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RESEARCH ARTICLE

Regular original article Serum IGF-1 changes associated with thyroid disorders.

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Abstract

Background: Thyroid hormones are involved in the regulation of the GH/IGF axis. Thyroid abnormalities are accompanied with changes in intermediary metabolism including alteration in body weight, insulin resistance and lipid profile. So this study was undertaken to determine the potential relationship between IGF-1 and thyroid hormone in hyperthyroid and hypothyroid patients.

Introduction: Thyroid hormones are involved in the regulation of IGF-1. It is a growth factor which is secreted from liver as a response to growth hormone, mediating the anabolic and linear growth promoting effect of pituitary GH protein.

Material & Methods : A cross sectional study was performed on 100 patients between age group of 15-60 years, along with 50 age matched healthy Control group in J. L. N. hospital Ajmer. Serum T_3 and TSH level were estimated by Radioimmunoassay (RIA) method, and serum Free T_4 and serum IGF-1 level by ELISA of Bio-Rad pw40.

Result: The decrease in serum IGF-1 level was observed statistically highly Significant ($p<0.0001$) in hypothyroid subjects and in hyperthyroid subjects ($p<0.0001$). There were significant correlations between IGF-1 and TSH in hypothyroid patients.

Discussion: Disturbances in thyroid hormones in thyroid diseases have an essential effect on the levels of IGF-1, involved in the regulation of energy balance. It has many receptors in various tissues and manifests insulin-like effect as well; it functions in many metabolic pathways including energy metabolism.

Conclusion: We concluded that measurement of IGF-1 possibly could prevent the false diagnosis of thyroid assessment and may offer more effective interventions to improve patients care and the economic aspect.

INTRODUCTION

Thyroid is an important and one of the largest endocrine gland that produces two main hormones, the principal one being 3, 3, 5-Triiodo- thyronine (T_3) and Thyroxin(T_4). Both these hormones are under control of thyroid stimulating hormone (TSH).

Thyroid hormone, Thyroxin, and Triiodothyronine play an important role in a wide range of physiological processes in mammals, including growth, development differentiation, and basal metabolic homeostasis [(6)].

Thyroid abnormalities are accompanied with changes in intermediary metabolism including alteration in body weight, insulin resistance and lipid profile [(9)].

Insulin like growth factor- 1 (IGF-1) also called Somatomedin C is a protein that in humans is encoded by IGF-1 gene. Human IGF-1 is a single chain 70-amino acid polypeptide cross-linked by 3 disulfide bridges, with a calculated molecular mass of 7.6 KD [16]. It is a growth factor which is secreted from liver as a response to growth hormone [20]. Normal thyroid status is a prerequisite for the normal growth and development of many tissues.

IGF-1 is secreted by many tissues and the secretory site seems to determine its actions. Most IGF-1 is secreted by the liver and is transported to other tissues, acting as an endocrine hormone [14]. IGF-1 is also secreted by other tissues including cartilagenous cells, and acts locally as a paracrine hormone [7]. The role of IGF-1 in the metabolism of many tissues including growth has been reviewed recently [15]. IGF-1 is an important growth hormone, mediating the anabolic and linear growth promoting effect of pituitary GH protein [23-24].

IGF-1 has many receptors in various tissues and manifests insulin-like effect as well; it functions in many metabolic pathways including energy metabolism [21]. IGF-1 has an important role in diabetic subjects [8] as well as in cancer development [19]. IGF-1 has growth-promoting effects on almost all cells in the body, particularly skeletal muscle, bone, cartilage, liver, kidney, nerve, skin, hematopoietic tissue, and lung cells [10].

Cianfarani et al (2005) [5] stated that IGF-1 concentration was reliable indicator of daily GH secretion, due to their dependency and relative stability in circulation. Investigations suggest that there is an increase in serum levels of IGF-1 in patients with hyperthyroidism (Roberto Valcavi et al; 1993**)** [17] and a decrease of these values in patients with hypothyroidism (J P Miell, et al; 1993) [13].

MATERIAL AND METHODS

A cross sectional study was conducted on 100 patients with 50 age matched healthy control between age group of 15-60 years in J. L. N. hospital Ajmer, Rajasthan , India. They were further divided into hyperthyroidism and hypothyroidism.

