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To Assess Hba1c In Non Diabetic Subclinical Hypothyroidism Patients

Mr. Dattu Vilas Hawale

Tutor Dept. of Biochemistry Jawaharlal Nehru Medical College, DattaMeghe Institute of Medical Sciences Sawangi (Meghe) Wardha-442001

Mr. GangaramLaxmanBhadarge

Tutor Dept. of Biochemistry Jawaharlal Nehru Medical College, DattaMeghe Institute of Medical Sciences Sawangi (Meghe) Wardha-442001

Dr. Pradip Jain
Professor and HOD Dept. of Biochemistry DattaMeghe Medical College-441110

Dr. Prakash Kute
Associate Professor Dept. of Biochemistry Jawaharlal Nehru Medical College, DattaMeghe Institute of Medical Sciences Sawangi (Meghe) Wardha-442001

Dr. V. Shegaonkar
Professor Dept. of Medicine Jawaharlal Nehru Medical College, DattaMeghe Institute of Medical Sciences Sawangi (Meghe) Wardha-442001

Address for Correspondence
Dr. Pradip Jain
Professor and HOD Dept. of Biochemistry
DattaMeghe Medical College-441110
Mob No. 9822566869

ABSTRACT

Introduction: ***India has the highest prevalence of prediabetes, hypothyroidism, and diabetes. In females, subclinical hypothyroidism (SH) is more prevalent than in men. Studies in non-diabetic hypothyroid patients have reported elevated HbA1c. Standard serum triiodothyronine (T3), thyroxine (T4) and serum thyroid stimulating hormone (TSH) levels dropping from 4.2 to 10 (mIU/L) are classified as SH.***

Aim: To study the HbA1c level in the non-diabetic SH patients and to compare the HbA1c level with the controls.

Materials and Methods:This study was a case-control study conducted between September 2020 and November 2020 in the Department of Medicine at DMMC & SMHRC, Nagpur in collaboration with ABVRH, Sawangi (Meghe). For the analysis, a total of 120 participants were considered, 60 in each case and 60 in the control groups. Parents and friends of patients who were matched by age and sex were monitored.

Results: Since there was no statistically significant difference in age, sex, FBS, haemoglobin, serum T3 and serum T4 levels between the case group with subclinical hypothyroidism and the control group with normal healthy subjects, the only difference between the case and control groups was serum TSH levels.

Conclusion:Our data suggest that the non-diabetic subjects with SH show high levels of the HbA1c. Therefore, the effect of altered levels of the serum TSH on the HbA1c must be considered when interpreting the HbA1c for the diagnosis of diabetes in the SH patients

Keywords: Subclinical Hypothyroidism, Glycosylated Hemoglobin, Serum TSH, T3 and T4.

INTRODUCTION:

