**East African Scholars Journal of Medical Sciences**
*Abbreviated Key Title: East African Scholars J Med Sci*
ISSN: 2617-4421 (Print) & ISSN: 2617-7188 (Online)
Published By East African Scholars Publisher, Kenya

OPEN ACCESS

Volume-7 | Issue-7 | Jul-2024 | DOI: 10.36349/easms.2024.v07i07.008

**Original Research Article**

# Assessment of Plasma Homocysteine in Patients with Hypothyroidism in a Nigerian Tertiary Hospital

Dalili M.S[1], Hadiru G.M[2], Dungus M.M[2*], Aisha S.K[2], Amali A.A[2], Hassan A.A[2], Gademi F.M[2], Fatima M.L[2], Halima M.A[2], Musa A.H[3], Mshelia D.S[4]

[1]Department of Chemical Pathology, Federal University of Health Sciences, Azare, Bauchi State
[2]Department of Chemical Pathology University of Maiduguri Teaching Hospital, Maiduguri, Borno State
[3]Department of Medical Laboratory Sciences, Faculty of Allied Health Sciences, University of Maiduguri, Borno State
[4]Department of Chemical Pathology, Faculty of Basic Clinical Sciences, University of Maiduguri, Borno State, Nigeria

**Article History**
**Received:** 11.06.2024
**Accepted:** 16.07.2024
**Published:** 24.07.2024

**Journal homepage:**
https://www.easpublisher.com

**Quick Response Code**

**Abstract:** ***Introduction*:** Hypothyroidism, a risk factor for atherosclerotic cardiovascular disease has been seen to be associated with hyperhomocysteinemia. The plasma levels of homocysteine and its relationship with hypothyroidism was assessed. ***Material and Methods*:** A total of 120 patients aged 20 – 60 years comprising of 60 hypothyroid and 60 euthyroid controls were assessed for the study. Evaluation of plasma homocystein was done using human homocysteine ELISA my BioSource. FT3, FT4 and TSH were also evaluated by enzyme linked immunosorbent assay (ELISA) technique using stat fax-2100. ***Result*:** In our study, we have found the values of FT3 in the subjects as 1.21± 0.89pg/ml lower than controls values of 1.92±0.66pg/ml, values of FT4 in subjects as 0.60±0.53ng/dl as compared to control group value of 1.40±0.30ng/dl, values of TSH as 2.07±1.19µiU/ml higher than the control group of 0.48±1.67µiU/ml. The mean values of plasma homocysteine (Hcy) for subjects was 34.50±10.01µmol/L higher than the control group with 9.30±2.11µmol/L. ***Conclusion*:** Our study findings suggest that patients with hypothyroidism also have a high plasma homocysteine known to pose cardiovascular complications.

**Keywords:** $fT_3$, $fT_4$, TSH, Homocysteine and Hypothyroidism.



## 1. INTRODUCTION

Disorder of thyroid gland poses a risk for cardiovascular diseases. High levels of thyroid stimulating hormone (TSH) and low thyroid hormone levels might affect atherosclerosis [1].

Studies have shown that thyroid hormones ($fT_3$ & $fT_4$) and thyroid stimulating hormone (TSH) affect lipid metabolism even in their normal plasma levels [2]. However, studies in hypothyroid individuals have shown that hypercholesterolemia and hyperlipoproteinemia could not fully and solely explain the increase in cardiovascular morbidity.

Thyroid hormones abnormalities particularly Hypothyroidism has been observed to pose cardiovascular risk such as atherosclerosis [2]. This has led researchers to look at the part homocysteine may play in cardiovascular disease. There is an association between raised plasma homocysteine concentrations and cardiovascular disease, in that individuals with moderate to severe concentration elevations may have an increased cardiovascular risk.

Homocysteine is derived from methionine by demethylation, can also be metabolized to cysteine by transulphuration, or remethylated using betaine or methyltetrahydrofolate. Thus elevated plasma homocysteine can be due to deficiencies of vitamins $B_{12}$, Folate or Vitamin $B_6$. There is also evidence that a mutation of the methylene tetrahydrofolate reductase (MTHFR) gene results in elevated plasma homocysteine levels [1]. Plasma homocysteine levels above 10µmol/L confer increase cardiovascular risk [1]. Concentrations of homocysteine increase with age, impaired renal function, hypothyroidism, Psoriasis and certain drugs such as methotrexate, theophylline and levodopa. Homocysteine could induce endothelial injury, oxidative stress, smooth muscle hypertrophy and oxidation of low density lipoprotein cholesterol, and the process of atherosclerosis and cardiovascular diseases [3]. It has often been shown to be related to occlusive vascular disease alone without the involvement of other familiar cardiovascular risk factors [4].

