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Hypothyroidism and Lipid Profile: A Comparative Study between Rural & Urban Hypothyroid Individuals

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ABSTRACT: Association between hypothyroidism & lipid profile has been a source of great interest among researchers. Hypothyroidism has been shown to be involved with altered lipid profile levels increasing the cardiovascular risk among hypothyroid subjects. We are studying the effect of hypothyroidism on lipid levels in rural population.**Objective of the study:** i)To study the relationship between Hypothyroidism and lipid profile. ii)To study the difference between lipid profile of rural and urban hypothyroid patients. **Material & methods:** For this study a group of 30 hypothyroid patients (both from rural & urban population) & control group of 30 subjects(both from rural & urban population) was choosen from the Medicine OPD of UPUMS, Saifai, Etawah (U.P.). Blood samples were taken after obtaining informed consent.TC,TG,HDL,LDL,VLDL were assayed using Enzymatic methods and Thyroid profile viz.(T3,T4 & TSH) was assayed. **Results:** Mean serum TC, TG & LDL were higher in Rural Hypothyroid patients as compared to Rural Controls. Similarly in Urban population, mean serum Total cholesterol, Triglyceride & LDL were higher in Urban Hypothyroid patients as compared to Urban Controls. **Conclusion:** Our analysis suggested that serum TC, LDL-C,TG and VLDL levels increased under Hypothyroidism(both in rural & urban) however, weak evidence suggested that hypothyroidism was associated with serum HDL-C levels.

Keywords : HYPOTHYROIDISM,LIPID PROFILE,RURAL,URBAN POPULATION

I. INTRODUCTION:

Association between hypothyroidism & lipid profile has been a source of great interest among researchers. Hypothyroidism has been shown to be involved with altered lipid profile levels increasing the cardiovascular risk among hypothyroid subjects[1]. Indeed, hypothyroidism is a common cause of secondary dyslipidemia[2]. This association is partly due to decreased levels of thyroid hormones, which lead to an atherogenic lipid profile characterized by increased levels of total cholesterol (TC) and lowdensity lipoprotein cholesterol (LDLC)[3]. It is a common disorder with a worldwide prevalence of about 7.5% to 8.5% in women and 2.8% to 4.4% in men[4].We are studying the effect of hypothyroidism on lipid levels in rural population, as such no study has been conducted on rural population, and we can evaluate that whether rural living standards has any beneficial effect on levels of lipid profile in hypothyroid subjects. In the past decades, some studies indicate that subclinical hypothyroidism (SCH), which is defined as normal levels of serum triiodothyronine (T3) and thyroxine(T4) as well as elevated levels of thyrotropin (TSH), is also associated with a moderate increase in the risk of CHD[5,6].

II. MATERIAL & METHODS:

This case control study was conducted in a tertiary care hospital of UP RIMS& R, Saifai,Etawah(U.P.) India. Sixty Hypothyroid patients divided into 30 rural & 30 urban Hypothyroid patients were compared with sixty healthy controls having 30 rural & 30 urban controls respectively. Inclusion criteria were TSH greater than 4.2 µIU/mL, decreased T4 (< 4.4µg/dL) and normal T3 (0.52-1.85ng/mL) levels. Healthy people with normal thyroid functions were selected as controls. Smokers & Alcoholics were excluded from the study along with known patients of Hypothyroidism or those on antithyroid medications. Proper history was taken from both cases & controls.After an informed consent, all patients and controls were subjected to complete

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physical examination and following investigations were done : Lipid profile like TC, TG, HDL, VLDL and LDL and thyroid function tests including serum TSH, T4 and T3. Samples were collected after an overnight fasting of 10-12 hours. Serum sample was separated by centrifugation at 3000 rpm for 10-15 minutes.The estimation of the T3,T4 & TSH was done by using ELISA method. The serum lipid profile was estimated by the enzymatic CHOD-PAP method for Total Cholesterol, by the GPO method for Triglyceride and by the PVS/PEGME method for HDL cholesterol.These estimations were carried out by using ERBA-XL 300 (Transasia) Fully automated analyzer. LDLCholesterol and VLDL Cholesterol were calculated by Friedwald's formula.All the kits used were commercially prepared, Calbiotech kit was used for Thyroid profile estimation while System packs kits were used for Lipid profile estimation. Calibration was performed using Randox quality control sera. The quality control was established using Erbapath and Erbanorm.

