ORIGINAL ARTICLE

Abnormalities of Renal and Lipid Profile in Patients with Thyroid Dysfunction and its Implications

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ABSTRACT

Background: Lipid and renal profile is markedly influenced by thyroid disorders; however, the relationship among them has not been analyzed in detail in human.

Methodology: The blood samples of thirty each hyperthyroid, hypothyroid patientand sex-matched clinically apparently healthy individuals were recruited for the present study. TG, LDL, HDL, total cholesterol, creatinine, urea and uric acid were determined with commercial kits.

Results: The results of the present study show that the lipid profile in the patients of hypothyroidism and hyperthyroidism differed significantly. The levels of TCh, TG and LDL were higher (189.45±6.83 mg/dl, 188.67±8.35 mg/dl and 98.27±5.87 mg/dl) in hypothyroid patients as compared to hyperthyroid group (244.39±5.26 mg/dl, 207.52±5.26 mg/dl and 107.56±2.76 mg/dl respectively). Renal profile of hypothyroidism and hyperthyroidism also differed significantly for creatinine, uric acid and urea. Higher levels of urea, uric acid and creatinine were recorded in hypothyroid patients (94.57±2.77 mg/dl, 8.10±0.28 mg/dl and 2.16±0.38mg/dl) in contrast to hyperthyroid group (87.63±1.98 mg/dl, 7.60±0.19 mg/dl and 1.07±0.16 mg/dl respectively) as compared to control.

Conclusion: The present study demonstrated that patients with hyperthyroidism had increased levels of TCh and LDL as compared to patients of hypothyroidism. Increased lipid contents remain associated with cardiovascular diseases hence the risk of cardiovascular and renal diseases remain higher in the patients with thyroid disorder.

Keywords: Thyroid disorders, cardiovascular disease, renal dysfunction, lipid profile, renal profile

INTRODUCTION

One of the largest gland in body remains thyroid gland itreleasestriiodothyronine (T3) and thyroxin (T4)[1].These are essential mediators act in metabolism and these hormones maintain homeostasis in body[2]. Thyroid diseases are caused by the disturbances in thyroid hormone secretion, inflammations or tumors of the thyroid gland[3]. Two common thyroid diseases are hyperthyroidism and hypothyroidism[4].Hyperthyroidism is a condition in which there are excessive thyroid hormones in circulation due to increase synthesis of hormones from hyperactive thyroid gland, caused by Graves' disease, multinodular goiter, sub-acutethyroiditisand tumors having symptoms like palpitation, anxiety, fatigue, weight loss, heat intolerance and muscle weakness[5]. Hypothyroidism is a clinical disorder due to iodine deficiency, autoimmune diseases and congenital abnormalities, resulting in the slowing down of metabolic processes[6].

All major metabolic pathways are affected by thyroid hormones, asin case of lipid metabolism, degradation, synthesis and mobilization of lipids are affected by means of thyroid hormones[7].In both, hyperthyroidismand hypothyroidism alterations observed in levels of total cholesterol (Tch), triglycerides (TG), low density lipoprotein (LDL),and high density lipoprotein (HDL) levels[8]. Triglyceride levels are found to be increased in hyperthyroid patients, may occur due to in-vivo increased turnover and non-esterified fatty acids are transported to the liver that than contribute in hepatic triglyceride synthesis and release[9].Due to increase cholesteryl ester transfer protein (CETP) contributes in transfer of cholesteryl esters from HDL to VLDL and increases enzyme namedhepatic lipase (HL) dependent catabolism of HDL-2 leading to its decreased levels. In

hyperthyroid patients, LDL-C levels are reduced because of increased expression of LDL receptors which results in LDL receptor mediated catabolism of LDL particles[10].Cholesterol levels are also low because of increased biliary excretion of cholesterol[11].Hypertriglyceridemia occurs in hypothyroidism despite of the LPL deficiency. The hypercholesterolemia occurs in hypothyroidism mainly due to decrease action of LDL receptors that results in decreased receptor- mediated catabolism of IDL and LDL[12]. The HDL-C levels increased due to decrease activity of CETP which results in decreased transfer of cholesteryl ester from HDL to VLDL[13].

