LIPID PROFILE PATTERN IN THYROID DISORDERS IN NORTH EASTERN NIGERIA.

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Abstracts.

Background: thyroid hormones are involved in regulation of lipid and lipoprotein metabolism therefore, thyroid dysfunctions induce significant changes in lipid and lipoprotein metabolism. However, lipid disorders in thyroid dysfunctions exhibit great individual variability and the pattern of changes in lipid fractions in thyroid disorders remain controversial.

Objectives: To determine lipid pattern in thyroid disorders in northeastern Nigeria.

Methods: 18 simple goiter, 41 thyrotoxicosis patients, and 41 control subjects were recruited at the surgery clinic and department of Chemical Pathology of University of Maiduguri Teaching Hospital. Thyroid function test and lipid profile were done for each subjects.

Results: The mean(SD) serum LDL and TGs levels in simple goiter patients were significantly higher than in the control subjects. However, total cholesterol and HDL did not show any significant difference. Similarly, the mean(SD) serum LDL and TGs levels in thyrotoxicosis patients were significantly higher than in the control subjects. In addition, total cholesterol and HDL did not show any significant difference. There was no significant difference in lipid components among thyroid disorder patients. The mean(SD) TC/HDL ratio was significantly higher in both simple goiter and thyrotoxicosis patients compared to that of the control subjects. However, the ratio did not show any significant difference among the thyroid disorder patients.

Conclusion: The lipid pattern did not only show dyslipidaemia in simple goiter patients alone but also in the thyrotoxicosis patients as well. Lipd profiles should therefore, be part of workup in the management of thyroid dysfunctions.

INTRODUCTION.

It is well known that thyroid hormones are involved in the regulation of lipd and lipoprotein metabolism, inducing significant changes in the concentration, structural composition, and transport of lipids and lipoproteins[1]. These are interfered in thyroid disorders[2-5].

Lipid disorders in thyroid dysfunctions exhibit great individual variability and hence the pattern of biochemical changes in plasma lipid fraction in thyroid dysfunctions remain controversial[5-9]. However, hypothyroidism is seen to be associated with hypercholesterolaemia, which can accelerate atherosclerosis[6]. In hyperthyroid states, the enhanced synthetic rate of cholesterol is accompanied by increased clearance, and normally hyperthyroidism is associated with either normal or even decreased total cholesterols[7], and recently high triglycerides has been found to be an independent risk factor for atherosclerosis[10]. Hence, it can be stated theoretically that atherosclerosis is

accelerated in both hypo- and hyperthyroid disorders.

Thyroid disorders are said to be common in Nigeria[11-16] including the northeastern Nigeria[17].

Although the changes that occur in the major plasma lipd fractions in specific thyroid dysfunctions are fairly well established, however, there is paucity of information on thyroid dysfunctions and plasma lipd and lipoproteins in northeastern Nigeria.

This study is therefore, set to determine the pattern of plasma lipid profile and to determine the values of lipd profile in evaluation of thyroid diseases in the region.

Materials and Methods.

Fifty-nine consecutive patients with provisional diagnosis of thyroid disorders from the surgery clinic of University of Maiduguri teaching Hospital (UMTH) who were not on any medication for thyroid disorders were recruited for the study. Ethical clearance obtained from the joint ethical committee of UMTH/University of Maiduguri, and informed consent obtained from each subject before recruitment.

Those excluded form the study were patients who had thyroidectomy or on medications for thyroid disease. Also excluded were subjects outside the region, pregnant mothers, diabetic patients, renal disease patients, and those on medications capable of altering lipid and lipoprotein metabolism.

Forty-one apparently healthy individuals matched for age and sex recruited as controls among hospital workers, patients' relatives and medical students. Those excluded among the controls were subjects outside the region, subjects who were diabetic, hypertensive, renal disease patients, or obese. Also excluded were subjects who smoke, take alcohol or on medications that may alter lipd and lipoprotein metabolism and those found to have subclinical thyroid disorders by thyroid function tests.