III. STATISTICAL ANALYSIS:

All the continuous variables were expressed as mean ± SD. All the results were discussed at 5% level of significance; P value < 0.05 was considered significant. Statistical Package for Social Sciences version 21.0 was taken for statistical analysis.

IV. RESULT:

Mean serum Total cholesterol, Triglyceride & LDL were higher in Rural Hypothyroid patients as compared to Rural Controls. Mean serum TC in Rural Hypothyroid was (213.83±61.70) mg/dL V/S (152.27±37.52) mg/dL in Rural euthyroid (P value <0.05). Mean serum TG in Rural Hypothyroid subjects was(154.56±70.5) mg/dL V/S (102.50±31.12) mg/dL in Controls**(**P value <0.05). Mean serum LDL in Rural Hypothyroid patients was (122.68±57.77) mg/dL V/S (72.67±35.57) mg/dL in Rural euthyroid (P value <0.05) **(Table I)**

Similarly in Urban population, mean serum Total cholesterol, Triglyceride & LDL were higher in Urban Hypothyroid patients as compared to Urban Controls. Mean serum TC in Urban Hypothyroid was (216.38±58.79) mg/dL V/S (158.90±39.30) mg/dL in Urban euthyroid(P value <0.05). Mean serum TG in Urban subjects was(148.17±47.90) mg/dL V/S (113.36.50±51.51) mg/dL in Controls(P value <0.05). Mean serum LDL in Urban Hypothyroid patients was (125.32±50.37) mg/dL V/S (78.58±38.81) mg/dL in Urban euthyroid (P value <0.05) **(Table II)**

There was no statistical significance measured in HDL levels both in Rural & Urban population. On comparing the thyroid profile between cases & controls we saw that there was a statistical significance (P value <0.05) between the levels of T4 & TSH in both cases & controls(Rural & Urban). There was no significance between the levels of T3,both in rural & urban cases.

Table I (Statistical analysis between Rural cases & controls)

Parameters (N=30)	Rural case (Mean±SD)	Rural control (Mean±SD)	t value	p value
T3(ng/mL)	1.2±0.7	1.4 ± 0.6	-1.169	NS
T4(µg/dL)	6.6±3.5	8.8±1.3	-3.257	<0.05
TSH(µIu/mL)	26.3±11.4	1.6±1.2	4.289	<0.05
TC(mg/dL)	213.8±61.7	152.3±37.5	4.669	<0.05
TG(mg/dL)	154.5±70.3	102.5±31.1	3.711	<0.05
HDL(mg/dL)	60.2±19.3	58.9±9.9	0.338	NS
LDL(mg/dL)	122.7±57.8	72.7±35.6	4.037	<0.05
VLDL(mg/dL)	30.9±14.0	20.7±6.5	3.067	<0.05

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Table II (Statistical analysis between Urban cases & controls)

Parameters(N=30)	Urban case (Mean±SD)	Urban control (Mean±SD)	t value	p value
T3(ng/mL)	1.2±0.6	1.7±0.5	-3.194	NS
T4(µg/dL)	6.5±3.4	9.6±1.6	-4.608	<0.05
TSH(µIu/mL)	28.3±16.9	1.9±1.1	3.916	<0.05
TC(mg/dL)	216.4±58.8	158.9±39.3	4.452	<0.05
TG(mg/dL)	148.1±47.9	113.3±51.5	2.710	<0.05
HDL(mg/dL)	61.4±14.3	57.6±12.5	1.093	NS
LDL(mg/dL)	125.3±50.4	78.6±38.8	4.026	<0.05
VLDL(mg/dL)	29.6±9.6	22.7±10.3	2.710	<0.05

