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General Medicine

EFFECT OF DERANGED THYROID PROFILE ON GLYCATED HEMOGLOBIN: PRE AND POST TREATMENT

Dr. Anubha srivastava — Md Medicine, Associate Professor, Department Of Internal Medicine, Mln Medical College, Prayagraj.

Dr. Sandeep rai* — Junior Resident, Department Of Internal Medicine, Mln Medical College, Prayagraj. *Corresponding Author

ABSTRACT **INTRODUCTION-** Glycated haemoglobin (A1C) levels depend on factors other than glycemic status and may have altered levels in different conditions. It has been postulated that A1C levels may vary due to altered thyroid status. **METHODS-**Non-Diabetic patients of overt hypo- and hyperthyroidism were selected. Age and sex-matched controls were recruited. Baseline values of A1C and reticulocyte count (for RBC turnover) was measured. These values were re-evaluated in randomly selected subgroups after achievement of euthyroid status. **RESULTS-**A1C values in patients initially selected, was found to be significantly higher in hypothyroid group as compared to controls though values did not differ significantly in hyperthyroid group. Post-treatment after achieving euthyroid status, A1C levels reduced significantly in hypothyroid group and no such significant effects were observed in hyperthyroid group. **CONCLUSION-** There is the need for evaluation of A1C in patients of hypothyroidism with more caution and prevent the patients from irrelevant investigations and work up for diabetes.

KEYWORDS : A1C, Hypothyroid, Hyperthyroid

INTRODUCTION

Thyroid disorders are perhaps the most common medical conditions throughout the world[1]. Thyroid hormones are seen to have an intimate relationship with insulin during cellular metabolism. Thyroid disorders can have a significant effect on blood glucose levels and, if left untreated, can affect glycemic control[2]. Hyperthyroidism has long been recognized to promote hyperglycemia[3]. A relationship between insulin resistance and oxidative stress has also been traced[4]. The interrelationship between thyroid dysfunction and insulin resistance has also been established by some studies that have shown normalization of long-term indicators of glycemic controls (HbA_{1c}) among non-diabetic thyroid disorder patients following thyroxine replacement therapy[5,6,7]. Such findings in turn indicate that inflated HbA_{1c} values in these patients are unrelated with diabetes and could be normalized only by managing the thyroid disorders, thus reducing an impending diabetic burden to a great extent.

AIMS AND OBJECTIVES

This study was designed to observe an effect of deranged thyroid profile on A1C levels in non-diabetic individuals, with overt hyper- and hypo-thyroidism and later see the effect of treatment on A1C levels.

METHODOLOGY

A prospective cohort study was conducted in SRN Hospital, Prayagraj from April 2018 to August 2019 with patients more than 18 years of age and either sex with newly diagnosed overt hyper- and hypo-thyroidism were enrolled and recruited as cases with euthyroid and euglycemic age and gender based control Patients with known diabetes or pre-diabetes such as those having deranged fasting and post- prandial plasma glucose were excluded from the study as per ADA 2019. Patients with anemia (Hb <10g/dl), hemoglobinopathies, renal insufficiency, liver dysfunction and pregnant females were also excluded from the study.

A baseline A1C was measured and were started on Thyroid Hormone Replacement Therapy(THRT) with levothyroxine in hypothyroidism and Methimazole in hyperthyroidism. The cases were followed after three months and six months from the date of start of therapy and were reinvestigated for TSH and A1C at follow up.

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 21.0 statistical Analysis Software. The values were represented in Number (%) and Mean±SD. To test the significance of two means the student 't' test was used. The ANOVA test was used to compare the within group and between group variances amongst the study groups. P value of <0.05 is taken as significant.

RESULTS

Table 1a: Comparison of Baseline general and clinical profile between hyperthyroid group and controls

