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ROLE OF LEPTIN IN HYPOTHYROID COMPLICATIONS

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ABSTRACT **Background:** Thyroid hormones are the fine regulators of metabolism. Any alteration of thyroid profile can affect the lipid metabolism. Leptin from adipose tissue can also alter both the thyroid hormone and lipid metabolism. **Aim:** In present study, we compare serum fasting leptin and LDL levels in hypothyroid patients when compared to healthy subjects and their effect on developing further complications. **Statistical Analysis:** Done by SPSS software 17 version. **Material and method:** 60 hypothyroid patients and 30 age and sex matched controls are selected. Serum TSH ,leptin, LDL was estimated. **Results** : TSH ,leptin and LDL is significantly different in case than control.Those who are having LDL > 160mg/dl is having significantly high leptin than the control group. **Discussion & Conclussion** : hypothyroid patients are having dyslipidemia. Leptin is having a role in cholesterol synthesis and lipid clearance.It is also having a regulating effect on TSH also.So leptin itself can aggrevate the dyslipidemia associated cardiovascular risk factors of hypothyroidism.

KEYWORDS : TSH, Leptin, Dyslipidemia

Introduction:-

Thyroid hormones and thyroid stimulating hormone (TSH) are the fine regulators of intermediate metabolism in our body[1-2]. So any alteration in thyroid profile will affect the metabolic spectra which ultimately disturbs appetite, body weight and adipose tissue and can also contribute in the pathogenesis of cardiovascular diseases and many more.[3-5]

Leptin, the `ob` gene product and lipostatic hormone by nature and correlates its functions with thyroid hormone[6-7], critically regulate the Thyroid Releasing Hormone(TRH) gene expression in paraventricular nucleus of the hypothalamus for normal functioning of thyroid axis[8]. Serum leptin concentration is increased in obesity, insulin resistance & dyslipidemia and as it increases the oxidative stress and calcification in vascular endothelium, can be a confounding factor for atherosclerosis[9-10].

So thyroid dysfunction can affect the functions of adipose tissue and together they can alter the metabolism and energy homeostasis. But the interrelationship between thyroid function and adipose tissue secreting cytokines are not yet clear[11]

Hypothyroidism and hyperthyroidism are the two ends of thyroid disorders. 42 million people in India are suffering from thyroid disorder[12] .Prevalence of hypothyroidism is 3.9% [13]. In hypothyroidism, increased TSH and decrease in T3 and T4, effect in increase of body weight and alteration of lipid profile[14-15].

Alteration of thyroid profile may affect the leptin secretions or may be altered leptin can disturb the thyroid function. Both together they can disrupt the normal lipid profile and precipitate atherosclerosis or cardiovascular risk.

Aim:

In present study, we compare serum fasting leptin and LDL levels in hypothyroid patients when compared to healthy subjects and their effect on developing further complications..

Materials and method

This Cross sectional, observational study was carried out in the Department of Biochemistry, Calcutta National Medical College, Kolkata, West Bengal. The study was six months was done during 15.05.2026 -31.12.2016. It was accepted by Institutional Ethics Committee and informed consents are being taken from study participants.

Inclusion criteria: A total of 60 hypothyroid (26 males and 34 females, aged 30 to 60 years) patients were selected for the study from the thyroid clinic of the College. 30 age and sex matched control subjects were also selected, with consent.

Exclusion criteria: Excluded from this study were those with neoplasm, other endocrine disorders like diabetes mellitus,liver dysfunction, renal failure, hypertension, secondary hypothyroidism, major surgery, psychiatric condition, GIT diseases, pregnancy, alcohol abuse, medications altering thyroid hormones , critically ill patients, autoimmune thyroid disease and patients on L-T4 treatment.

Sample Collection: 5 ml of blood was collected aseptically using standard protocols. The serum was separated by centrifugation (3000 rpm for 5 min) immediately and analysis was done.

Methods for analysis of test parameters:

Estimation of (S) TSH was done by Sandwich Elisa (Aspen Laboratories Pvt Ltd)[16].

Estimation of (S) leptin was done by Sandwich Elisa (RayBiot, Inc)[17].
Estimation of (S) LDL was done by Direct method (Erba Lachema, diagnostics)[18].

Statistical Analysis : Done by SPSS software 17 version.

