ORIGINAL ARTICLE

Age and Sex Related Changes in Thyroid Functions in Normal Healthy Subjects of Jammu Region

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Abstract

The study was conducted on 150 normal healthy subjects of different age groups of both sexes (belonging to Jammu region only) to find out the pattern of physiological variations in the levels of the thyroid hormones viz. T_3 (triiodothyronine), T_4 (thyroxine) and TSH (thyroid stimulating hormone). The blood levels of T_3, T_4 and TSH of these subjects were found out by using radioimmunossay technique. The serum T_3 and T_4 levels decreased progressively with age with the highest levels being observed in children and lowest in the elderly. The serum T_3 levels of males and females did not show any difference in any age group, whereas the mean serum T_4 level in the adult females was more than that of adult male though the difference is statistically insignificant. There was, however, no difference between the serum T_4 levels of males and females of children, adolescents and elderly groups. The mean serum TSH level was found to increase progressively with age and did not show any significant difference in males and females in any age group.

Key Words

Triiodothyronine, Thyroxine, Thyroid stimulating hormone

Introduction

The thyroid gland is requires iodine for hormone synthesis, hence adequate dietary intake of iodine is, therefore, essential (1). The daily dietary intake of iodine varies widely throughout the world, depending on iodine content of soil and water and on dietary practice (2). The population iodine intake level is a major determinant of the types of thyroid abnormalities prevalent in a particular community (3). The relation of the thyroid gland to the aging process is of interest because of the importance of the organ in regulating the rates of various body functions (4). Thyroxine (T_4) and triiodothyronine (T_3) are the two main metabolically active hormones of the thyroid gland. It was found that during a normal human life span, serum T_3 is low at the time of birth, increases markedly during early infancy, remains high during childhood, is reduced (during) after adolescence, then remains stable until late middle age and ultimately decreases in old age. Reports regarding age related changes in serum T_4 levels are conflicting. Some studies reported stable T_4 levels for men throughout life, and T_4 values lower in females older than 60 years(5-9).

TSH values increased significantly in females over age 60. Throughout all decades, males had stable TSH levels that were slightly higher than the female levels before age 60 and lower thereafter (4-6). Estrogens cause increased secretion of thyroid binding globulin (TBG). On the other hand, TBG levels are depressed by androgens (10).

The present study has been undertaken to define the pattern of physiological variations in the level of T_3, T_4 and TSH of healthy subjects (both males and females) in Jammu region (Goitre belt) and also to define the range of thyroid functions in normal healthy subjects.

Material and Methods

The study was conducted on 150 subjects belonging to Jammu region. The subjects chosen for the study were

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ambulatory and apparently in normal nutritional state without any abnormalities on routine physical examination. A detailed history was taken to rule out the presence of any thyroid disorder (hyperthyroidism or hypothyroidism) or intake of drugs known to affect thyroid functions. Also the presence of any chronic illnesses such as renal failure, malignant neoplasm, hepatic cirrhosis and diabetes mellitus and other diseases known to affect thyroid functions was ruled out.

The subjects were classified into three groups according to their age: -

Group A : 50 subjects (01-20 years).
Group A was further divided into 2 sub groups:
Group A1 – 25 children of age group (01-10 years).
Group A2 – 25 adolescents of age group (11-20 years).
Group B : 50 adult subjects of age group 21 to 60 years.
Group C : 50 elderly subjects of more than 60 years of age.

The number of males and females was equal in both the groups.The blood sample was taken from non-fasting subjects as fasting causes a rapid fall in serum T_3 concentration. The tests were performed by radio-immunoassay method as per the protocol given in the RIAK-4A, RIAK-5A and RIAK-9 kits for T_3, T_4 and TSH respectively, supplied by BARC, Mumbai.

Graphs showing standard curve for T_3 and T_4 were plotted with counts on y-axis versus standard concentration of T_3 and T_4 on x-axis. The sample T_3 and T_4 concentrations were read from the standard curve. Similar procedure was adopted for reading sample TSH concentration from the standard curve. Difference in means of T_3, T_4 and TSH of males and females of different age groups was statistically evaluated using 'unpaired' t-test.