On recruitment, age (years) and sex were noted and subjects weight (Kg), height(m) and blood pressure(mmHg) were taken. BMI was calculated as BMI=Kg/M2. Ten(10) ml of fasting venous blood was collected from the antecubital vein aseptically and dispensed into a plain container, allowed to clot and retracted for 15 minutes. The samples centrifuged at 3000rpm for 10 minutes and serum separated into other fresh containers and stored at -20°C until analysis within 2 weeks of sample collection.

The serum TSH, T_4 and T_3 levels were determined by Enzyme Linked Immunosorbent Assay(ELISA) method using competitive enzyme 2nd generation method of Chpro[18]. The reagent kits were manufacture by Dailab Company Austria. Also analyzed from the serum were total cholesterol[19], triglycerides[20], and high-density lipoprotein(HDL)[21], while the values of Low-density lipoprotein(LDL) calculated using the Friedwald formula[22].

Data obtained were analyzed using statistical software SPSS version 11. Student's t-test was used to compare the means of variables. The level of significance was set at $p<0.05$. Also determined was specificity and sensitivity of lipid profile values against thyroid diseases using Galen and Gambino methods[23].

RESULTS.

From the study, 18 cases were simple goiter patients, 4(22.2%) males and 14(77.8%) females with male: female ratio of 1:3.5, while 41 were thyrotoxicosis patients, 11(26.8%) males and 30(73.2%) females with male: fermale ratio of 1:2.7. Of the 41 control subjects 18(43.1%) were males and 23(56.9%) were females.

The mean(SD) age of the simple goiter patients, 33.5(9.4) years, (range 19-48 years) was significantly higher than that of the thyrotoxicosis patients, 30.9(7.2) years,(range 18-49 years) and the controls, 30.6(7.5) years, (range 20-47 years), $p<0.05$. However, there was no significant difference in the ages of thyrotoxicosis patients and the controls, $p>0.05$.

The mean(SD) BMI of simple goiter patients, 25.4(1.8)kg/m^2 was not significantly different to that of the controls, 25.8(1.1)kg/m^2, $p>0.05$. However, the mean(SD) BMI of the thyrotoxicosis patients, 22.5(3.1)kg/m^2 was significantly lower than

that of the simple goiter patients values and the controls values, $p<0.05$ in both.

Comparison of the mean(SD) systolic blood pressure of simple goiter patients, 124.3(3.6)mmHg and that of the controls, 123.2(4.7)mmHg showed no statistically significant difference, $p>0.05$. However, although the mean(SD) systolic blood pressure of the thyrotoxicosis patients, 132.4(3.1)mmHg was within the normal range, it was significantly higher when compared to that of simple goiter patients values and the controls values, $p<0.05$ in both cases. There was no significant difference in the diastolic blood pressures when compared in all the subjects.

Table 2 shows comparisons of mean(SD) serum levels of T_3,T_4,and TSH in subjects. The mean(SD) serum T_3 level of thyrotoxicosis patients, 0.07(0.04)nmol/L was significantly higher than that of simple goiter patients, 0.02(0.01)nmol/L, t=8.922, p=0.000 and the controls, 0.02(0.01)nmol/L, t=8.922, p<0.000. While the mean(SD) serum level of T3 of simple goiter patients, 0.02(0.01)nmol/L was not statistically different when compared to that of the controls, 0.02(0.01)nmol/L, t=0.669, p=0.654. The mean(SD) serum level of t4 of thyrotoxicosis patients, 176.7(59.4)nmol/L was also significantly higher than in simple goiter patients, 152.0(47.3)nmol/L, t=3.209, p=0.012, and the controls, 103.1(27.4)nmol/L, t=7.209, p=0.000. The mean(SD) serum level of T_4 in simple goiter patients, 152.0(47.3)nmol/L was also significantly higher than in the control patients, 103.1(27.4)nmol/L,t=5.006, p=0.001. Although the mean(SD) serum TSH level of thyrotoxicosis patients, 1.2(1.1)mU/L was lower as against that of simple goiter patients, 1.7(2.0)mU/L,t=1.727, p=0.710, and that of the control subjects, 1.7(1.0)mU/L, t=1.829, p=0.671, the difference was not statistically significant. Similarly, the difference in the mean(SD) serum TSH level of simple goiter patients and the control was not statistically significant.

