STUDY OF THYROID HORMONES AND TSH LEVELS IN PATIENTS WITH HYPOTHYROIDISM IN KARACHI

Pages with reference to book, From 39 To 43

R.A. Khan, Perveen Akhter, Nasim Jahan (Pakistan Atomic Energy Medical Centre, Jinnah Postgraduate Medical Centre, Karachi.)
Farida Agha (Pakistan Medical Research Council, Research Centre, Jinnah Postgraduate Medical Centre, Karachi.)

Abstract

Sixty six clinically proven hypothyroid subjects were studied using radioimmunoassay techniques for estimation of serum thyroid hormones and pituitary TSH concentrations. The mean level for serum TSH was significantly elevated while the mean levels for serum T4, 13 and Free T4 were significantly low. A significant positive correlation was found between 14 and T3 and between T4 and FTI. Serum TSH was found to have a significant negative correlation with FTI. There was no significant difference in the mean of various hormones between the males and females. Serum TSH was considered to be the most diagnosis of hypothyroidism (JPMA 37:39 , 1987).

INTRODUCTION

The clinical features of hypothyroidism are one of the most insidious of all diseases. Sometimes symptoms are present for years before diagnosis is confirmed. Even severe myxedema could be missed by one who fails to appreciate the slow progress of the disease process. Milder form of the disease often escapes diagnosis because of vague and non specific signs and symptoms. Confirmation of the diagnosis is made by estimation of thyroid horniones, that is low T4 and 13 after correction for the concentration of binding proteins. On occasions T3, T4 , estimations will not keep in the diagnosis because of certain amount of overlap between euthyroid and hypothyroid range and abnormality of the levels of binding capacity of thyroid binding globulin. This study was undertaken to estimate the levels of thyroid hormones and pituitary TSH in subjects with hypothyroidism.

MATERIAL AND METHODS

Sixty six patients with clinically proven hypothyroidism attending the Radioisotope Centre Pakistan Atomic Energy Medical Centre, Jinnah Postgraduate Medical Centre, Karachi were studied.
Name, age, sex, socioeconomic status and the place of origin were recorded. Blood was drawn fof the estimation of thyroid hormones and pituitary TSH. Iodine-uptake for two hours, 24 hours and 48 hours was also done in some cases. Serum thyroxine (T4), tri-iodothyronine (T3) and serum thyrotropin (TSH) were measured by standard double antibody radioimmunoassays (RIA) using RIA kits supplied by Ammersham International (U.K.). Two types of RIA kits were used, the Simple RIA and the Amerlex RIA kit. The principle of the assay was similar, but the method was modified in Amerlex RIA and the normal ranges given in the kit were slightly different. Serum T4, T3 and TSH in 41 cases were measured by simple RIA and in 25 cases by Amerlex RIA. The thyroid hormone binding capacity was measured by 13 uptake (MAA) simple RIA kit. An indirect “Free” 14 index (FTI) was calculated by the formula.
In 25 patients the free-thyroxine (FT4) was measured by Amerlex RIA kit only.
Forty one apparently healthy subjects selected from medical and para-medical staff of Jinnah Postgraduate Medical Centre and Radioisotope Centre, Karachi were taken as controls. The T4, T3, TSH and T3 -uptake in 15 normal subjects were measured by simple RIA kit and in 26 subjects by

Amerlex RIA kit. The Free-T4 was estimated by Amerlex RIA.
Each hormone assay was performed in duplicate serum samples. A set of quality control sera, (supplied from Amersham International. U.K.) in duplicate was also analysed with each hormone assay to check the accuracy of the results. The radioactivity was counted in Mini-Assay type 6-20 Gamma counter. The results were further checked by counting the tubes in Multi detector Computerised Gamma Counter (model 1612 Nuclear Enterprises) using 4 parameter non linear curve fitting model. The coefficient of correlation "r" between various hormones was calculated by Karl Pearson formula. The value for "t" was calculated and the corresponding value of "p" was noted from the table.

