

# Study of Glycosylated Haemoglobin (HbA1c) Levels in Non-Diabetic Patients with Hypothyroidism

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## ABSTRACT

**Introduction:** HbA1c used for the assessment of glycemic status of the diabetic patients is widely recommended for its use for diagnosing diabetes. A positive association between thyroid disorder and diabetes mellitus is well recognized but to study the effect of thyroid disorders on glucose metabolism in non diabetic patients is an area for extensive research. Objective of the study was to study the glycosylated haemoglobin (HbA1c) levels in Non diabetic patients with hypothyroidism.

**Material and methods:** Patients attending teaching hospitals attached to BMCRI who fulfilled the inclusion criteria were taken into study during the period from November 2017-May 2019. It was a cross sectional study. Descriptive statistics like mean, standard deviation were calculated. Inferential statistics like Mann-whitney test was used to compare the parameters between two groups.

**Results:** During the period of study, 130 patients were studied of these, 65 were cases who were non diabetic patients with hypothyroidism, 65 controls who were non diabetic euthyroid patients. Among 65 cases 5 patients had normal HbA1C levels (7.7%) and 60 patients had increased HbA1C levels (Pre-diabetes) (92.3%), among 65 controls 56 patients had normal HbA1C levels (86.2%) and 9 patients had increased HbA1C levels (13.8%).

**Conclusion:** From the results of the present study it can be concluded HbA1c levels were significantly higher in non diabetic patients with hypothyroidism when compared to non diabetic patients with normal thyroid function (mean HbA1C levels were  $5.87 \pm 0.23$  vs  $5.42 \pm 0.24$ ) ( $P < 0.0001$ ) which was statistically significant. Therefore it is suggested that the effects of the hypothyroidism on the HbA1c must be considered when interpreting the HbA1c for the diagnosis of prediabetes.

**Keywords:** HbA1c, Pre-diabetes, Hypothyroidism

diabetic patients is widely and the American Diabetes Association (ADA) recommended its use for diagnosing diabetes.<sup>4</sup>

The glycosylated hemoglobin represents the fraction of hemoglobin that undergoes non-enzymatic glycosylation over the circulatory life span of the erythrocytes (usually 120 days).<sup>5</sup>

A positive association between thyroid disorder and diabetes mellitus is well recognized but to study the effect of thyroid disorders on glucose metabolism in non diabetic patients (i.e. patients diagnosed with only thyroid dysfunction and not diabetes) is an area for extensive research.

Theory cites different causes for increased HbA1c levels in patients of Hypothyroidism.<sup>6</sup>

Decreased metabolism leading to decreased turnover of proteins and thus prolonging their half - life.

Increased oxidative stress causing increased glycation of proteins.

Theory cites different causes for increased HbA1c levels in patients of Hyperthyroidism.<sup>7</sup>

1. Permissive influence of T3 is seen in the glycogenolytic, gluconeogenic effect and thyroid hormones are known to increase hepatic glucose output.

Thus Present study was planned to assess correlation between thyroid dysfunction and (HbA1c) glycosylated haemoglobin levels in non-diabetic patient .

The effects of the thyroid dysfunction on the HbA1c must be considered when interpreting the HbA1c for the diagnosis of diabetes or prediabetes.

Rana Bhattacharjee et al conducted in Department of Endocrinology and Metabolism, IPGME and SSKM Hospital, Kolkata, West Bengal, Study of Effects of thyroid status on glycated haemoglobin, this case control study was conducted on 127 subjects in those 47 hypothyroid, 34 hyperthyroid and 46 controls. Data suggests HbA1c levels were found to be significantly higher in hypothyroid

## INTRODUCTION

Galaganda as mentioned in Susrutha Samhitha which was written in 1500BC gives the signs and symptoms of thyroid dysfunction and its treatment.<sup>1</sup> Dysfunction and anatomic abnormalities of the thyroid are among the most common diseases of the endocrine glands.<sup>2</sup>

Almost one-third of the world's population lives in areas of iodine deficiency. The prevalence of goitre in areas of severe iodine deficiency can be as high as 80%.<sup>3</sup>

In iodine-replete areas, most persons with thyroid disorders have autoimmune disease, ranging from primary atrophic hypothyroidism, Hashimoto's thyroiditis to thyrotoxicosis caused by Graves' disease.