Table 3 shows profile of serum lipoproteins in subjects.

The mean(SD) serum LDL, 3.0(1.0)mmol/L and TG, 1.5(0.8)mmol/L in simple goiter patients were statistically significantly higher compare to that of the controls, 2.3(0.0)mmol/L and 1.3(0.2)mmol/L, t=1.631,p=0.000. Meanwhile the mean(SD) of serum total cholesterol, 5.0(0.9)mmol/L and HDL, 1.1(0.5)mmol/L in simple goiter patients did not show any statistically significantly difference compared to that of the controls, 4.6(0.2)mmol/L, t=1.863,p=0.481, and 1.3(0.4)mmol/L, t=1.055, p=0.530 respectively. Similarly, the mean(SD) serum LDL, 2.9(1.4)mmol/L and TG, 1.4(0.6)mmol/L were also significantly higher in thyrotoxicosis patients when compared to that of the controls,2.3(0.0)mmol/L, t=2.675,p=0.002, and 1.3(0.2)mmol/L, t=1.160, p=0.000, respectively. The mean(SD) serum total cholesterol, 4.8(1.4)mmol/L and HDL, 1.2(1.2)mmol/L did not show any statistically significant difference when compared to that of the controls, 4.6(0.2)mmol/L, t=0.753,p=0.100 and 1.3(0.4)mmol/L, t=0.633, p=0.276 respectively. Meanwhile, although the mean(SD) of all the components of lipid profile, except that of HDL, were higher in simple goiter patients than that in the thyrotoxicosis patients, the difference were not statistically significant.

The mean(SD) TC/HDL ratio in simple goiter patients, 5.2(2.2) is significantly higher when compared to that of the controls, 3.9(1.4). Similarly, the ratio in thyrotoxicosis patients, 5.3(2.2) was significantly higher when compared to that of the controls, 3.9(1.4). While the difference observed in the mean(SD) of the ratio in simple goiter patients and that of the thyrotoxicosis patients was not statistically significant.

The sensitivity was higher in TG(88%) and HDL(88%) in thyrotoxicosis patients and in HDL(83%) and LDL(78%) in simple goiter patients.

Table 1. Demographic profile of subjects in the study.

Variables	simple goiter(n=18)	Thyrotoxicosis(n=41)	Controls(n=39).
Female	14	30	23
Males	4	11	16
Age(years)	33.5(9.4)	30.9(7.2)	30.6(7.6)
BMI(Kg/m2)	25.4(1.8)	22.5(3.1)	25.8(1.1)
Systolic BP(mmHg)	124.3(3.6)	132.4(3.1)	123.2(4.7)
Diastolic BP(mmHg)	69.5(2.8)	68.4(4.2)	70.5(1.1).

Table 2: Profile of mean(SD) serum levels T3, T4 and TSH in subjects.

Variables	Simple goiter	Thyrotoxicosis	Controls.
T3(nmol/L)	0.02(0.01)	0.07(0.04)	0.02(0.01)
T4(nmol/L)	152.0(47.3)	178.4(57.4)	103.1(27.4)
TSH(mU/L)	1.7(2.0)	1.2(1.1)	1.7(1.0).

Table 3: Mean(SD) of lipid profile in subjects in the study.

Variables	Simple goiter	Thyrotoxicosis	Controls
TC(mmol/L)	5.0(0.9)	4.8(1.4)	4.6(0.2)
LDL(mmol/L)	3.0(1.0)	2.9(1.4)	2.3(0.7)
HDL(mmol/L)	1.1(0.5)	1.2(1.2)	1.3(0.4)
TGs(mmol/L)	1.5(0.8)	1.4(0.6)	1.3(0.2)
TC/HDL ratio	5.2(2.2)	5.3(2.2)	3.9(1.4).

Table 4: Sensitivity of components of lipid profile in thyroid disorder patients.

Variables	Simple goiter	Thyrotoxicosis
TC	67%	78%
LDL	78%	78%
HDL	83%	88%
TG	72%	88%.

