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Original Research Article

Clinical Prospective Cross-Sectional Study to Explore the Relationship between Hypothyroidism and Hormone Therapy with Respect to Chronic Inflammation

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Abstract:

Background: Hypothyroidism is a common condition and harmful effects are caused on cardiovascular system both by overt and subclinical hypothyroidism. This is caused by several mechanisms which cause increased risks of atherosclerosis and coronary heart disease. A number of inflammatory biomarkers in circulation are related with increased risk of acute coronary syndrome. This study was done to compare the status of inflammatory markers like secretory phospholipase A2 group 2A (PLA2G2A) and Adiponectin (ADP) in hypothyroidism.

Objectives: This study was done to identify the possible relationship between hormone treatment and the risk of atherosclerosis in hypothyroid patients and to explore the status of inflammation with respect to PLA2G2A and ADP in hypothyroid patients.

Setting and Design: This study was done as a cross-sectional study in 60 hypothyroid patients attending General medicine / Endocrinology OPD in PSG hospitals.

Material and Methods: Blood samples were taken from hypothyroid patients and analysed for PLA2G2A and ADP using ELISA kit.

Statistical Analysis: SPSS version 19 used for statistical analysis. Independent sample t test and ANOVA used and results were expressed in mean ± standard deviation.

Results: In this study we observed that when the duration of the disease increased, there was a rise in PLA2G2A and fall in ADP with no statistical significance. Then thyroxine dose was compared with these markers and the mean value of PLA2G2A was high in patients with low dose thyroxine (8.79 ±3.98) followed by high dose thyroxine (8.08± 4.28) and then by patients not on drug (7.12 ± 4.22). Also, ADP value was high in patients with high dose thyroxine (4.72±3.24) compared to low dose thyroxine (3.64±1.97) and patients not on thyroxine group (3.65±1.98).

Conclusion: This study revealed that when the duration of hypothyroidism increased, there was a rise in level of PLA2G2A and fall in level of ADP suggesting a relationship between hypothyroidism and chronic inflammation. Patients on inadequate dose of thyroxine had higher chance of developing atherosclerosis than compared to patients on adequate or higher dose of thyroxine explaining the need for adequate dose as prescribed in the patient diagnosed with hypothyroidism as replacement therapy based on their body weight.

Keywords: Adiponectin, Atherosclerosis, Hypothyroidism, PLA2G2A, Thyroxine.

Introduction

Thyroid hormone is essential for normal development. In humans they play a vital role in maintenance of metabolic functions and also on functioning of other organ systems. Hypothyroidism is an endocrine disorder characterized by low T4 and elevated TSH. They are the common endocrine disorders with prevalence of 4-15% in world. In Indian adults the prevalence of hypothyroidism was less than 10%. A study done in Cochin revealed prevalence of hypothyroidism as 3.9% [1]. Hypothyroidism is a common condition and harmful effects are caused on cardiovascular system both by overt and subclinical hypothyroidism [2]. This is caused by several different mechanisms which cause increased risks of atherosclerosis and coronary heart disease [3,4]. A number of inflammatory biomarkers in circulation are related with increased risk of acute coronary syndrome [5]. Phospholipase A2 is an esterase that hydrolyses membrane

phospholipids to generate free fatty acids like arachidonic acid and lysophospholipids. The phospholipaseA2 group IIa (PLA2G2A) isoform belongs to the family of secretory PLA2. Elevated levels of PLA2G2A are observed in many diseases associated with inflammation including rheumatoid arthritis, pancreatitis, and septic shock. Secretory Phospholipase A2 group 2A (PLA2G2A) is one of such inflammatory markers for atherosclerosis, which is a chronic inflammatory condition.

Adiponectin (ADP), which is a hormone derived from adipose tissue is proven to have anti-inflammatory and anti-atherogenic effects. Many diseases are related to decreased levels of ADP such as Type 2 diabetes, Hypertension, Metabolic syndrome, Atherosclerosis etc. Some biological actions of ADP acts together with thyroid hormones like reduction of body fat by increased thermogenesis and lipid oxidation. Only very few studies were available on hypothyroidism and inflammation [6],[7] and no study was conducted on inflammatory markers PLA2G2A and Adiponectin with hypothyroidism in India. This study aimed to identify the possible relationship between hormone treatment and the risk of atherosclerosis in hypothyroid patients and to explore the status of inflammation with respect to PLA2G2A and Adiponectin in hypothyroid patients.

