International Journal of Advanced Research in Medicine

E-ISSN: 2706-9575
P-ISSN: 2706-9567
IJARM 2021; 3(2): 415-418
Received: 06-09-2021
Accepted: 29-10-2021

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Hemoglobin and thyroid dysfunction in postmenopausal women: Descriptive clinical study

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DOI: https://doi.org/10.22271/27069567.2021.v3.i2g.282

Abstract
Clinical hyperthyroidism has been associated with systolic hypertension, increased pulse pressure, and possibly hyperhomocysteinemia. Additionally, patients with overt hyperthyroidism have a hypercoagulable state and an increased risk of thrombosis. Project was submitted to ethical committee, got approval from the ethical committee. Test and control population were recruited after obtaining all necessary consent in their local regional language. Haemoglobin and its effect on thyroid profile were evaluated. Mean haemoglobin values for euthyroid subjects were10.3g%, sub-clinical hypothyroid 11.1g%, overt hypothyroid 10.7g% and hyperthyroid subjects 10.1g%. Result indicate that Free T3 and haemoglobin have negative correlation. This means, as the Hb increases Free T3 decreases and vice versa. Similarly Free T4 and haemoglobin also have negative correlation. Whereas TSH and haemoglobin have positive correlation, that is, as haemoglobin increases TSH also increases and vice versa.

Keywords: hemoglobin, thyroid dysfunction, postmenopausal women

Introduction
In hypothyroidism, the main functional cardiovascular disturbances involve decreased heart rate, elevated peripheral vascular resistance, increased diastolic blood pressure and cardiac afterload, reduced blood volume and cardiac preload, and diminished cardiac output. Impaired left ventricular systolic contractility at least during exercise and delayed left ventricular diastolic relaxation at rest and during exercise are common in both overt and subclinical hypothyroidism. Hypothyroidism is also associated with diastolic heart failure in the elderly [1]. In hyperthyroidism, hemodynamic changes result mainly from increased β1-adrenergic activity. Increased triiodothyronine levels exert positive inotropic and chronotropic effects, leading to enhanced heart rate and systolic contractility and, consequently, increased cardiac output. Increased triiodothyronine stimulates sarcoplasmic reticulum Ca-ATPase, leading to systolic and diastolic dysfunction. Moreover, triiodothyronine reduces peripheral vascular resistance, causing a decrease in diastolic blood pressure and cardiac afterload, which further raises cardiac output. Decreased vascular resistance accounts for activation of renin-angiotensin-aldosterone system, which increases blood volume and cardiac preload, augmenting cardiac output even more [2].
Biondi *et al*. found that even patients with subclinical hyperthyroidism had significantly higher average heart rate, enhanced systolic function, impaired diastolic function with prolonged isovolumic relaxation time, and increased left ventricular mass compared with euthyroid subjects [3].
As mentioned above, thyroid disease is related to the development of dyslipidemia which is a well-known atherogenic factor. Dyslipidemia induces insulin resistance oxidative stress, via a vice-vicious cycle. Insulin resistance, hypertension, inflammation, oxidative stress, and coagulation deficits are also promoted by thyroid disease, independently of dyslipidemia.
The above associations support a multifactorial origin of atherosclerosis in thyroid disease, with dyslipidemia playing an important role [4].
Overt hypothyroidism has been associated with diastolic hypertension and hyperhomocysteinemia. Increased levels of high-sensitivity C-reactive protein and coagulation deficits have been reported in patients with hypothyroidism. Higher levels of homeostasis model assessment and lower levels of Matsuda indexes, suggesting insulin resistance, have been found in patients with overt hypothyroidism compared with euthyroid subjects in some but not in all studies.

Impaired intracellular glucose catabolism and GLUT4 translocation, decreased glycogen synthesis and glucose oxidation, and altered blood flow, have been proposed as underlying mechanisms.

Increased intima-media thickness of the common carotid artery has been reported in some studies in patients with overt hypothyroidism. A higher frequency and/or severity of coronary heart disease and an increased ischemic stroke risk have been reported in patients with overt hypothyroidism.

Clinical hyperthyroidism has been associated with systolic hypertension, increased pulse pressure, and possibly hyperhomocysteinemia. Additionally, patients with overt hyperthyroidism have a hypercoagulable state and an increased risk of thrombosis. Angina pectoris is a frequent disorder, especially in older patients with hyperthyroidism and underlying cardiac disease, and is due to increased heart rate and contractility and high myocardial oxygen demand Some cases of patients with hyperthyroidism due to Graves' disease presenting with coronary artery spasm have been reported. Hyperthyroidism has been associated with a higher risk for ischemic stroke among young adults during a 5-year follow up which was probably associated with atrial fibrillation (AF), hypercoagulability and rarely antiphospholipid antibody syndrome [5].