Group 1: hypothyroid subjects (n=50)

Group 2: hyperthyroid subjects (n=50)

Group 3: healthy control subjects (n=50)

EXCLUSION CRITERIA:

Patients with Atherosclerosis, diabetes mellitus, on treatment concerning thyroid dysfunction, with any inflammatory or medical condition which would have influenced the parameters under study, were excluded from the study. Participants gave written consent before taking part in the study.

Blood samples were collected by venupuncture by aseptic technique and samples with signs of hemolysis were discarded. Then centrifuged at 2500-3000 RPM, serum separated from the samples were analyzed for following biochemical parameters :- T_3 and TSH by Radioimmunoassay (RIA) method, serum Free T_4 and serum IGF-1 level by ELISA of Bio-Rad pw40.

The statistical analysis was done by the unpaired two tailed 't' test and the Pearson's correlation coefficient by using online calculator. The data were presented as mean with SD. The statistical significance was kept as a P value of < 0.05.

RESULT:

This study was conducted to study the status of serum IGF-1 levels in hypothyroid and hyperthyroid subjects. The mean ± SD value of serum IGF-1 level in healthy control subjects was 192.16±30.8 ng/ml, in hypothyroid subjects was 123.42±16.8 ng/ml and in hyperthyroid subjects was 150.44±18.8 ng/ml.

The decrease in serum level was observed statistically highly Significant ($p<0.0001$) in hypothyroid subjects (Table II, Fig.2) and in hyperthyroid subjects ($p<0.0001$) (Table III, Fig.3) when compared with healthy control subjects. Comparison of hypothyroid subjects with hyperthyroid subjects shows that the decrease in IGF-1 level is statistically highly significant ($p<0.0001$).

Pearson correlation (r) analysis was used to determine the correlation of serum IGF-1 levels with TSH in thyroid dysfunction. IGF-1 significantly inversely correlated with TSH in hypothyroid subjects ($r= -0.62$) and in hyperthyroid subjects ($r= -0.17$), respectively Fig.-2, Fig-3.

TABLE-1
SERUM THYROID HORMONE LEVELS OF HYPOTHYROID AND HYPERTHYROID SUBJECTS

S. NO.	PARAMETER	CONTROL	HYPOTHYROID SUBJECTS	HYPERTHYROID SUBJECTS
1.	T_3(ng/ml)	1.34±0.39	0.59±0.36	2.41±0.64
2.	FT_4(ng/dl)	1.1±0.3	0.46±0.2	3.1±0.7
3.	TSH(µIU/ml)	2.29±0.9	49.1±27.9	0.08±0.05

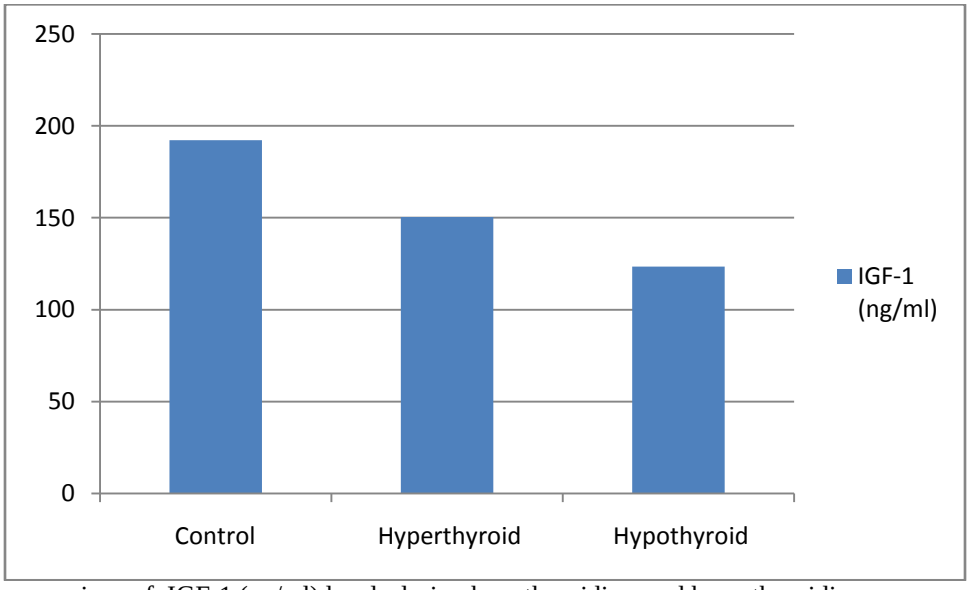

Fig.-1 : The comparison of IGF-1 (ng/ml) levels during hypothyroidism and hyperthyroidism**.**

