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ESTIMATION OF GLYCATED ALBUMIN LEVELS IN VARIOUS THYROID DISORDERS

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ABSTRACT

Background: Glycation is the linking of sugar molecule to various compounds such as glucose, lipid or protein. As albumin is one of major protein in our circulation, to which sugar has bonded to form Glycated albumin. Albumin is present not only in blood but also in major organs and body fluids and it serves to maintain cell shape and distribution of hormones.

Objective: The present study was designed to compare the levels of GA in Various thyroid disorders group with Normal healthy control group.

Materials and Methods: The present cross sectional study includes 200 cases, (n=50 in each group) newly diagnosed hyperthyroidism, hypothyroidism, subclinical hypothyroidism and normal controls between 30-55 years of both genders. Serum samples obtained for the estimation of T₃, T₄, TSH and glycated albumin. Statistical analysis done by using SPSS, version 16.0. One-way ANOVA was performed. All P-values which were ≤ 0.05 were considered as statistically significant.

Results: Glycated albumin values were found to be significantly correlated among the different groups ($p=0.001$). GA levels significantly increased in hypothyroidism, subclinical hypothyroidism and lowered in hyperthyroidism group compared to normal group. Significant correlation was found between T₃, T₄, TSH and GA levels.

Conclusion: The present study showed increased levels of GA among experimental groups when compared with the normal control group. Hence It was concluded that estimation of serum GA will be useful as a novel parameter in thyroid disease cases.

Keywords: Glycated albumin, Hypothyroidism, subclinical hypothyroidism, Hyperthyroidism

INTRODUCTION

Thyroid gland is a body organ located in front of the neck. It has two lobes, one on each side of trachea. The thyroid gland takes iodine from blood and synthesizes two active hormones called triiodothyronine (T₃) and thyroxine (T₄) and these hormonal production regulated by TSH [1]. Thyroid hormones control the body's cell metabolism. When thyroid hormones are released into the bloodstream, cells increase the rate at which they convert oxygen and nutrients into

energy and heat for the body's use [2]. Abnormalities of thyroid gland function are more common among individuals with developmental disabilities than in the general population, But overt hypothyroidism and subclinical hypothyroidisms are become relatively common now a days in general population as well [3,4]. When thyroid gland is overactive and produces too much thyroid hormone an individual develops hyperthyroidism and Subclinical Hypothyroidism is defined as a condition in which serum TSH

concentration above the statistically defined upper limit of the reference range, when the serum free T4 concentration is within its reference range [5,6]. Primary hypothyroidism and thyrotoxicosis are very common in adult female genders with prevalence rate 3.5 per thousand and 0.8 per thousand respectively. There is increased T3 and T4 levels with decreased or normal TSH levels in case of thyrotoxicosis especially in developed countries[7]. Glycated albumin formed by non enzymatic glycation in which reducing sugars are covalently attached to amino acid residues especially serine, lysine residues of protein[8]. The reducing carbonyl group of glucose can react with the amine groups of human serum albumin (HSA) to form glycated albumin (GA) (Schiff-base) which results in a 162 Da molecular weight increase for each glucose-induced glycation on HSA. This is followed by the Schiff-base reorganized itself to the more stable aminomethyl ketone by the Amadori rearrangement [9]

In hypothyroid patients the Glycated protein levels have been increased and in case of hypothyroid cases its levels were found to be decreased [10]. Compared to normal subjects the GA levels higher in primary hypothyroidism cases and lower in Grave's disease. As thyroid hormone promotes albumin metabolism the mean concentration of albumin and total protein in serum were lower in hyperthyroid patients than the hypothyroid patients[11]. It has been proved from the previous studies that GA can be used to monitor short term glycemic control than glycated hemoglobin[12]. We therefore hypothesized that GA levels do not reflect accurately glycemia in hypothyroidism.