HbA1c used for the assessment of glycemic status of the

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patients.<sup>8</sup>

Meekyoungkim et al conducted cross sectional study of 45 patients of non diabetic overt hypothyroidism. The study compared with euthyroid as controls. HbA1c levels were higher in patients with hypothyroidism compared with control subjects.<sup>9</sup>

Vidya Sagar et al conducted a case-control study which was conducted on total 209 subjects. 109 patients were allotted in case group of non diabetic sub clinical hypothyroidism and 100 in control group. HbA1c levels increased in subclinical hypothyroid patients.<sup>10</sup>

Current research aimed to Study the Glycosylated haemoglobin (HbA1c) levels in Non diabetic patients with hypothyroidism

## MATERIAL AND METHODS

The Cross sectional was conducted on patients presented (Outpatient/Inpatient) to the hospitals attached to Bangalore Medical College & Research Institute during the study period from November 2017-May 2019.

Sample size: 65 non diabetic patients with hypothyroidism and 65 non diabetic patients with normal thyroid function.

### Inclusion criteria

1. Patients who will give valid written informed consent for the study
  2. Patients who have hypothyroidism, according to ATA guidelines.<sup>11,12</sup>
  3. Patients who give Non diabetic history
- Patients who have Normal Thyroid function, according to ATA guidelines.<sup>11,12</sup>

### Exclusion criteria

1. Patients who give diabetic history and who are Diabetic, according to ADA guidelines<sup>2</sup>

2. Patients who have hyperthyroidism
3. Patients who have history of Recent (< 3 months) blood transfusion
4. Patients who have history of any haematological disorder

### Experimental protocol

After obtaining Institutional ethical committee clearance, cases were selected as per the inclusion criteria mentioned above and written informed consent was taken. Relevant blood investigations were done. Patients were grouped Hypothyroid and Euthyroid based on TSH T3 T4 LEVELS as per ATA guidelines<sup>14</sup> and patients were grouped Non Diabetic, PreDiabetic, Diabetic Based on HbA1c, FBS, PPBS levels as per ADA guidelines<sup>15</sup> then studied the HbA1c levels in Hypothyroid patients who were Non diabetic and in Euthyroid patients who were Non diabetic also .

### STATISTICAL ANALYSIS

Descriptive analysis like frequency and percentage were calculated. Inferential statistics like chi square test was applied for categorical data. P value was set significant at 0.05.

### RESULTS

During the period of study 130 patients were studied, among these 65 non diabetic patients with hypothyroidism and 65 non diabetic patients with normal thyroid function.

Of the 130 patients, 65 cases were non diabetic hypothyroid patients, 65 controls who were non diabetic euthyroid patients (Table 2). Among 65 non diabetic patients with hypothyroid 5 patients have normal HbA1c levels (7.7%) and 60 patients have increased HbA1c levels (Pre-diabetes) (92.3%), among 65 non diabetic patients with normal thyroid function 56 patients have normal HbA1c levels (86.2%) and 9 patients have increased HbA1c levels (13.8%) P value -0.00 which was significant (Table 1).

HbA1c levels were significantly higher in non diabetic patients with thyroid dysfunction when compared to non diabetic patients with normal thyroid function (P value -0.00) (table-2).

The mean age of the patients in the cases was 38.31 ± 11.257 years and the mean age of the patients in the controls 32.37 ± 11.704 years (table 3).

Among cases 62 were female and 3 were male patients among controls 49 were female and 16 were male. Among cases the mean HbA1c levels was 5.87 ± 0.23, among controls HbA1c levels was 5.42 ± 0.24 (table 4).

Among cases 5 patients had normal HbA1c levels and 60 patients had increased HbA1c levels (Pre-diabetes), among controls 56 patients had normal HbA1c levels and 9 patients had increased HbA1c levels (table 5).

The mean TSH values in cases was 16.67. ± 22.60 the mean

Variables	Mean ± SD	
	Cases	Controls
Age, in years	38.31±11.257	32.37±11.704
HbA1c, %	5.87±0.23	5.42±0.24
TSH, uU/ml	16.67±22.06	2.59±1.04
T3, ng/ml	1.18±0.74	1.17±0.74
T4, ug/dl	8.71±3.58	8.69±3.57
FBS, mg/dl	75.47±8.16	75.47±8.16
PPBS, mg/dl	108.06±8.59	108.09±8.57
Total number of patients, N=130		

**Table-1:** Summary of characteristics of patients

Total (N= 130)	Normal (HbA1c < 5.7%)	Pre diabetes (HbA1c 5.7% to 6.4%)
Cases (65)	5 (7.7%)	60 (92.3%)
Controls (65)	56 (86.2%)	9 (13.8%)