Material and Methods

This study was done as a cross sectional study. Patients attending Medicine and Endocrinology OPD of age greater than 18years with clinical diagnosis of hypothyroidism including old and new patients were included in the study.

Exclusion criteria were post operated and radiation cases of thyroid, patients on drugs like Statins, Steroids, Metformin, age less than 18 years and those who on other system medication (ayurveda, siddha). The proposal of study was accepted by institutional Human Ethics Committee (IHEC) preceding start of the study.

The details and the purpose of the study protocol were explained to each participant individually and their doubts were clarified before obtaining informed consent. Samples collected and separated using serum separator tube after allowing clotting for two hours at room temperature. Centrifugation done for 15 minutes 1000 RPM then stored at -20°C. Enzyme-linked immunosorbent assay (ELISA) method was used for measuring PLA2G2A and Adiponectin levels.

Results

IBM SPSS software 19.0 version was used for statistical analysis. Results were expressed as mean ± standard deviation. Independent-samples t-test was used to compare the parameters between the two experimental groups and one-way ANOVA test was used for comparing the parameters between multiple groups. Statistical significance was set at P values ≥ 0.05 in all cases.

Out of 60 patients in our study, most of them (61.7%) were from 21 to 40 years of age and 96.7% were female patients. Around 38.3% patients were overweight, 15% patients were obese. Nearly half of the patients had family history of hypothyroidism. Around 20% were newly diagnosed hypothyroid patients. In this study nearly 60% of patients had TSH value less than 10mIU/L. Most of the patients were on regular thyroid replacement therapy except few cases. Above general characteristics of participants are depicted in Table 1. Study population was divided into three groups in relation to duration as new cases, < 5 years and more than 5 years; in relation to TSH (mIU/L) as <25, 26-50 and more than 50.

Mean difference in the rise of PLA2G2A with reference to the duration of disease was 7.00±4.15 in Group 1, in Group 2 it was 8.15± 4.54 and Group 3 it was 8.81± 3.68; there was no statistical significance (P value 0.46) among the 3 groups (Fig.1).The analysis of mean serum Adiponectin level was high in newly diagnosed hypothyroid patients (4.81± 1.32) followed by < 5 years duration (4.09±2.34) and ≥ 5 years of duration (3.53±2.18) with no statistical significant difference among the 3 groups by one way Anova test (P value 0.66) (Fig.2).

Values of PLA2G2A were increased in patients with elevated TSH; but adiponectin was decreased (Fig 3& 4). Similarly, we analyzed the dose of thyroxine with that of serum PLA2G2A in our patients using one way Anova test and it was found that the mean was high (8.79 ± 3.98) in patients with low dose thyroxine followed by high dose thyroxine (8.08 ± 4.28) and with a P value 0.44 (Fig 5). Also, with adiponectin the mean was found to be higher in patients with high dose thyroxine (4.72 ± 3.24) when compared to the patients on low dose thyroxine (3.64 ± 1.97) with P value 0.31 (Fig.6). But none of these results were statistically significant.

Table 1:

Variables	n (%)
Age	
S 20 years	3 (5)
21 to 40 years	37 (61.7)
41 to 60 years	17 (28.3)
> 60 years	3(5)
Sex	
Female	8(96.7)
Male	2(3.3)
BMI	
Overweight	23 (38.3)
Normal weight	22 (36.7)
Obese	9(15)
Underweight	6(10)
Pregnancy status	
Pregnant	6(10.3)
Family history	
Present	26 (43.3)
Absent	34 (56.7)
Disease duration	
Newly diagnosed	12 (20)
<5 years	23 (38.3)
25 years	25 (41.7)
TSH values (mly/L)	
<10	36 (60)
11 to 25	12(20)
26 to 50	8(13.3)
>50	4 (6.7)
Thyroxine treatment	
Regular intake	42 (87.5)
Not on regular medication	6 (12.5)

