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General Medicine

EFFECT OF THYROID HORMONE ON HbA1c LEVELS IN PATIENTS WITH NEWLY DETECTED HYPOTHYROIDISM

KEY WORDS: Thyroid hormone, Hypothyroidism, HbA1c, TSH.

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ABSTRACT

Introduction: HbA1c is an important parameter in diagnosis of diabetes. However, Glycated hemoglobin (HbA1c) may not accurately reflect the level of glycemia in conditions of altered erythrocyte turnover.
Objective: to determine HbA1c levels in non-diabetic patients with newly detected hypothyroidism and to determine the effect of thyroid hormone replacement therapy on HbA1c levels.
Material and method: A prospective study was carried out July 2019 to December 2019 in the Department of Medicine in a tertiary care teaching institute in Jhalawar, District, Rajasthan. Total 128 Patients with newly detected hypothyroidism were included in this study. Thyroid hormone replacement was prescribed for 3 months to all patients. Paired t-test (2-tailed) was used to compare means of different parameters before and after the restoration of euthyroid state.
Results: Thyroid replacement therapy showed a statistically significant difference in haemoglobin level ($p=0.008$), thyroid profile ($p=0.001$) and HbA1c level ($p=0.007$) of study participants. There was a significant negative correlation between glycosylated haemoglobin and serum T4 levels ($r=-0.42, p<0.05$). Serum TSH level shows significantly positive correlation with glycosylated haemoglobin ($r=0.26, p<0.05$).
Conclusion: The study revealed a statistically significant reduction in mean HbA1c after thyroid replacement therapy which concludes that correction of hypothyroid states was associated with fall in HbA1c levels. A significantly positive correlation was found between Serum TSH level and glycosylated hemoglobin. It implies that that thyroid hormone affects HbA1c values.

INTRODUCTION:-

As per the International Diabetes Federation, 422 million people are living with diabetes across the world, and it is expected to rise to a whooping figure of 592 million in 2035, of which 79.4 million diabetics will be from India.[1] India is declared as the "diabetic capital" of the world by WHO.[2]Thyroid disorders are also very common in the general population and it is second only to diabetes as the most common condition to affect the endocrine system.[3,4]

Insulin and thyroid hormones are intimately involved in cellular metabolism and thus excess or deficit of either of these hormones result in the functional derangement of the other.[5] Thyroid disease is a pathological state that can adversely affect glycemic control in general population and has the potential to affect the health.[6]

The American Diabetic Association has approved the use of glycated hemoglobin (HbA1c) as a gold-standard measure of long-term glycaemic control with the ability to reflect the cumulative glycaemic history of the preceding 2–3 months and consider better predictor than fasting or 2-h glucose.[7] A value ≥ 5.7% but < 6.5% was considered to represent pre-diabetes, while a value ≥ 6.5% was considered diagnostic of diabetes mellitus.[8,9]

Glycosylated Hemoglobin is formed by the glycation of the valine of the ß-chain of hemoglobin and represents the fraction of hemoglobin that undergoes non-enzymatic glycation over the circulatory life span of the erythrocytes which is usually120 days.[10,11,12]It not only depends on the ambient level of glycemia over the preceding 2-3 months but also on the erythrocyte turnover in circulation.[13]Glycated hemoglobin may not accurately reflect the level of glycemia in conditions of altered erythrocyte turnover. Conditions such as hypothyroidism, iron and vitamin B12 deficiency and renal failure which are associated with a low erythrocytes turnover with a predominance of older cells due to paucity of younger RBCs and reticulocytes in circulation are associated with a falsely elevated HbA1c. [14,15,16] Therefore HbA1c levels do not accurately reflect glycemic levels in patients with hypothyroidism.That's why thyroid hormonereplacement is associated with a decrease in glycosylatedhaemoglobin (HbA1c) level, which is influenced byincreased erythropoiesis rather than by changes in glucoselevel.[17]Considering the above literature we planned a study to re-assess the glycemic status of hypothyroid patients after initiation of thyroxine replacement therapy.

Aim & Objectives:-

1. To determine HbA1c levels in non-diabetic patients with newly detected hypothyroidism.
2. To determine the effect of thyroid hormone replacement therapy on HbA1c levels.

Methodology: A prospective study was carried out from July 2019 to December 2019 in the Department of Medicine in a tertiary care teaching hospital in south-eastern Rajasthan. Total 128 Patients with newly detected hypothyroidism attending the OPD of Medicine Department, SRG Hospital attached to Jhalawar Medical College, Jhalawar during study period satisfying the inclusion and exclusion criteria were included in this study.