TABLE-2
IGF-1 LEVELS OF CONTROL AND HYPOTHYROID SUBJECTS

S.NO.	BIOCHEMICAL PARAMETER	CONTROL	HYPOTHYROID SUBJECT	t Value	p* value
1	IGF-1(ng/ml)	192.16±30.8	123.42±16.8	13.3	<0.0001

TABLE-3
IGF-1 LEVELS OF CONTROL AND HYPERTHYROID SUBJECTS

S. No	BIOCHEMICAL PARAMETER	CONTROL	HYPERTHYROID SUBJECTS	t Value	p* value

1	IGF-1 (ng/ml)	192.16±30.8	150.44±18.8	8.1	<0.0001

TABLE-4
COMPARISION OF TSH WITH IGF-1

SUBJECTS	TSH	IGF-1	p*VALUE
HYPOTHYROID SUBJECTS	49.1±27.91	123.4±16.8	<0.0001
HYPERTHYROID SUBJECTS	0.08±0.05	150.4±18.8	<0.0001

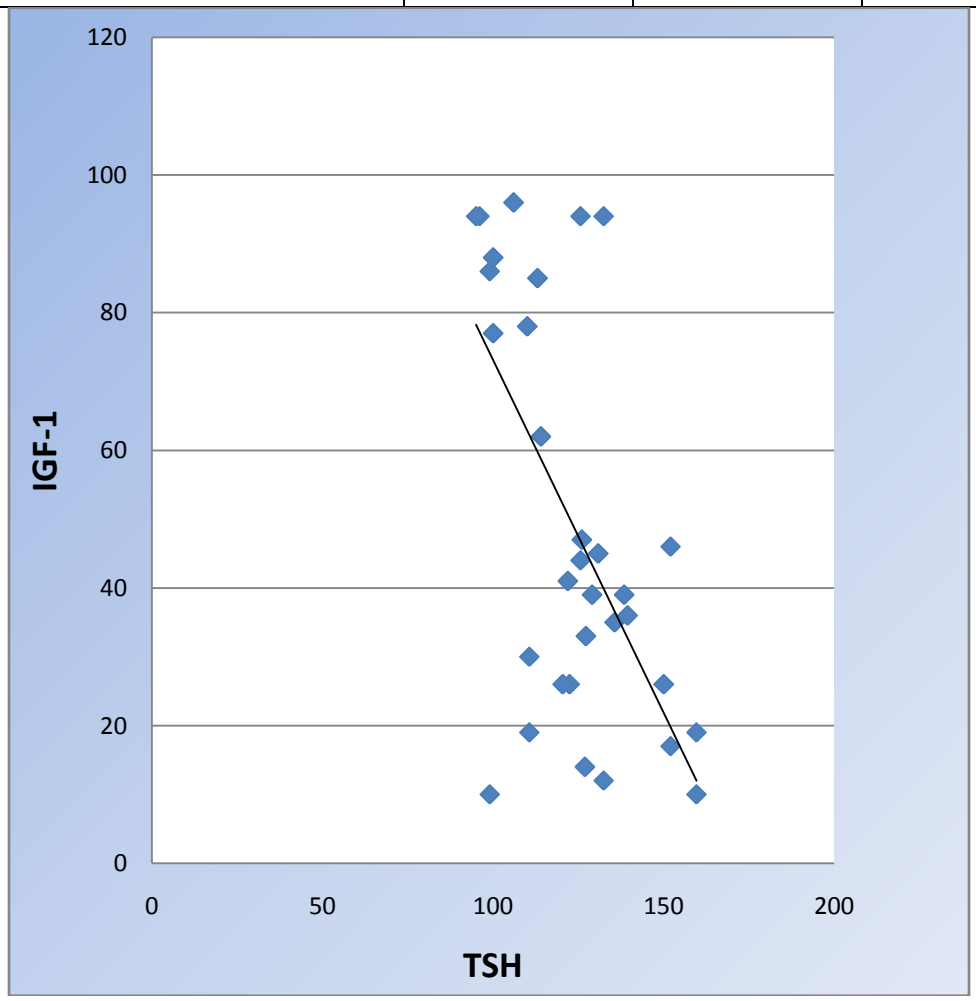

Fig.2 Linear correlation between serum IGF-1 and TSH in Hypothyroid subjects.

