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Original Research Article

Evaluation of serum Adiponectin and lipid fractions in newly diagnosed hypothyroid patients

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Abstract: Thyroid abnormalities are accompanied by changes in intermediary metabolism including alteration in body weight, insulin resistance, lipid profile. Changes in adiponectin have been reported in patients with thyroid dysfunction. But the evidence is controversial. This study was done to evaluate the levels of serum adiponectin levels and lipid fractions in newly diagnosed hypothyroid patients and compare with euthroid controls. A case control study was carried out on patients attending OPD, Department of Medicine RMRI, Bareilly. 100 cases of newly diagnosed hypothyroid cases were taken. 100 age and sex matched euthyroid subjects were taken as a control. All the biochemical parameters (adiponectin, plasma glucose, serum cholesterol, triglyceride, HDL-C, LDL-C, VLDL-C) were evaluated in both the groups. Statistical analysis was done using SPSS 20.0 version. Data was expressed in "mean ±SD". Student t- test and Pearson correlation coefficient was used to find out any significance. The result of this study showed that the level of adiponectin (Hypothyroid; 6.12±2.02 µg/ml; control; 6.59±1.44 µg/ml) decreased marginally (p=0.059) which is statistically insignificant. The levels of total cholesterol, triglyceride, LDL-C, VLDL were significantly increased which is statistically highly significant (p=.000). In our present study the findings suggests that total cholesterol, triglyceride, VLDL and LDL-C levels were significantly increased in hypothyroid patients compared with control group where HDL-C levels were slightly increased. This finding indicates that thyroid dysfunction alters lipids metabolism in our body. These lipid parameters should be evaluated and monitored regularly to predict the future outcome of cardiovascular diseases. The marginal increase of adiponectin level indicates that metabolic changes associated with thyroid disorder are not due to variations in serum alteration of adiponectin though more extensive study with increased sample size may provide more insights.
Keywords: Hypothyroidism. Adiponectin, Cholesterol, Triglyceride, HDL-C, LDL-C

INTRODUCTION

Dysfunction and metabolic abnormalities of thyroid are among the most common disease of the endocrine glands [1]. Estimates of the incidence of hypothyroidism vary depending on the population studied. The burden of thyroid disease in general population of India is enormous [2]. Data from various studies suggest that, in India approximately 42 million people suffer from thyroid abnormalities [3]. The incidence of hypothyroidism is higher among women, the elderly and in some racial groups [4].

Thyroid dysfunction leads to changes in intermediary metabolism including alteration in body weight, insulin resistance and lipid profile [5]. The changes are due to cumulative effect of thyroid hormones on various metabolisms occurring on various organs like liver, muscle and also adipose tissue. Adipose tissue is nowadays recognized as a highly

active metabolic and endocrine gland which secretes various adipokines, like adiponectin, resistin, leptin. Among the various adipokines only adiponectin shows anti-inflammatory and antiatherogenic properties [6]. Though adiponectin is secreted from adipose tissue, its levels are decreased in obese and also type 2 diabetes [7,8]. Adiponectin and thyroid hormones share some common physiological role like thermogenesis lipid oxidation [9]. Changes in adiponectin level have been reported in thyroid patients but the evidence is controversial [10,11]. Another interesting finding is that high levels of TSH receptors are also expressed on adipocytes [12]. This indicates the possible role of TSH in the regulation of adipocyte function including adiponectin secretion.

Studies regarding adiponectin level in thyroid dysfunction are very limited, mainly in Indian population. Therefore in the present study we evaluated serum levels of adiponectin along with serum cholesterol, triglyceride, LDL-C, HDL-C in newly diagnosed hypothyroid patients.

MATERIAL AND METHOD

The present case control study was conducted in the Department Biochemistry of Rajshree Medical Research Institute, Bareilly, India during the period from February 2015 to September 2016.The study was performed on the patients attending the Medicine OPD of RMRI hospital. Ethical clearance was procured from Institutional Ethical Committee with vide reference no RMRI.Bly/2014-15/101. 100 cases of newly diagnosed hypothyroid patients age group between 25 to 45 years were selected. Selection criteria of the patients were based on biochemical laboratory investigation (increase TSH> 6.16 μIU/ml and decrease T_3, T_4 , fT_3 and fT_4 respectively) and clinical sign and symptoms. 100 age, sex matched healthy euthyroid controls were taken and all the biochemical parameters (Blood glucose, Adiponectin, Cholesterol, Triglyceride, HDL-C, LDL-C, LDL-C, VLDL) were measured in both the groups.

