



## **Evaluating Blood sugar levels in patients diagnosed with primary hypothyroidism: A study at a tertiary care hospital**

<sup>1</sup>Veena Bhaskar S Gowda, Associate Professor, Department of Biochemistry, East Point College of Medical Sciences & Research Centre, Bidarahalli, Bangalore, Karnataka, India

<sup>2</sup>Shyamali Chatterjee, Tutor, Department of Biochemistry, East Point College of Medical Sciences & Research Centre, Bidarahalli, Bangalore, Karnataka, India

**Corresponding Author:** Veena Bhaskar S Gowda, Associate Professor, Department of Biochemistry, East Point College of Medical Sciences & Research Centre, Bidarahalli, Bangalore, Karnataka, India

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### **Abstract**

**Introduction:** Many studies have proven that patients with hypothyroidism end up in Type 2 Diabetes Mellitus over a period of time. However not much information is known about the status of blood sugar levels in patients diagnosed with hypothyroidism for the first time. Thus, the authors were interested to know status of blood sugar levels in patients with primary hypothyroidism at diagnosis.

**Materials & Methods:** The study was conducted in Department of Biochemistry in collaboration with Department of Medicine, East Point College of Medical Sciences & Research Centre between December 2018 & December 2019. Thyroid function tests (TFT) of all patients attending Hospital during the time period was studied. Those found to be hypothyroid (TSH: Thyroid stimulating hormone  $>4.5\mu\text{IU/ml}$ ) were enrolled for the study & random blood sugar (RBS) evaluated.

**Results:** Of 4217 samples processed for TFT, 576 were hypothyroid. 75 of these patients were diagnosed to be

hypothyroid for the first time in whom RBS was analysed. No significance was found when mean T3, T4 & TSH was compared between hypothyroid & those with hypothyroidism for the first time. Significant correlation was found between age & TSH, age & RBS as well as TSH & RBS of patients diagnosed with hypothyroidism for the first time.

**Discussion & Conclusion:** The study concludes that though RBS levels were within normal limits for patients with primary hypothyroidism for the first time, a significant correlation with TSH signifies that patients with higher TSH levels are at increased risk of high blood sugar levels.

**Keywords:** Hypothyroidism, Blood sugar levels, Diabetes Mellitus, Healthy lifestyle, Thyroid function test

### **Introduction**

The two most common endocrine disorders in clinical practice: Diabetes mellitus (DM) and thyroid disorders, with mutual influence and association on each other has

long been reported<sup>1</sup>. Whereas the role of autoimmunity in type I DM along with autoimmune thyroid disease has been observed, a complex mechanism between type II DM and thyroid disorder is attributed to disturbed expression of genes leading to impaired glucose utilization by the muscles, increased hepatic glucose output and increased glucose absorption from intestine<sup>2</sup>. The association between hypothyroidism and metabolic syndrome has been proposed and its indirect relation to diabetes onset has been reported as well<sup>3</sup>. A large prospective population based cohort study found that low & low normal thyroid function was associated with an increased risk of diabetes mellitus<sup>4</sup>.

With this background, the researchers were interested to know the status of blood sugar levels in patient population diagnosed with primary hypothyroidism attending one of the new medical colleges in East Bengaluru, East Point College of Medical Sciences & Research Centre.

#### **Aims & objectives**

To evaluate blood sugar levels in patients diagnosed with primary hypothyroidism for the first time and also to see if blood sugar levels are elevated in patients with high TSH (Thyroid stimulating hormone) levels.

#### **Materials and methods**

The study was conducted in the Department of Biochemistry & Department of General medicine, East Point College of Medical Sciences & Research Centre (EPCMS&RC), Bidarahalli, Bengaluru. All patients between 18-75 years (Inpatients & outpatients of both gender) undergoing thyroid function test (TFT-Total T3, Total T4 & TSH) from December 2018 to December 2019 at Central laboratory, EPCMS & RC were included in the study. After cleaning the area with