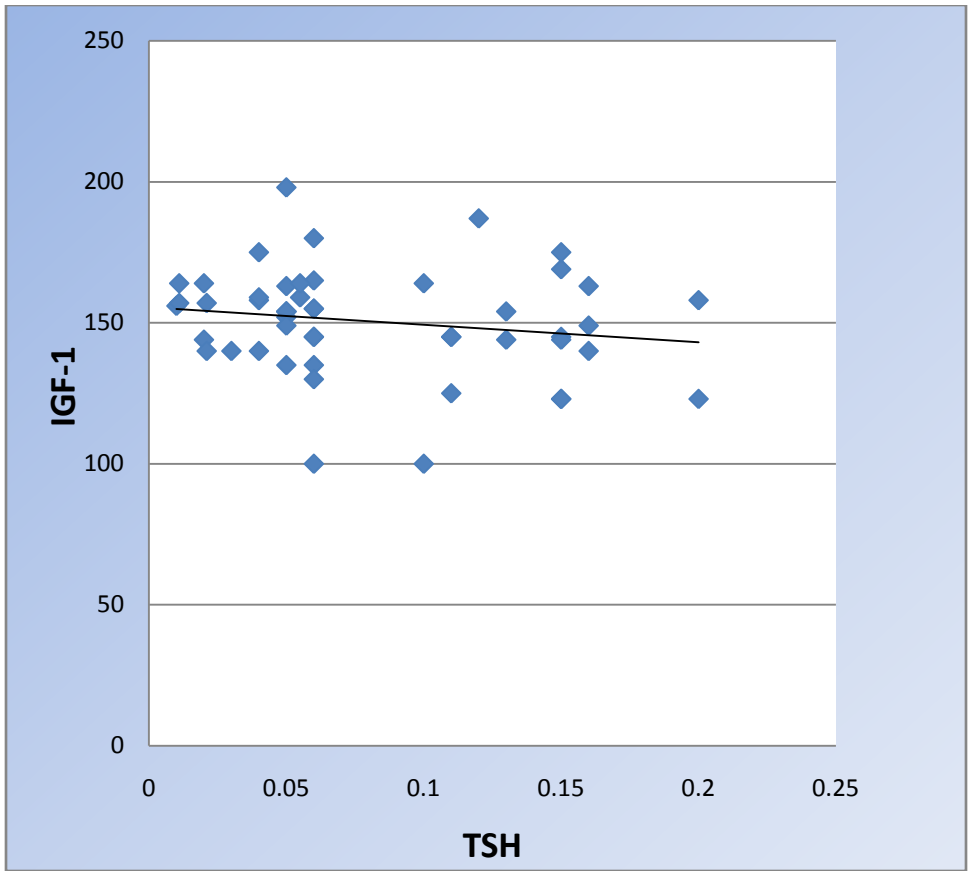

Fig.3 Linear correlation between serum IGF-1 and TSH in Hyperthyroid subjects.

DISCUSSION:

IGF-1, a potent mitogen for numerous cell types, promotes the progression of mitosis via the promotion of DNA synthesis, and has long-term effects on cell proliferation, differentiation and apoptosis [(12)]. Thyroid hormones play a role in the regulation of insulin-like growth factor type 1 (IGF-1) that functions as the major mediator of growth hormone (GH)-stimulated somatic growth, as well as a mediator of GH-independent anabolic responses in many cells and tissues [(2)].