RESULTS

CONTROLS

Of 41 normal subjects, 29 were males and 12 females. The mean (±SE) age was 31.82 (±1.82) for males and 28.41 (±2.71) for females. Their ages ranged between 18 to 58 years and 22 to 56 years respectively. All the females (100%) and 27 (93.1%) males belonged to Karachi, while 1 (3.44%) male belonged to Punjab and 1 (3.44%) to Bangladesh. Twenty two (75.86%) males and 9 (75%) females were of middle class, 3 (10.34%) males and 3 (25%) females were of high socioeconomic strata and only 4 (13.79%) males belonged to poor class.
The normal ranges for T4, T3, TSH, T3 -uptake and FT4, given in the kits of simple and Amerlex RIA and those found in normal males and females of this study are shown in Table-I.

TABLE – I

Range of Thyroid Hormones and TSH in Normal Subjects by Simple and Amerlex RIA.

Simple RIA	T_4 (SIU)	T_3 (SIU)	TSH (SIU)	T_3-Uptake (%)	FT_4 (SIU)	FTI (SIU)
Normal Males	63.00-144.00	1.92-2.92	0.6-5.0	25.08-34.4	–	18.69-43.47
Normal Females	92.66-146.72	1.31-2.74	1.5-6.9	26.23-33.14	–	27.89-45.93
KIT Range	63.00-173.00	1.21-3.08	0.0-10.0	25.5-34.40	–	17.80-46.10
Amerlex RIA	–	–	–	–	–	–
Normal Males	77.86-139.00	1.17-2.90	0.0-2.75	–	17.25-23.94	–
Normal Females	93.95-166.00	1.09-2.24	1.2-2.29	–	13.26-28.70	–
KIT Range	54.00-142.00	0.80-2.46	0.0-5.50	–	8.80-23.00	–

All the ranges found in normal subjects of this study were within the range given in the kits except in Amerlex RIA group, the upper limit of T4 and Free T4 in females and T3 in males slightly exceeded the kit range.

TABLE – II

Mean Values of Thyroid Hormones and TSH in Normal Subjects by Simple and Amerlex RIA.

Hormones	Simple RIA		Amerlex RIA	
	Males (No)	Females (No)	Males (No)	Females (No)
T_4 (SIU)	116.36 ± 6.99 (10)	115.11 ± 6.69 (7)	106.11 ± 3.93 (19)	120.54 ± 13.24 (5)
T_3 (SIU)	2.43 ± 0.09 (10)	2.26 ± 0.25 (7)	1.86 ± 0.08 (19)	1.75 ± 0.24 (5)
TSH (SIU)	3.28 ± 0.37 (10)	4.49 ± 0.81 (7)	1.27 ± 0.17 (19)	1.64 ± 0.18 (5)
T_3-Uptake (%)	30.21 ± 0.94 (10)	30.03 ± 1.04 (7)	21.87 ± 1.30 (19)	21.98 ± 2.50 (5)
F-T_4 (SIU)	–	–		
F-T_3-I	34.96 ± 2.02 (10)	34.59 ± 2.50 (7)	–	–

Results are mean (SE).

Table II, shows the mean (± SE) of thyroid hormones and TSH in normal males and females by simple and Amerlex RIA. There was no significant difference in the mean levels between males and females in the two groups.

PATIENTS

Of 66 patients with hypothyroidism 19 (28.78%) were males and 47 (71.27%) females, F:M ratio was 2.5:1. Their ages ranged between 100 months to 60 years and 2.5 to 65 years respectively. The mean (±SE) age for males was 32.01 (± 5.03) and for females was 36.03 (± 2.09).

Fifteen (78.94%) males and 34 (72.34%) females were of poor class while in middle class there were 4 (21.05%) males and 13 (27.65%) females. The majority of males (84.2%) and females (87.23%) belonged to Karachi. Only 2 (10.52%) males belonged to Punjab and one (5.26%) to Sind. In females 2 (4.25%) were fromSind, one (2.12%) from Punjab, one (2.12%) from Swat and 2 (4.25%) were from India. The 24 hours- iodine uptake was low in both male and female patients. The mean was 9.96% in females and 10.9% in males.

TABLE – III

Mean Values of Thyroid Hormones and TSH in Hypothyroid Patients by Simple and Amerlex RIA.