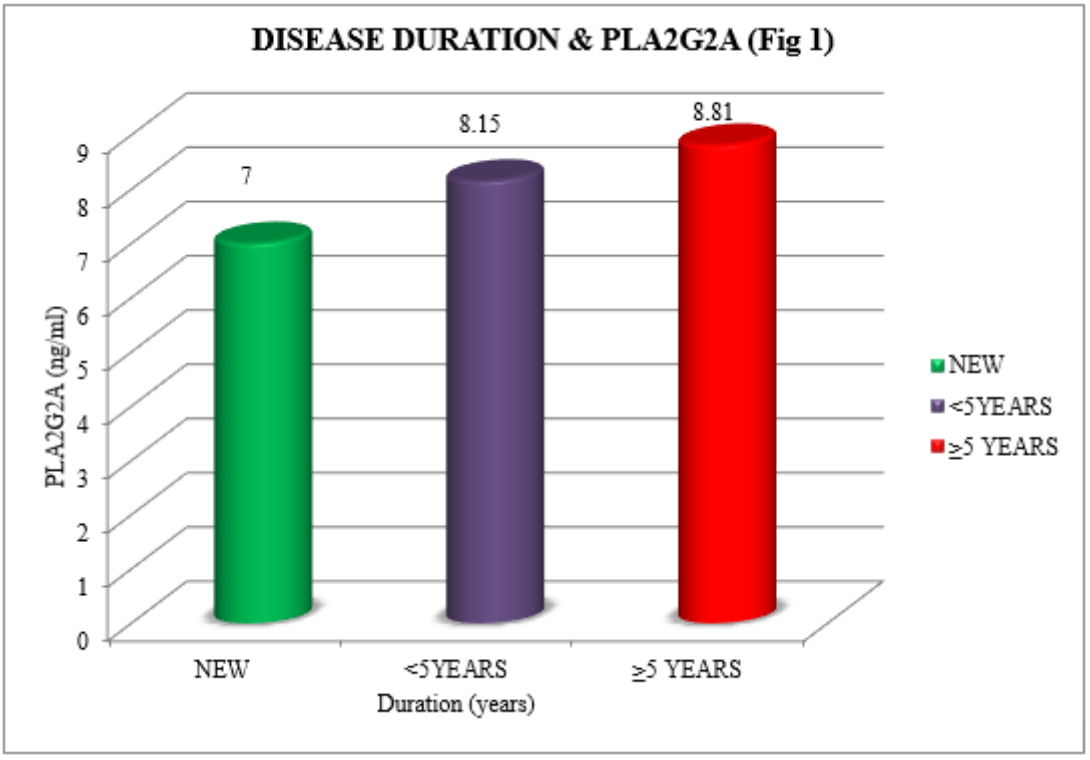
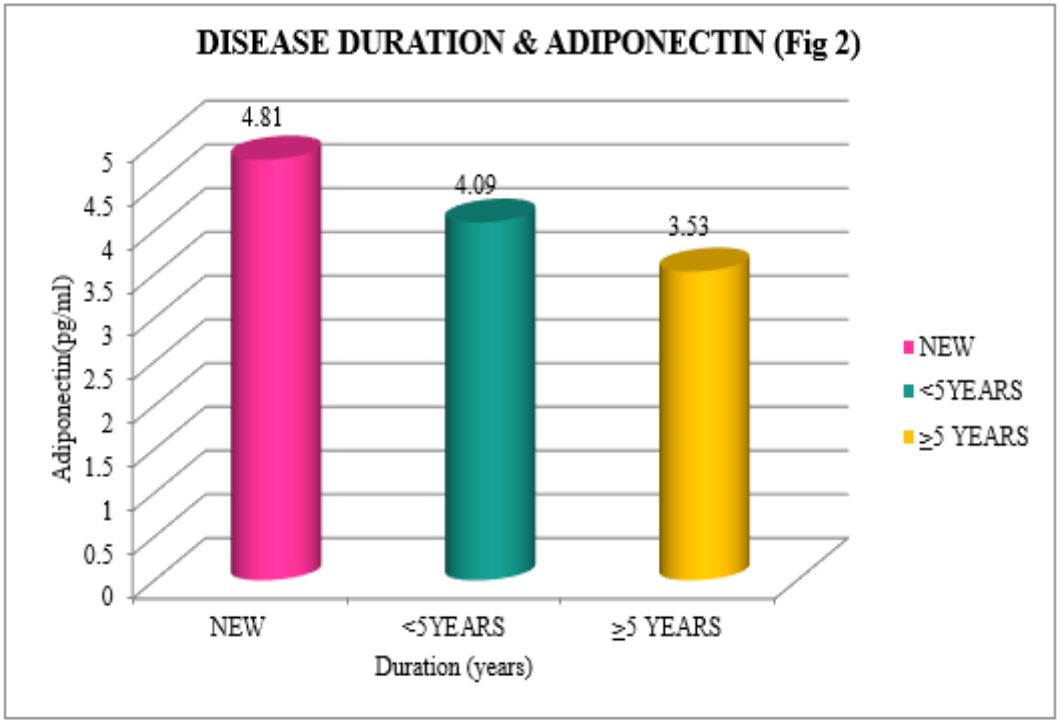