Results:-

Table 1 Showing the demographic profile and students t test of parameters between case and control group

	N	Mean	Std. Deviation	Std. Error Mean	t	df	Sig. (2-tailed)
TSH control	30	2.4160	2.09961	.38333	6.303	29	.000
TSH case	38	10.1247	3.60324	.58452	17.321	37	.000
LDL control	30	87.4000	18.50927	3.37932	25.863	29	.000
LDL case	60	150.5667	63.06826	8.14208	18.492	59	.000
Leptin control	30	7.3040	3.15613	.57623	12.676	29	.000
Leptin case	60	11.1653	4.63585	.59849	18.656	59	.000

*. The mean difference is significant at the 0.05 level.
Students` t test showed significant difference of mean in case and control group for all three parameters

Table 2 : showing ANOVA analysis of LDL & LEPTIN in between 3 groups

LDL	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	265036.155	2	132518.077	194.163	.000
Within Groups	59378.334	87	682.510		
Total	324414.489	89			
LEPTIN	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	1177.110	2	588.555	75.530	.000
Within Groups	677.936	87	7.792		
Total	1855.046	89			

*. The mean difference is significant at the 0.05 level.

Case group was further divided into 2 sub-groups on the basis of serum LDL value 160 mg/dl as a cut off.

One way ANOVA showed significant difference of LDL and Leptin value within the 3 groups.

Post –hoc Bonferroni showed LDL was significantly different in between three groups but the serum level of Leptin was not significantly different in case group who had LDL < 160 mg /dl when compared with control ,though the rest of the two comparisons were significant

Table 3: post hoc Bonferroni (with 95% Confidence intervel) showing Multiple Comparisons of LDL in between groups

LDL					LEPTIN				
(I) grouping	(J) grouping	Mean Difference (I-J)	Std. Error	Sig.	(I) grouping	(J) grouping	Mean Difference (I-J)	Std. Error	Sig.
.00	1.00	-20.88947*	6.38052	.005	.00	1.00	-.94913	.68177	.502
	2.00	-136.19091*	7.33304	.000		2.00	-8.89143*	.78355	.000
1.00	.00	20.88947*	6.38052	.005	1.00	.00	.94913	.68177	.502
	2.00	-115.30144*	6.99885	.000		2.00	-7.94230*	.74784	.000
2.00	.00	136.19091*	7.33304	.000	2.00	.00	8.89143*	.78355	.000
	1.00	115.30144*	6.99885	.000		1.00	7.94230*	.74784	.000

*. The mean difference is significant at the 0.05 level.

Discussion:-

In our study we found that hypothyroid patients are having increased leptin level along with increased serum LDL.Our study is in similarity with many other[19]. We sub-grouped the hypothyroid patients in two on basis of their serum LDL level. Results are showing that those who are having LDL> 160 mg /dl ,their serum leptin level is significantly increased when compared to control and the other group with LDL <160 mg/dl. But those with serum LDL <160 mg/dl ,their leptin is not significantly increased than the control group.

Thyroid hormone alters the lipid profile by effecting its synthesis, absorption ,storage and catabolism[20]. Regulatory enzyme of cholesterol synthesis in liver is HMGCR (3-Hydroxy-3-Methyl-Glutaryl Coenzyme A Reductase) which is regulated by many hormones like insulin,glucagon,estrogen,glucocorticoid and thyroid hormone[21].In hypothyroid state HMGCR mRNA synthesis reduced which causes decreased hepatic cholesterol synthesis but this is outweighted by reduced LDL receptor expression and cholesterol absorption ,resulted in increased LDL concentration[22-23]. TSH has a direct effect on leptin secretion by stimulating TSH receptor on adipocytes. On the counter say, leptin critically regulate the Thyroid Releasing Hormone(TRH) gene expression in paraventricular nucleus of the hypothalamus [8]. But the interrelationship between thyroid hormone and leptin is not clearly understood. Leptin is `ob` gene product and lipostatic in nature[6-7]. By increasing the oxidative stress and vascular endothelium calcification leptin can precipitate atherosclerosis[2].

According to ATP- III [24]serum level of LDL >160mg/dl is a risk factor for atherosclerosis and other cardiovascular disorders. In our study we found those who are having LDL > 160mg/dl ,their leptin level is significantly increased than the control. Moreover increased leptin causes decrease in adiponetin level which is cardioprotective.

So leptin can aggravate the atherogenic potential of hypothyroid state along with increasing LDL.So while assessing hypothyroid patients along with the lipid profile serum leptin level should be assessed specially those who are having LDL at criticaaly high level it can predict the degree of cardiovascular risk and according to that mode of treatment can be altered.