A study done earlier, indicated that an increase in plasma homocysteine level of 4µmol/L had 40%

***Corresponding Author:** Dr Musa Dungus Musa
Department of Chemical Pathology University of Maiduguri Teaching Hospital, Maiduguri, Borno State

increase in relative risk for coronary heart disease compared with healthy controls [5]. Hyperhomocysteinemia in overt hypothyroidism is a common finding in many studies [6, 7].

Furthermore, in subclinical hypothyroidism patients, homocysteine level was reported to be higher as compared with euthyroid controls [8]. Furthermore, homocysteine level had been reported to be associated with carotid intima-media thickness in patients with clinical hypothyroidism [9].

## 2. MATERIALS AND METHODS

### 2.1 Patients

A total of 120 patients aged 20-60years comprising of 60 hypothyroid and 60 euthyroid controls were consecutively recruited at the endocrinology clinic of the University of Maiduguri Teaching Hospital. Euthyroidism was defined as $fT_3$, $fT_4$ and TSH within their reference limits. Patients were excluded if they are hypertensive, Diabetic, Pregnant and any major condition lasted beyond six months (Liver, Kidney and Heart failure). Patients with previous history of thyroid disease such as hyperthyroidism, hypothyroidism, carcinoma of thyroid, were excluded. Patients on drugs that affect thyroid hormones levels such as thyroid supplements and antithyroid agents, amiodarone, lithium corticosteroids etc were all excluded. Informed consent was obtained from all participants. The study was approved by ethical committee of the University of Maiduguri Teaching Hospital.

### 2.2 Measurements

Measurements of weight, height, body mass index (BMI) and blood pressure were done. Weight measurement was done using a weighing scale (OHAUS pioneer PA413) with subjects putting on light clothes and no shoes. The height was assessed using stadiometer and the BMI was estimated using weight in kg divided by height in meter square (wt/kg)/(ht/$m^2$). The blood pressure was measured twice in the sitting position on the left arm using an accuson's sphygmomanometer. Whole blood specimens (5mls) were collected after an overnight fast from the antecubital vein using aseptic procedures for measurements of serum $fT_3$, $fT_4$ and TSH. Serum was separated from the cell using Pasteur pipette and spun at 300 rpm for 10 minutes using swinging bucket centrifuge and stored frozen at -20$^0$C until time of analysis. The $fT_3$, $fT_4$ and TSH levels were measured using enzyme link immunosorbent assay (ELISA) kit, Perkins Elmer.

The serum homocysteine was evaluated using human homocysteine ELISA Kit (Competitive Elisa) myBio-source.com) with reference interval of 5 – 15µmol/L. The normal ranges for $fT_3$, $fT_4$ & TSH were 2.3 – 41pg/ml, 5.0 – 11.0µg/dl and 0.5 – 5.0µiU/L respectively. Hypothyroidism is when $fT_3$ is < 1.4, $fT_4$<0.8 & TSH>0.53 and hyperhomocysteinemia is when plasma homocysteine level is > 15µmol/L.

### 2.3 Statistic Analysis

The data analysis was performed using SPSS version 18.0. The data was expressed as mean ±standard deviation (SD). Student's t-test was used for non-paired group analysis. Mean values of P< 0.05 were considered statistically significant.

## 3. RESULT

The mean age distribution for both cases and control was found to be 40.10 ± 4.3 years, 42.3 ± 4.8 years with predictive value of 0.17 are not statistically significant. On the other hand, the body mass index (BMI) of cases and controls was found to be 24.10± 4.5 kg/$m^2$, 21.30± 2.4 kg/$m^2$ were also not statistically significant (*p*-0.09). The mean values of systolic blood pressure of both groups were 125.30 ± 1.42 mmHg, 121.25 ± 2.10 mmHg and their diastolic blood pressure counterparts were 78.4 ± 2.13 mmHg, 73.58 ± 1.40 mmHg with predictive values of 0.07 and 0.05 respectively were also not statistically significant (Table 1).

**Table 1: Mean Values of Age, Body Mass Index (BMI) and Blood Pressure**

| Parameter | Cases | Control | p-value |
|---|---|---|---|
| Age (Years) | 40.10 ± 4.3 | 42.3 ± 4.8 | 0.17 |
| Body Mass Index (BMI) (kg/$m^2$) | 24.1 ± 4.5 | 21.3 ± 2.4 | 0.09 |
| Systolic Blood Pressure (mmHg) | 125.30 ± 1.42 | 121.25 ± 2.10 | 0.07 |
| Diastolic Blood Pressure (mmHg) | 78.40 ± 2.13 | 73.58 ± 1.40 | 0.05 |

*p*<0.05 is considered Significant

The mean values of free $T_3$ ($fT_3$) in both cases and controls were found to be 1.21 ± 0.89 pg/ml and 1.92 ± 0.66 pg/ml with the predictive value of 0.001 were statistically significant.