Figure 1:



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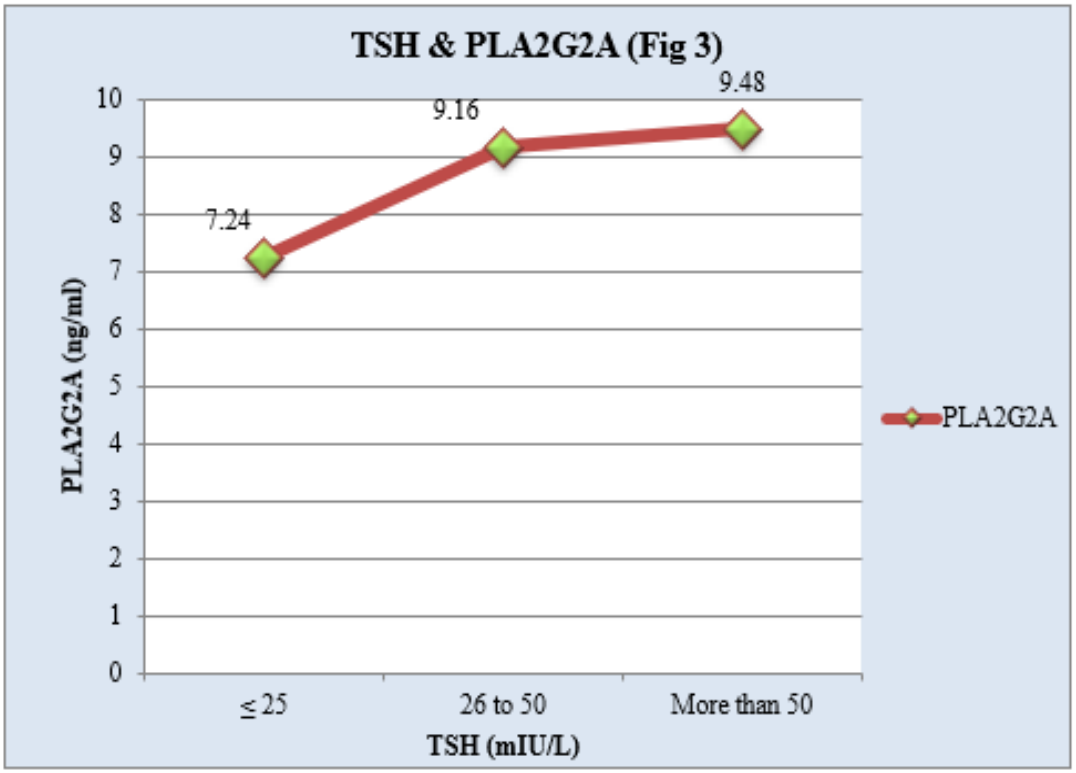

