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Assessment of Lipids Profile in Hyperthyroidism Sudanese Patients in North Kordofan State, Sudan

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ABSTRACT

The objective of this study was to find out possible relationship between thyroid hormones and lipids profile levels in Elobeid city, North Kordofan State, during the period from March 2011 to March 2012. A total of 250 subjects were selected for this study. Out of 250 subjects, 150 were patients, Female to Male ratio was 2.75: 1.0 (100 patients were hyperthyroidism before treatment (new cases), 50 patients were currently under treatment (Evert hyperthyroidism) and 100 were apparently healthy individuals (ascertained as controls). Thyroid hormones were measured using ELISA technique. For cholesterol, triglycerides using enzymatic spectrophotometeric method and precipitation enzymatic method for HDL-C and LDL-C.T_3 and T_4 were significantly increased in new cases (3.9 ± 1.1 *p*-value <0.00) and (16.9 ±3.1 *p*-value <0.00) compared with control group (1.08 ± 0.4) and (8.07 ± 1.6) for T_3 and T_4, respectively.TSH was significantly reduced (0.05 ± 0.06 *p*-value <0.00) compared with control (2.6 ± 0.17). In patients under treatment T3, T_4 and TSH were not altered in comparison with control *p*-value (0.272, 0.633 and 0.061), respectively. Lipids profile, the total Cholesterol, LDL-C and HDL-C were significantly decreased (107 ± 10.9 *p*-values <0.00, (46.6 ± 10.4 *p*-values <0.039), and (35.6 ± 3.3 *p*-values <0.00) in compression with control groups (154 ± 67), (52 ± 7.2) and (79.3±12.9) for lipds profile respectivly. There was negative correlation between the level of lipids profile and thyroid hormones level (T3 and T4) and positively correlated with the triglycerides. It was concluded that T3 and T4, as well as triglycerides, are elevated in hyperthyroidism, while cholesterol is decreased.

المستخلص

هدفت هذه الدراسة الى ايجاد العلاقة بين هرمونات الغدة الدرقية ومستوى الدهون في البلازما لدي الاشخاص المصابين بفرط الدرقية. شملت الدراسة 250 شخصا منهم 150 شخصا مصابا بفرط الغدة الدرقية من الجنسين (نسبة الاناث للذكور 2.75 :1) تم تقسيمهم الي مجموعتين (100 شخص مصاب بنشاط الغده قبل تناول العلاج و50 شخص مصاب تحت تاثير العلاج) بالاضافه الى 100 شخص اصحاء كمجوعة ضابطة. تم تحليل عينات هرمونات الغدة الدرقية باستخدام تقنية الانزيم المناعي المرتبط بينما تم تحليل عينات الدهون بالطريقة الانزيمية المعتمدة على المطياف الضوئي.

أوضحت النتائج ان هناك زيادة في هرمونات الغدة الدرقية (T3 = 1.1 ± 3.9) ذو دلاله معنويه اقل من 0.00 وأن قيمة T4

(16.9±3.1) ذات دلالة معنوية اقل من 0.00. عند المقارنه مع المجموعه الضابطه (T3 = 0.4±1.08) و T4 تساوي (8.07±1.36). بينما لم يحدث تغير في هرمونات الغدة الدرقية لدى الاشخاص المصابين الذين هم تحت تاثير العلاج.
عند مقارنه تركيز الدهون في المرضى الذين يعانون من فرط الغدة الدرقية قبل تناول العلاج بالمجموعة الضابطة تبين وجود انخفاض ذو دلاله معنويه اقل من0.00 في مستوي الكلسترول(10.9± 107.3), كلسترول البروتين الدهني منخفض الكثافه (10.4±46.9) وكلسترول البروتين الدهني عالي الكثافة (3.3±35.6) مقارنة بالمجموعة الضابطة (7.2±52), (67±154) و (12.9±79.3) على التوالي بينما وجدت الجلسريدات الثلاثية بها زيادة (14.6 ± 122) ذات قيمة معنوية (0.00) مقارنة مع المجموعة الطبيعية (16.7 ± 67). أظهرت الدراسة وجود علاقة عكسية بين هرمونات الغدة الدرقية T3 و T4 ومستوى تركيز الدهون في البلازما. خلصت الدراسة الى ان نشاط الغدة الدرقية قد زاد من مستويات هرمونات الغدة الدرقية و الجلسريدات الثلاثية بينما مستوي الكلسترول انخفض.