MATERIALS AND METHODS

The present cross-sectional study was conducted from December 2010 to January 2012 in MAPIMS&R hospital Melmaruvathur, Tamil Nadu respectively. A total of 150 cases were selected (n=25 in each group) newly diagnosed hyperthyroidism, subclinical hypothyroidism, hypothyroidism and normal control between the

ages of 30-58 years of both sexes (M:F ratio 65:85) were selected for this cross sectional study from the outpatient department of endocrinology in MAPIMS&R and were compared with 50 (M: F 20:30) control subjects. After the full explanation of the study, written informed consent was obtained from each study subject. The study was approved by the Ethics committee of the institution prior (EC No-MAPIMS/RC/NOV/2010/24) the informed consent was obtained from all the subjects. Demographic and anthropometric details like age, weight, height, duration of disease, duration of treatment were recorded for all the study subjects. Family history of Thyroid disease and hypertension, smoking and alcohol consumption habits were obtained from the medical records of the study subjects. Patient on treatment for any disorder, lipid lowering drugs, diabetes, malignancy and pregnant women were excluded. Blood samples were collected for the biochemical estimations such as T₃, T₄, and TSH using Hitachi auto analyzer by Electro Chemiluminescence immune assay (ECLIA) method. Plasma glycated albumin (GA) levels were measured by an enzymatic method using albumin specific protease, ketoamine oxidase and albumin assay reagent on the Hitachi autoanalyser 912 (Lucica GA-L, Asahi Kasei Pharma Corp, Tokyo, Japan) [13,14] GA was hydrolyzed to amino acids by albumin specific protease and then oxidized by ketoamine oxidase to produce hydrogen peroxide, which was measured quantitatively. The GA value was calculated as the percentage of GA relative to total albumin, which was measured with bromocresol purple method. The measured values of GA was not influenced by the substances such as bilirubin F up to 14.6 mg/dl, bilirubin C up to 15.2 mg/dl, glucose up to 1000 mg/dl, ascorbic acid up to 100 mg/dl.

The statistical analysis was done by using SPSS version 16.0. One Way ANOVA method was applied to observe association of microalbuminuria with GA and duration of

diabetes. P value < 0.0001 was considered as statistically significant.

RESULTS

The mean values of thyroid hormones among experimental group along with the normal group has shown in fig 1. GA values were much more elevated in hypothyroidism group compared to subclinical hypothyroidism group shown in figure 2 and the values were lower than the normal level in hyperthyroidism group and higher than normal in hypothyroidism group which is statistically significant. Figure 3 shows the GA values and FPG levels of different groups which were below normal in case of hyperthyroidism and above normal in subclinical hypothyroidism which is statistically significant. GA values found to be significant among the groups ($p=0.001$). In hypothyroidism specificity and the sensitivity was found to be 100% and 98.4% and in hyperthyroidism it is 94.8% and 72%. Where as in Subclinical hypothyroidism it is around 95.5% and 78%. Compared to hypothyroidism group the albumin values in hyperthyroidism group found to be decreased which is statistically correlated negatively with hypothyroidism but no statistical significant correlation with total proteins. While comparing with the normal GA levels as 12-16 mg % the sensitivity, specificity, positive predictive value (PPV) of GA for hyperthyroidism, hypothyroidism, and subclinical hypothyroidism. fig 4 and fig 5 showing the serum MDA and protein carbonylation levels in the experimental groups which are elevated in hypothyroidism group as well as in subclinical hypothyroid group. At the same time serum antioxidants such as GSH levels decreased in respect to increase of oxidants in all the groups except normal group.

DISCUSSION

Thyroid hormone exert profound effects in the regulation of glucose homeostasis, including modification of circulating insulin levels and other

counter regulating hormones [15]. thyroid disorders has got a major impact on glucose control. When thyroid dysfunction the glucose homeostatic balance is broken and it is mainly associated with increased hepatic gluconeogenesis which is a characteristic of excess of thyroid hormones *i.e* Hyperthyroidism [16]. In hypothyroidism glucose homeostasis also get affected although it's clinical impactless it's because of less disposal of glucose [17]. At the same time insulin resistance has been reported in subclinical hypothyroidism with altered glucose levels [18].