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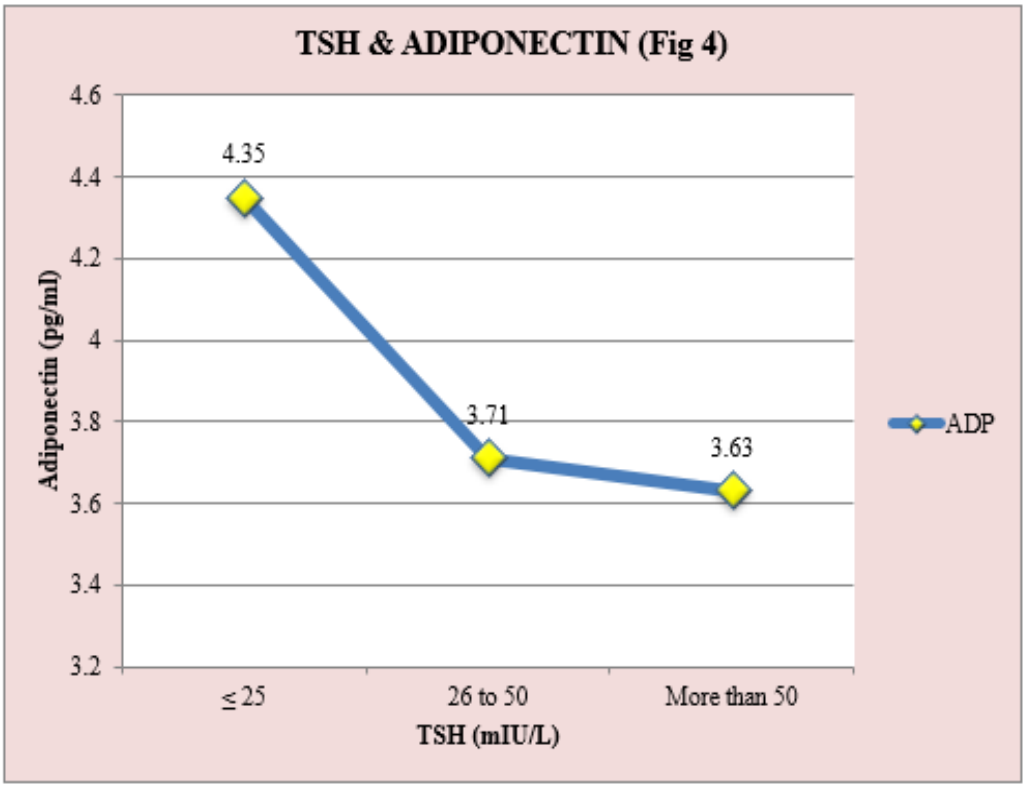

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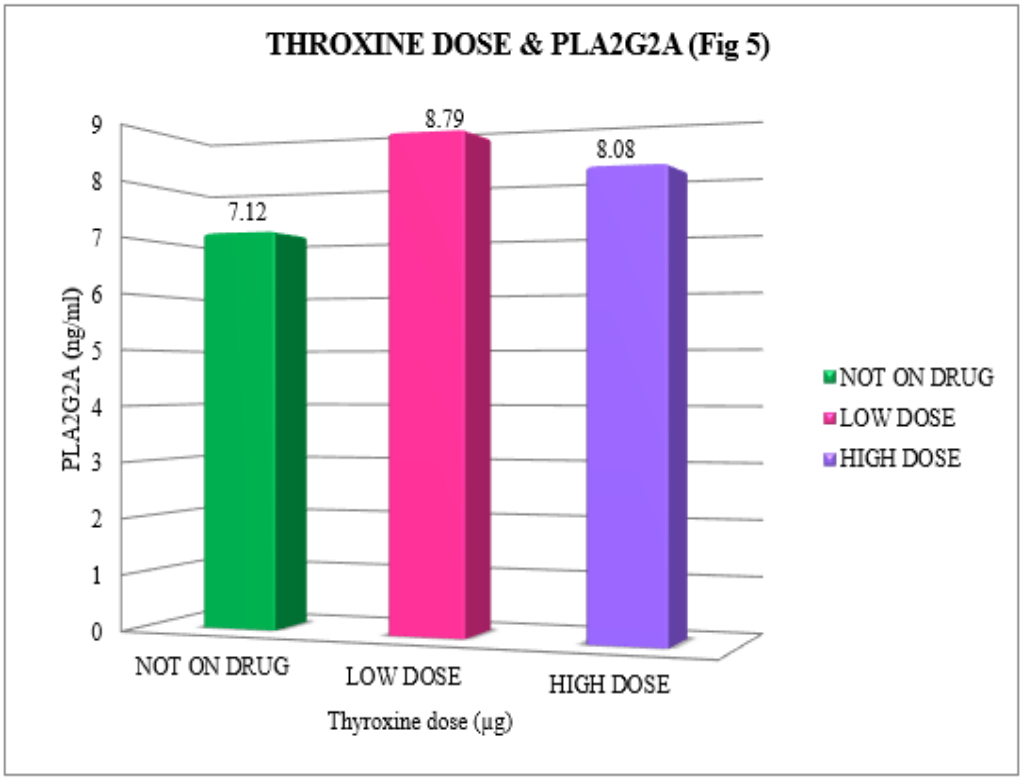