Subclinical hyperthyroidism has been also associated with hypertension in some but not all studies. Ochs *et al*. found a possible association, while the meta-analysis by Singh *et al*. found no significant association. Jeong *et al*. in a study of 382 patients with ischemic stroke found no difference in the prevalence of subclinical hyperthyroidism (1.6%) compared to the general population [6].

Methodology

Estimation of serum T3, T4, TSH by chemiluminescences immunoassay method

Principle*:* In this method, the immobilization takes place at the surface of an opaque chemiluminescent reaction cell through the interaction of streptavidin coated on the opaque reaction cell and exogenously added biotinylated monoclonal antibody coupled to the analyte of interest. Upon mixing monoclonal biotinylated antibody, the enzyme labeled antibody and the test serum containing the native antigen, reaction results between the native antigen and the antibodies, without competition or stearic hindrance, to form a soluble sandwich complex. After equilibrium is attained, the antibody bound fraction is separated from unbound antigen by decantation or aspiration. The enzyme activity, determined by reaction with a substrate that generates light, in the antibody-bound fraction is directly proportional to the native antigen concentration. By utilizing several different serum reference of known antigen values, a dosage response curve can be generated from which the antigen concentration of an unknown analyte can be ascertained.

Inclusion criteria

- Postmenopausal women attending outpatient and inpatient of Medicine Department

Exclusion criteria

- Known cases of diabetes mellitus
- Known cases of Thyroid dysfunction,
- Known cases of hypertension,
- Known cases of chronic kidney disease.
- Patients on Hormone replacement therapy
- Diagnosed cases of Ovarian and uterine malignancy
- Patients on drugs like iodide, amiodarone, salicylates, propranolol, octreotide, phenytoin, lithium, glucocorticoid, amphetamine, aminoglutethemide, somatostatins.

Results

Haemoglobin and its effect on thyroid profile were evaluated. Mean haemoglobin values for euthyroid subject's were10.3g%, sub-clinical hypothyroid 11.1g%, overt hypothyroid 10.7g% and hyperthyroid subject's 10.1g%. Result indicate that Free T3 and haemoglobin have negative correlation. This means, as the Hb increases Free T3 decreases and vice versa. Similarly Free T4 and haemoglobin also have negative correlation. Whereas TSH and haemoglobin have positive correlation, that is, as haemoglobin increases TSH also increases and vice versa.

Table 1: Effect of haemoglobin on thyroid profile

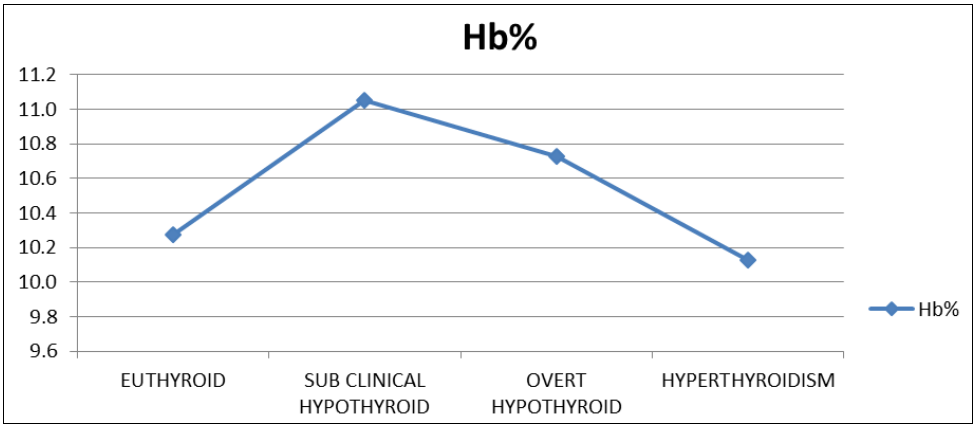
	Euthyroid		**Sub clinical hypothyroidism**		**Overt hypothyroidism**		**Hyperthyroidism**	
Variable	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.
N	25		20		4		13	
Hb%	10.3	1.2	11.1	1.1	10.7	1.5	10.1	1.4

The mean Haemoglobin values for Euthyroid (10.3g%), sub-clinical hypothyroid (11.1g%), overt hypothyroid (10.7g%) and hyperthyroidism (10.1g%). The P value was >0.05. Hence there was no statistically significant difference between the groups.

Table 2: Comparison of haemoglobin with thyroid profile

Pearson correlation	**Free t3 vs hb%**	**Free t4 vs hb%**	**Tsh vs hb%**
Correlation coefficient	-0.1907	-0.1096	0.1318
P value	>0.05	>0.05	>0.05

Table 2 shows that, Free T3 and Haemoglobin have negative correlation (means as the Hb Increases the Free T3 Decreases and Vice Versa), similarly Free T4 and Haemoglobin have negative correlation whereas TSH and Haemoglobin have positive correlation (means as the Hb Increases the TSH also Increases and Vice Versa). But all the three parameters are not statistically significant.



