

**EFFECTS OF THYROXINE REPLACEMENT ON GLYCOSYLATED HEMOGLOBIN LEVELS IN NON DIABETIC PATIENTS WITH OVERT HYPOTHYROIDISM**

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**ABSTRACT**

HbA1c is used for screening as well as for diagnosing Diabetes Mellitus. It depends on ambient levels of glycemia over the preceding 2-3 months but also on the RBC turnover from the bone marrow. HbA1c may not accurately reflect the level of glycemia in conditions of altered erythrocyte turnover, one such condition being hypothyroidism, thereby causing false elevation of HbA1c which can result in false diagnosis of pre diabetes or diabetes mellitus. The aim of this study is to assess changes in HbA1c levels independent of changes in plasma glucose levels after initiation of thyroxine replacement in non diabetic patients with overt hypothyroidism. In these patients the post treatment FBS and PPBS were within normal limits. The HbA1c estimation was done and was found to be increased. The average HbA1c was around 5.83%. This led to false diagnosis of dysglycemia in 67% of patients. False diagnosis of impaired glucose tolerance -60% and diabetes was 7%. After thyroxine replacement and achievement of euthyroidal state follow up was done for 3 months post achieving euthyroidal state. The T4 and T4 on the average was found to be TSH-3.66 and T4- 7.85 within normal range, although there was no difference in fasting and post prandial blood sugars the mean HbA1c decreased to 5.25%. Therefore in hypothyroid patients diagnosis of pre diabetes or diabetes should only be based on fasting blood glucose and post prandial blood glucose. So we conclude that HbA1c is not a valid test for diagnosis of prediabetes or diabetes in the presence of hypothyroidism.

**KEYWORDS:** HYPOTHYROID, FBS, HBA1C, PPBS, TSH, T4.**INTRODUCTION**

HbA1c is used for screening as well as for diagnosing Diabetes Mellitus. It depends on ambient levels of glycemia over the preceding 2-3 months but also on the RBC turnover from the bone marrow. HbA1c may not accurately reflect the level of glycemia in conditions of altered erythrocyte turnover, one such condition being hypothyroidism, thereby causing false elevation of HbA1c which can result in false diagnosis of pre diabetes or diabetes mellitus. There is no current guidelines regarding the use of hba1c for the diagnosis of diabetes mellitus in hypothyroid patient. This study. The aim of this study is to assess changes in HbA1c levels independent of changes in plasma glucose levels after initiation of thyroxine replacement in non diabetic patients with overt hypothyroidism.

**MATERIALS AND METHODS****Study population****Source of data**

The study was conducted on 100 patients admitted to Government Rajaji Hospital & Madurai Medical College.

**Inclusion Criteria**

All patients with Overt Hypothyroidism.

**Exclusion Criteria**

- Diabetes mellitus (FBS:  $\geq 126$ mg/dl, PPBS:  $\geq 200$  mg/dl)
- Impaired glucose tolerance (2h post 75g OGTT is between 140- 199 mg/dl.
- Hb < 10 g/dl
- Known hemoglobinopathies
- Renal or Liver diseases.
- Pregnant patients

**Design of Study**

Prospective study.

**Period of Study**

6 Months

**Consent:** Individual written and informed consent.

**Procedure Methodology**

Informed consent was obtained from all patients enrolled for the study. In all the patients relevant information was collected in a predesigned proforma.

The patients are selected based on clinical examinations, biochemical tests. The patients are followed over a period of six months with TSH and HbA1c levels. initially baseline TSH, FBS, PPBS and HBA1C are obtained, patients are then started on thyroxine treatment. After thyroxine replacement and achievement of euthyroidal state , again TSH FBS PPBS and HBA1C are taken and compared with the post treatment values.

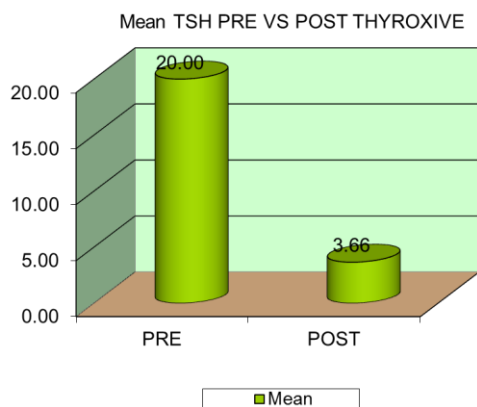
**RESULTS**

**Table 1: This table compares TSH values before and after thyroxine replacement.**

TSH	PRE	POST
Mean	20.00	3.66
S.D	9.16	0.81
P'	<0.001	Sig

The mean TSH before and after thyroxine treatment has significantly declined and it is statistically significant with a standarad deviation of 0.81 after treatment. P value <0.001.