The following patients were excluded from our study

- Subjects taking medication affecting thyroid hormone levels such as antithyroid agents and hypolipidemic agents were excluded from our study.
- Diabetes, Tuberculosis, hypertension, cancer, known cases of HIV.
- Pregnant women and women with contraceptive pills.
- Obese subject BMI >35.

All the patients were explained about aim, objective of the study and written consent was obtained. Detail history was taken from all the patients. Height and weight of all the subjects were measured. The body mass index (BMI) of the subjects was calculated as per convention:

$$\text{BMI} = \frac{Weight\ in\ Kg}{Height\ in\ m^2}$$

Biochemical analysis

The blood of the subjects was collected after an overnight fast. The serum was extracted immediately and stored at -20^o C until analyzed. Thyroid profile (T_3, T_4, fT_3, fT_4, TSH) test was done using ELISA method (Avantor, USA). Serum adiponectin level was estimated by quantitative sandwich ELISA method (CUSA Biotech, USA). Plasma fasting glucose level was done by glucose oxidase/peroxidase method (ACCUREX, India). Total cholesterol was estimated by enzymatic end point cholesterol esterase-peroxidase method (ACCUREX, India). Triglycerides were measured by glycerol phosphate oxidase- peroxidase method (ACCUREX, India). HDL-C was estimated by direct enzymatic end point assay based on precipitation method (ERBA, Germany). LDL -C and VLDL were calculated using Friedewald's formula [13].

Statistical analysis

Statistical analysis was performed using SPSS version 20.0. All data were expressed as "mean ±SD". Student t- test and Pearson's correlation coefficient was used to find out statistical significance. p value which were $\leq$ 0.05 were considered to be statistically significant. ROC curve analysis was done to find out the cut off value of various parameters.

RESULTS

The demographic characteristics and BMI of our study population for hypothyroid patients and control groups is shown in Table-1. The mean BMI of hypothyroid patients were significantly higher than the control group (BMI for hypothyroid 25.44±1.99; for control 23.52±1.56) with p value <0.0001. In our study the number of female patients (56/100) was more than that of males (44/100). The maximum number of patients in our study was in the age group of 36 to 45 years (n=59).

Table -2 shows the normal values of TSH, T_3, T_4, fT_3, fT_4 as well observed values in hypothyroid subjects and controls. We found that TSH value was significantly high ($p<0.0001$) in hypothyroid cases (47.77±23.79 µIU/ml) while T_3, T_4, fT_3, fT_4 were significantly low ($p<0.0001$).

Comparison of various biochemical parameters is shown in Table-3. The mean serum adiponectin level in hypothyroid patient was 6.59±1.44 µg/ml as compared with control group it was found 6.12±2.02 µg/ml ($p=0.059$). The levels of total cholesterol (246.89±34.98mg/dl) triglyceride (183.82±64.30mg/dl) LDL-C (160.95±28.53mg/dl) were significantly higher than the control group ($p=<0.0001$). But there was no significant increase for HDL- C for hypothyroid group (HDL-C for hypothyroid group 46.30±10.63; for control 49.18±11.67) as compared with euthroid control with p value 0.07.

Table-4 shows correlations of various parameters with TSH in hypothyroid cases. Total cholesterol shows a strong positive correlation with TSH (r=0.74) where adiponectin shows negative correlation with TSH (r = -.20).

Figure-1 shows negative correlation of adiponectin with BMI in hypothyroid patients with r value - 0.62.

When plotted in ROC curve in hypothyroid patients vs. control groups best cut off value obtained for total cholesterol was 211.6 mg/dl with 87% sensitivity and 90% specificity with AUC 0.952 (Figure-2). For triglyceride the best cut off value obtained was 161 mg/dl with 60 % sensitivity and 75% specificity (Figure-3). Best cut off value for LDL cholesterol was obtained 137.85 mg/dl with 77% sensitivity and 89% specificity (Figure-4).