DISCUSSION.

Thyroid disorders are common in the west[11,13] and central[12,16] part of Nigeria. These are also common in the northeastern part of the country[17]. This is supported by the sample size obtained in this study compared to the period of study despite the number subjects excluded.

The range of age at on set of thyroid disorders, simple goiter (range 19-48years) and thyrotoxicosis (18-49years) were similar. In addition, the well-known fact that thyroid dysfunction is more common in females than in males is clearly apparent in this study where male: female ratio was 1:3.5 in simple goiter patients and 1:1.27 in thyrotoxicoisis patients.

Simple goiter patients who are still in the compensatory states do not usually manifest common features of hypothyroidism especially weight gain hence the similarity of the BMI in them and that in the controls. However, the typical feature of weight lost in hyperthyroid dysfunction was found in this study where the mean BMI of this group of patients was lower compare to that of the simple goiter patients and the controls.

Although the mean systolic blood pressure in thyrotoxicosis patients was significantly higher than in the simple goiter

patients and the controls, it was within the normal range. This is because the hypertensives among them were excluded from the study. The results of thyroid function tests enhances the categorizations of patents in each group where values of simple goiter patients were almost similar o that of the control group while that of the thyrotoxicosis patients were higher. T_3 and T_4 were higher in thyrotoxicosis patients while TSH is lower compare to those of simple goiter patients and the controls. This is in keeping with findings of other studies[12,18,24]. This may imply that primary thyrotoxicosis is also common because the mean value of TSH in thyrotoxicosis patients was not typically lower. The findings in this study where T_3 but T_4 levels in simple goiter patients were similar to that of the controls accords with the work of Franklyn[25], where T_3 is said to be maintain at euthyroid state during adequate compensation.

Thyroid dysfunctions are complex and are subject to biochemical change, including that of lipids, and clinical changes that interplay in the evaluation of the disorder. Several cross-sectional studies suggest that serum total cholesterol concentration is elevated in individuals with thyroid failure when compared with that of euthyroid controls[18,24,27,28]. In other studies, the observed difference was not significant[19,29]. In this study, the observed differences in serum total cholesterol among the thyroid disorder patients or even when compared to that of the controls was not statistically significant. However, both mean serums LDL and TGs in thyroid disorder patents were significantly higher than those of the controls were. This is in keeping with a report from Jos, north central Nigeria[30]. This indicated that dysmetabolism of serum lipids in this environment may start even when the thyroid dysfunction is almost compensated for.

Usually, the biochemical changes which include that of lipids occurring in endemic goiter are complex and in turn partly determines the state of the serum lipids[24,26]. Consequently, the results of findings in this study indicate the need for investigation of lipid profile even when the goiter is termed simple, as treatment of the dyslipidaemia will potentially decrease the risk of death from cardiovascular cause[31].

The compositions and transport of lipoproteins are seriously interfered in thyroid diseases, due to altered clearance of LDL cholesterol from the plasma by changes in the number of LDL receptor on the liver cell surfaces, and because the promoter of the LDL receptor gene contains a thyroid hormone responsive element (TRE), T_3 modulates gene expression of the LDL receptor. Notwithstanding, the magnitude of the changes in plasma LDL depends both on the severity and the duration of the disease[32,33]. This is in contrast to findings in this study since the mean duration of the disorder in simple goiter patients was 3.5 years compared to the mean in thyrotoxicosis, 1.9 years. Yet, the observed difference in serum LDL in simple goiter and thyrotoxicosis patients was not statistically significant. However, although HDL in thyroid disorder patients was not significantly different from that of the control, the significantly elevated LDL as well as the TG in thyroid disorder patients, a similar findings in Jos, may predispose these patients to increase risk of atherosclerosis. Therefore, thyroid disorder patients including simple goiter patients could benefit from investigations and treatment of dyslipidaemia. Triglycerides were elevated in patients with thyroid disorders in this study. This could be due to increased hepatic lipogenesis in thyrotoxicosis patients[7], while that in simple goiter patients may be due decreased clearance[7]. These findings indicate that patients with thyroid disorders are at increase risk of atherosclerosis.