alcohol, blood for TFT was collected from antecubital fossa in plain vacutainer tubes assuring fasting status, allowed to clot & centrifuged to separate serum. The separated serum was processed for Total T3, Total T4, TSH by Chemiluminescence Immunoassay method using Beckman Coulter Access 2 instrument. Those with TSH >4.5  $\mu$ IU/ml & diagnosed with hypothyroidism for the first time were enrolled for the study. The patients were explained about the aims & objectives of the study & after being convinced an Informed consent was taken. Following enrolment, Random blood sugar (RBS) level was analysed. Blood collected in grey capped fluoride tubes was processed for glucose estimation by Hexokinase method using Beckman Coulter AU 480 instrument. Patients less than 18 years of age, known hypothyroid patients on treatment as well as known diabetics were excluded from the study. Statistical analysis was done using SPSS 16 to compare the means between two groups using independent "t" test (Table 1) & Pearson correlation analysis for correlating age, TSH & RBS of patients diagnosed with hypothyroidism for the first time. p value <0.05 was considered significant. The study was approved by Institutional Research & Ethics Committee.

#### **Results**

The results of thyroid function tests (Total T3, Total T4, TSH) of all patients undergoing TFT & blood glucose values of patients identified to be suffering from hypothyroidism for the first time is expressed as mean  $\pm$  SD (Table 1). Normal values for T3 was 0.7-2.0 ng/ml, T4 was 4.6 - 11  $\mu$ g/dl & for TSH was 0.4-4.5  $\mu$ IU/ml [5].

Table 1: Age, Gender & TFT values of Hypothyroid as well as First time hypothyroid patients

Hypothyroid patients (n=576)					First time Hypothyroid patients (n=75)						
Age (Mean)	Sex		T3 (Mean ±SD) ng/ml	T4 (Mean ±SD) µg/dl	TSH (Mean ±SD) µIU/ml	Age (Mean)	Sex		T3 (Mean ±SD) ng/ml	T4 (Mean ±SD) µg/dl	TSH (Mean ±SD) µIU/ml
	M (%)	F (%)					M (%)	F (%)			
37.63	66 (11.45%)	510 (88.54%)	0.99±0.258	8.20±2.781	14.51±16.530	40.53	9 (12%)	66 (88%)	0.93±0.303	8.36±3.440	13.64±15.464

Table 2: Comparison between known hypothyroids & those diagnosed with hypothyroidism for the first time

Parameter	Known Hypothyroid n	1st time Hypothyroid n	Mean		Standard deviation		"t" value	P value
			Known Hypothyroid	1st time hypothyroid	Known Hypothyroid	1st time hypothyroid		
Total T3	299	35	0.999	0.937	0.258	0.303	1.321	0.187
Total T4	297	35	8.204	8.369	2.781	3.440	0.324	0.746
TSH	501	75	14.515	13.646	16.530	15.464	0.428	0.669

4217 samples were processed for thyroid function test at Central Laboratory, EPCMS & RC, between December 2018 to December 2019. 576 of these samples (13.65%) were identified to be hypothyroid (Patients were identified to be hypothyroid biochemically if TSH was more than 4.5µIU/ml)<sup>5</sup>. 66 were male (11.45%) & 510 female patients(88.54%).The mean age of patients identified to be hypothyroid was 37.63 years with a age group range of 18-75 years involved in the study. Total T3, Total T4 & TSH were analysed for all patients identified to be hypothyroid. The mean Total T3 was 0.99 ± 0.258 ng/ml, mean Total T4 was 8.20± 2.781 µg/dl and mean TSH was 14.51± 16.530 µIU/ml for all the hypothyroid samples studied.

75 out of 576 (13.02%) hypothyroid patients were diagnosed with hypothyroidism for the first time. 9 were male (12%) & 66 (88%) were female patients. The mean age of patients identified to be hypothyroid for the first time was 40.53 years with a age group range of 20-74 years. The mean Total T3 of patients identified to be hypothyroid for the first time was 0.93± 0.303 ng/ml, Total T4 8.36± 3.440 µg/dl & TSH 13.64 ± 15.464 µIU/ml. Random blood glucose levels of these 75 patients was analysed on the day of being identified as hypothyroid. The mean blood glucose level of these patients was 103.84 mg/dl(74.6 -136). No significance was detected when the mean between two groups for Total T3, Total T4 & TSH was compared (Table 2). Pearson correlation when applied for age, TSH & RBS for patients diagnosed with

hypothyroidism for the first time showed significant correlation between age & TSH ( $p < 0.001$ ) as well as between age & RBS ( $p < 0.001$ ). A significant correlation was also observed between TSH & RBS ( $p < 0.001$ ).