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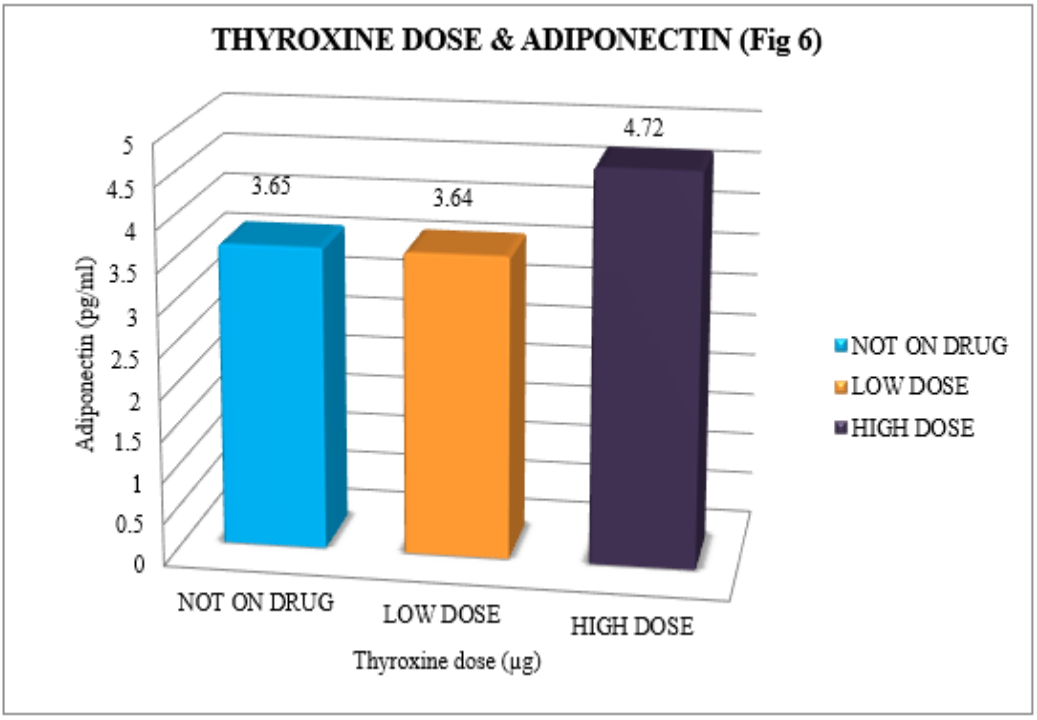

Figure 6:

Discussion:

This cross-sectional study was done to explore the relationship between hypothyroidism and hormonal therapy with respect to chronic inflammation. It is mainly focused at identifying the plausible relationship between hormone treatment and the risk of development of atherosclerosis in patients with hypothyroidism and also aimed at exploring the status of inflammation with respect to PLA2G2A and Adiponectin in hypothyroid patients.

In our study predominant of patients were in 21-40 years similar to Pilla E et al study results[8]. As PLA2G2A is a marker of inflammation, it is expected to considerably rise as the duration of the disease increases. Here though we could establish a mean difference in the rise of PLA2G2A with reference to the duration of disease, there was no statistical significance among the 3 groups.