In the recent past, TC/HDL ratio has been found to predict risk for coronary artery disease better than elevated LDL, TGs or decreased HDL alone[34]. A study reported a ratio of 4.4 in normal women[35]. In this study, the TC/HDL ratio was 3.9 in the controls.

The TC/HDL ratios in the thyroid disorder patients are higher than in the controls. This concurs with findings eslswhere[35]. Thus, implying that these patients are at a greater risk for coronary artery disease despite the normal HDL values found in them. The ratio rather than an individual lipid profile component

could be use in monitoring therapeutic interventions[36]. The finding of significant elevation of serum LDL, TGs, and TC/HDL ratio in thyroid disorder patients compared to that of the controls calls for further study to determine the prevalence of cardiovascular disease in these patients in this environment.

In conclusion, Thyroid dysfunctions are still a major health problem in many parts of the world, especially in the developing countries including Nigeria. The significance and roles of lipids in the aetiology of atherosclerosis are well known. An evaluation of serum lipid fractions and lipoproteins in these disorders is therefore considered necessary as part of their work-up.

REFERENCES.

(1) HUESCA-Gomez C, Franco M, Luc G, et al. Chronic hypothyroidism induced abnormal structure of high-density lipoprotein and impaired kinetics of apolipoproteins in the rat. Metabolic 2002;51:443-450.

(2) Soutar AK and Knight BL. Structure and regulation of the LDL receptor and its gene. Br. Med. Bull. 1990;46:891-916.

(3) Danese MD, Powe NR, Sawin CT, Ladenson PN. Screening for mild thyroid failure at the periodic Health examination: a decision and cost-effectiveness analysis. JAMA 1996; 276:285-292.

(4) Vanderpump MPJ, Tunbridge WMP, French JM, Appleton D, Bates D, Clark F. The development of ischeamic heart disease in relation to autoimmune thyroid disease in a 20-year follow-up study of an English community. Thyroid 1996; 6:155-156.

(5) Kung AWC, Pang RWC, Janus ED. Elevated serum lipoprotein (a) in subclinical hypothyroidism. Clin. Endocrinol. 1995; 43:445-449.

(6) Duntas LN. Thyroid diseases and lipids. Thyroid 2002;12:28-93.

(7) Cachefo A, Bouches P, Vidon C, et al. hepatic lipogenesis and cholesterol synthesis in hypothyroid patients. J. Clin. Endocrinol. Metab. 2001; 86:5353-5357.

(8) Pucci E, Chivato L, Pinchera A. Thyroid and lipid metabolism. Int. J. Obes. Relate. Metab. Disrod.2000; 24:5109-5112.

(9) Verdugo C, Perrot L, ponsin G, Valentin C, berthezene F. Time-course of alterations of high-density lipoproteins(HDL) during thyroxin administration to hypothyroid women. Eur. J. Clin. Invest. 1987;17:313-316.

(10) Michael E.Z. Hypertriglyceridaemia and cardiovascular disease: a review: Third report of National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood cholesterol in Adult (Adult Treatment Panel 111). American College of Physician Annual session, San Francisco, CA, 2005.

(11) Osotimehin B, Hofferberg r. serum thyroglobulin measurement in various thyroidal disorders. Afri. J. Med. med. Sci.1980; 9:89-95.

(12) Isichei UP, Das SC, Egbuta JO, Banwo AI, Morimoto I, Nagataki S. Endemic Goitre studies in Plateau State, Nigeria. Iodine Deficiency disorders. Newsletters. WHO/UNICEF/ICCIDD publication 1989; 5:5-7.

(13) Olurin E.O. Thyrotoxicosis in Nigeria; A study of 46 patients. Postgrad. Med. J.1972; 48:609.

(14) Ekpechi Ol. Pathogenesis of endemic goiter in Nigeria. British J. Nur.1967; 21:537-545.

(15) Wilson DC. Goitre in Coylon and Nigeria. British J. Nurt.1954; 8:90-99.

