

Original research article

Study of serum glycated hemoglobin and bound sialic acid in newly diagnosed non diabetic hypothyroid patients

¹Dr Mallikarjun Suligavi, ²Dr. Mandayal Jamatia, ³Dr. Abhijith D, ⁴Dr. K Pratibha, ⁵Dr. Ullas Mahesh

¹Assistant professor, Department of Biochemistry, DM WIMS, Wayanad, Kerala, India

²Assistant professor, Department of Biochemistry, JNUIMSRC. Jaipur, Rajasthan, India

³Assistant Professor, Department of Biochemistry, JSS Medical College, JSSAHER, Mysooru, Karnataka, India

⁴Professor and Head, Department of Biochemistry, ESICMC & PGIMSR, Bengaluru, Karnataka, India

⁵Professor, Malla Reddy Medical College, Telangana India

Corresponding Author:

Dr. K Pratibha

Abstract

Introduction: Hypothyroidism is most common endocrine disorder resulting in decreased levels of thyroid hormones. Hypothyroidism can be divided into primary, central and congenital hypothyroidism. Iodine deficiency is the most common cause of primary hypothyroidism. In areas with sufficient dietary iodine, most common cause is hashimoto's thyroiditis.

Materials and Methods: Patients attending the OPD and those admitted in wards of Department of General Medicine at a tertiary centre, Bangalore who are newly diagnosed with non diabetic hypothyroidism are selected for the study as cases. The healthy individuals who are age and sex matched to cases are taken as controls. Study is carried out for the period of 18 months from November 2015 to April 2017.

Results: A total number of 200 subjects were studied which included:

- 100 Controls
- 100 patients with newly diagnosed non diabetic hypothyroidism.

Discussion: Hypothyroidism is defined as decreased levels of thyroid hormones in blood due to underactive thyroid. The thyroid gland produces hormones that regulate the body's metabolic rate as well as heart and digestive function, muscle control, brain development and bone maintenance.

Conclusion: From this study it can be concluded that newly diagnosed non diabetic hypothyroid patients show elevated glycated hemoglobin levels in spite of normal fasting blood sugar levels.

Keywords: Hypothyroidism, glycated hemoglobin, thyroid gland.

Introduction

Hypothyroidism is most common endocrine disorder resulting in decreased levels of thyroid hormones. Hypothyroidism can be divided into primary, central and congenital hypothyroidism. Iodine deficiency is the most common cause of primary hypothyroidism. In areas with sufficient dietary iodine, most common cause is hashimoto's thyroiditis. Hashimoto's thyroiditis may present with the mass effect of a Goiter (enlarged thyroid gland). Though signs and symptoms vary according to severity of disease, there is no effect on blood glucose levels.

However, earlier studies have stated that there is comparable insulin resistance in patients with clinical and subclinical hypothyroidism with increased levels of HbA1c. The American Diabetic Association (ADA) have guidelines for diagnosing prediabetes and diabetes if HbA1c levels fall between 5.7%-6.4% and more than 6.4% respectively. So there is a chance of diagnosing diabetes wrongly in cases of hypothyroidism patients. HbA1c is diagnostic as well as for monitoring glycemic control for diabetes. Few studies have also shown that HbA1c also altered in patients on hemodialysis, haemolytic anemia, recent blood transfusion, after blood loss, haemoglobin variants (HBC, HBS, HBF), increased erythropoiesis secondary to hemolysis or blood loss, excess intake of vitamin C & E in spite of normal blood glucose levels. Sialic acid is a generic term for the N- or O-substituted derivatives of neuraminic acid, which play a central role in the biomedical functioning of humans. The normal range of total sialic acid (TSA) level in serum/plasma is 1.58-2.22 mmol/L.

Materials and Methods

Source of Data

Patients attending the OPD and those admitted in wards of Department of General Medicine at a tertiary centre, Bangalore who are newly diagnosed with non-diabetic hypothyroidism are selected for the study

as cases. The healthy individuals who are age and sex matched to cases are taken as controls. Study is carried out for the period of 18 months from November 2015 to April 2017.

Inclusion Criteria

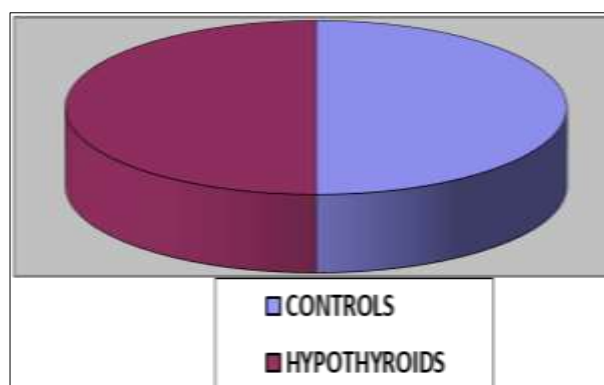
1. Newly diagnosed non diabetic hypothyroid patients between the age group of 18-40 years, irrespective of their sex are included in our study.