KEYWORDS: evert hyperthyroidism, high density lipoprotein, low density lipoprotein, Enzyme-Linked Immunosorbent Assay (ELISA).

INTRODUCTION

Hyperthyroidism is a term for overactive tissue within the thyroid gland, resulting in overproduction and thus an excess of circulating free thyroid hormones: thyroxin (T_4), triiodothyronine (T_3), or both [(1)].

Human hyperthyroidism is accompanied by multiple abnormalities with increased energy expenditure and excessive mobilization and utilization of metabolic substrates [(2)].

With respect to lipid metabolism it is clear that the breakdown of triglycerides (TGs) stored in adipose tissue is enhanced by thyroid hormones excess, resulting in concentration and turnover of non-esterified fatty acids (NEFA) [(3)]. This increased availability of fatty acids is associated with a rise in the lipid oxidation rate [(2)].

At the hepatic level this contributes to an elevated production rate of ketone bodies [(3)]. Hyperthyroid patients have also low plasma cholesterol levels may be due to an increased biliary excretion of cholesterol [(4)].

However, hyperthyrodism was reported as public health problem in Kordofan state. Most of the studies done on thyroid patients directed to assess thyroid function (T_3, T_4). However, information concerning lipid profile is lacking or insufficient.

MATERIALS and METHODS

This study was conducted in Elobeid teaching hospital, North Kordofan state; samples were collected during the period from March 2011 to March 2012 from patients who underwent routinely medical assessment by medical doctors.

Blood samples were obtained from 150 subjects 40 male and 110 female. Age of the subjects ranged from 16 to 65 years, divided into two groups (100 new cases before starting the treatment and 50 with patients of hyperthyroidism under treatment) beside 100 subjects as control subjects. All patients included in this study were proved to be hyperthyroidism (clinically and according to laboratory diagnosis). Hypertensive patients, diabetics, pregnant, smokers, obese, alcoholic, those on lipid and contraceptive medications, and patients with renal and liver diseases were excluded, because these factors may affect the plasma lipid levels. Venous blood samples were drawn after 8 to12 hours of overnight fasting. Blood samples were left

to clot, after that; they were separated and kept in two plain tubes. One sample was stored in refrigerator at –20 ºC and later assayed to determine (T_3, T_4, and TSH) in hyperthyroidism patients, using ELISA state fax 2100 with human regents. Another sample used to measure lipids profile including; total cholesterol, triglycerides (TG), LDL-C, and HDL-C. These were measured by the Biosystem semi automated system using the Biosystem diagnostic kits.

Quality control: The precision and accuracy of all methods used in this study were checked using commercially prepared control sera and results ±2SD were accepted.

Statistical analysis

Computer software of Statistical Package for Social Science (SPSS) version 17 was used for data analysis. The mean and standard deviation, Linear regression as well as, Chi-square test with 95% confidence level were used. *P* value of less than or equal to 0.05 was considered statistically significant.

RESULTS

One hundred and fifty patients with thyroid disorder disease (divided into two groups, one hundred subjected were new cases and fifty subjected were Evert hyperthyroidism) were investigated for lipids profile. Moreover, one hundred control persons were subjected to the same investigations.

In this study the mean ages of new cases were 36.6 ± 7.9 years ranging (16-65 years), and mean age of new cases under treatment was 34.6±9.18 years ranging(15-65years), while mean age of control persons was 33±7.6 years ranging (17-65) years. There was no significant difference between ages of the three groups. The results of the present study that showed, approximate ratio of female to male Sudanese hyperthyroidism was 2.75:1 with percentage of 73 % females and 27 % males.

Table (1) illustrates the findings of thyroid level in control subjects and patients suffering hyperthyroidism (new cases).

T_3 and T_4 were significantly increased in new cases (3.9 ± 1.1) *p*-value <0.000) and (16.9±3.1 *p*-value <0.000) compared with control group (1.08±0.4) and (8.07±1.6) for T_3 and T_4, respectively.

TSH on the other hand was significantly reduced (0.05 ± 0.06 *p* value <0.000) compared with control (2.6±0.17).