Reference

1. Krotkiewski, M. Thyroid hormones in the pathogenesis and treatment of obesity. Eur J Pharmacol 440, 85–98 (2002).
2. Potenza, M., Via, M. A. & Yanagisawa, R. T. Excess thyroid hormone and carbohydrate metabolism. Endocr Pract 15, 254–262 (2009).
3. Chen, H. H., Yeh, S. Y., Lin, C. L., Chang, S. N. & Kao, C. H. Increased depression, diabetes and diabetic complications in Graves'disease patients in Asia. QJM 107, 727–733 (2014).
4. Gronich, N. et al. Hypothyroidism is a Risk Factor for New-Onset Diabetes: A Cohort Study. Diabetes Care 38, 1657–1664 (2015).
5. Gierach, M., Gierach, J. & Junik, R. Insulin resistance and thyroid disorders. Endokrynol Pol 65, 70–76 (2014).
6. Zhang Y, Proenca R, Maffei M, Barone M, Leopold L & Friedman JM. Positional cloning of the mouse obese gene and its human homologue. Nature 1994 372 425–432.
7. Mantzoros CS. The role of leptin in human obesity and disease: a review of current evidence. Annals of Internal Medicine 1999 130,671–680.
8. Flier, J.S., Harris, M. & Hollenberg, A.N. (2000) Leptin, nutrition, and the thyroid. the why, the wherefore, and the wiring. Journal of Clinical Investigation, 105, 859–861.
9. Bouloumie A, Drexler HCA, Lafontan M & Busse R. . Leptin induce oxidative stress in human endothelial cells. FASEB Journal 1999 ,13 1231–1238.
10. Parhami F, Tintut Y, Ballard A, Fogelman AM & Demer LL. Leptin enhances the calcification of vascular cells: artery wall as a target of leptin. Circulation Research 2001 88 954–960.
11. Zimmermann-Belsing, T., Brabant, G., Holst, J.J. & Feldt-Rasmussen, U. (2003) Circulating leptin and thyroid dysfunction. European Journal of Endocrinology, 149, 257–271.
12. [Last accessed on 2011 April 2]. Availabl from: http://www.ias.ac.in/currsci/oct252000/n%20kochupillai.PDF .
13. Usha Menon V, Sundaram KR, Unnikrishnan AG, Jayakumar RV, Nair V, Kumar H. High prevalence of undetected thyroid disorders in an iodine sufficient adult south Indian population. J Indian Med Assoc. 2009;107:72–7. [PubMed: 19585813].
14. Pucci E, Chiovato L, Pinchera A: Thyroid and lipid metabolism. Int J Obesity Rel Metab Dis 2000, 24:S109-S112.13.
15. Diekman MJ, Anghelescu N, Endert E, Bakker O, Wiersinga WM: Changes in plasma low-density lipoprotein (LDL)- and highdensity lipoprotein cholesterol in hypo- and hyperthyroid patients are related to changes in free thyroxine, not to polymorphisms in LDL receptor or cholesterol ester transfer protein genes. J Clin Endocrinol Metab 2000, 85:1857-1862.
16. Schall RF, Fraser AS, Hansen HW, Kern CW and Teneso HJ. A Sensitive Manual Enzyme Immunoassay for Thyroxine. Clin. Chem 1978;24 (10): 1801.
17. Zhou YT .Intuction by leptin of uncoupling protein -2 and enzymes of fatty acid oxidation.Proceeding of the National Academy of Science (USA)94: 6386-6390 (1997).
18. Pisani T, Gebski CP, Leary ET et al. Accurate direct deyermination of low density lipoprotein cholesterol assay. Arch Pathol Lab Med 1995; 119: 1127.
19. Tsao TS. ACRP30,A new hormone controlling fat and glucose metabolism.European Journal of Pharmacology 440 (2-3) : 213-221(2002).
20. Pearce EN. Update in lipid alterations in subclinical hypothyroidism. J Clin Endocrinol Metab. 2012; 97: 326-333.
21. Mullur R, Liu YY, Brent GA. Thyroid hormone regulation of metabolism. Physiol Rev. 2014; 94: 355-382.
22. Ness GC, Chambers CM. Feedback and hormonal regulation of hepatic 3-hydroxy-3-methylglutaryl coenzyme A reductase: the concept of cholesterol buffering capacity. Proc Soc Exp Biol Med. 2000; 224: 8-19.
23. Gälman C, Bonde Y, Matasconi M, Angelin B, Rudling M. Dramatically increased intestinal absorption of cholesterol following hypophysectomy is normalized by thyroid hormone. Gastroenterology. 2008; 134: 1127-1136.
24. [Last accessed on 2013 December]. Available from www.nhlbi.nih.gov.