SN	Characteristic	Hyperthyroid (n=23)		Controls (n=50)		Statistical significance (Independent samples 't'-test)	
		Mean	SD	Mean	SD	't'	'p'
1.	Age	37.61	7.90	39.54	8.41	0.928	0.356
2.	Gender Male Female	14 (60.9%) 9 (39.1%)		21 (42.0%) 29 (58.0%)		x^2=2.25; p=0.134	
3.	Hb (gm/dl)	11.68	0.45	11.81	0.57	-0.924	0.359
4.	TLC (thousands/ cumm)	7.81	1.67	7.09	1.72	1.666	0.100
5.	S.Bilirubin (mg/dl)	0.51	0.18	0.48	0.15	0.618	0.538
6.	SGOT (IU/L)	26.00	7.91	26.80	6.81	-0.441	0.660
7.	SGPT (IU/L)	24.92	7.99	26.95	7.00	-1.100	0.275
8.	S.Urea (mg/dl)	28.92	5.72	28.26	5.46	0.477	0.635
9.	S.Creatinine (mg/dl)	1.04	0.19	1.07	0.20	-0.561	0.577
10.	fT3 (pg/ml)	9.14	2.80	2.64	0.55	15.860	<0.001
11.	fT4 (ng/dl)	8.13	5.01	1.14	0.17	9.931	<0.001
12.	TSH (µIU/ml)	0.02	0.02	3.36	0.88	-18.128	<0.001
13.	HbA_{1c}	5.23	0.20	5.17	0.30	1.460	0.149
14.	Reticulocyte count	1.37	0.39	1.36	0.36	0.908	0.367
15.	FPG(mg/dl)	92.70	3.99	91.59	5.21	0.192	0.848
16.	PPG(mg/dl)	132.60	5.19	131.24	5.38	0.910	0.366

Table 1A demonstrates comparison of baseline characteristics between hyperthyroid group and controls and it was inferred that no significant difference between two groups was observed for any of the parameters except thyroid hormones (fT3, fT4 and TSH).

Table 1b: Comparison of Baseline general and clinical profile between hypothyroid cases and controls

SN	Characteristic	Hypothyroid (n=60)		Controls (n=50)		Significance of difference (Independent samples 't'-test)	
		Mean	SD	Mean	SD	't'	'p'
1.	Age	40.58	9.28	39.54	8.41	0.612	0.542

2.	Gender Male Female	15 (25.0%) 45 (75.0%)		21 (42.0%) 29 (58.0%)		x^2=3.58; p=0.058	
3.	Hb (gm/dl)	11.86	0.60	11.81	0.57	0.492	0.624
4.	TLC (thousands/ cumm)	7.21	1.76	7.09	1.72	0.344	0.732
5.	S.Bilirubin (mg/dl)	0.48	0.15	0.48	0.15	0.072	0.943
6.	SGOT (IU/L)	26.07	7.21	26.80	6.81	-0.543	0.588
7.	SGPT (IU/L)	26.02	7.18	26.95	7.00	-0.682	0.497
8.	S.Urea (mg/dl)	28.28	5.33	28.26	5.46	0.020	0.984
9.	S.Creatinine (mg/dl)	1.06	0.19	1.07	0.20	-0.378	0.706
10.	fT3 (pg/ml)	2.26	0.45	2.64	0.55	-4.042	<0.001
11.	fT4 (ng/dl)	1.14	0.27	1.14	0.17	-0.090	0.928
12.	TSH (µIU/ml)	24.59	17.49	3.36	0.88	8.570	<0.001
13.	HbA_{1c}	5.77	0.15	5.17	0.30	4.179	<0.001
14.	Reticulocyte count	0.85	0.32	1.36	0.36	13.484	<0.001
15.	FPG(mg/dl)	90.92	5.69	91.59	5.21	-7.756	<0.001
16.	PPG(mg/dl)	130.46	5.17	131.24	5.38	-0.641	0.523

Table 1B demonstrates comparison between hypothyroid group and controls. It was observed that in hypothyroidism cases values of A1C and reticulocyte count were significantly higher as compared to that in controls (p<0.001).

Table 2: Comparison of in TSH levels and HbA_{1c} Levels before and after TRT among cases completing follow-up

SN	Parameter	Baseline		Follow-up		Change		Significance of change (Paired 't'-test)	
		Mean	SD	Mean	SD	Mean	SD	't'	'p'
Hyperthyroidism									
1.	TSH (µIU/ml) (n=13)	0.02	0.02	3.69	0.93	3.67	0.93	18.94	<0.001
2.	HbA_{1c} (n=13)	5.22	0.22	5.12	0.26	-0.10	0.20	1.842	0.090
Hypothyroidism									
1.	TSH (µIU/ml) (n=40)	27.33	19.76	4.06	0.56	-23.26	19.69	7.47	<0.001
2.	HbA_{1c} (n=40)	5.78	0.16	5.46	0.11	-0.38	0.14	14.41	<0.001

In Table 2, hyperthyroid group, mean TSH levels at baseline were 0.02±0.02 µIU/ml which were found to be 3.69±0.93µIU/ml at follow-up, thus showing a significant increase of 3.67±0.93 µIU/ml (p<0.001). On the other hand, mean HbA1c levels were 5.22±0.22% at baseline which dropped to 5.12±0.26% at follow-up, showing a decline of 0.10±0.20%, though was not significant statistically (p=0.090).