The proteinmetabolic abnormalities including increased serum creatinine and uric acid levelin hypothyroidism due to reduction in glomerular filtration rate. Decreased renal plasma flow and impaired glomerular filtration are the secondary causes of hyperuricemiain hypothyroidism[14]. Extent to which liver synthesizes urea was increased in rats with hypothyroidism as activities of some of the enzymes were altered[15].Hyperthyroidism also affects protein metabolism, as protein breakdown is increased and hyperuricemia occurs because of increased purine nucleotide turnover and reducedrenal urate excretion[16]. Thyroid dysfunction affects serum creatinine concentration in hyperthyroidism as GFR is increased; there is increase in creatinine clearance and increase in creatinine tubular secretion which cause low creatinine levels[17]. Serum creatinine is also decreased due to reduction in overall muscle mass[18].Due to excessive protein catabolism, urea nitrogen production is increased and its excretion is decreased which causes high level of blood urea nitrogen (BUN) in hyperthyroid patient[19]. So the present study was designed to assess the implications for thyroid hormone inflections responsible for cardiovascular disease progression and renal dysfunction in patients with thyroid disorders.

MATERIALS AND METHODS

Blood samples were taken from thirty hyperthyroid and thirty hypothyroid patients each for the sake of present study. Afterwards for the controls thirty more healthy individuals were included in the study. All the protocols applied were according to the REC (Research Ethical Committee) of IMBB (Institute of Molecular biology and Biotechnology) at University of Lahore. For the purpose 5ml venous blood was drawn from anticubital vein of each of the subject. All the samples were centrifuged within an hour of their collection from the patients so the serum may be separated and is then allowed to store at -70°C until it is used.

DETERMINATION OF LIPID PROFILE

For the determination of Lipid profile method of Gidez*et al*.[20] was employed. All the blood samples were centrifuged prior to their analysis so that plasma and RBCs may be separated. Apart from that the concentrations of total cholesterol, triglycerides and LDL in the serum of patients were evaluated by the help of ELISA kit commercially available manufactured by (Randox Laboratories, Crumlin, England). For the sake of HDL determination within the plasma same kits were employed as that were used to determine the levels of low density of lipoprotein (LDL) and very low density lipoproteins (VLDL) which were precipitated with heparin-$MnCl_2$ solution.

DETERMINATION OF CREATININE

Determination of creatinine was done by the method of Krishnegowda*et al*.[21]for this purpose spectrophotometer with special cuvets made up of quartz was used for the absorbance measurement. While chemicals used were of analytical grade. Reagents were especially prepared by the using double distilled water for keeping its sensitivity intact as reagents once prepared are then stored in amber colored standard flasks which were then kept in refrigerator at 4^oC. Stock solution of acetate buffer of concentration 10mM at the pH 5.4 was also synthesized for the sake of study.

DETERMINATION OF URIC ACID

Lippi,[22] method was used especially for the determination of uric acid which uses a special kit named uric acid calorimeter assay kit. Uric acid is the final product in the result of Purine metabolism. Uric acid is converted to certain products like allantoin by the expense of specialized enzyme named uricaseand this allantoinis further changed into hydrogen peroxide. Following hydrogen peroxide is found to be involved in several phenolic compounds and 4 aminoantipyrine by their catalytic action of peroxidase which synthesized a red coloured quinoneimine dye complex. Colour intensity is believed to be directly proportional to the amount of uric acid present in the sample. Finally their absorbance was measured at 520 nm by the help spectrophotometer.

DETERMINATION OF UREA (PHENYLALANINE ASSAY):

Friedman and Young,[23] specialized method was used for the determination of Urea. For this reason first of all, media is diluted to5 µL of the 100 mM, then standard solution for urea with almost 995 µL of Urea Assay Buffer was prepared to about 0.5 mM of standard solution. These different ratios were added in amounts(0, 2, 4, 6, 8, and 10 µL) of the 0.5 mM Urea standard solution into a 96 well plate in which one is kept blank while 1,2,3,4,5th well were considered as standards. Then they were added with Assay buffer of urea in each of 96 wells so, to bring the final volume to 50µL. Serum was then allowed to centrifuge at 13000rpm for almost ten minutes at temperature of 4°C in a sense to remove all insoluble materials. Serum was then added in the wells for analysis.

