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Study to evaluate the association of Leptin with Dyslipidemia in Hypothyroid Patients

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Abstract

Objective: Aim of the present study was to evaluate the levels of leptin in hypothyroid patients and to find a possible association of leptin with dyslipidemia in hypothyroid patients.

Material & Methods: The present study was conducted on 100 previously diagnosed hypothyroid (PDH) patients and 100 newly diagnosed hypothyroid (NDH) patients attending the outpatient clinics or admitted in wards of J.L.N. Hospitals, Ajmer. 100 healthy control subjects of same age group of either gender were selected for the study. Blood samples were drawn from patients and controls, after overnight fast of at least 8 hours. Estimation of S.Leptin, free T_3, free T_4, and TSH was done by using Enzyme- Linked Immunosorbant Assay (ELISA) technique. S. Total Cholesterol, S.Triglycerides & S.HDL were determined on semi automated clinical chemistry analyzer whereas VLDL and LDL were calculated by using Friedewald's formula. Differences in the parameters among the groups were analyzed by ANOVA test followed by its Tukey HSD post hoc analysis. Correlations between variables were tested using the Pearson rho (r: Correlation coefficient) correlation test.

Results: Findings of the present study shows that the levels of S.fT_3 (1.79 ± 0.29 pg/mL) and S.fT_4 (0.34 ± 0.11 ng/dL) were significantly lower in NDH group compared to PDH group (fT_3 = 3.00 ± 0.32 pg/mL & fT_4 = 0.81 ± 0.15 ng/dL) and control group (fT_3 = 3.12 ± 0.31 pg/mL & fT_4 = 0.85 ± 0.11ng/dL) whereas S.TSH levels were significantly higher in NDH group (40.59 ± 13.55 µIU/mL) compared to PDH group (5.34 ± 1.47 µIU/mL) and control group (3.23 ± 1.04 µIU/mL) [Table 1; Figure 1]. Leptin levels were significantly higher in NDH group (21.37 ± 6.44 ng/mL) compared to PDH group (16.51 ± 4.47 ng/mL) and control group (11.15 ± 5.29 ng/mL) [Table 2]. A highly significant variation ($p<0.0001$) in the levels of leptin was found between the groups.

Conclusion: It was suggested that thyroid dysfunction does not affect the leptin levels and also thyroid hormones were not involved in the synthesis and secretion of leptin. Dyslipidemia in hypothyroid patients was primarily due to thyroid dysfunction and leptin shows a non-significant association with lipid profile. Further studies are required to gain more insight into the relationship between leptin and thyroid dysfunction.

Keywords: Leptin, Hypothyroidism

Introduction

Hypothyroidism is one of the most common disorders which occur from hormone deficiency. In developed countries the prevalence of hypothyroidism is about 4%–5%, whereas in India, it is reported to be around 10.95%[1]. Hypothyroidism can be easily diagnosed by the estimation of blood levels of thyroid hormones. Hypothyroidism shows diverse clinical manifestations which include lethargy, cold intolerance, weight gain, fatigue, menstrual irregularities etc[2]. In patients with overt hypothyroidism, dyslipidemia with elevated levels of total cholesterol and LDL-cholesterol is a common finding[3].

Leptin and thyroid hormones both have an effect on each other. Both of them through complex mechanisms may regulate the metabolism and composition of the body. Leptin not only shows its effect on energy consumption and appetite but also helps in the conversion of T_4 to T_3 by regulating the activity of central and peripheral iodothyronine deiodinase[4].

In hypothyroidism increase in the levels of serum leptin is probably due to the reduced effect of thyroid hormones on leptin receptor and adipocytes whereas in hyperthyroidism decrease in the levels of serum leptin is probably due to increased thyroid hormone levels which stimulates the sympathetic system particularly adregenic receptors which blocks the leptin receptors and inhibit leptin secretion in adipose tissue. On the other hand, TSH probably through TSH receptors shows a direct effect on adipocytes and consequently stimulates leptin secretion[5,6,7].

Material & Methods:

Subjects:

The present study was conducted on 100 previously diagnosed hypothyroid (PDH) patients and 100 newly diagnosed hypothyroid (NDH) patients attending the outpatient clinics or admitted in wards of Medicine Department, J.L.N. Hospital, Ajmer. 100 healthy control subjects of same age group of either gender were selected for the study. Patients with congestive heart failure, chronic renal failure and diabetes mellitus were excluded from the study.