As deficiency or over production of thyroid hormones plays major role in glucose homeostasis, so we tried to assess the glycated products such as glycated albumin levels in various thyroid disorders. In our study GA levels significantly correlated ($p=0.001$) when inter comparison was done among different groups and we found GA levels are above normal in case of hypothyroidism, subclinical hypothyroidism and lower the normal values in case of hyperthyroidism. The albumin values were found to be decreased in hyperthyroidism group compared to hypothyroidism which was statistically significant. The increased GA levels in hypothyroid patients along with non clinical hyperglycemia because of deterioration of protein metabolism which further decreases turnover of proteins and increase of half life of proteins. And the increase in glycation of proteins via auto oxidative glycation in case of increased oxidative stress [19]. There is marked increase in protein carbonylation, serum Malondialdehyde and decreased glutathione levels in hypothyroid cases explaining increased peroxidation of lipids might be a contributing factor for increased protein glycation [20]. Low grade inflammation and free radical formation causes increase in higher immunoglobulin production explains glycation of these immunoglobulins. Disturbance in glucose homeostasis with decreased glucose absorption and utilization leads to insulin resistance this further causes glycation of proteins. In case of

subclinical hypothyroidism the GA levels were not that higher compared with hypothyroid group. The GA levels were lower in hyperthyroid in contrast to hypothyroid and subclinical hypothyroid groups but with higher plasma glucose levels[21,22,23]. Previous studies showed that there is increase in glycated HbA1c which corresponds to raise in glucose concentration but with the low levels of Glycated albumin which is very contradictive[24].

CONCLUSION

There are only studies reported about HbA1C levels in thyroid disorders so we tried to estimate glycated products such as GA other than HbA1C, and present study suggests an increase GA levels in all the thyroid disorders with which we conclude, that we can consider GA as a diagnostic criterion in thyroid disorders.