RESULTS

The data presented in Figure 01 shows that the lipid profile in the patients of hypothyroidism and hyperthyroidism differed significantly for TCh (p=.032), TG (p=.043), HDL (p=.019), LDL (p=.026) respectively. The levels of TCh, TG,HDL and LDL were higher (244.39±5.26 mg/dl, 207.52±5.26 mg/dl, 65.95±2.76 mg/dl and 107.56±2.76 mg/dl respectively) in hypothyroid patients as compared to hyperthyroid group (189.45±6.83 mg/dl, 188.67±8.35 mg/dl, 53.45±2.87 mg/dl and 98.27±5.87 mg/dlrespectively) and when both were compared to control. Renal profile of hypothyroidism and hyperthyroidism differed significantly for urea (p=.001), uric Acid (p=.032) and creatinine (p=.019) respectively in figure 02. Higher levels of urea, uric acid and creatinine were recorded in hypothyroid patients (94.57±2.77 mg/dl, 8.10±0.28 mg/dl and 2.16±0.38mg/dl) in contrast to hyperthyroid group (87.63±1.98mg/dl, 7.60±0.19mg/dl and 1.07±0.16mg/dl respectively)as compared to control.

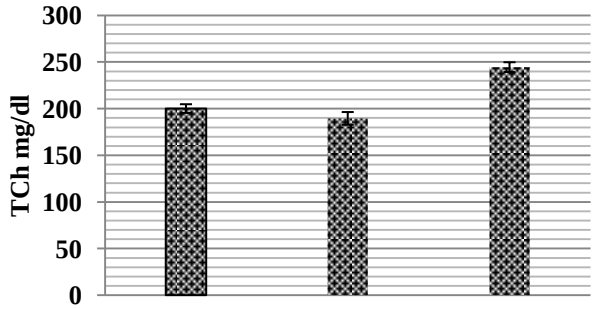
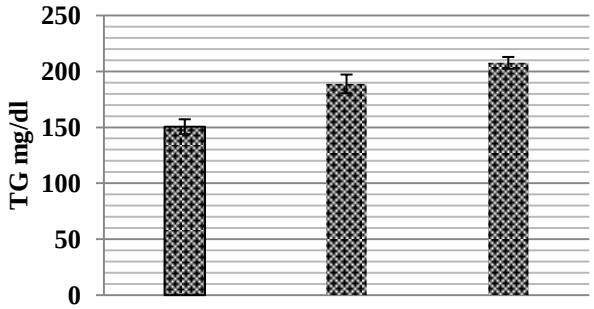


FIGURE (A)



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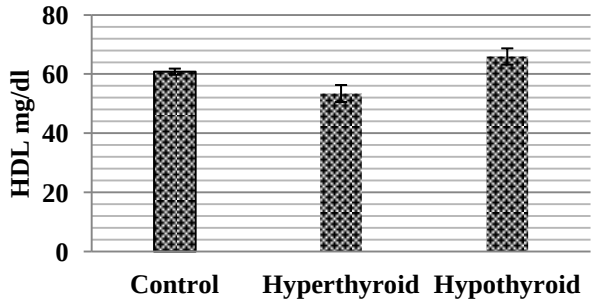

FIGURE (C)

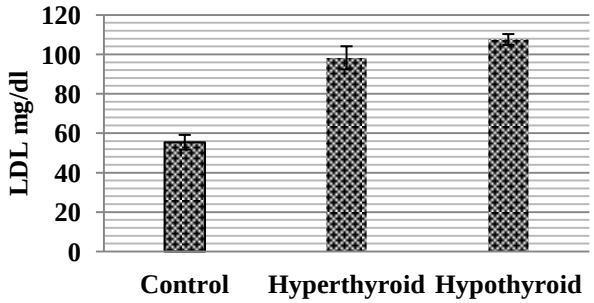

FIGURE (D)

Figure 1: Lipid Profile of Patients with Thyroid Disorders Responsible for Cardiovascular Disease Progression

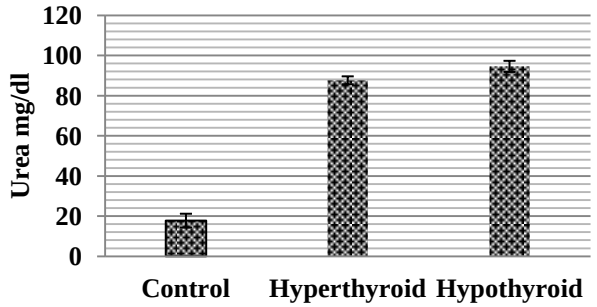

FIGURE (A)