Sample collection & Measurement:

Blood samples were drawn from patients and controls, after overnight fast of at least 8 hours. Five ml blood was collected in plain vial and was allowed to clot for 30 minutes at room temperature and then centrifuged at 2500 rotations per minute (rpm) for 15 minutes to obtain clear non-haemolysed serum. Estimation of S.Leptin, free T_3, free T_4, and TSH was done by using Enzyme- Linked Immunosorbant Assay (ELISA) technique. Estimation of S.Total Cholesterol, S.Triglycerides & S.HDL were done on semi-automated clinical chemistry analyzer whereas S.VLDL and S.LDL were calculated by using Friedewald's formula.

Statistical Analysis:

Variables were presented as Mean ± Standard deviation (S.D.). Differences in the parameters among the groups were analyzed by ANOVA test followed by its Tukey HSD post hoc analysis. Correlations between variables were tested using the Pearson rho (r: Correlation coefficient) correlation test. The accepted level of significance for all statistical analyses used in the study was $P \leq 0.05$ (two tailed P value).

Results

In the present study it was observed that the levels of $S.fT_3$ (1.79 ± 0.29 pg/mL) and $S.fT_4$ (0.34 ± 0.11 ng/dL) were significantly lower in NDH group compared to PDH group (fT_3 = 3.00 ± 0.32 pg/mL & fT_4 = 0.81 ± 0.15 ng/dL) and control group (fT_3 = 3.12 ± 0.31 pg/mL & fT_4 = 0.85 ± 0.11ng/dL) whereas S.TSH levels were significantly higher in NDH group (40.59 ± 13.55µIU/mL) compared to PDH group (5.34 ± 1.47 µIU/mL) and control group (3.23 ± 1.04 µIU/mL) [Table 1; Figure 1].

TABLE No.1

General and Biochemical parameters

S.No.	Parameter	Control group [Mean ±S.D.]	NDH group [Mean ±S.D.]	PDH group [Mean± S.D.]
1	**Age (Years)**	40.41 ± 5.81	43.89 ± 5.30	46.04 ± 5.71
2	**BMI (Kg/m^2)**	23.88 ± 1.54	26.84 ± 1.41	24.45 ± 1.01
3	**fT_3 (pg/mL)**	3.12 ± 0.31	1.79 ± 0.29	3.00 ± 0.32

Volume 4, Issue 5; September-October 2021; Page No1482-1488

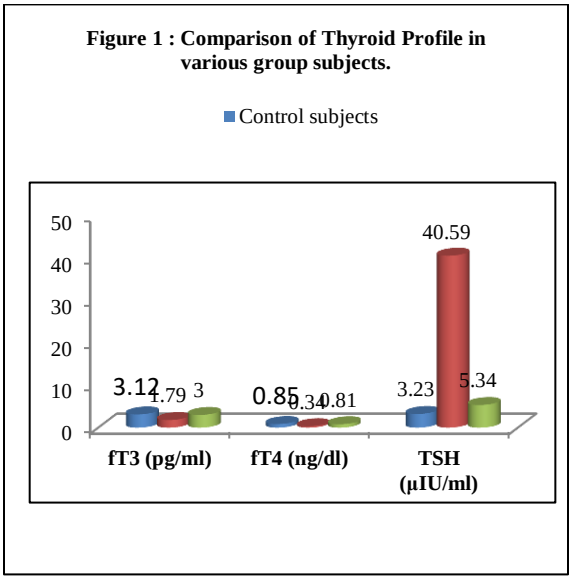
4	**fT_4 (ng/dL)**	0.85 ± 0.11	0.34 ± 0.11	0.81 ± 0.15
5	**TSH (µIU/mL)**	3.23 ± 1.04	40.59 ± 13.55	5.34 ± 1.47
6	**Total Cholesterol (mg/dL)**	170.43 ± 18.50	236.73 ± 23.71	196.37 ± 16.57
7	**Triglyceride (mg/dL)**	141.55 ± 13.03	198.06 ± 16.26	159.54 ± 13.94
8	**HDL (mg/dL)**	39.22 ± 6.89	27.8 ± 4.05	29.57 ± 4.83
9	**VLDL (mg/dL)**	28.31 ± 2.60	39.61 ± 3.25	31.90 ± 2.78
10	**LDL (mg/dL)**	102.9 ± 19.33	169.31 ± 23.84	134.89 ± 17.71