Exclusion criteria: Patients with history of

- Diabetes mellitus
- Pregnancy
- Renal insufficiency
- Liver dysfunction
- Thyroidectomy/semi thyroidectomy patients
- Ingestion of large amounts of vitamin C and E
- Recent transfusions
- Increased erythropoiesis secondary to hemolysis or blood loss
- Hemodialysis
- Uraemia
- HbS traits
- Increased HbF

-are excluded from the study

Results

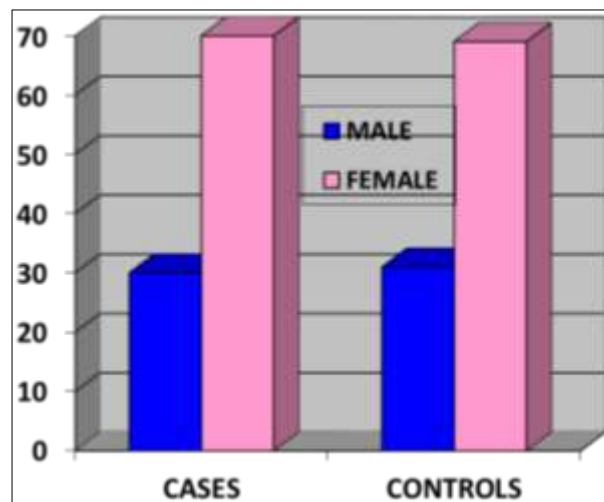


Graph 1: A total number of 200 subjects were studied which included:

- 100 Controls
- 100 patients with newly diagnosed non diabetic hypothyroidism.

Following biochemical parameters were analysed in fasting state in both the groups:

- Serum TSH.
- Serum free T3
- Serum free T4
- HbA1c
- Serum sialic acid



Graph 2: Gender distribution

Table 1:

	Cases	Controls
Male	30	31
Female	70	69

- In this study, a total number of 139 females and 61 males were studied.
- The total number of women in control group were 69 and men were 31.
- The total number of women who were hypothyroid were 70 and men were 30.

Discussion

Hypothyroidism is defined as decreased levels of thyroid hormones in blood due to underactive thyroid. The thyroid gland produces hormones that regulate the body's metabolic rate as well as heart and digestive function, muscle control, brain development and bone maintenance.

Diabetes and hypothyroidism are two endocrine diseases which contribute a large share to the health burden of the world. It has been known that one tenth of diabetics have hypothyroidism, which points towards an underlying relationship between the two. But the reasons for this frequent coexistence are largely unexplained. Sialic acid is an indicator of risk of atherosclerosis and cardiovascular diseases. Previous studies have shown that in hypothyroid patients there is increase in the level of serum sialic acid. In our study we have taken non diabetic hypothyroids as cases to find out the correlation of HbA1c and serum sialic acid with hypothyroidism.

We evaluated our results and compared with those obtained by various other studies. Our analysis is as follows.

In our study the serum samples of 100 newly diagnosed non diabetic hypothyroid patients and 100 samples of controls were taken and serum glycosylated hemoglobin and sialic acid were estimated along with thyroid profile.

The gender distribution in both groups were comparable as shown in graph 1. The gender distribution of newly diagnosed non diabetic hypothyroid cases in our study showed female preponderance. The unpaired 't' test of both groups in age distribution showed matched data. The mean age group in control was 29.49 ± 6.64 and the mean age group in newly diagnosed non diabetic hypothyroid was 28.69 ± 6.32 with statistically no significant difference between both groups.

Serum TSH

Our study included newly diagnosed non diabetic hypothyroid patients based mainly on serum TSH levels and presentation of signs and symptoms. It included both clinical and subclinical hypothyroid patients.

The mean serum TSH levels in newly diagnosed non diabetic hypothyroid patients was significantly more than controls in our study. The mean serum TSH levels in hypothyroid was 19.26 ± 4.83 compared to 2.73 ± 1.3 mean serum levels of controls with p value of <0.0001 .

Serum FT3

The mean serum levels of FT3 in newly diagnosed non diabetic hypothyroid patients with value of 1.69 ± 0.48 was significantly less than the mean serum level of controls with value of 3.41 ± 0.52 with p value of <0.0001 .

Serum FT4

The mean serum levels of FT4 in newly diagnosed non diabetic hypothyroid patients with value 0.62 ± 0.33 was significantly less than the mean serum level of controls with value of 0.98 ± 0.24 with p value of <0.0001

HbA1c

The present study shows a significantly increased levels of glycated hemoglobin in newly diagnosed non diabetic hypothyroid individuals with mean serum HbA1c level 5.93 ± 0.32 as compared to normal controls where mean serum HbA1c level was 5.37 ± 0.22 with $p < 0.0001$. This finding is in accordance with the study done by Alap L Christy *et al.*

By this study, it can be stated that most of the patients suffering from hypothyroidism show increased levels of glycated hemoglobin, although they are non-diabetic.