The mean values of free $T_4$ ($fT_4$) for the cases and controls were 0.60 ± 0.53ng/dl, 1.40 ± 0.30 ng/dl respectively were statistically significant (*p*-0.001). The thyroid stimulating hormone (TSH) mean values for both cases and controls were found to be 2.07 ± 1.19µiU/ml and 0.48 ± 1.67µiU/ml were also statistically significant (p-0.003). The mean values of homocysteine for cases and control respectively were 34.50± 10.01µmol/L, 9.30± 2.11µmol/L were statistically significant (p-0.00). Table II

**Table II: Mean values of thyroid hormones and Homocysteine**

| S/No. | Parameters | Cases | Control | p-values |
|---|---|---|---|---|
| 1 | $fT_3$ (Triiodothyronine) (pg/ml) | 1.21 ± 0.89 | 1.92 ± 0.66 | 0.001 |
| 2 | $fT_4$ (Tetraiodothyronine) (ng/dl) | 0.6 ± 0.53 | 1.40 ± 0.30 | 0.001 |
| 3 | TSH (Thyroid Stimulating Hormone) (µiU/ml) | 2.07 ± 1.19 | 0.48 ± 1.67 | 0.003 |
| 4 | Homocysteine (µmol/L) | 34.5± 10.01 | 9.30 ± 2.11 | 0.00 |

$p<0.05$ is considered significant

## 4. DISCUSSION

Thyroid hormones are known to be catabolize in function and regulate various metabolic processes. They influence homocysteine metabolism through the activity of hepatic enzymes involved in the remethylation pathway of homocysteine, methionine synthase, and methylene tetrahydrofolate reductase [10, 11].

Homocysteine metabolism can also be influenced by low levels of thyroid hormones as a result of their effects in reducing glomerular filtration rates (GFR) with resultant elevation of creatinine and homocysteine plasma levels [12, 13]. These are in agreement with our study which suggested that, thyroid function might influence the homocysteine metabolism, leading to hyperhomocysteinemia. This could suppose that homocysteine might be related to thyroid function and atherosclerosis.

In a study by Yun Zhang *et al.*, patients with hyperhomocysteinemia an independent risk factor for cardiovascular disease have been to also have lower $fT_4$ levels, indicative of low normal thyroid function [14]. In another study by Boushey *et al.*, indicated that an increase in plasma homocysteine level of 4µmol/L conferred a 40% increase in relative risk of coronary heart disease compared with healthy controls [15].

Elevated plasma homocysteine levels occurs in approximately 5 – 7% of the general population [16]. A good number of epidemiologic evidence has shown that the presence of mild homocysteinemia is an independent risk factor for atherosclerosis in the coronary, cerebral and peripheral vasculature [17].

Hyperhomocysteinemia occurs in nutritional deficiencies (Folate, Vitamin $B_{12}$, Vitamin $B_6$, Selenium), genetic disorders, endocrine disorders (hypothyroidism, diabetes Mellitus, hypogonadism, Cushing's Syndrome), other diseases (Chronic Kidney disease, Malignancies), in active Smokers and could be induced by some medications (Methotrexate, Phenytoin, Carbamazepine) [18, 19].

On the other hand, elevated plasma homocysteine is a risk factor of cognitive impairment ischemic stroke [20], and osteoporosis-induced fractures [21].

## 5. CONCLUSION/RECOMMENDATION

In view of this study, patients with hypothyroidism have been seen to also have hyperhomocysteinemia that is known as a risk factor for atherosclerosis and cardiovascular disease. Screening of hypothyroid patients for homocysteine would go a long way in identifying these patients with higher risk of cardiovascular disease and possible prevention of the disease.