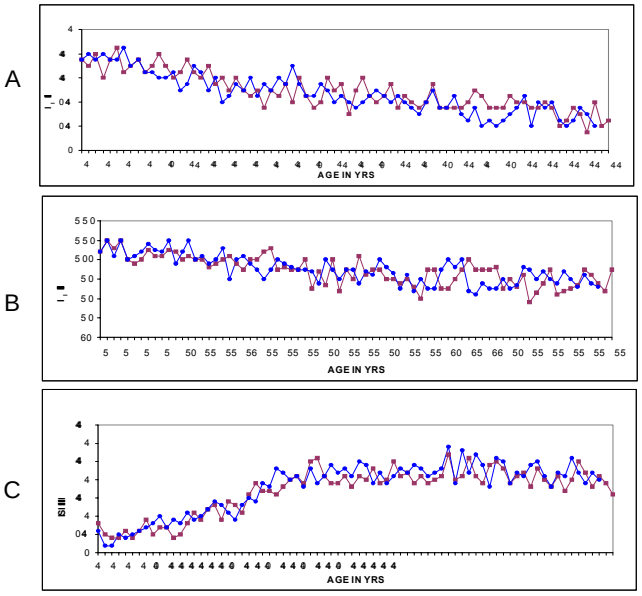
Results

In our study, we observed that serum T_3 and T_4 levels decrease progressively with age with highest serum levels of these hormones present in children and lowest in the elderly. The mean serum TSH level, however, was in the lower limit in children and increased progressively with age (Table 1 and Fig. 1). There was no difference in serum T_3 levels of males and females in any age group. The serum T_4 levels of males and females of children, adolescents and elderly also did not show any difference whereas the mean serum T_4 level in the adult females was more than that of adult males though this difference was statistically insignificant. The mean serum TSH levels of males and females also did not show any significant difference in any age group (Table 1 and Fig. 2)

Table 1: Comparison of Thyroid Function Tests of Different Age Groups in Both Sexes

GROUP							

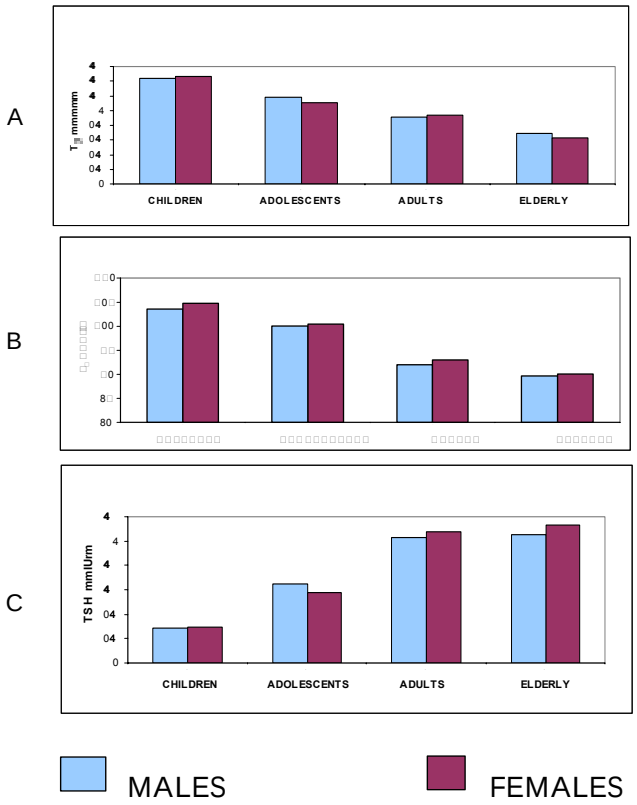
Fig. 1: Distribution of T_3, T_4 and TSH Values in Different Age Groups



Male Subjects
Female subjects

A: T_3 values in different age groups.
B: T_4 values in different age groups.
C: TSH values in different age groups.

