP (mm of Hg)	0.008	0.93	-0.19	0.04	0.01	0.92	
Diastolic BP(mm of Hg)	-0.09	0.36	-0.22	0.02	-0.14	0.14	

Mean of BMI, W.C, FBS, HbA1c, TC, TG, LDL and VLDL were higher in cases as compared to HDL which is higher in control group as compared to case group (Table 2).

Serum T3 values correlates positively and significantly with waist circumference and triglyceride also, while T4 correlates positively and significantly with waist circumference, fasting sugar level, triglycerides and LDL-C while correlates only positively with, HbA1c and HDL-C, whereas TSH correlates positively only with LDL and HDL Levels.(Table 3)

4. Discussion

Thyroid hormones & TSH plays a very important role in maintaining homeostatis of blood glucose & lipid metabolism thereby affecting the parameter of MetS i.e lipid profile, blood pressure, blood sugar level. Hypothyroidism is found to be associated with MetS leading to obesity, dyslipidemia and increased risk of atherogenic CVD.¹⁴

Indians is on a very high risk with respect to CVD, and their numbers are consistently rising. MetS is considered to be contributing to various cardiometabolic risk factors like increased BMI, WC, obesity and raised blood pressure also biochemical parameters like increased blood sugar level and raised triglyceride and low HDL-C.¹⁵

Various documented studies have been carried out in Indian subcontinent on MetS, however data available is very limited on correlation of thyroid hormones with different variable risk factors contributing to MetS leading to CVD.

In various studies, it is documented that there is a significant association between thyroid hormones and TSH with metabolic risk factors leading to CVD.^{16,17}

Our study findings also indicate in the direction that the altered thyroid hormones and TSH levels may predict the MetS on the cases leading to CVD. Bakker et al.¹⁸ in their study documented that TSH seemed to affect the various CVD risk factor. Which is in accordance to our study which also indicate a close relationship between TSH and CVD risk factors

Recently, after a 10-year cohort study researchers concluded that deranged HbA1c and TSH levels have been found to be the associated with CVD.¹⁹

In subjects having increased level TSH levels i.e TSH \geq 10, the CVD events increased as compared to normal TSH level subjects.²⁰

Reference range of TSH is linearly and positively associated with body mass index(20), similarly in our study we have also found that TSH is associated with BMI.

Both diastolic and systolic blood pressures,²¹ and deranged lipid profile²² have conflicting effects on cardiovascular health.²³ An increased risk of CVD is present in subjects suffering from thyroid disorder i.e of hypothyroidism.²⁴ Similar findings have been found out in our study also.

In a study conducted by Kim et al.²⁵ HbA1c was also found to be elevated in hypothyroid patient as compared to control group $(5.54\pm 0.43\% \text{ vs. } 5.34\pm 0.31\%)$ in hypothyroid patients (cases) and euthyroid healthy controls respectively;

In another study it is documented that hypothyroid patients are compared with euthyroid. HbA1c in the hypothyroid patients was (6.32 $\pm 0.75\%$ vs. $5.87\pm0.46\%$) in the euthyroid group, the correlation being statistically significant.²⁶

Our study also shows similar finding when HbA1c values of hypothyroid patients were compared with control group i.e $(6.21\pm2.33 \text{ vs. } 4.43\pm1.10)$

Komarica et al²⁷ also shows in their study that correlation of TSH and HbA1c is significant.

Our study is also in accordance with this study which state that TSH is associated with HbA1c.

5. Conclusion

In the light of our study findings, we can conclude that there is a likely association of thyroid hormones, TSH, HbA1c with CVD. Our study also highlights the importance of analysis of risk of CVD in patients of thyroid disorders. It is still not clear whether alterations in thyroid hormones, TSH and HbA1c can have an impact on CVD progression. It is therefore suggested that the patients of thyroid disorders need to be screened for CVD during routine investigations for early detection and treatment of the disease. Hence, we contemplate that there may be an association of HbA1c, TSH and thyroid hormones in the development CVD.

6. Source of Funding

None

7. Conflict of Interest

None

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