Table-1: Demographic characteristic and BMI of study population

Parameters	Controls (n=100) (Mean±SD)	Hypothyroid cases(n=100) (Mean±SD)
Age(Yrs)	36.63±5.38	36.74±5.2
Mean age of Males	36.06±5.48	36.79±5.70
Mean age of Females	37.07±5.31	36.69±4.74
BMI(Kg/ m^2)	23.52±1.56	25.44±1.99

Table-2: Thyroid profile in hypothyroid cases and control

Parameter	Normal range	Controls (Mean±SD)	Hypothyroid cases (Mean±SD)	p-value
T3 (ng/ml)	0.52-1.85	1.18±0.32	0.48±0.18	<0.0001
T4 (µg/dl)	Males: 4.4-10.8 Females: 4.8-11.6	7.25±1.98	2.87±1.20	<0.0001
FT3(pg/ml)	1.4-4.2	2.96±1.10	0.98±0.39	<0.0001
FT4(ng/dl)	0.8-2.0	1.33±0.42	0.57±0.34	<0.0001
TSH (µIU/ml)	0.39-6.16	2.71±1.35	47.77±23.79	<0.0001

Table-3: Comparison of biochemical parameters between two groups

Parameters	Controls (Mean±SD)	Hypothyroid cases (Mean±SD)	p- value
Fasting plasma glucose(mg/dl)	83.25±10.76	86.41±8.96	0.025
Adiponectin (µg/ml)	6.59±1.44	6.12±2.02	0.059
Total Cholesterol (mg/dl)	172.42±32.62	246.89±34.98	<0.0001
Triglyceride (mg/dl)	132.95±38.33	183.82±64.30	<0.0001
HDL-C (mg/dl)	46.30±10.63	49.18±11.67	0.07
LDL-C (mg/dl)	99.52±30.79	160.95±28.53	<0.0001
VLDL-C(mg/dl)	26.59±7.66	36.76±12.86	<0.0001

Table-4: Correlation of different biochemical parameters with TSH in hypothyroid cases

Parameters	r value
Total Cholesterol	0.74
Triglyceride	0.53
HDL-C	0.56
LDL-C	0.44
VLDL-C	0.53
Adiponectin	-0.20