Fig. 2: Comparison of T_3, T_4 and TSH levels in males and females of different age groups



A: Comparison of male & female T_3 values in different age groups.
B: Comparison of male & female T_4 values in different age groups.
C: Comparison of male & female TSH values in different age groups.

Discussion

Thyroid function probably decreases with senescence and the decrease is probably the result of the aging process (4-6). It is observed that during a normal human life span, serum T_3 is low at the time of birth, increases markedly during early infancy, remains high during childhood and is reduced after adolescence, then remains stable until late middle age and ultimately decreases in old age (5,6). Several studies reveal that mean T_4 values remain stable throughout life in males but in females under age 60, T_4 values are significantly higher than in older women. This is believed to result from a decline in estrogen dependent Thyroid Binding Globulin concentration after the age of sixty (4-6). Our results also show that T_3 and T_4 decrease with age with highest serum levels of these hormones in children and lowest in the elderly.

In our study, the highest mean T_3 value (1.456 ng/ml) was observed in the children (1-10 yrs.), it fell to 1.114ng/ml in adolescents and further decreased to 0.913ng/ml in adults and to 0.658ng/ml in elderly people. No significant difference was found between males and females in any age group. Similar findings of progressive decrease of T_3 levels from childhood onwards to adolescence were observed in several studies (6,11). Some attributed these values to the progressive change in the relative thyroid output of T_3 and T_4 and not due to a decrease in TBG because there is no significant change in the levels of serum concentration of TBG in young children and adults (6,12). However, others observed that this change in T_3 levels was due to decreasing TBG levels since T_3 like T_4 is largely transported bound to TBG; the fall in mean T_3 and TBG approximated 29% and 30% respectively between 1 and 15 years in their studies (7-9). In the present study also, the mean T_3 value in adolescents (11-20 yrs) fell to 1.114ng/ml from 1.456ng/ml in children (1-10 yrs). It has been observed that increased metabolic activity during infancy and childhood leads to increased peripheral utilisation of thyroid hormone (13).

Some previous studies contradicted these findings (7-9,13). However subsequent studies done to correlate the relationship between thyroid growth (as determined by ultrasonography) and chronological age, body surface area (BSA) showed varied results. It has been observed that marked changes occur in thyroid function during puberty as an adaptation to body and sexual development. Adaptation of the hypothalamo–pituitary–thyroid gland axis in response to increase energy expenditure has been suggested. A prepubertal surge of TSH between 9.0 and 9.5 years, followed by a transient increase in circulating thyroid hormones (T_4 and T_3) may account for this adaptation (9). With ongoing puberty, however, decreasing or constant TSH levels have been reported, as well as progressive decrease in circulating thyroid hormones (13).

In some studies done in adolescents, in both genders, the thyroid volume was best related to BSA (7,8). The increase in thyroid volume was found to be similar in boys and girls upto age of menarche, when girls have a distinct thyroid growth spurt, suggesting that female sex steroids might have an additional positive influence on

thyroid function as well. Several authors have identified sex steroid receptors in normal and pathological human thyroid tissues and suggested that estrogens might have a positive influence and androgens a rather restraining influence on the thyroid gland itself (14,15).

In our study, the mean T_3 value was found to decrease further with age; the mean T_3 value of adults being 0.913ng/ml and that of elderly, 0.658ng/ml and the difference between the two was statistically significant ($p< 0.01$). Similar findings were reported by several other studies (5,16). This could be because of decreased thyroidal production and release with advancing age (5,9) or because of decrease in peripheral conversion of T_4 to T_3 (5,6,16). It is also possible that degradation rate of T_3 increases in old age leading to decreased serum T_3 levels (5). The decrease in serum T_3 in elderly could not be secondary to age related difference in concentration of TBG, because the TBG levels were found to increase in elderly . However no correlation was found between TBG and T_3 in elderly (5). Other studies failed to show any decrease in serum T_3 values in older persons (11).