In our study we found decrease level of IGF-1 in patients with thyroid dysfunction. The IGF-1 serum level were significantly lower in hyperthyroid (150.44±18.8) and hypothyroid group (123.42±16.8) as compared to control group (192.16±30.8).) this was similar with the study of Akin et al; (2009) [(1)].

Bona G et al; (1999) [(2)] also reported that thyroid hormones are involved in the regulation of the GH/IGF axis. Hypothyroidism is associated with a reduction in GH pulsatility and in GH-response to stimulatory tests. In hypothyroidism, serum levels of IGF-1 and IGFBP-3 fall and these changes are reversed after short term replacement with L-T4.

Cavaliere H et al; (1987) [(3)] found a significant and positive correlation between (IGF-1) Sm-C and serum T4 and T3 concentrations. Plasma (IGF-1) Sm-C basal levels were significantly lower in primary hypothyroid subjects. The subnormal response of plasma (IGF-1) Sm-C during effective thyroid hormone therapy could be an additional factor involved in growth failure of endemic cretins.

In our study we found serum IGF-1 levels decrease in hypothyroid status and correlate negatively with TSH levels. GH/IGF-1 axis may be influenced in clinical or sub clinically hypothyroid patients. This study was correlated with the study of P. Iglesias et al; (2001) [(11)] according to them thyroid status affects GH/IGF axis. Hypothyroidism is associated with significant reductions of IGF-1 and IGFBP-3, and IGFBP-1 is elevated in both hypothyroidism and hyperthyroidism.

Yen-Jui Chang et al; (2014) [22] also found that IGF-1 secretion was inhibited by hypothyroidism. The physiological functions of the Ghrelin/GHS-R axis, namely stimulating GH release and increasing food intake, are interrupted, while the GH/IGF-1 axis operates independently from hypothyroidism.

Ceren Eke Koyuncu et al; (2013) [4] previously concluded that serum IGF-1 levels decrease in hypothyroid status and correlate negatively with TSH levels. In accordance with that study we also found a significant negative correlation of IGF-1 with TSH in hypothyroid subjects (r= -0.62) and in hyperthyroid subjects (r= -0.17).

CONCLUSIONS:

Changing in serum level of IGF-1 may be considered as a marker for diagnosis of thyroid dysfunction. Thus the measurement of IGF-1 possibly can prevent the false diagnosis of thyroid assessment and may offer more effective interventions to improve patients' care and the economic aspect.

Recommendations: Our study has some limitations : In our study sample size were too small, A larger sample size would have given more reliable results .it covered only a particular age group. In this study there were no different group for male and female. Further study is required.

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References :