Inclusion criteria

- All patients >18 years of age with newly detected hypothyroidism i.e., elevated thyroid stimulating hormone and low thyroxin levels.
- Exclusion criteria
- Patients with Diabetes mellitus
- Patients with Anemia
- Patients with Renal insufficiency
- Patients with Liver dysfunction
- Patients with Severe hypertriglyceridemia
- Seriously ill patients requiring immediate hospitalization,
- Non-co-operative patients or patients not proving written consent.

Ethical clearance was taken from the Institutional Ethics Committee before commencing the study. Nature and purpose of study was explained in detailed to all participants and written consent was obtained from all the study participants before the study. Body weight was measured in kilograms using a spring weighing machine to the nearest 0.5 kg with light clothes on. Height was measured in the standing position with bare foot against the wall and was calculated to the nearest 0.5cm. Blood samples of the study participants were obtained in the morning hours after an overnight fast for fasting plasma glucose (FPG), hemoglobin (Hb), HbA1c, serum T3, T4, TSH, serum creatinine, liver function test, renal function test and lipid profile. Each patient then was given 75 gm anhydrous glucose mixed in 200 mL water and asked to drink slowly over 3 minutes. Repeat samples for plasma glucose were collected after 2 hours. Thyroid hormone replacement was prescribed for 3 months to all patients. The thyroxin dose was increased periodically in step wise manner, based on estimation of TSH till the patients were rendered euthyroid. Once the patient restored to the euthyroid state, they were allowed to continue the same dose of thyroxin and reassessed after three months. with following investigations: fasting plasma glucose (FPG), hemoglobin (Hb), HbA1c, serum T3, T4, TSH, serum creatinine and post glucose load 2 hours plasma glucose (PGPG). Data thus collected was entered in MS excel 10 and analyzed using SPSS trial version 20. Pearson's correlation test was applied to determine various correlations. Paired t-test (2-tailed) was used to compare means of different parameters before and after the restoration of euthyroid state. P value < 0.05 was considered as statistically significant.

RESULT:-

A prospective study was carried out on newly diagnosed hypothyroid patients attending Medicine OPD of SRG Hospital during study period. Based on inclusion and exclusion criteria a total 128 patients of hypothyroidism were enrolled in study. Base line investigation were assessed for all and based on test result thyroid replacement therapy was initiated. Patients were followed for three months and thereafter same investigations were repeated after achieving euthuroid states. During follow up, 06 patients could not be traced in spite of all efforts and they were excluded from study. So effective number of participants was 122 and they were assessed.

Table 1 Baseline characteristics of study participants.

Parameters	Male (n=43) (Mean ± SD)	Female (n=79) (Mean ± SD)	Total (n=122) (Mean ± SD)
Age (years)	39.8±09.4	36.6±11.8	37.72±10.6
Weight (kg)	68.3±12.8	52.5±14.6	58.06±13.8
BMI (kg/m^2)	28.2±5.2	29.1±6.6	28.7±6.1
Obese participants (%)	27 (62.79%)	48(60.75%)	75(61.48%)
Haemoglobin (gm%)	12.3±1.8	11.6±2.1	11.85±2.0
TSH (IU/mL)	97.5±55.8	99.3±56.4	98.67±56.2
T4 (ng/ml)	11.6±7.2	08.2±6.2	9.39±6.8
T3 (ng/ml)	1.2±0.8	0.8±0.4	0.94±0.5
FPG (mg/dl)	89.6±12.6	88.3±11.4	88.76±12.2
PGPG (mg/dl)	124.7±24.2	128.2±31.6	126.97±29.4
HbA1c (%)	5.7±0.6	5.8±0.4	5.7±0.5
S. creatinine (mg/dl)	0.78±0.3	0.77±0.2	0.77±0.3

Table 1 depict base line characteristic of study participants. Mean age of study participants was 37.72±10.6 years. Thyroid dysfunction was more common in females (M:F::1:1.83). Most of study participants were obese (61.48%). Females have lower hemoglobin level (11.6 gm%) than males (12.3 gm%) although difference was not statistically significant. The body mass index (28.7) of hypothyroid patients was significantly higher as compared to standard range of BMI. Pre-diabetic condition according to HbA1c level was found in 37.2% males and 35.44% females. Fasting and after 75 gm of glucose load, plasma glucose was within normal range.