(16) Isichei UP, Das Sc, Egbuta JO, Banwo AI, Morimoto I, Nagataki S. Endemic goiter in Plateau State, Nigeria. In: Vichayamiat A, Nitiyanant W, Eastman C, Nagataki S (eds) Recent progress in Thyroidology, Bangkok, Crystal house press, 1989: pp368-372.

(17) Dogo D, Yawe T. The pattern of thyroid diseases in northern Nigeria. Annals of Borno 1994;11/12: 287-292.

(18) Chopra IJ. A radioimmunoassay of thyroxine and triiodothyronine. J. Clin. Endocrinol.1971;33:865.

(19) Zak B. cholesterol methodologies. A

review. Clin. Chem. 1977; 23:1201.

(20) Klotzsch SG, Mc-Namara JR. Triglyceride measurements: A review of methods and interferences. Clin. Chem. 1990; 36:1605-1613.

(21) Warnick GR, Cheung MC, Albers JJ. Comparisons of current methods for hig-density lipoproteins quantification. Clin Chem. 1979; 25:596.

(22) Friedwald WT, Levy RI, Fredrickson DS. Estimation of the concentration of Low-density lipoprotein cholesterol without the use of the preparative ultra centrifugation. Clin. Chem.1972; 18:499.

(23) Galen RS, Gambino SR. Beyond Normality-the predictive value and efficiency of medical diagnosis. New York; John Wile and sons 1975.

(24) Das SC, Isichei UP, Egbuta JO, Ihezue CH. Thyroid function rpfile and differential serum lipids and lipoproteins in Africans with endemic goiter. Afri. J. Med.med Sci. 1994; 23:238-247.

(25) Franklyn JA. Hypothyroidism. Medicine 2005; 33:27-29.

(26) Isichei UP, Egbuta JO, Das SC, Ezeogu A. Aberations in serum proteins and thyroid size in Nigeria on Jos Plateau and their relation to thyrometabolic function. Afri. J. Med. med. Sci 1993; 22:77-87.

(27) Canaris GJ, Monuitz NR, major G, Ridgway C. the Colorado thyroid Disease Prevalence Study. Arch. Intern. Med. 2000; 160:526-534.

(28) Guo CY, Weetman AP, Eastell R. Longitudinal change[illegible]one mineral density and bo[illegible]nover in postmenopausal wo[illegible]n thyroxine. Clin. Edocrinol.(oxf) 1997:49:301-307.

(29) Parle JV, Franklyn JA, Cross KW, Jones SR, and Sheppard MC. Circulating lipids and minor abnormalities of thyroid function. Clin. Endocrinol. 1992; 37:411-414..

(30) Das SC, Isichei UP. Hypothyroidism and its effect on thyroid tissues and lipids. Indian J. Expt. Boil. 1988;2:92-94.

(31) Danese MD, Ladenson PW, Meinert CL, Powe NR. Effect of thyroxine therapy on serum lipoproteins in patients with mild thyroid failure: a quantitative review of the literature. J. Clin. Endocrinol. Metab. 2000;85:2993-3001.

(32) Verdugo C, Perrot L, ponsin G, Valentin C, Berthezene F. Time-course of alterations of high-density lipoproteins (HDL) during thyroxin administration to hypothyroid women. Eur. J. Clin. Invest. 1987; 17:313-316.

(33) Mueller B, Zulewski H, Huber P, Ratcliff JG, Staub JJ. Impaired action of thyroid hormone associated with smoking in women with hypothyroidism. N. Engl. J. Med. 1995; 333:964-969.

(34) Catelli WP, Garrison RT, Wilson PWF, et al. Incidence of coronary hert disease and lipoprotein cholesterol level: The Framingham Study. JAMA 1986;256:2835-2838.

(35) Scottolini AG, Bhagavan NV, Oshiro TH, Ade SY. Serum High-Density Lipoprotein Cholesterol Concentrations in hypo-and-hyperthyroidism. Clin. Chem.1980;26/5:584-587.

(36) Sasidharan VK. Effect of thyroid hormones on lipid metabolism and related atherosclerotic risk factors. Biomedicine 1996;16:64-68.