In hypothyroid group, mean TSH levels were 27.33±19.76 µIU/ml at baseline which declined to 4.06±0.56 µIU/ml at follow-up, thus showing a significant decline of 23.26±19.69 µIU/ml (p<0.001). Mean HbA_{1c} levels were 5.78±0.19% at baseline which was 5.46±0.11% at follow-up, thus showing a decline of 0.38±0.14% and was significant (p<0.001).

DISCUSSION

Out of 133 patients enrolled 83 patients (62.4%) had deranged thyroid profile and the other 50 Euthyroid patients were taken as controls. Hypothyroidism was more common in our study, 60 patients (45.1%) were hypothyroid and 23(17.3%) patients were hyperthyroid. Our study showed higher prevalence of hypothyroidism in comparison to hyperthyroidism similar to the study done by Ambika Gopalakrishnan et al[8]. In our study mean age(in years) of patients in hypothyroid group was 40.58±9.58 and hyperthyroid group was 37.61±7.60. This result was similar to study done by Nagarkar et al[9] who showed that the prevalence of thyroid disorders was significantly higher in higher aged (≥ 31years) patients as compared to lower aged (≤30 years) patients (14.1% vs. 85.9%,P<0.001).

In our study mean baseline A1C values in hypothyroid patients were compared with age and sex matched controls and it was found that values were significantly higher in hypothyroid group(5.77±0.155) in comparison to healthy controls(5.17±0.30) . Anantarapu et al[6] did a similar study in context of A1C values in hypothyroid patients and made a demonstration that HbA1c values are falsely elevated in hypothyroid patients. Similar observations were demonstrated by Kim et al[7](5.54 ± 0.43%*vs*. 5.34 ± 0.31% in hypothyroid patients and controls respectively; p < 0.001), despite the lower level of plasma fasting glucose in the hypothyroid individuals.

Contrary to the findings demonstrated in hypothyroid group, there was no significant difference observed between A1C and hyperthyroid group in comparison to healthy controls (cases 5.23±0.20, controls 5.17±0.30,p value 0.149) which was statistically insignificant. Similar observations were obtained in a study conducted by Rana Bhattacharjee et al[5].

In 40 hypothyroid patients were given levothyroxine treatment and were followed up with Thyroid profile at 3 months and 6 months. After attainment of euthyroid status mean A1C was measured and it was found to be 5.46±0.11 which was statically significant as compared to pretreatment group (5.78±0.16,p<0.001). Similar observations were obtained by Rana Bhattacharjee et al[5](5.7 ± 0.75 [pretreatment] vs. 5.4 ± 0.75 [posttreatment]; $P < 0.001$).Kim et al[7] did a similar follow up study enrolling 30 hypothyroid patients who were given thyroid hormone replacement and concluded that A1C values returns to normal post treatment(pre treatment 5.57±0.26,post treatment 5.37±0.32,p value <0.001).

In hyperthyroid group 13 out of 23 patients were enrolled for follow up and were put on anti-thyroid medication.A1C values were measured at follow up once these patients were rendered euthyroid which was sustained. It was observed that there was no statistically significant difference in A1C values post treatment.(pre therapy 5.12±0.20 post therapy 5.17±0.30 p=0.583).These results were consistent with the results obtained by Rana Bhattacharjee et al[5](5.35 ± 0.45 [pretreatment] vs. 5.35 ± 0.3 [posttreatment]; $P = 0.323$).

CONCLUSION

A1C is an integral part of diagnosis of Diabetes. As we are aware about fallacies of A1C in Anemia, Hemoglobinopathies, CRF**,** we propose by this study that A1C levels are falsely elevated in patients of hypothyroidism. A1C alone is less reliable marker for assessment of dysglycemia in hypothyroid patients. A1C levels in hypothyroid patients leads to false diagnosis of prediabetes and diabetes Following levothyroxine replacement, A1C levels reduced significantly in patients with hypothyroidism. Patients with hyperthyroidism do not show such correlation between glycated hemoglobin levels and thyroid hormone levels both pre and post-treatment. So, caution should to be taken while interpreting A1C values in patients with thyroid dysfunction. So tests like serum fructosamine assay and glyclated albumin have been proposed to overcome this fallacy .

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