Table 2: Comparison of pretreatment and post treatment parameter of study participants (n=122)

Parameters	Pre-treatment (Mean ± SD)	Post - treatment (Mean ± SD)	P value
Weight (kg)	58.06±13.8	55.3±14.6	0.13
BMI (kg/m^2)	28.78±6.1	27.34±6.4	0.07
Obese participants (number)	75(61.48%)	57 (46.72%)	-
Haemoglobin (gm%)	11.85±2.0	12.5±1.8	0.008
TSH (IU/mL)	98.67±56.2	3.6±2.4	0.0001
T4 (ng/ml)	9.39±6.8	104.7±28.6	0.0001
T3 (ng/ml)	0.94±0.5	0.72±0.2	0.0001
FPG (mg/dl)	88.76±12.2	89.6±13.6	0.61
PGPG (mg/dl)	126.97±29.4	127.4±28.4	0.90
HbA1c (%)	5.7±0.5	5.5±0.4	0.007

P value <0.05 was consider statistically significant Table 2 depicts changes in parameters before and after thyroid replacement therapy. Post treatment mean weight (p=0.13) and BMI (p=0.07) were reduced although difference was not statistically significant. Number of obese patient was reduced from 75 (61.48%) to 57 (46.72%). Thyroid replacement therapy showed a statistically significant difference in haemoglobin level (p=0.008), thyroid profile (p=0.001) and HbA1c level (p=0.007) although FPG and PGPG were remain unaffected by therapy.

Table 3: Correlation of HbA1c levels with thyroid hormone levels in study participants.

Parameters	TSH		T_3		T_4	
	r	p	r	p	r	p
HbA1c	0.26	<0.05	-0.056	>0.05	-0.42	<0.05

P value <0.05 was consider statistically significant. Table 3 depicts correlation of HbA1c with TSH, T_3 and T_4. There was a significant negative correlation between glycosylated haemoglobin and serum T_4 levels ($r = -0.42$, $p < 0.05$). Negative correlation was found between glycosylated haemoglobin and serum T3 levels although it was not significant ($r = 0.056$, $p > 0.05$). Serum TSH level shows significantly positive correlation with glycosylated haemoglobin ($r = 0.26$, $p < 0.05$).

DISCUSSION:

The present study was aimed to determine the effect of thyroid hormone on the levels of glycated haemoglobin in patients with newly detected hypothyroidism. Those patients with FPG or PGPG in the diabetic range (i.e FPG ≥ 126 mg/dL and PGP ≥ 200 mg/dL were excluded from the study since they would require anti-diabetic medication or the rapeutic lifestyle change, in addition to thyroxin treatment. Thus to eliminate the risk of a confounding factor of impact ofdiabetes treatment on HbA1c, the patients with FPG or PGPG in the diabetic range were excluded. The reason for choosing three months follow up was on account of the approximately 120days life span of the RBCs in circulation[12,18].

In present study, there was a statistically significant reduction in mean HbA1c after thyroid replacement therapy when compared to pretreatment values (p =0.007). The study results are similar to study conducted by Kim MK et al[17] and Mohammed Ismail et al[19].

In our study, significantly positive correlation was found between Serum TSH level and glycosylated haemoglobin. Kim MK et al showed a strong positive correlation between

TSH and glycated haemoglobin in the 45 cases that were studied by them.[17]. Our result of a positive correlation between HbA1c and TSH is also consistent with the results by Velija-Asimiet al[20]. They examined the effects of treatment of subclinical hypothyroidism on metabolic control and hyperinsulinemia and concluded that the correlation between TSH and HbA1c were positive and significant and normalised TSH levels will result in decreased levels of fasting insulin, FBS, PPBS and HbA1c.

Edina BilicKomaricaet al[21]conducted a study to understand the effects of treatment of L thyroxine on glucose regulation in patients with subclinical hypothyroidism. The patients were followed up after 6 months of L thyroxine and physical activity and after 6 months with the normalised TSH values FBS, PPBS, HbA1c, fasting insulin and lipids were significantly reduced thus concluding that normalizing TSH levels with thyroxine treatment will control blood sugar better.

Vibha Uppalet al[22] correlated the levels of insulin and HbA1c with thyroid hormones and reported that the levels of HbA1c have a positive and significant correlation with TSH level.

The study results are in accordance with previous studies and imply that thyroid hormones exert influence over glycated haemoglobin values. The study results suggest that with treatment of the hypothyroid state the HbA1c levels fall. The study is limited by having only a small number of patients and by the absence of a control group.

CONCLUSION:

there was a statistically significant reduction in mean HbA1c after thyroid replacement therapy which implies that correction of hypothyroid states was associated with fall in HbA1c levels. A significantly positive correlation was found between Serum TSH level and glycosylated hemoglobin, concluding that thyroid hormone affects HbA1c values. Future studies with large sample sizes are required to precisely quantitate the effect of thyroid hormones supplements on HbA1c levels and also to determine the proper underlying mechanism which brings about the above-mentioned results

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