## REFERENCES


1. Martin, A. Crook. Cardiovascular risk factors. In clinical Biochemistry and Metabolic Medicine 8th Edition. Greenwich, UK: P. 329, ISBN-13, 978-1-4441-4414-7. 2012.
2. Åsvold, B. O., Bjøro, T., Platou, C., & Vatten, L. J. (2012). Thyroid function and the risk of coronary heart disease: 12-year follow-up of the HUNT S tudy in N orway. *Clinical endocrinology*, *77*(6), 911-917.
3. Medina, M. Á., Urdiales, J. L., & Amores-Sánchez, M. I. (2001). Roles of homocysteine in cell metabolism: old and new functions. *European journal of biochemistry*, *268*(14), 3871-3882.
4. Den Heijer, M., Lewington, S., & Clarke, R. (2005). Homocysteine, MTHFR and risk of venous thrombosis: a meta-analysis of published epidemiological studies. *Journal of Thrombosis and Haemostasis*, *3*(2), 292-299.
5. Boushey, C. J., Beresford, S. A., Omenn, G. S., & Motulsky, A. G. (1995). A quantitative assessment of plasma homocysteine as a risk factor for vascular disease: probable benefits of increasing folic acid intakes. *Jama*, *274*(13), 1049-1057.
6. Nedrebø, B. G., Ericsson, U. B., Nygård, O., Refsum, H., Ueland, P. M., Aakvaag, A., ... & Lien, E. A. (1998). Plasma total homocysteine levels in hyperthyroid and hypothyroid patients. *Metabolism*, *47*(1), 89-93.
7. Morris, M. S., Bostom, A. G., Jacques, P. F., Selhub, J., & Rosenberg, I. H. (2001). Hyperhomocysteinemia and hypercholesterolemia associated with hypothyroidism in the third US National Health and Nutrition Examination Survey. *Atherosclerosis*, *155*(1), 195-200.
8. Şengül, E., Çetinarslan, B., Tarkun, İ., Cantürk, Z., & Türemen, E. (2004). Homocysteine concentrations in subclinical hypothyroidism. *Endocrine research*, *30*(3), 351-359.

9. Gunduz, M., Gunduz, E., Kircelli, F., Okur, N., & Ozkaya, M. (2012). Role of surrogate markers of atherosclerosis in clinical and subclinical thyroidism. *International Journal of Endocrinology*, *2012*(1), 109797.
10. Chan, M. M. S., & Stokstad, E. R. (1980). Metabolic responses of folic acid and related compounds to thyroxine in rats. *Biochimica et Biophysica Acta (BBA)-General Subjects*, *632*(2), 244-253.
11. Nair, C. P., Viswanathan, G., & Noronha, J. M. (1994). Folate-mediated incorporation of ring-2-carbon of histidine into nucleic acids: influence of thyroid hormone. *Metabolism*, *43*(12), 1575-1578.
12. Lien, E. A., Nedrebø, B. G., Varhaug, J. E., Nygard, O., Aakvaag, A., & Ueland, P. M. (2000). Plasma total homocysteine levels during short-term iatrogenic hypothyroidism. *The Journal of Clinical Endocrinology & Metabolism*, *85*(3), 1049-1053.
13. Nedrebø, B. G., Nygard, O., Ueland, P. M., & Lien, E. A. (2001). Plasma total homocysteine in hyper- and hypothyroid patients before and during 12 months of treatment. *Clinical chemistry*, *47*(9), 1738-1741.
14. Zhang, Y., Wang, Q., Li, Q., & Lu, P. (2015). Association between hyperhomocysteinemia and thyroid hormones in euthyroid diabetic subjects. *BioMed Research International*, *2015*(1), 196379.
15. Boushey, C. J., Beresford, S. A., Omenn, G. S., & Motulsky, A. G. (1995). A quantitative assessment of plasma homocysteine as a risk factor for vascular disease: probable benefits of increasing folic acid intakes. *Jama*, *274*(13), 1049-1057.
16. Welch, G. N., & Loscalzo, J. (1998). Homocysteine and atherothrombosis. *New England journal of medicine*, *338*(15), 1042-1050.
17. Kang, S. S., Wong, P. W., & Malinow, M. R. (1992). Hyperhomocyst (e) inemia as a risk factor for occlusive vascular disease.
18. Fonseca, V., Guba, S. C., & Fink, L. M. (1999). Hyperhomocysteinemia and the endocrine system: implications for atherosclerosis and thrombosis. *Endocrine reviews*, *20*(5), 738-759.
19. Gonzalez, S., Huerta, J. M., Álvarez-Uría, J., Patterson, Á. M., Lasheras, C., & Fernández, S. (2004). Serum selenium is associated with plasma homocysteine concentrations in elderly humans. *The Journal of nutrition*, *134*(7), 1736-1740.
20. Seshadri, S., Beiser, A., Selhub, J., Jacques, P. F., Rosenberg, I. H., D'Agostino, R. B., ... & Wolf, P. A. (2002). Plasma homocysteine as a risk factor for dementia and Alzheimer's disease. *New England journal of medicine*, *346*(7), 476-483.
21. Raisz, L. G, & Homocysteine, L. G. (2004). Homocysteine and osteoporotic fractures. N. Engl J Med, 350, 2089 – 90.


**Cite This Article:** Dalili M.S, Hadiru G.M, Dungus M.M, Aisha S.K, Amali A.A, Hassan A.A, Gademi F.M, Fatima M.L, Halima M.A, Musa A.H, Mshelia D.S (2024). Assessment of Plasma Homocysteine in Patients with Hypothyroidism in a Nigerian Tertiary Hospital. *East African Scholars J Med Sci*, *7*(7), 317-320.