Levels of Total Cholesterol, Triglycerides, V.L.D.L & L.D.L were significantly higher in NDH group (T.Chol.= 236.73 ± 23.71 mg/dL, Triglycerides = 198.06 ± 16.26 mg/dL, V.L.D.L = 39.61 ± 3.25 mg/dL & L.D.L = 169.31 ± 23.84 mg/dL) compared to PDH group (T.Chol.= 196.37 ± 16.57 mg/dL, Triglycerides = 159.54 ± 13.94 mg/dL, V.L.D.L = 31.90 ± 2.78 mg/dL & L.D.L = 134.89 ± 17.71 mg/dL) and controls (T.Chol.= 170.43 ± 18.50 mg/dL, Triglycerides = 141.55 ± 13.03 mg/dL, V.L.D.L = 28.31 ± 2.60 mg/dL & L.D.L = 102.9 ± 19.33 mg/dL) whereas HDL levels were significantly lower in NDH group (198.06 ± 16.26 mg/dL) compared to PDH group (29.57 ± 4.83 mg/dL) and controls (39.22 ± 6.89 mg/dL).

Leptin levels were significantly higher in NDH group (21.37 ± 6.44 ng/mL) compared to PDH group (16.51 ± 4.47 ng/mL) and control group (11.15 ± 5.29 ng/mL) [Table 2]. A highly significant variation ($p<0.0001$) in the levels of leptin was found between the groups.

In the present study a non significant correlation of leptin with $S.fT_3$, $S.fT_4$ and TSH was found both in NDH and PDH group whereas BMI shows a significant positive correlation with leptin in NDH group in comparison to a non-significant correlation in PDH group [Table 3; Figure 2,3].

Figure 1 : Comparison of Thyroid Profile in various group subjects.



Volume 4, Issue 5; September-October 2021; Page No1482-1488

TABLE No. 2

S.No.	Parameter	Control group [Mean ±S.D.]	NDH group [Mean ±S.D.]	PDH group [Mean± S.D.]
1	**Leptin (ng/mL)**	11.15 ± 5.29	21.37 ± 6.44	16.51 ± 4.47

TABLE No. 3

Correlation of S. Leptin with various variables (fT_3, fT_4, TSH and BMI) in PDH group and NDH group

Parameter	r value		p value		Significance	
	PDH group	NDH group	PDH group	NDH group	PDH group	NDH group
fT_3	-0.049	-0.171	0.628	0.088	NS	NS
fT_4	-0.045	-0.073	0.656	0.470	NS	NS
TSH	0.033	0.165	0.744	0.100	NS	NS
BMI	0.096	0.237	0.342	0.017	NS	S

TABLE No.4

Correlation of S. Leptin with Lipid Profile in PDH group and NDH group

Parameter	r value		p value		Significance	
	PDH group	NDH group	PDH group	NDH group	PDH group	NDH group
Total Cholesterol (mg/dL)	-0.149	0.098	0.138	0.332	NS	NS
Triglyceride (mg/dL)	0.000	0.146	1	0.147	NS	NS
HDL (mg/dL)	-0.128	0.010	0.204	0.921	NS	NS
VLDL (mg/dL)	0.000	0.146	1	0.147	NS	NS
LDL (mg/dL)	-0.104	0.076	0.303	0.452	NS	NS

Volume 4, Issue 5; September-October 2021; Page No1482-1488

Figure 2 : Correlation of S. Leptin with fT4 in Newly diagnosed hypothyroid subjects.

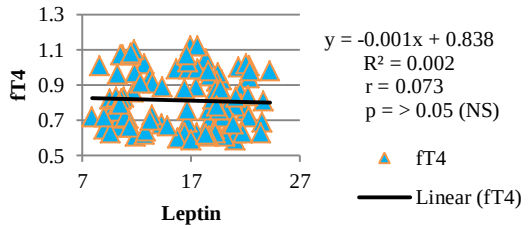
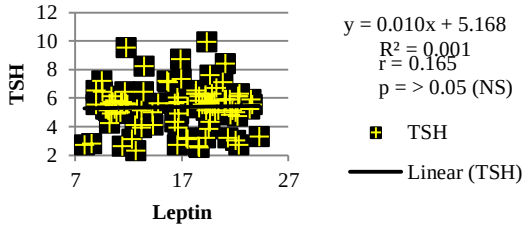


Figure 3 : Correlation of S. Leptin with TSH in Newly diagnosed hypothyroid subjects.