### **Discussion**

Glucose metabolism is affected by thyroid hormones by several mechanisms<sup>1</sup>. A study by Erdogan et al found metabolic syndrome to be in high frequency in subclinical & overt hypothyroid patients than in healthy controls<sup>6</sup>. An increasing global prevalence of the two endocrine disorders: Thyroid disorders and type 2 DM has been noticed and the frequency of thyroid disorders being second to type 2 DM in endocrine clinics has been observed too<sup>7</sup>. BM Singh & others have proposed that it would be good practice to screen females with hypothyroidism for evidence of metabolic syndrome<sup>8</sup>. They have also concluded that hypothyroidism leads to a state of Insulin resistance<sup>8</sup>. Many studies have proved that since thyroid dysfunctions & diabetes are related to endocrine glands, they are inter connected. Hence, the researchers were interested to find the blood sugar status in hypothyroid patients identified for the first time & later as a continuation of the study to evaluate the time taken for the hypothyroid patients to become diabetic.

The authors were interested to know if patients diagnosed with primary hypothyroidism for the first time have an altered blood sugar level at presentation or it develops over time due to the common metabolic derangement associated with hypothyroidism & T2 diabetes mellitus. To the best of authors knowledge no evidence was found regarding the coexistence of diabetes in patients with hypothyroidism diagnosed for the first time. So the authors were interested to know

the blood sugar levels at diagnosis of hypothyroidism. Wang C has proposed that many factors are indicated of contributing to Type 2 Diabetes Mellitus in patients with thyroid abnormalities<sup>1</sup>. He has also concluded in his review article that heavily disturbed lipid metabolism due to thyroid dyscrasias was responsible for the cardiovascular events with micro & macro-angiopathies in patients with thyroid disorders<sup>1</sup>. Hollowell & others in the NHANES III study found 4.6 % of total participants to be hypothyroid and a higher prevalence of thyroid disease in women compared to men<sup>9</sup>. The current study however observed 13.65% of total participants to be hypothyroid and a very high prevalence of hypothyroidism was observed in females (88.54%). When the number of patients presenting with hypothyroidism for the first time was evaluated, it was 13.02% and Women contributed to a higher proportion compared to men in this group as well (88%). The current study, comprising of patient population from both urban & rural areas, observed the mean age of hypothyroid patients was 37.63 years & those diagnosed to be hypothyroid for the first time was 40.53 years. The mean age of patients with hypothyroidism was 36.1 years in the study by Singh & others whereas it was 40.53 in the current study. This could be because unlike the former study having patients in the age group between 18-45 years the current study included patients in a wide range between 18-75 years thus increasing the mean age. Lee SA & others in their study recognised that patients with thyroid disorders in the age group between 20 to 34 years showed a higher rate of Diabetes when they had low continuity of care in contrast to other studies wherein diabetes occurred in middle aged or older individuals<sup>10</sup>. A significant correlation between age &

TSH as well as age & RBS of patients with hypothyroidism for first time in the current study signifies that patients of higher age groups are at risk for hypothyroidism & might end up having high blood sugar levels thus adding double burden of metabolic disorders compared to younger age groups diagnosed with hypothyroidism for the first time. In view of the high prevalence of hypothyroidism in the population studied, with a high prevalence in women & considering the age group affected, the researchers highlight the significance of educating patients about maintaining healthy lifestyle & preventing them from turning into diabetics to reduce the risk of co morbidities. Also, since the prevalence of hypothyroidism is more in females, they have to be educated regarding the consequences of not adhering to treatment & reduced continuity of care as well as sensitized about the risk of developing T2 DM, metabolic syndrome which adds up to the financial as well as emotional burden to the family.

Unlike in the study by BM Singh & others where the mean TSH was 45.8 $\mu$ IU/ml, the mean TSH in patients with hypothyroidism was 14.51 $\mu$ IU/ml & that in patients diagnosed with hypothyroidism for the first time was 13.64  $\mu$ IU/ml in the current study. However similar to the blood sugar levels (92.9mg/dl) seen in the study by Singh & others, random blood sugar levels were within normal range (103.84mg/dl) in the current study as well.