Also, there was no study done so far with regard to establishment of correlation between duration of hypothyroidism and PLA2G2A levels and we are aimed at doing so.

Whereas, when compared the Adiponectin which is also an inflammatory marker for atherosclerosis which is supposed to be decreased with that of disease duration, there was a rise in the mean value of Adiponectin in newly diagnosed hypothyroid patients, followed by patients with less than 5 years of disease duration and then by ≥ 5 years of duration of disease. Few studies have shown that hypothyroidism reduced the levels of Adiponectin [7,8]. This study also analyzed the level of TSH with respect to the inflammatory markers. In three groups of patients based on the level of TSH, the level of PLA2G2A increased with an increase in TSH level. But there was no much difference in rise between group 2 and 3 because patients with higher TSH would be on higher dose of Thyroxine [7,8].

Similarly Adiponectin level decreased as the TSH level increased. Few studies have shown that Adiponectin value decrease as the TSH increase [9]. In relation to treatment with thyroxine the value of PLA2G2A for these patients found, that the mean was high in patients with low dose thyroxine followed by high dose thyroxine and then by patients not on drug.

High mean value in the low dose group may be due to the reason that the thyroxine dose would not have been adequate enough for them.

Similarly, this study analyzed the value of Adiponectin with the thyroxine treatment same as that for PLA2G2A.Here also it was found that the mean was high in patients with high dose thyroxine compared to low dose thyroxine and patients not on thyroxine group which suggested that the low dose group did not receive adequate amount of thyroxine. There were no studies done regarding the influence of thyroxine dose on chronic inflammation.

Lack of statistical significance in this study may be due to small sample size and also it was a cross sectional study. Since few limitations pertaining to

this study, further Randomized controlled trials with regular follow ups in a large scale of patients may overcome the limitations in future.

Conclusion

This study revealed that when the duration of hypothyroidism increased, there was a rise in level of PLA2G2A and fall in level of Adiponectin suggesting a relationship between hypothyroidism and chronic inflammation. This study also found that patients on inadequate dose of thyroxine had higher chance of developing atherosclerosis than compared to patients on adequate or higher dose of thyroxine explaining the need for adequate dose as prescribed in the patient diagnosed with hypothyroidism as replacement therapy based on their body weight. This study recommends further larger studies with large number of sample population to establish the significant association between inflammatory markers and hypothyroidism.

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References

1. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian journal of endocrinology and metabolism. 2011 Jul 1; 15(6):78.
2. Klein I, Danzi S. Thyroid disease and the heart. Circulation. 2007 Oct 9; 116(15):1725-35.
3. Cappola AR, Ladenson PW. Hypothyroidism and atherosclerosis. J Clin Endocrinol Metab. 2003;88:2438–44
4. Libby P. Inflammation in atherosclerosis. Arteriosclerosis, thrombosis, and vascular biology. 2012 Sep 1; 32(9):2045-51.
5. Welsh P, Packard CJ, Sattar N. Novel antecedent plasma biomarkers of cardiovascular disease: improved evaluation methods and comparator benchmarks raise the bar. Current opinion in lipidology. 2008 Dec 1; 19(6):563-71.
6. Nik MH, Darabi M, Ziaee A, Hajmanoochehri F. Serum phospholipase A2-IIA, hs CRP, and lipids in women with subclinical hypothyroidism. International journal of endocrinology and metabolism. 2014 Jul;12(3)
7. Aragao CN, Souza LL, Cabanelas A, Oliveira KJ, Pazos-Moura CC. Effect of experimental hypo-and hyperthyroidism on serum adiponectin. Metabolism. 2007 Jan 31; 56(1): 6-11
8. Pilla E. Impact of adipocytokines-leptin and adiponectin on thyroid stimulating hormone among hypothyroid patients. Asian Journal of Medical Sciences (E-ISSN 2091-0576; P-ISSN 2467-9100). 2014 Jun 27; 5(2):67-72.
9. Ichiki T. Thyroid hormone and atherosclerosis. Vascular pharmacology. 2010 Apr 30; 52(3): 151-6.