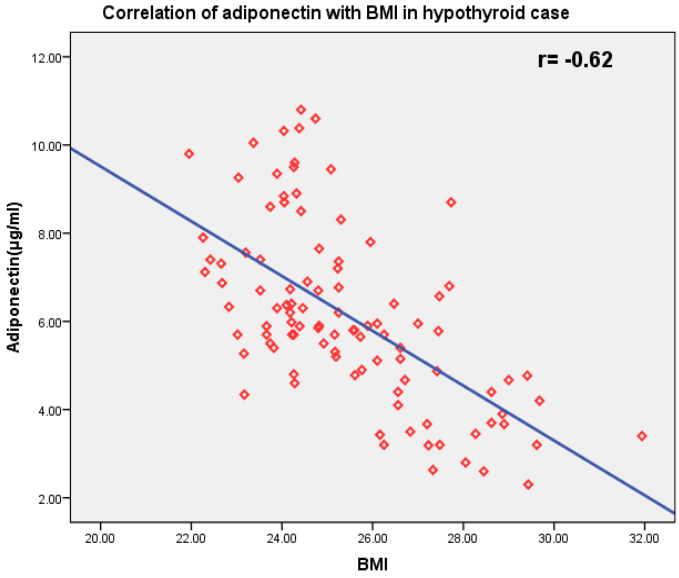

Fig-1: Correlation of Adiponectin with BMI in hypothyroid cases

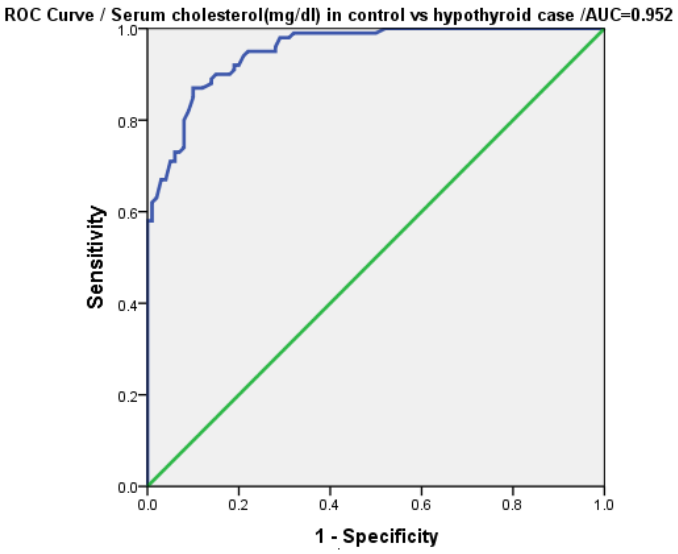

Fig-2: ROC curve/ Serum cholesterol (mg/dl) in control vs. hypothyroid cases

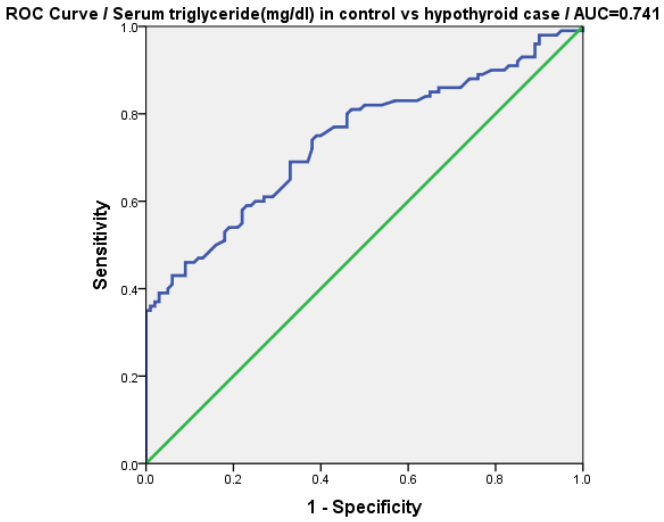

Fig-3: ROC Curve/Serum Triglyceride in control vs. hypothyroid cases

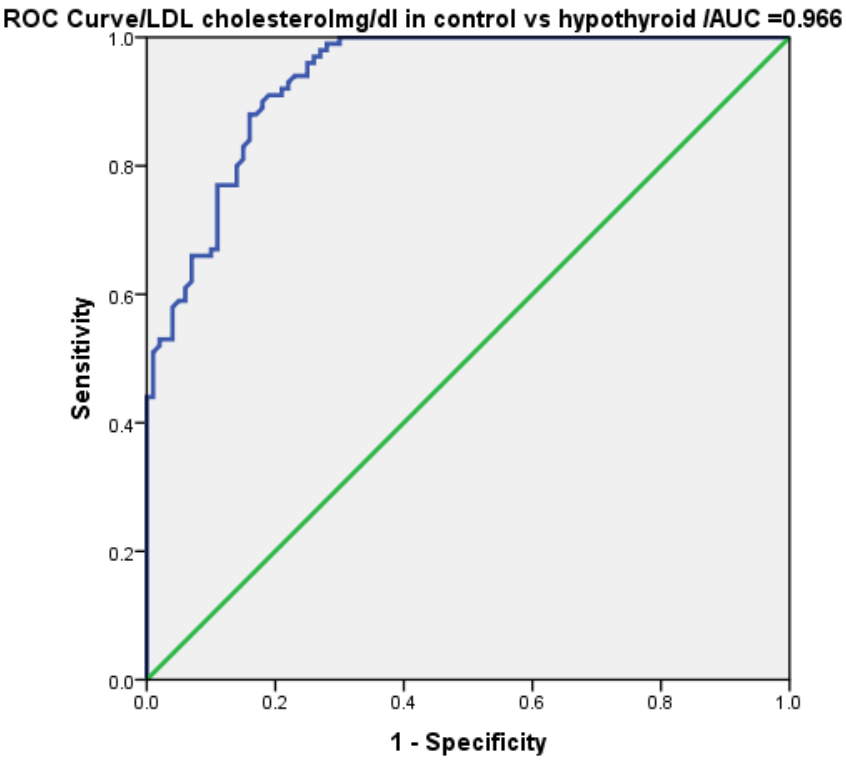

Fig-4: ROC Curve / Serum LDL-C (mg/dl) in control vs. hypothyroid cases

DISCUSSION

Adiponectin is mainly derived from adipose tissue and circulates at a high concentration in human plasma. In our present study we found that the level was decreased marginally in hypothyroid patients (6.12±2.02 µg/ml) as compare to euthyroid control (6.59±1.44 µg/ml) which is statistically insignificant (p=0.059). We found that there was a positive association between thyroid hormones and serum adiponectin level and negative association between TSH and adiponectin (r= -0.20). Santini F et al. conducted similar studies in agreement to our result and found that metabolic changes associated with thyroid disorder are not due to variations in serum alteration of adiponectin[11]. Another important finding in our study was that there was a negative correlation between BMI and serum adiponectin level (r= -0.62). Study conducted by Wei Shiung Yang *et al*. showed that Hypoadiponectinemia was associated with obesity and weight reduction increased the plasma level of adiponectin [7,14]. In our study the marginally decrease of adiponectin in hypothyroid subjects may be due to consequence of increase BMI of hypothyroid group (mean±SD 25.44±1.99) in comparison to control group (mean±SD 23.52±1.56). Study conducted by Miyao et al. shows that dyslipidemia is associated with low plasma adiponectin level in non diabetic women [15]. They found that low plasma adiponectin leads to hypertriglyceridemia and low high density cholesterol (HDL-C) level in non diabetic women. In our study we found that all the lipid parameters (total cholesterol, triglyceride, LDL-C, VLDL-C) were significantly increased (p =.000) compare to euthroid controls. But the mean value of high density lipoproteins were slightly increased in hypothyroid patients (hypothyroid patients; 49.18±11.67mg/dl ; control; 46.30±10.63mg/dl) which is statistically insignificant (p=0.07). Such findings are in accordance to study conducted by Sanjiv Kumar Bansal et al.[16]. However such marginal increase of HDL-C is not antiatherogenic because hypothyroidism may induce dysfunctional HDL-C with increase pro-oxidative and pro-inflammatory properties [17]. Our findings contradict the study conducted by Sridevi V et al. regarding the levels of HDL-C in hypothyroid subjects [18]. They found that there was decrease in HDL-C in hypothyroid subjects compare to euthyroid control.