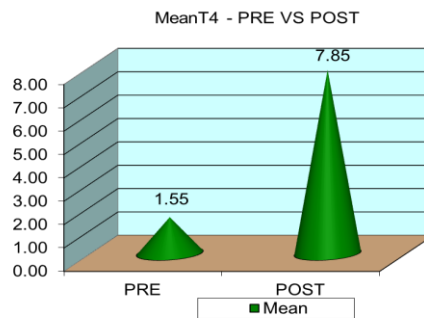
This chart compares the mean TSH levels pre and post thyroxine replacement.



**Table 2: The table shows the difference in T4 levels before and after thyroxine replacement.**

T4	PRE	POST
Mean	1.55	7.85
S.D	0.81	1.94
P'	<0.001	Sig

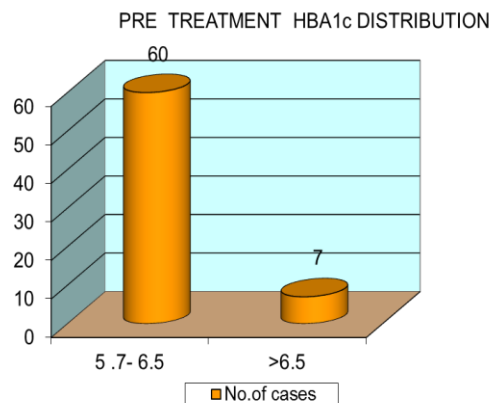
From this table we see that the T4 levels have significantly increased post treatment with a standard deviation of 1.94. p value <0.001 which is statistically significant.



**Table 3: Pre Treatment HbA1C.**

HbA1c	No. of cases
< 5.7	33
5.7- 6.5	60
>6.5	7
Total	100

From this chart we can infer that the baseline HbA1c was significantly high around 67% in hypothyroid patients inspite of having normal blood sugar levels. 7 out of 100 patients even had HbA1c in the diabetic range.



**Table 4: Hba1c Post Thyroxine Replacement.**

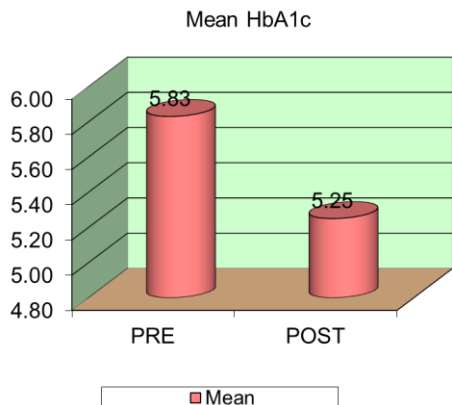
HbA1c	No. of cases
< 5.7	100
< 5.7- 6.5	0
> 6.5	0
Total	100

This table shows that all the patients in the study population had a normal HbA1c level after thyroxine replacement and achievement of a euthyroid state.

**Table 5: Hba1c Pre and Post Thyroxine Replacement- Comparison.**

HbA1c	PRE	POST
Mean	5.83	5.25
S.D	0.35	0.21
P'	<0.001	Sig

The mean HbA1c significantly decreased post thyroxine replacement and achievement of euthyroidal state. P value is <0.001 which is statistically significant.



## DISCUSSION

In our study majority of the patients belong to age group 36-45(43%). Females were more in number (85%). The baseline TSH values on an average was between (10-20) in 66% of the study population. T4 levels were between 1.1-2.0 in 49% of patients. In these patients the post treatment FBS and PPBS were with normal limits. The HbA1c estimation was done and was found to be increased. The average HbA1c was around 5.83%. This lead to false diagnosis of dysglycemia in 67% of patients. False diagnosis of impaired glucose tolerance - 60% and diabetes was 7%. This false elevation of HbA1c was also demonstrated by Kim and cols who showed that HbA1c in 45 hypothyroid patients was higher than in control group study by Anantarapu et al. also demonstrated false elevation of HbA1c values in patients with hypothyroidism which was lowered by thyroid hormone replacement without any change in fasting or OGTT values.

After thyroxine replacement and achievement of euthyroidal state, The T4 and T4 on the average was found to be TSH-3.66 and T4- 7.85 within normal range, although there was no difference in fasting and post prandial blood sugars the mean HbA1c decreased to 5.25%. These findings were similar to a study done by Kwon HS et al published in diabetes care journal in 2010 which showed no changes in FBS and PPBS following correction of hypothyroidism.

## CONCLUSION

Its concluded from the above study that HbA1c are falsely elevated out of proportion to the level of glycemia in patients with hypothyroidism which leads to false diagnosis of dysglycemia and it is lowered without any change in blood sugar levels after thyroine replacement and achievement of a euthyroidal state. Therefore in hypothyroid patients diagnosis of pre diabetes or diabetes should only be based on fasting blood glucose and post prandial blood glucose.

So we conclude that HbA1c is not a valid test for diagnosis of prediabetes or diabetes in the presence of hypothyroidism.

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