1. Akin, F.,Yaylali, G.F.Turgut, S.Kaptanoglu, B. "Growth hormone/insulin-like growth factor axis in patients with subclinical thyroid dysfunction". Growth Horm. IGF Res.,2009;19: 252–255.
2. Bona G, Rapa A, Boccardo G, Silvestro L, chiorboli E. **"**IGF-1 and IGFBP in congenital and acquired hypothyroidism after long-term replacement treatment". Minerva Endocrinol.,1999 Jun;24(2):51-5.
3. Cavaliere H, Knobel M, Medeiros-Neto G. "Effect of thyroid hormone therapy on plasma insulin-like growth factor I levels in normal subjects, hypothyroid patients and endemic cretins". Horm. Res., 1987; 25(3):132-9.
4. Ceren Eke Koyuncu, Sembol Turkmen Yildirmak, Mustafa Temizel, TevfikOzpacaci, Pinar Gunel, MustafaCakmak and Yuksel Gulen Ozbanazi "Serum Resistin and Insulin like growth factor-1 Levels in Patients with Hypothyroidism and Hyperthyroidism". Journal of thyroid research, 2013; 2013: 306750.
5. Cianfarani S, Liguori A, Germani D. "IGF-I and IGFBP-3 assessment in the management of childhood onset growth hormone deficiency". EndocrDev, 2005; 9: 66-75.
6. Dayan CM, Panicker V.(2009) "Novel insights into thyroid hormones from the study of common genetic variation". Nature Rev. Endocrinology, 5(4): 211–18.
7. D'Ercole AJ, Applewhite GT, Underwood LE. Evidence that somatomedin is synthesized by multiple tissues in the fetus. Dev Biol 1980;**75:**315–28.
8. D. G. Dills, C Allen, M Palta, D J Zacccaro, R Klein, and D D' Alessio."Insulin-like growth factor-1 is related to glycemic control in children and adolescents with newly diagnosed insulin-dependent diabetes." J ClinEndocrinoMetab, 1995; 80(7): 2139-43.
9. E. Pucci, L. Chiovatoand A. (2000) . Pinchera. "Thyroid and Lipid metabolism". International journal of obesity, 24(2):S109-S112.
10. Fuentes EN, Zuloaga R, Valdes JA, Molina A, Alvarez M "Skeletal muscle plasticity induced by seasonal acclimatization involves IGF1 signaling: implications in ribosomal biogenesis and protein synthesis". Comp Biochem Physiol B Biochem Mol Biol. 2014 Oct;176:48-57.
11. Iglesias P, Bayon C, Mendez J, Gancedo PG, Grande C, Diez JJ. "Serum insulin-like growth factor type 1, insulin-like growth factor-binding protein-1, and insulin-like growth factor-binding protein-3 concentrations in patients with thyroid dysfunction". Thyroid, 2001; 11(11): 1043-8.
12. Jones JI, Clemmons DR. Insulin-like growth factors and their binding proteins: biological actions. Endocr Rev. 1995;16:3–34.
13. J. P. Miell, A M Taylor, M Zini, H. G. Maheshwari, R J Ross, and R Valcavi. "Effect of hypothyroidism and hyperthyroidism on insulin-like growth factors and growth hormone and IGF-binding proteins"J ClinEndocrinolMetab, 1993; 76(4): 950-5.

14. Merimee T, Laron Z, eds. Growth hormone, IGF-I and growth: new views of old concepts. Modern endocrinology and diabetes, Vol. 4. London-Tel Aviv: Freund Publishing House Ltd, 1996.
15. Nilsson A, Isgaard J, Lindhahl A, *et al*. Regulation by growth hormone of number of chondrocytes containing IGF-I in rat growth plate. *Science* 1986;**233**:571–4.
16. Rinderknecht, E., Humbel, R. E. (1978) "The amino acid sequence of human insulin-like growth factor I and its structural homology with proinsulin". J. Biol. Chem. 253: 2769-2776.
17. Roberto valcavi, Carlos Dieguer, Michele Zini, CovadongaMuruais, Felipe Casanueva and ItaloPortioli. "Influence of hyperthyroidism on growth hormone secretion". Clinical Endocrinology, 1993; 38(5): 515-522.
18. Rosenfeld RG, Roberts CT, Jr, eds. The IGF system—molecular biology, physiology and clinical applications. Totowa,NY: Humana Press, 1999.
19. Stanilov NS, Karakolev IA, Deliysky TS, Jovchev JP, Stanilova SA. "Association of Insulin-like growth factor-1 receptor polymorphism with colorectal cancer development". Mol Bio Rep, 2014; 10: 3708.
20. Sumida Y, Yonei Y, Tanaka S, Mori K, Kanemasa k, Imai S, Taketani H, Hra T, Seko Y, Ishiba H, Okajima A, Yamaquchi K, Moriquchi M, Yasui k, Minami M, Itoh Y. "Lower levels of insulin-like growth factor-1 standard deviation score are associated with histological severity of nonalcoholic fatty liver disease".Hepatology research, 2014; 10: 12408.
21. W.F. Ganong, Ganong medical Physiology, 16 Edition, 2002.
22. Yen-Jui Chang, Chii-Min Hwu, Chii-Chang Yeh, Paulus S. Wang and Shyi-Wu Wang. "Effects of Subacute Hypothyroidism on Metabolism and Growth-Related Molecules." Molecules, 2014;19:11178-11195.
23. Zapf J, Froesch ER. Insulin-like growth factor I actions on somatic growth. In: Kostyo J, ed. Handbook of physiology,Vol. V, Section 7. Philadelphia: American Physiological Society, 1999:663–99.
24. Z Laron. Insulin-like growth factor 1 (IGF-1): a growth hormoneJ Clin Pathol: Mol Pathol 2001;**54**:311–316.