V. DISCUSSION:

Thyroid hormones affect the metabolism of lipids[7].Several studies have assessed these effects in patients with hypothyroidism. These studies have reported increased levels of total cholesterol & LDL-cholesterol[8,9]. Our study showed significant dyslipidaemic changes in hypothyroid patients as compared to euthyroid controls. From our study we saw that the levels of Total cholesterol, Triglyceride, LDL & VLDL were all higher & statistically significant (both rural & urban cases) as compared to control groups, but we didn't find any correlation between levels of HDL in both cases & controls. The elevation in total cholesterol and LDL-C in hypothyroidism is accounted for by the effect of thyroid hormone on lipoprotein-lipase activity[10] and the expression of the LDL receptor[11], and these changes probably play an important role in atherogenesis in untreated hypothyroidism. Triglycerides and LDL-C levels were significantly high in hypothyroid patients when compared with the controls in our study. Thyroid hormones have profound effects on the cardiovascular system[12]. By affecting the metabolism of lipids, hypothyroidism accelerates the process of atherogenesis and elevates cardiovascular risk. Changes in LDL-C are mainly attributable to altered clearance of LDL-C from plasma by the changes in the number of LDL receptors on liver cell surfaces [13].

Hussein Kadhem Al-Hakeim et.al.(2009)[14] reported a significant increase (P<0.05) in serum cholesterol, LDL-C and LDL-C/HDL-C ratio in hypothyroid patients as compared with the control. A significant decrease(P<0.05) was also observed in the HDL-C levels in hypothyroid patients in comparison to control group. There is no significant difference noticed between hypothyroid and control groups in serum level of triglyceride & VLDL. In a substantial number of studies, total cholesterol and/or LDL cholesterol seem to be elevated in subclinical hypothyroidism compared with controls[15,16]. In this respect, in our case control study, subjects with hypothyroidism had significantly higher levels of TC, TG, LDL &VLDL, thus displaying a atherogenic lipid profile when compared with healthy individuals. Even more contradictory results have been presented on HDL-C levels. They are reported as either lower[17,18]or comparable[19,20]with control groups. Overt hypothyroidism is associated with increased risk of cardiovascular disease , which is attributed to increased TC and LDL-C. Inconsistent results have been reported in literature regarding the association between subclinical hypothyroidism, serum lipids and cardiovascular disease[21,22]. By contrast, a number of studies showed that TC, LDLC, and TG were elevated in SCH compared with controls. In a population based sample of 2799 elderly subjects, SCH was associated with elevation in total cholesterol [23]. Among 25862 participants in a statewide health fair in Colorado, fasting TC, TG, and LDLC levels were significantly greater in patients with SCH than those euthyroid subjects[24]. In a community based study of 2108 participants, serum TSH was