Further, with p value of < 0.0001 , HbA1c in newly diagnosed non diabetic hypothyroid patient showed statistically significant moderately positive correlation with TSH with r value of 0.4315. and weak negative correlation with FT3 and FT4 with r values of -0.2398 and -0.2841 respectively with p value of 0.0162 and 0.0042 respectively.

Alap L Christy *et al.* in their study also established positive correlation between HbA1c and Serum TSH. The causal relationship has to be further strengthened with more studies.

The exact mechanism of false elevation in glycated hemoglobin levels in newly diagnosed non diabetic hypothyroid is unknown so far. It may be attributed to the effect of thyroid hormones on erythropoiesis and RBC life span. Nithin Sinha *et al.* in 2012 attributed elevated HbA1c levels in hypothyroidism to the iron deficiency in hypothyroid patients. However further studies are needed to establish a cause for elevated HbA1c levels in hypothyroid patients.

The mean glycated hemoglobin levels in newly diagnosed hypothyroid patients fall in the range of prediabetic diagnostic criteria suggested by American diabetic Association which suggests range of 5.7-6.4% for prediabetes. Hence care must be taken before newly diagnosing patient as diabetic or prediabetic based on glycated hemoglobin alone. With this study we can also state that newly diagnosed hypothyroid patients should not be diagnosed as diabetic if glycated hemoglobin are elevated without proper further investigations.

Sialic acid

The present study shows a significantly increased levels of bound serum sialic acid with $p < 0.0001$ in newly diagnosed non diabetic hypothyroid individuals with mean serum bound sialic acid level 2.29 ± 0.28 as compared to normal controls where mean serum bound sialic acid level is 1.81 ± 0.18 . This finding is in accordance with the study done by Mustafa Altay *et al.*

The bound serum sialic acid in newly diagnosed non diabetic hypothyroid patient showed statistically significant mild positive correlation with TSH with r value of 0.2303 and p value of 0.0212.

Mustafa Altay *et al.* also established positive correlation of sialic acid with atherosclerosis in hypothyroids.

Since sialic acid is an indicator of risk of atherosclerosis and cardiovascular diseases, further studies should be made to understand risk of atherosclerosis and cardiovascular diseases in hypothyroid patients.

Conclusion

From this study it can be concluded that newly diagnosed non diabetic hypothyroid patients show elevated glycated hemoglobin levels in spite of normal fasting blood sugar levels.

The exact mechanism of false elevation in glycated hemoglobin levels in newly diagnosed non diabetic hypothyroid is unknown so far. It may be attributed to the effect of thyroid hormones on erythropoiesis and RBC life span. Further studies are needed in this regard.

With mean HbA1c value of 5.93 ± 0.32 in newly diagnosed non diabetic hypothyroids, most of the cases in the study fall in the range of prediabetic according to American Diabetic Association. Hence it can be concluded that proper investigations should be carried out before diagnosing a newly diagnosed hypothyroid patient as prediabetic/diabetic based on HbA1c alone.

Further elevated HbA1c levels showed positive correlation with TSH in spite of normal fasting blood sugar levels.

Our study also showed that there is increase in the level of serum sialic acid in newly diagnosed non diabetic hypothyroid patients. Since Sialic acid is an indicator of risk of atherosclerosis and cardiovascular diseases. it can be concluded that these patients can develop atherosclerosis and cardiovascular diseases if untreated. Further studies should be made to understand risk of atherosclerosis and cardiovascular diseases in hypothyroid patients.

Summary

- Our study comprised of total 200 subjects, of which 100 subjects were newly diagnosed cases of hypothyroidism who were non diabetic and 100 subjects were age and sex matched healthy controls.

- After obtaining an informed consent, 5 ml of venous blood was collected after overnight fasting.
- Serum TSH, FT3, FT4 were analyzed using Chemiluminescence immunoassay in automated Access -2 analyser from Beckman Coulter.
- HbA1c was estimated by using HbA1c analyser by HPLC method.
- The serum sialic acid was measured using acidic ninhydrin method by Yao K *et al.*
- The measured parameters were expressed as mean $\pm$ SD. Statistical analysis was done using Graph Pad Prism 6. Unpaired t test was used to compare the groups. Relationship between the variables was assessed by Karl Pearson's coefficient of correlation.
- Serum level of HbA1c and bound sialic acid is significantly increased in newly diagnosed non diabetic hypothyroid patients as compared to normal healthy controls and there was a positive correlation of Serum HbA1c and serum sialic acid with Serum TSH in hypothyroid group.
- It was concluded that all the newly diagnosed hypothyroidism patients with elevated HbA1c levels should be properly investigated before diagnosing them as prediabetic/diabetic.

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