Graph 1: Comparison of haemoglobin with thyroid profile

Discussion

Haemoglobin and its effect on thyroid profile were evaluated. Mean haemoglobin values calculated for test and controls. Result indicated that Free T3/T4 and haemoglobin have negative correlation. This means, as the Hb increases as Free T3/T4 decreases and vice versa. Whereas TSH and haemoglobin have positive correlation, that is, as haemoglobin increases TSH also increases and vice versa. All the three parameters were not statistically significant.

Unlike previous studies, there was no statistical significance in Thyroid dysfunction and Non HDL-C, LDL, VLDL, apo lipoprotein a.

Hence, according to the study, there is a significant correlation between lipid profile and thyroid dysfunction. Moreover, hypothyroidism may present without any symptoms in post-menopausal women. Thyroid dysfunction causing lipid profile abnormality is a risk factor for developing CAD and CVA. So it becomes even more important to check the lipid profile and thyroid profile of post-menopausal women.

While the association between thyroid dysfunction and alteration in lipid profile is an undisputed fact, the situation is less clear when post-menopausal women are concerned. The relationship between thyroid dysfunction and reversibly elevated lipid levels has been widely investigated, but the results remain highly controversial.

There was a significant increase in the total cholesterol and LDL levels in study/case group when compared with euthyroid controls, but the variation in HDL and triglycerides were not significant.

A recent meta-analysis of the effect of treatment with thyroxine on lipid profile in mild thyroid failure cases by Mark D. Danese and colleagues has demonstrated a mean reduction in the total cholesterol level of 7.9 mg per decilitre (0.2 mmol per litre) and in the LDL cholesterol level of 10 mg per decilitre (0.26 mmol per litre). Changes in high-density lipoprotein (HDL) cholesterol were heterogeneous among the studies and were not statistically significant.

Wanjia and Wang *et al*, studies were done at two Chinese hospitals from 2004 – 2010 in adult patients who previously had TSH, thyroid hormone and cholesterol blood tests done. One study by Wanjia and colleagues looked at 521 patients recently diagnosed with heart disease, while the other study by Wang and colleagues looked at 3,709 patients who were seen for a routine medical visit. Both studies consisted only of patients who were not taking any medications nor had health problems that could impact the TSH, thyroid hormone or cholesterol tests. Both studies reported that patients with TSH levels at the upper limit of the normal range were more likely to have higher cholesterol levels as compared with those with lower TSH levels [7, 8].

Omprakash Mathur, Ranjana Yadav Monika *et al*., in 2013 conducted a study. In this study, 25 patients of clinically established hypothyroidism and 25 patients of diabetes attending the Out Patient Department, Department of Medicine, MDM Hospital (Jodhpur) were evaluated for lipid profile. Hypothyroidism is a condition characterized by abnormally low thyroid hormone production and diabetes mellitus is also common endocrine disorder which is defined as group of metabolic diseases characterized by hyperglycemia. Serum total cholesterol of hypothyroids and diabetic patients showed a highly significant relationship as compared to controls. Serum triglycerides showed a very significant relationship, serum LDL-c also showed a highly significant relationship while serum VLDL-c of hypothyroid patients showed a significant relationship and in diabetic patient's very significant relationship as compared to controls. Study concluded that estimation of serum lipid profile is simple, reliable, economic and sensitive that can now be considered as an adjunct in the management of hypothyroidism and diabetes mellitus [9].

Kuldip Singh *et al*. in 2011., did a study in which serum lipid profile such as total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, very low density lipoprotein cholesterol and triglyceride from 100 patients in the age range of 15-65 years of both sex having subclinical hypothyroidism were compared with euthyroid controls to observe that whether subclinical hypothyroidism is associated with abnormal lipid levels or not in a population based sample from Northern Indians study. A significant increase in triglycerides and very low density lipoprotein cholesterol levels were observed in patients of subclinical hypothyroidism with respect to euthyroid controls while a nominal increase in serum cholesterol, low -density lipoprotein and high -density lipoprotein levels were recorded. However, there was no statistical difference found in any of the lipid fraction levels with change in the severity of subclinical hypothyroidism. All these observation suggested that subclinical hypothyroidism did not have a marked impact on any of the fraction of lipids [10].

Conclusion

Free T3 and Haemoglobin have negative correlation (means as the Hb Increases the Free T3 Decreases and Vice Versa), similarly Free T4 and Haemoglobin have negative

correlation whereas TSH and Haemoglobin have positive correlation (means as the Hb Increases the TSH also Increases and Vice Versa). But all the three parameters are not statistically significant.

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