positively correlated with TC, TG, and LDLC, but these associations were no longer observed after adjustment for age and sex. In this study, no associations were observed between serum TSH and HDLC[25]. HDL-C has been variably reported to be low or unchanged in SCH[26]. In our study TC, TG, LDL &VLDL concentrations were higher in patients with serum TSH greater than 10mU/L than those with serum TSH equal to or less than 10mU/L. We found weak evidence for effects of hypothyroidism on serum HDL-C levels in our study. These results may contribute to the contrasting effects of thyroxine on enzymes related to HDLC metabolism. Plasma cholesteryl ester transfer protein concentration decreased with slight reductions in serum thyroxine level in SH patients, which may result in higher HDLC level[27]. On the other hand, the activities of hepatic lipase, lecithin cholesterol acyl transferase, and ATPbinding cassette transporter also decreased in SH patients, which may lead to lower HDLC levels[28]. These 2 contrasting effects neutralized one another, and the HDLC level may remain stable. Xiao-Li Liu et. al.(2014)[29] reported that serum TC, LDLC, and TG levels increased under subclinical hypothyroidism ; however, weak evidence suggested subclinical hypothyroidism was associated with serum HDLC levels. Higher serum TC, LDLC, and TG levels increased the risk of CHD; therefore, the cardiovascular status of SH patients should be monitored carefully. In a population based sample from Northern India of 100 patients in the age range of 15-65 years having SH, a significant increase in triglycerides and VLDL cholesterol levels were observed in patients of SH with respect to euthyroid controls while a nominal increase in serum cholesterol, LDL and HDL levels were recorded. However, there was no statistical difference found in any of the lipid fraction levels with change in the severity of SH[30]. In another study of dyslipidemia in an Indian population of 100 patients with SH and 52 euthyroid controls above the age of 20 years, total cholesterol, triglyceride and LDL in the age group of 40-50 years were significantly elevated in SH[31]. Several epidemiologic studies have shown that increased lipid concentration is associated with hypothyroidism, this explains the increased prevalence of cardiovascular disease in patients with hypothyroidism[32,33]. In hypothyroid patients, the most frequent lipid abnormality is hypercholesterolaemia, mainly due to an increased concentration of low density lipoproteins (LDL), resulting from decreased activity of LDL receptors and, consequently reduced catabolism of LDL. Decreased thyroid function not only increases the number of LDL particles, but also promotes their oxidability, making them even more atherogenic. Plasma triglycerides are increased because of an enhanced esterification of fatty acids at hepatic level. The detailed mechanisms responsible for the effects of TSH on the lipid profile remained unclear. Traditionally, the main function of TSH is to stimulate the synthesis and release of thyroid hormones in the thyroid gland via the specific cell membrane receptor-TSHR. It is now recognized that TSHR is expressed widely in a variety of extrathyroidal organs including kidney, bone marrow and adipose tissue[34],and act as a physiological regulator in the growth and development of adipocytes[35]. More importantly, emerging evidence suggests that TSH not only acts on the thyroid gland, but also targets on several other organs and tissues. The mechanisms for the regulation of cholesterol homeostasis include effects on biosynthesis, uptake, and metabolism; and the liver is vital for both endogenous synthesis and elimination of cholesterol. N. Karthick et. al. (2013)[36]studied significant dyslipidaemic changes in Subclinical hypothyroid women as compared to euthyroid controls. Serum total cholesterol and triglyceride levels were significantly higher as compared to those in controls. LDL levels were higher in SH women, but did not reach statistical significance and lower levels of HDL were noticed in SH subjects as compared to those in euthyroid women. A positive association was also reported between serum TSH and lipid parameters in this study group.

VI. CONCLUSION:

Our analysis suggested that serum TC, LDL-C,TG and VLDL levels increased under Hypothyroidism(both in rural & urban) however, weak evidence suggested that hypothyroidism was associated with serum HDL-C levels. Higher serum TC, LDL-C and TG levels increases the risk of coronary heart disease, therefore cardiovascular status of Hypothyroid patients should be monitored carefully. This study shows the significant positive correlation between serum TSH and lipid profile, showing that increase in serum TSH is one of the early markers of hypothyroidism. So hypothyroidism could be one of the reason for secondary hyperlipidaemia and should be taken as an independent risk factor for atherosclerosis along with hypertension , diabetes, obesity etc. An impaired lipid profile is an important reason for

cardiovascular and cerebrovascular diseases. Furthermore, the same amount of statistical significance was noted between hypothyroidism and lipid profile both in rural & urban hypothyroid patients on comparing them with their control groups. This observation might be indicative of that, the alteration of lipid parameters in hypothyroid patients is not altered by social habits, dietary habits or status of living, but is only dependent on the disease state i.e. Hypothyroidism. Also due to alteration of lipid profile at the same level, the relative risk of cardiovascular disease in both rural & urban hypothyroid patients will be same.

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