Also the mean values of the total cholesterol, high density lipoprotein cholesterol and low density lipoproteins cholesterol were significantly decreased, (107 ± 10.9 *p*-values < 0.000), (46.6 ± 10.4 *p*-values <0.000), and (35.6 ± 3.3 *p*-values <0.000) in comparison with control groups (154 ± 67), (52 ± 7.2) and (79.3 ± 12.9), respectivly, while triglycerides slightly increased (122 ± 14.6 *p* - value 0.00) compared with control group (67 ± 16.7).

Table 1: Biochemical parameters in control and new cases suffering from hyperthyroidism

Variables	Control n = 100	New Cases n =100	*p*-value
Triiodotyronine (T_3) (ng/ml)	1.08 ± 0.4	3.9 ± 1.1	0.00
Thyroxine (T_4) (µg/dl)	8.07 ±1.36	16.9 ±3.1	0.00
Thyroid stimulating hormone TSH(miu/l)	2.6 ±1.17	0.05 ± 0.06	0.00
Triglycerides (TG) (mg/dl)	67 ± 16.7	122 ± 14.6	0.00

Total Cholesterol (mg/dl)	154.67 ±14.9	107.3 ± 10.9	0.00
High density lipoprotein (HDL) (mg/dl)	52 ±7.2	35.6 ± 3.3	0.00
Low density lipoprotein (LDL) (mg/dl)	79.3 ± 12.9	46.9 ± 10.4	0.00

- Results given in mean and ±SD
- P - value equal or less than 0.05 levels considered significant

Table (2) Shows the level of thyroid hormones and lipids in evert hyperthyroidism compared with control. No alteration of thyroid hormones level, (1.16 ± 0.42 *p*-value 0.272), (7.9 ± 0.94 *p*-value 0.663) and (2.25 ± 1.07 *p*-value 0.061) was seen when compared with control group (1.08 ± 0.4), (8.07 ± 1.36) and (2.6 ± 1.17) for T_3, T_4 and TSH, respectively. Lipids, total cholesterol, HDL-C and LDL-C were significantly decreased (131.98 ± 14.17 *p*-values <0.000), (45.04±5.43 *p*-values <0.000), and (68.36 ± 12.76 *p*-values <0.039) in comparison with control groups (154 ± 67), (52 ± 7.2) and (79.3 ± 12.9), respectivly, while triglycerides slightly increased (91.98 ± 12.63 *p* – value 0.00) compared with the control group (67 ± 16.7). Table (3) shows a comparison of thyroid hormones and lipoprotein in females and males in new case of hyperthyroidism. Table (4) illustrates the correlation between thyroid hormones and lipids profile in new hyperthyroidism patients.

Table 2: The level of thyroid hormones and lipids in evert hyperthyroidism compared with control

Variables	**control n =100**	**Evert hyperthyroidim n =50**	***p*-value**
Triiodotyronine (T_3) (ng/ml	1.08±0.4	1.16 ± 0.42	0.272
Thyroxine (T_4) (µg/dl)	8.07±1.36	7.9 ± 0.94	0.663
Thyroid stimulating hormone TSH (miu/l)	2.6±1.17	2.25 ± 1.07	0.061
Triglycerides (TG)	67 +16.7	91.98 ± 12.63	0.00
Total Cholesterol (mg/dl)	154.67±14.9	131.98 ± 14.17	0.00
High density lipoprotein (HDL) (mg/dl)	52±7.2	45.04 ± 5.43	0.00
Low density lipoprotein (LDL) (mg/dl)	79.3 +12.9	68.36 ± 12.76	0.039

- Results are given in mean and ± SD.
- P.value equal to or less than 0.05 was considered significant.

Table 3: Comparison of thyroid hormones and lipoprotein in females and males in new case of hyperthyroidism

Variables	Sex	Mean	*p*-value
T_3	Female	3.98 ± 1.17	0.470
	Male	3.87 ± 1.12	
T_4	Female	17.53 ± 3.5	0.938
	Male	15.28 ±2.89	
TSH	Female	0.053 ± 0.061	0.215
	Male	0.052±0.06	
LDL-C	Female	47.8±10.6	0.070
	Male	46.0±10.1	
HDL-C	Female	35.8±3.4	0.606
	Male	35.2±3.	