It is found that patients with diabetes mellitus become hypothyroid over a period of years. However the association vice versa is not studied. Layal Chakar & others in their study have concluded that low and low normal thyroid function are related to an increased risk of diabetes<sup>4</sup>. They also raised a concern that despite the

high occurrence of thyroid dysfunction & diabetes in the general population, the relation between the two remained unexplored and suggested further research to determine the extent of association of thyroid hormones to accelerate the development of diabetes or if it was due to a common genetic predisposition<sup>4</sup>. The current study, trying to evaluate blood glucose levels at presentation of hypothyroidism, found that blood glucose levels were within normal limits for all patients diagnosed with hypothyroidism for the first time (mean RBS: 101.16mg/dl) thus indicating that, at the time of being diagnosed with hypothyroidism, there was no sign of coexisting diabetes mellitus & they might progress to diabetes over a period of time with high risk as proposed by Layal Chaker & others. Also a significant correlation between TSH & blood sugar levels in the current study signifies that patients with hypothyroidism for the first time especially those with a high TSH levels are at higher risk of increased blood sugar levels compared to those with TSH on the lower side & thus need to be evaluated thoroughly at presentation. Hence the study proposes that patients with high TSH levels at presentation should be educated to inculcate a healthy life style & eating habits to reduced the chances of progressing to DM. In view of the findings in current study with regards to high prevalence of hypothyroidism in general population as well as females of Asian origin, the authors propose that further studies are required to monitor how long it takes for hypothyroid patients to become diabetic with respect to all age groups & in all populations. The researchers are interested to continue the study, by following up patients diagnosed to be hypothyroid for the first time every six months & monitor the time by

which they become diabetic & the time taken for the same.

Duntas & others have concluded that insulin resistance in subclinical hypothyroidism was due to diminished rate of insulin stimulated glucose transport caused due to altered expression of glucose transporter type 2 gene (GLUT 2) translocation<sup>11</sup>. Hypothyroidism has been shown to be directly associated with insulin resistance in various studies<sup>12,13,14</sup>.

Lack of thyroid hormone is associated with decrease in insulin sensitivity & glucose intolerance, whereas treatment of hypothyroidism is shown to improve insulin sensitivity<sup>4,12,15</sup>. Since controlling thyroid hormone levels within normal range is found to help prevent development of DM in patients with thyroid dysfunction<sup>16</sup>, as well as based on the observation in the current study, the researchers recommend all hypothyroids diagnosed for the first time to be started hypothyroid treatment right away & educate the patients about possibilities of developing T2 DM.

Strengths of the study are, the study was conducted over a period of one year and 4217 patients undergoing TFT were studied. However the weakness of the study is that only TFT & blood sugar levels were measured and no other parameter studied. The reason being, patients realising they were hypothyroid based on their TSH levels, had no mood to cooperate for other factors like collecting their blood samples for lipid profile, HbA1c, or cooperate for giving their height & weight for BMI.

### **Conclusion**

Lee SA & others have concluded that having known the relationship between thyroid disorders & diabetes mellitus, efforts to minimise the effects of thyroid disorders on development of type 2 diabetes mellitus

should be considered. Unlike patients with T2 DM, who are usually middle or older age group & progress to Hypothyroidism over a period of time, Patients diagnosed with hypothyroidism for the first time are much younger and it would be wise to educate them about the chances of progressing to T2 DM as well as its consequences. The current authors reinforce the same as well, based on the findings that patients diagnosed with hypothyroidism for the first time have normal blood sugar levels but are at high risk of developing T2DM over a period of time as seen by other researchers. Thus the emphasis should be to educate patients about adopting healthy lifestyle, adhere to the recommended treatment for hypothyroidism, have a plan for continuity of care, thereby reduce the chances of developing T2 DM & thus the financial & emotional burden on the family. In view of the same, the authors would like to continue the study by following up the patients every six months for blood sugar levels & see when exactly the blood sugar levels get deranged & how long it takes for an hypothyroid patient to develop insulin resistance, glucose intolerance & dyslipidemia.

### **Abbreviations**

1. DM: Diabetes mellitus
2. TSH: Thyroid stimulating hormone
3. EPCMS&RC : East Point College of Medical Sciences & Research Centre
4. RBS : Random blood sugar
5. TFT : Thyroid function tests (Total T3, Total T4, TSH) of all patients undergoing
6. GLUT 2: Glucose transporter type 2



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