In hypothyroidism though the main rate limiting enzyme of cholesterol biosynthesis i.e. HMG CoA reductase activity is reduced but total cholesterol and LDL- C levels are increased in patients[19]. The mechanism behind this is due to decrease LDL-receptor's activity, which results in decrease catabolism of LDL and IDL [20,21]. Decrease lipoprotein lipase activity results low clearance of triglyceride rich lipoproteins in hypothyroid patients, which leads to increase levels of triglycerides and VLDL [22]. Hypothyroid patients may exhibit raised HDL-C level. This is due to increased concentration of HDL_2 particle. In hypothyroidism hepatic lipase (HL) activity is reduced and as a result a decrease HDL_2 catabolism is observed [23]. Decrease activity of the CETP results in reduced transfer of cholesteryl esters from HDL to VLDL, which results in increase HDL cholesterol level [24]. Outcome in our study have also been in accordance with the proposed mechanism but we found that there was a marginal increase of HDL-C which is statistically insignificant when compared with euthyroid controls. When ROC curve analysis was done it shows the best cut off value of cholesterol in serum is 211.6 mg/ dl compare to healthy control with 87% sensitivity and 90% specificity and the area under curve was 0.952. For LDL-C the best cut off value we found is 137.85 mg/dl with 77% sensitivity and 89% specificity (AUC= 0.935). Up on ROC analysis of triglyceride best cut off value is 161 mg/dl with 60% sensitivity and 75% specificity.

CONCLUSION

In our present study the findings suggest that total cholesterol, triglyceride, VLDL and LDL-C levels were significantly increased in hypothyroid patients compared with control group where HDL-C levels were slightly increased. This finding suggests that thyroid hormone affect metabolism of lipids in our body and hypothyroidism surely plays a major role in the development of dyslipidemia. Raised LDL-C cholesterol concentration is an established risk factor for cardiovascular diseases. So those lipid parameters should be estimated and monitored regularly to prevent the future cardiovascular diseases. We found marginally decrease serum adiponectin level in hypothyroid patients which was not statistically significant. We can conclude that serum levels of adiponectin are not influenced by low activity of thyroid glands. The slight decrease of adiponectin value in hypothyroid patients indicating the need for further studies with increased sample size.

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