Table 4: The correlation between thyroid hormones and lipids profile in new hyperthyroidism patients

Variables	TC	TAG	HDL	LDL
	r^2	r^2	r^2	r^2
T3	-0.524**	+0.409**	-.0365**	-0.507**
T4	-0.243**	+0.103**	-0.141**	-0.254**
TSH	+0.05*	-0.039*	+0.050*	+0.116**

**Correlation is significant at <0.01 level (2-tailed).
*Correlation is significant at 0.05 levels (2-tailed).

r^2 = strength of correlation, (-) inversely correlation, (+) proportional correlation.

DISCUSSION

In this study, the prevalence of hyperthyroidism was more common in women than in men with a ratio of 2.75: 1 Showed low ratio when compared with previous international study that reported hyperthyroidism is generally affects females and males with a ratio of approximately 10:1 respectively [5]. This difference in the prevalence may result from immunological changes that increase thyroid hormone levels.

This study revealed that, there is significant difference when compare the mean concentration of thyroid hormones (T_3, T_4 and TSH) of the newly discovered group with controls group, resulting in p-value (<0.000, <0.000 and <0.000) for the T_3.T_4 and TSH respectively. In evert hyperthyroidism T3, T4 and TSH were nor altered in comparison with control *p*-values (0.272, 0.633 and 0.061) for T_3,T_4 and TSH respectively. This finding is confirmed by previous study [6].

Our results showed that there was significant difference between mean concentration of lipids profile (Cholesterol, triglycerides, LDL-C and HDL-C) of the new cases group with controls group. *p*-values (<0.000, <0.000,

<0.000 and <0.000) for cholesterol, triglycerides, LDL-C and HDL-C) respectively. The presented results showed negative correlation between triiodthyronin (T3) and lipid levels (total Cholesterol, LDL-C and HDL-C) (r^2 0.524, 0.365 and 0.507) respectively, while T3 had positive correlation with the triglycerides (r^2 0.409).On others hand TSH hormones had proportional correlation with total Cholesterol, LDL-C and HDL-C (0.05, 0.05 and 0.116, respectively.

Both T_4 and T_3 can mediate thyroid hormone responses, T_3 is more potent and binds the thyroid hormone receptor with 15 fold greater affinity than T_4 [(7)].

The presented results also showed no significant differences in the concentration of LDL-C and HDL-C was observed between the values of females and males for the new cases group with *p*-values = (0.07 and 0.606) for LDL-C and HDL-C respectively

The results of the present study showed that total cholesterol, HDL-C and LDL in new cases were decreased in hyperthyroidism in comparison with control group.

Our study agrees with studies conducted by Cachefo, *et al.* 2001, Rizos, *et al*. 2011, and Nouh, *et al.* 2008, they found that hyperthyroidism is associated with decrease the level of total cholesterol, HDL-C, and LDL-C, while TGs is slightly increased.[(8,9)]

Our findings disagree with results obtained by Sahr, 2011, who found that hyperthyroid did not affect lipid levels of patients in Saudi Arabia.

It has been hypothesized that the low plasma cholesterol level of hyperthyroidism patients may be due to an increased clearance rate [(4)]. However, thyroid hormones induce the 3-hydroxy-3-methylglutaryl-coenzyme A(HMG-CoA) reductase, which is the first step in cholesterol biosynthesis [(10)]. On the other hand, the LDL receptors are increased resulting in low cholesterol concentration [(11,12)]. Thyroid hormones can influence HDL metabolism by increasing cholesterol ester transfer protein (CETP) activity, which exchanges cholesteryl esters from HDL_2 to the very low density lipoproteins (VLDL) and TGs to the opposite direction [(13)].

Also our study showed that triglycerides (TGs) of new cases (122 ± 14.6) were significantly increased when compared with controls subjects (67 ± 16.7, p-value < 0.000).

The elevation of triglycerides (TGs) may be due to breakdown of TGs stored in a dipose tissue which is enhanced by thyroid hormones excess [(3)].

Our findings agreed with findings reported by Esko, *et al.* 1972, where they found that in thyrotoxicosis the mean triglyceride level was slightly increased above that of control subjects. Thyroid hormones control both production and removal of plasma triglycerides [(14)].

CONCLUSIONS

The present study concluded that, thyroid dysfunction was more common among females than males. In addition, Hyperthyroidism was associated with decrease in total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol and slightly increase in serum triglycerides compared with control.

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