Simple RIA	T_4 (SIU) (No)	T_3 (SIU) (No)	TSH(SIU) (No)	T_3-Uptake(%) (No)	FT_4 (SIU)	FTI
Hypothyroid Males	6.62 γ 2.15 (11)	0.50 ± 0.12 (11)	90.39 ± 7.12 (11)	23.58 ± 0.71 (11)	– –	1.48 ± 0.49 (11)
(Normal males)	(116.36 ± 6.99) (10)	(2.43 ± 0.09) (10)	(3.28 ± 0.37) (10)	(30.21 ± 0.94) (10)	–	(34.96 ± 2.02) (10)
Hypothyroid Females	6.65 ± 1.17 (30)	0.51 ± 0.07 (30)	85.39 ± 5.07 (30)	22.59 ± 0.38 (30)	–	1.71 ± 0.39 (30)
(Normal Females)	(115.11 ± 6.69) (7)	(2.26 ± 0.25) (7)	(4.49 ± 0.81) (7)	(30.03 ± 1.04) (7)	–	(34.59 ± 2.50) (7)
Amerlex RIA	–	–	–	–	–	–
Hypothyroid Males	9.70 ± 2.81 (8)	0.52 ± 0.17 (8)	93.6 ± 15.33 (8)	23.98 ± 0.25 (8)	1.91 ± 0.43 (8)	1.49 ± 0.65 (8)
(Normal Males)	(106.11 ± 3.93) (19)	(1.86 ± 0.08) (19)	(1.27 ± 0.17) (19)	–	(21.87 ± 1.30) (19)	–
Hypothyroid Females	9.03 ± 1.53 (17)	0.55 ± 0.17 (17)	92.11 ± 8.45 (17)	22.82 ± 0.45 (16)	1.49 ± 0.22 (14)	1.86 ± 0.37 (17)
(Normal Females)	(120.54 ± 13.24) (5)	(1.75 ± 0.24) (5)	(1.64 ± 0.18) (5)	–	(21.98 ± 2.50) (5)	–

Results are mean (SE)

Table III shows the mean (± SE) of thyroid hormones and TSH levels in male and female patients by simple and Amerlex RIA. There was no significant difference in the mean of various hormones between the two sexes.

The difference in the mean levels of all hormones between the patients and controls was found to be highly significant. The mean levels for T4, T3 -uptake and Free T4 were significantly low ($P < 0.001$) in both male and female patients, hereas the mean serum TSH was significantly ($P < 0.0001$) high in these cases.

The free-T4 index (FTI) calculated from T4 and T3 uptake was also very low. The mean difference of FTI between patients and controls was highly significant ($p <,0.001$)

The mean T3/T4 ratio was 0.21 in males and 0.094 was in females. The ratio was found to be higher than normal males (0.018) and females (0.017).

The range for serum T4, T3, TSH, T3-uptake and FT4 in patients is shown in the Table IV.

TABLE – IV

Range of Thyroid Hormones and TSH Levels in Hypothyroid Patients by Simple and Amerlex RIA.

Simple RIA	T_4 (SIU)	T_3 (SIU)	TSH (SIU)	T_3-Uptake (%)	FT_4 (SIU)	FTI (SIU)
Hypothyroid Males	0.00 −20.59	0.00 −1.15	58.0 −127.68	19.62 −28.69	–	0.00 −4.80
(Normal Males)	63.00 −144.00)	(1.92 −2.92)	(0.6 −5.0)	(25.08 −34.40)	–	(18.69 −43.47)
Hypothyroid Females	0.0 −24.45	0.00 – 1.59	48.0 −138.74	18.50 −26.4	–	0.00 −10.04
(Normal Females)	92.66 −146.72)	(1.31−2.74)	(1.5−6.9)	(26.23−33.14)	–	(27.89−45.93)
Amerlex RIA						
Hypothyroid Males	0.0–21.88	0.0−1.46	31.5−184.5	23.24−25.09	0.25−3.86	0.00−5.14
(Normal Males)	(77.86−139.0)	(1.17−2.9)	(0.0−2.75)	–	(17.25−23.94)	–
Hypothyroid Females	0.64−28.31	0.1−2.77	55.0−205.14	18.5−26.26	0.62−2.96	0.1−2.7
(Normal Females)	(93.95−166.0)	(1.09−2.42)	(1.2−2.29)	–	(13.26−28.7)	–

Significant difference was noted between the patients and controls in various hormonal ranges. The range for TSH in patients was remarkably higher than in controls. The ranges for T4 , T3 and FT4 were significantly lower than normal. The range for T3 -uptake was also low in patients.

A positive correlation was seen between T4 and T3 in both male (r0.57, $p < 0.05$) and female (r0 33, $p < 0.05$) patients by simple RIA and in males (r~0.65, $p < 0.05$) by Amerlex RIA. Serum TSH was found to have a negative correlation with T4 and T3 in both male and female patients, but it was not statistically significant.