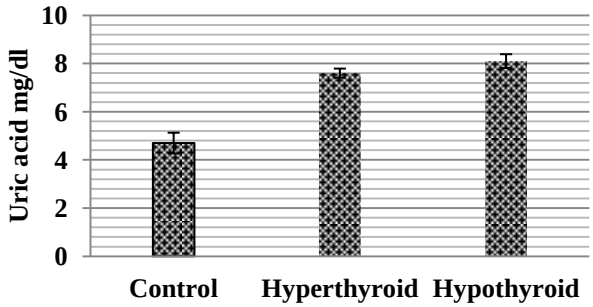

FIGURE (B)

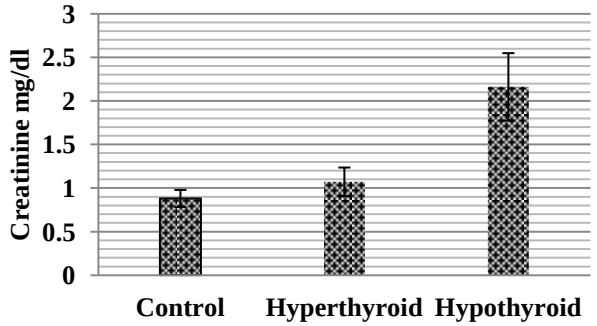

FIGURE (C)

Figure 2: Renal Profile Of Patients With Thyroid Disorders Responsible For Renal Dysfunction

STATISTICAL ANALYSIS

The study design of the present study was comparative to lipid and renal profile in hyperthyroid and hypothyroid patients susceptible to cardiovascular and renal complications. Independent t-test was performed to assess the significance between different variables performed.P value was set at < 0.05.

DISCUSSION

In the present study, insignificant increase in serum HDL levels was observed in hypothyroid patients as compared to control group. The outcome was correlated with the study of Dullaart*et al*.[13]. They observed that HDL-C levels increased due to decrease activity of CETP which result in decrease transfer of cholesteryl ester from HDL to VLDL[24].In hyperthyroid patients, significant reduction in HDL level was found in the present study as compared to control group as the result was highly correlated with the work of Altahir*et al.*[25].They also observed low HDL level in hyperthyroid patients. Significant elevation in serum total cholesterol levels was observed in hypothyroid patients as compared to control group as the findings were correlated with the study of Guyton *et al*.[26].A significant reduction in serum TCh was observed in hyperthyroid patients as compared to control group and similar findings were suggested by Altahir*et al.*[25]. They also estimated lipid profile in hyperthyroid patients and found that TCh levels were lowered in those patients. It has been revealed that the reduced HMG-CoA reductase activity is due to decreased thyroid function, so LDL levels were elevated in patients with overt hypothyroidism[27,28]. The significant increases in serum LDL levels were observed not only in the hypothyroid patients but also in the hyperthyroidpatients as compared to control group, the results were in contrary to Alterihy*et al*.[29].The significant increase in serum triglyceride levels was observed in both hypothyroid and hyperthyroid patients as compared to control group. In the present study, significant elevation in serum creatinine levels was observed in hyperthyroid patients as compared to control group and the results were contrary with results of Stojanoski*et al*.[30], as they observed reduced creatinine levels in hyperthyroid patients. In patients with hyperthyroidism, body mass is decreased that results in decrease in muscle mass that causes lower serum creatinine concentration[31]. Significant increase in serum

creatinine levels was observed in hypothyroid patients as compared to control group, the result was correlated with the study of Karanikas*et al*.[14]. They observed that in hypothyroid patients serum creatinine level increased due to reduction in glomerular filtration rate[32].A significant increase in serum urea levels was observed in hypothyroid patients as compared to control group in the present study. The result was correlated with the study of Marti*et al*.[15].Patients of hyperthyroidism had significant elevation in serum urea concentration as compared to control group. The outcome was highly correlated with results of Aizawa*et al*.[19] who also observed high serum urea concentration. Significant increase in serum uric acid levels was observed in hypothyroid patients as compared to control group, similar findings were revealed by Khan and Majumder,[33]. The hyperuricemia may be due to reduction in both the renal plasma flow and urate excretion in hypothyroidism[34,35]. Significant elevation in serum uric acid was observed in hyperthyroid patients as compared to control group. The result was highly associated with several studies which observed high serum uric acid concentration. The increase in serum uric acid levels in hyperthyroid patients is due to increase purine nucleotide turnover[36].

CONCLUSION

The present study concludes that hypothyroidism affects more negatively on lipid and renal profile than hyperthyroidism. It is suggested that early detection and treatment of thyroid dysfunction may be helpful in reduction of cardiovascular and renal disease.

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