Thyroid disorders are very prevalent in the general population and after diabetes mellitus, are the second most common disease affecting the endocrine system. The main feature of hypothyroidism is reduced thyroid hormone production.[1] Subclinical hypothyroidism is characterised as an elevated serum TSH level and normal free T3 (FT3), free T4 (FT4), T3 and T4 concentrations.[2] Subclinical hypothyroidism (SH) is a disease characterised by the lack of clinical signs and symptoms as a condition with elevated serum levels of the thyroid stimulating hormone TSH and normal serum concentrations of thyroid hormones.[3] In 5-18 percent of cases, progression from subclinical to overt hypothyroidism is anticipated. The chance of crossing SH to MH will be higher if TSH is > 10 mIU/L. In 80 percent of SH, antithyroid antibodies were found, and 80 percent of these patients had serum TSH <10 mIU/L. The evaluation of anti-TPO antibodies is believed to ensure proper assessment of SH patients as an excellent predictor of the transition to overt hypothyroidism.[4,5]A positive correlation between thyroid and diabetes mellitus is well known, but an area for systematic research is to study the effects of thyroid disorders on glucose metabolism in non-diabetic patients. The current research was designed to determine the association in non-diabetic patients between subclinical hypothyroidism and glycosylated haemoglobin levels.[6-7] The concentration of HbA1c depends not only on the prevailing glycaemia, but also on the life span of the erythrocytes, so conditions affecting the turnover or survival of the erythrocyte can lead to a false increase or decrease in the levels of HbA1C.[8-9] A value of 5.7 percent to 6.5 percent is pre-diabetes, while a value of 6.5 percent is considered diabetes mellitus. Several factors other than glycemic status, including altered red blood cell (RBC) turnover, may affect levels of HbA1c. In thyrotoxic states, RBC turnover is raised, while hypothyroidism has the opposite effect.We hypothesise that due to altered thyroid status, HbA1c levels can change, likely due to RBC turnover changes. Therefore, we measured HbA1c levels based on fasting and 2h post-glucose plasma glucose requirements in hypothyroid and thyrotoxic individuals who do not have diabetes or pre-diabetes. After euthyroidism was achieved, we also followed up on some of the patients and assessed HbA1c again.[10] India has a higher prevalence of hypothyroidism, diabetes and pre-diabetes. Subclinical hypothyroidism (SH) in females is more common than in males. Studies have shown that non-diabetic hypothyroid patients have elevated HbA1c. SH is characterised by normal serum levels of triiodothyronine (T3), thyroxine (T4) and serum levels of thyroid stimulating hormone (TSH) falling from 4.2 to 10 mU/L.[11] The use of HbA1c for screening and diagnosis of diabetes has recently been approved by the American Diabetes Association (ADA) and the World Health Organization (WHO). Both organisations have indicated that the HbA1c level is known to be diabetes at 6.5 percent and the ADA has also suggested that the HbA1c level is pre-diabetes diagnostic at 5.7 to 6.4 percent.[12-13] The concentration of HbA1c not only depends on the prevailing glycaemia, but also on the life span of the erythrocytes, and so the conditions affecting the turnover or survival of the erythrocyte lead to falsely high or low levels of HbA1c.[14] A research performed by Kim MK et al. found that there was a spurious elevation of HbA1c even in the absence of diabetes in patients with hypothyroidism.[15]

The current research was conducted to measure the levels of HbA1c in non-diabetic subjects with SH, i.e. those with FBS < 110 mg/dl, and to determine the impact of SH on HBA1c in non-diabetic subjects.

MATERIALS AND METHODS:

This study was a case-control study conducted between September 2020 and November 2020 in the Medicine Department at DMMC & SMHRC, Nagpur, in collaboration with ABVRH, Sawangi (Meghe). For the analysis, a total of 120 participants were considered, 60 in each case

and 60 in the control groups. Parents and friends of patients who were matched by age and sex were monitored.

Inclusion criteria

- Non-diabetics
- Subclinical hypothyroidism
- Patients who consent to the participation.

Exclusion criteria

- Diabetes
- Anemia
- Renal insufficiency
- Liver dysfunction
- Severe hypertriglyceridemia
- Hypothyroid patients already on thyroid hormone replacement
- Abnormal haemoglobinopathy
- Hemolytic disorder
- Recent (< 3 months) blood transfusion

BLOOD SAMPLE COLLECTION AND PROCESSING

5 ML blood was collected from each subject by venipuncture with standard blood collection technique and distributed in plain vial for serum separation for the estimation of TFT and EDTA vial for HbA1C estimation and in fluoride vial for the estimation of fasting blood sugar.

BIOCHEMICAL ANALYSIS

TSH were estimated by Two-site immunoenzymatic ("sandwich") assay method[16], T3 were estimated by Competitive binding immunoenzymatic assay method[17] T4 were estimated by Competitive binding immunoenzymatic assay[18]. HbA1c were estimated by HPLC method[19], FBS were estimated by GOD-POD method[20]. Hemoglobin were estimated on Beckman coulter counter.

STATISTICAL ANALYSIS

Haemoglobin, FBS, Serum T3, T4, TSH, HbA1c were measured. All data were collected and analyzed statistically to determine the significance of different parameters. All values were given as mean±SD. Comparison between the case and the control groups were made using Student's t-test (unpaired), and the p-value of less than 0.05 was considered statistically significant. Box and Whisker Plot and regression graph were presented for correlation between serum TSH and HbA1c.

RESULTS

A total of 120 subjects were enrolled in this study, of which 60 subjects were in the case group and 60 were in the control group. All the subjects were from the 21-70 age groups.

Table 1: Comparison of Age and Sex in the Case and the Control Group

PARAMETERS	CASE (MEAN±SD)	CONTROL (MEAN±SD)
Age (Year)	44.46±13.28	46.56±17.44
Sex (M/F)	34/26	30/30

Table 1 shows the mean age of the case group and the control group were 44.46±13.28 and 46.56±17.44 respectively.Number of Male & female patients were 34 and 26 respectively. In control group there were 30 males and 30 females.