**Table-2:** Outcome of patients

	N	Minimum	Maximum	Mean	Std. Deviation
Cases	65	18	69	38.31	11.257
Controls	65	18	69	32.37	11.704

**Table-3:** Distribution of the subjects based on age

	Cases		Controls	
	Frequency	Percent	Frequency	Percent
Females	62	95.4	49	75.4
Males	3	4.6	16	24.6
Total	65	100.0	65	100.0
Chi-square value – 8.87; p value – 0.002*; *significant				
<b>Table-4:</b> Distribution of the subjects based on gender				

	Cases		Controls	
	Frequency	Percent	Frequency	Percent
Normal	5	7.7	56	86.2
Pre-diabetes	60	92.3	9	13.8
Total	65	100.0	65	100.0
Chi-square value – 77.21; p value – 0.00*				
<b>Table-5:</b> Distribution of the subjects based on hba1c levels				

	Minimum	Maximum	Mean	S.D	Mean diff	p value
Cases	.04	150.0	16.67	22.60	14.07	0.00*
Controls	1.10	4.80	2.59	1.04		
*significant						
<b>Table-6:</b> Distribution of the subjects based on TSH						

TSH values in controls were  $2.59 \pm 1.04$ . The mean T3 value in cases was  $1.18 \pm 0.74$ , the mean T3 value in controls was  $1.17 \pm 0.74$ , the mean T4 value in cases was  $8.71 \pm 3.58$ , the mean T4 value in controls was  $8.69 \pm 3.57$  (table-6).

## DISCUSSION

This study was conducted to study the Glycosylated haemoglobin (HbA1c) levels in non diabetic patients with hypothyroidism. During the period of study, 130 patients were studied of these, 65 non diabetic patients with hypothyroid and 65 non diabetic patients with normal thyroid function.

### Age distribution

In our study, the average age among cases was 38 years and among the controls was 32 years.

In a study by Vidya Sagar Ram et al, conducted on 209 patients at Uttar Pradesh University of Medical Sciences, Saifai, Uttar Pradesh, a similar mean age group of 46 years among cases and 47 years among controls was seen.<sup>11</sup>

Mayur Goradhanbhai et al conducted on 200 patients at Karamsad medical college, Gujarat on a similar mean age group of 49 years among cases and 48 years among controls was seen.<sup>12</sup>

### Sex distribution

Our study comprised of 111 females and 19 males. Among the cases, there were 62 females (95.4%) and 3 males (4.6%). While among the controls, there were 49 females (75.4%) and 16 males (24.6%).

In a study by Vidya Sagar Ram et al, there were 209 patients, 179 females and 30 males.<sup>11</sup> In Mayur Goradhanbhai et al study there were 200 patients, 120 females and 80 males.<sup>12</sup>

### HbA1c levels

Among the cases the mean HbA1C levels were  $5.87 \pm 0.23$ , among controls HbA1c levels were  $5.42 \pm 0.24$ , (p value <0.0001). There was a significant increase in HbA1c levels

in cases compared to controls

In the study by Vidya Sagar Ram et al among the cases the mean HbA1C levels were  $5.65 \pm 0.34$ , among controls HbA1c levels were  $5.13 \pm 0.31$ , (p value <0.0001). There was a significant increase in HbA1c levels in cases compared to controls<sup>11</sup>

Mayur Goradhanbhai et al also showed among the cases the mean HbA1C levels were  $5.70 \pm 0.35$ , among controls HbA1c levels were  $5.26 \pm 0.17$ , (p value <0.0001).<sup>12</sup> There was a significant increase in HbA1c levels in cases compared to controls.

Our study also showed similar results. HbA1c levels were significantly higher in non diabetic patients with hypothyroid when compared to non diabetic patients with normal thyroid function. (p value=0.00).

### Limitations of the study

1. Not included hyperthyroid patients.
2. On correction of thyroid dysfunction HbA1c levels not studied

## CONCLUSION

From the results of the present study it can be concluded HbA1c levels were significantly higher in non diabetic patients with Hypothyroid when compared to non diabetic patients with normal thyroid function (mean HbA1C levels were  $5.87 \pm 0.23$  vs  $5.42 \pm 0.24$ ) (P <0.0001), which was statistically significant. Therefore it is suggested that the effects of the hypothyroid on the HbA1c must be considered when interpreting the HbA1c for the diagnosis of Pre-diabetes

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