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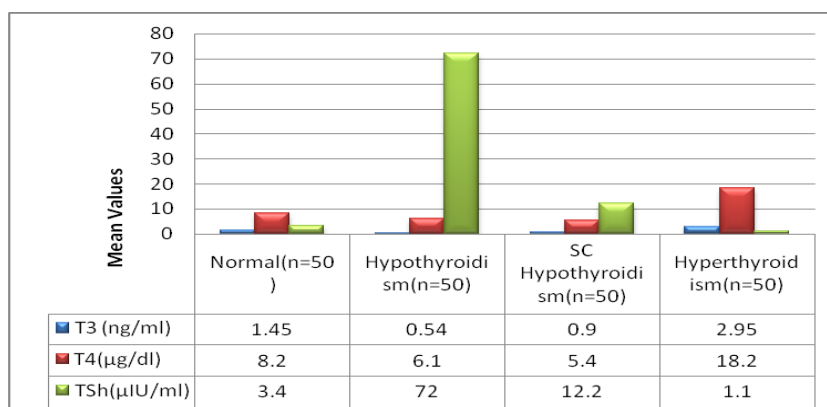
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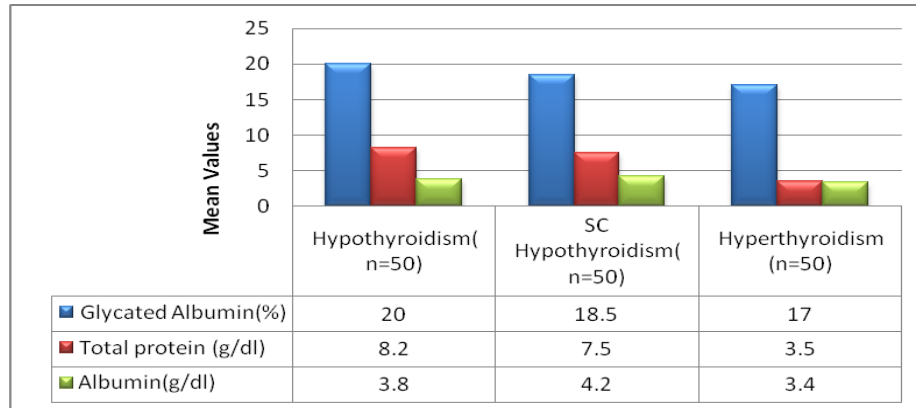
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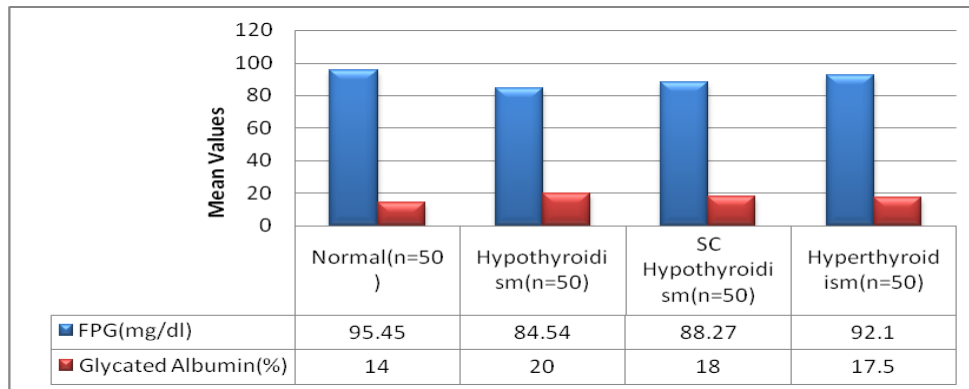
[Table/Fig-1] The mean values of T₃, T₄, and TSH among different groups



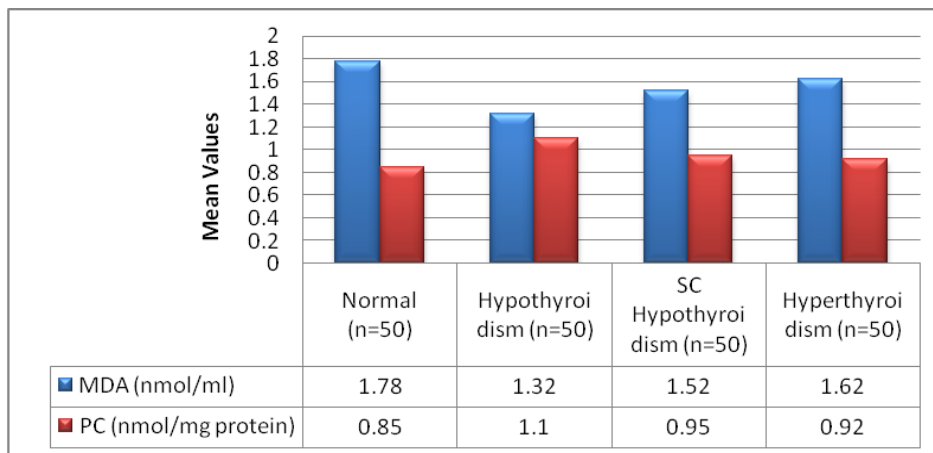
[Tab/Fig2] Comparison of GA levels with Total proteins and albumin among experimental group. P value<0.001 is significant.



[Tab/Fig 3] Comparison of Fasting plasma glucose levels with GA levels among experimental groups with normal group. P value<0.001 is significant.



[Table/fig 4] serum MDA and protein carbonyl levels in experimental groups compared with normal group. P value<0.001 is significant.



[Table/Fig 5] Comparison of serum antioxidant GSH levels in experimental groups with the normal group. P value < 0.001 is significant.