Table 2: Comparison of the Various Parameters in the Case and the Control Groups.

PARAMETERS	STUDY GROUP MEAN±SD	CONTROL MEAN±SD	P-VALUE
FBS (mg/dl)	96.20±8.90	95.82±12.29	P = 0.8465
Haemoglobin (gm/dl)	13.21 ± 1.38	13.35 ± 1.64	P = 0.6405
T3 (ng/ml)	1.07±0.22	1.11±0.19	P = 0.2887
T4 (µg/dl)	8.04±1.17	8.39±1.26	P = 0.1175
TSH (mIU/L)	6.98±0.89	2.62±0.81	P < 0.0001
HbA1c (%)	6.20±0.50	5.80±0.77	P = 0.0010

Fasting blood sugar levels for control group was 95.82±12.29and for study group was 96.20±8.90 respectively. There was no statistically significant difference between the case and the control groups. Similarly, haemoglobin levels were 13.21 ± 1.38 and 13.35 ± 1.64 in case and control groups respectively with p value 0.6405.The mean serum TSH level was 6.98±0.89 and 2.62±0.81 in the case and the control groups, respectively. There was statistically significant difference with the p-value of < 0.0001 and the levels of S. TSH (mIU/L) were significantly higher in the study group compared with the control group.

The mean HbA1c levels were 6.20±0.50 % and 5.80±0.77 % in the case and the control groups respectively. There was statistically significant difference with the p-value of P = 0.0010. The levels of HbA1c (%) were significantly higher in the study group compared with the control group.

DISCUSSION:

Subclinical hypothyroidism is an endocrine condition commonly found currently. The goal of this study was to evaluate the impact of thyroid hormone on glycosylated haemoglobin levels in both deficient and normal states. Studying the effects of thyroid hormones on HbA1c is important in order to help us better understand the levels of HbA1c in patients with thyroid dysfunction.The inclusion and exclusion criteria was formulated, taking into consideration the many other non-glycaemic factors affecting glycosylated haemoglobin. Acute and chronic blood loss, hemolytic anaemia, other anaemia, hemoglobin variations, blood urea and serum creatinine were omitted in certain confusing medical conditions.[21] The mean serum TSH level in the case group with SH and the control group was statistically significantly different ($p < 0.0001$). The levels of serum TSH were significantly higher in the study group which consists of subjects of SH compared with the control group comprising of normal healthy individuals. The mean HbA1c level in the case group and the control group was statistically significant ($p < 0.0010$).As there was no statistically significant difference between the case group with Subclinical hypothyroidism and the control group with normal healthy individuals for the age, sex, FBS, haemoglobin, serum T3 and serum T4 levels, the only difference in the case and the control groups were the levels of serum TSH. Also, the levels of serum T3, serum T4 and Haemoglobin were normal in both the groups. So, we can say that the levels of HbA1c in both the groups were not affected by age, sex, and the levels of FBS, serum T3, serum T4 and Serum TSH levels were significantly higher in the cases with subclinical hypothyroidism than normal healthy individuals and the study result also showed that HbA1c levels were significantly higher in the cases than the controls.

Ram VS et al. (2017)found no significant change in haemoglobin, serum T3 and serum T4 levels, the only difference in the case and the control groups were the levels of serum TSH. Also, the levels of serum T3, serum T4 and Haemoglobin were normal in both the groups.[22]
Billic-Komarica E et al, also found a positive and statistically significant (r=0.46) correlation between the level of serum TSH and HbA1c levels.[22-25]

CONCLUSION:

Our data shows that HbA1c levels are misleadingly high in non-diabetic subjects with SH. Therefore when interpreting HbA1c for the diagnosis of diabetes in patients with SH, the impact of altered levels of serum TSH on HbA1c must be noted.Baseline HbA1c levels were found to be significantly higher in hypothyroid patients compared to control individuals despite similar glucose levels. HbA1c reduced significantly with treatment in hypothyroid patients without a significant change in glucose levels. Significant baseline or post treatment change was not observed in hyperthyroid patients. Our study suggests that HbA1c data should be interpreted with caution in patients with hypothyroidism.

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