There was a highly significant positive correlation between T4 and FTI in males (r0.96, $p < 0.001$) and females ($r=0.71$, $p < 0.001$) by simple RIA and in both males ($r=0.62$, $p < 0.05$) and females (r0.89, $p < 0.001$) by Amerlex RIA. Serum TSH was found to have a negative correlation with FTI, in both male ($r= -0.41$, $p < 0.001$) and female (r -0.65, $p < 0.001$) patients by Simple RIA and in males ($r= -0.51$, $p < 0.001$) patients by Simple RIA and in males (r -0.51, $p < 0.05$) by Amerlex RIA.

DISCUSSION

The diagnosis of hypothyroidism can be confirmed by' the estimation of thyroid hormones. There is in general a good correlation between T3 and T4 levels over a wide range of concentration[1]. In hypothyroidism both T4 and T3 levels are depressed while in subjects with mild thyroid failure T3 levels were significantly low and a positive correlation between T4 and T3 was also noted in the present study. T3 level alone is not sufçicient for the diagnosis of hypothyroidism, siiice a small proportion of hypothyroid patients have normal T3 values.

Measurement of FT4 concentration is believed to be the most direct indicator of thyroid status of an individual[3]. Normally the concentration of FT4 are effectively independent of binding protein concentration[4] Consequently abnormal concentration of FT4 are generally an indication of thyroid malfunction[5]. In all patients with hypothyroidism the FT4 is reduced. Similar reduction in FT4 levels was found in present study. A significant positive correlation between T4 and FTI[6] was also noted in

the present series. Once a reduced FT4 index has been found it is important to determine whether the cause of the disease is primary-owing to the thyroid disease, or secondary involving the hypothalamic pituitary axis. An elevation in serum TSH establishes the diagnosis of primary hypothyroidism[2-7]. if the serum TSH concentration is normal or borderline then the diagnosis of pituitary or hypothalamic hypothyroidism is made and further steps are taken to evaluate the possibility of a deficiency of other pituitary hormones.

A significant elevation in TSH levels was seen in the patients of this study and a negative correlation was found between serum TSH and free thyroxine index (FTI), confirming the diagnosis of hypothyraidism it is concluded that estimation of serum TSH should be considered as the most useful and sensitive single test that can be performed for the diagnosis of hypothyroidism including neonatal hypothyroidism. This is a base line data that shows the hormonal pattern and establishes the levels of thyroid hormones and pituitary TSH in hypothyroid patients studied in Karachi.

Further studies are needed to establish the hormonal levels in different thyroid disorders to ascertain the etiology and incidence rate. Early detection of congenital hypothyroidism is also important whichi if left untreated, can lead to permanent neurological damage and cretinism[8].

REFERENCES

1. Evered, D.C. Diseases of the thyroid in “Investigations of endocrine disorders”. Clin. Endocrinol. Metab., 1 974; 3: 425.
2. Evered, D.C., Ormston, B..J Smith, P.A., Hall, R. and Bird, T. Grades of hypothyroidism. ~Br. Med. J.,1973;1: 657.
3. Weilby, M. and O’Halloran, M.W. Measurement of the plasma free thyroxine level as a test of thyroid function. Br. Med. J., 1966; 2 : 668.
4. Robbins, J. and Rail, J.E. The interaction of thyroid hormones and protein in biological fluids. Recent Prog. Horm. Res., 1957; 13:16 1.
5. Braverman, L.E., Abreau, C.M., Brock, P., Kleinmann, R., Founder, L., Odstrchel, G. and Schoe-maker, HJ. Measurement of serum free thyroxine by RIA in various clinical states. J. Nuci. Med., 1980; 21: 233.
6. Clark, F. and Brown, HJ. Free thyroxine index. Br. Med. J.,1970;1 :543,672.
7. Hall, R., Amos, J. and Ormston, BJ. Radioimmunoassay of human serum thyrotrophin. Br. Med.J., l971;1:582.
8. AIm, 3., Hagenfeldt, L., Larsson, A. and Lundberg, K. Incidence of congenital hypothyroidism; retrospective study of neonatal laboratory screening versus clinical symptoms as indicators leading to diagnosis. Br. Med. 3., 1984; 289: 1171.