Discussion

Hypothyroidism is a common endocrinological problem which plays a significant role in metabolic and development processes worldwide as well as in India. Hypothyroidism is a common disorder and because of its nonspecific clinical presentation, it remains under-diagnosed[8]. As compared to the general population, patients with hypothyroidism show a greater propensity for co-morbidities and complications. We observed that hypothyroidism was more prevalent in women than men[9].

Hyperlipidemia is a very common condition associated with hypothyroidism and after diabetes mellitus, hypothyroidism is the second only reason for the development of secondary hyperlipidemia. Thyroid hormones affect the synthesis, mobilization and breakdown of lipids: two major target points are the expression of low-density lipoprotein (LDL) receptors and subsequent cellular uptake of LDL and very low-density lipoprotein (VLDL)[11]. Indeed, a deficit in the expression of the hepatic LDL receptor gene decreases the rate of LDL-cholesterol clearance, and is claimed to be responsible for elevated serum lipid levels in patients with hypothyroidism[12].

The effect of hypothyroidism in lipid metabolism shows an increase in the levels of total cholesterol, triglycerides and LDL-cholesterol whereas the level of HDL-cholesterol decreases. S.fT_4 shows a highly significant negative correlation with T. Cholesterol both in NDH and PDH group while S.TSH shows a highly significant positive correlation with T. Cholesterol both in NDH and PDH group. A weak negative correlation of S.fT_4 with T.G., VLDL and LDL was found in NDH group in comparison to a strong negative correlation in PDH group while a weak positive correlation of S.TSH with T.G. and LDL was found both in NDH and PDH group. HDL shows a non significant correlation with S.fT_4 in NDH group in comparison to a highly significant correlation in PDH group while HDL shows a non significant correlation with TSH in NDH group in comparison to a weak negative correlation in PDH group. The relationship between thyroid hormones and lipid profile is evident from this correlation trend.

Leptin is also known as satiety hormone which is secreted by adipose tissue and considered as an important factor in the regulation of food intake and energy storage. In circulation leptin occurs in both free and bound forms and concentration of serum leptin is directly proportional to the amount of body fat present. Both alterations in the levels of leptin and thyroid dysfunction are associated with noticeable changes in energy expenditure and body weight therefore it is important to understand the association between them and to study their mutual interactions[13,14]. In the beginning, leptin was considered as a hormone which is intended to prevent obesity but after various studies it was now recognized that leptin also controls the switch from the fed to the starved state which represents a significant interaction between leptin and thyroid hormones[15,16]. In our study a non significant correlation of S.Leptin with S.fT_3, S.fT_4 and S.TSH was found both in NDH and PDH group and as far as lipid profile is concerned, a non significant correlation with S.Leptin was found both in NDH and PDH group. BMI shows a significant positive correlation with S.Leptin in NDH group in comparison to a non significant correlation in PDH group.

Leptin not only shows its effect on energy consumption and appetite but also helps in the conversion of T_4 to T_3 by regulating the activity of central and peripheral iodothyronine deiodinase[17]. In

Volume 4, Issue 5; September-October 2021; Page No1482-1488

hypothyroidism increase in the levels of serum leptin is probably due to the reduced effect of thyroid hormones on leptin receptor and adipocytes[18,19]. A recently published study on females with higher levels of serum leptin reported that sex hormones are involved in the regulation of leptin synthesis. Another possible explanation of these sex based differences in leptin concentration is due to differences in the body composition[20].

Conclusion:

Thyroid hormones and thyroid stimulating hormone controls the regulation of a broad spectra of metabolic parameters. Dyslipidemia in hypothyroid patients was primarily due to thyroid dysfunction and leptin shows a non-significant association with lipid profile. Leptin shows its effect on energy expenditure possibly due to the mediation of thyroid hormones but further studies regarding the role of thyroid hormones on leptin are still required to gain more insight into the relationship between leptin and thyroid dysfunction.

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Volume 4, Issue 5; September-October 2021; Page No1482-1488