Our study showed a progressive decrease in serum T_4 concentration with mean T_4 level of 104.12 ng/ml in children; 100.24ng/ml in adolescents; 92.33ng/ml in adults and 89.91ng/ml in elderly. In our study, though the mean T_4 level in adolescents was lower than that of children, it decreased further in adults from mean T_4 value of 100.24ng/ml to 92.33ng/ml ($p < 0.01$). These results did not match with the results of some of the studies, which reported a gradual decrease of T_4 levels from infancy till these reached a nadir during the middle to end of the adolescent growth period suggesting that during adolescence there is an increase in the cellular uptake of thyroxine because of increase in muscular mass, which coincides with an increase in the BMR (6).

Present study showed the mean T_4 concentration in the elderly group to be lower than that of adults, although the difference was statistically insignificant. Similar age related decrease in serum T_4 concentration in older people was reported by other studies . This decrease could be ascribed to a primary retardation of processes for hormone metabolism within the cell i.e. these changes could be a consequence of the seeming hypometabolism associated with aging (11,12). Some authors have observed that physiological changes in thyroid hormone concentrations might be related to changes in the overall physical functions in the elderly (4).

Our study show no significant difference in male and female T_4 values in children, adolescents and elderly. However, the mean T_4 level in the adult females (93.0 ng/ml) was more than that of males (91.96 ng/ml), but the difference between the two was statistically insignificant. This is in contrast to other studies, which found significant difference in serum T_4 concentration in male and female adults (5,6). This is explained by increased binding of T_4 with TBG in adult females. Present study failed to show similar results, probably because in a bid to stick to exclusion criteria for selecting patients, exact matching of age between the two sexes could not be accomplished. It has been observed that these sex-related differences may be masked unless samples are carefully age matched and obtained from young patients in full sexual maturity .

In the present study, mean TSH value in the children was in the lower limit of normal range i.e. 0.58mIU/ml. The mean TSH value increased to 1.23mIU/ml in adolescents, was 2.11mIU/ml in adults and 2.17mIU/ml in the elderly. There was no significant difference between TSH values of adult and elderly people though the difference in TSH concentration between children and adolescents was statistically significant ($p < 0.05$). Similar results were reported in other studies (17). It is possible that with increasing age there occurs a decrease in the sensitivity of the pituitary to slight deficiencies of thyroid hormone, so that more marked deficiency than younger individuals would be required to elicit hypersecretion of TSH.

It was observed that TSH values increased significantly in females over 60 years of age whereas males had stable TSH levels that were slightly higher than the female results before sixty years and lower thereafter (5). In our study, however, the mean TSH level of males and females did not show any significant difference in any age group. This could be due to the fact that subjects could not be exactly matched for height and weight.

In another study, which included healthy centenarians (unique group of very selected individuals free of major age related disease), it was found that serum

TSH concentrations 'decrease' with age and it was suggested that studies showing an increase in basal TSH levels might have not carefully excluded subjects with primary 'sub-clinical' hypothyroidism (16). These authors also suggested that a resetting of the pituitary threshold of TSH feedback suppression occurs in healthy elderly leading to reduced TSH levels for a given concentration of circulating thyroid hormone.

As a result of conclusions drawn from the present study in different age groups, the normal range for healthy subjects of different age groups of Jammu region can be established as shown in Table 2:

Table 2:

A very interesting and significant observation is that different laboratories reported varied results of T_3 and T_4 when T_3 standards and an unknown serum prepared by these workers were sent to 18 different laboratories. It is being concluded that the heterogeneity of normal T_3 values obtained in different laboratories is probably due to intrinsic methodological differences and due to these differences, it cannot be elucidated whether T_3 levels differ between communities.

Therefore, in view of the fact that age - related changes occur in thyroid status, it becomes imperative that clinical laboratories should establish normal values for different age groups in order to avoid diagnostic misinterpretations and therapeutic failures (6).

To sum up our observations, serum T_3 levels decline significantly progressively with age while serum T_4 levels decline significantly only from adolescent to adult group. The serum TSH levels, on the other hand, increase significantly only from children to adolescents. There is no significant difference in the mean serum T_3, T_4 and TSH values in males and females in any age group.

References

1. Weetman PA. The thyroid gland and disorders of thyroid function. In: Warrel D, Cox T, Firth J et al (eds).Oxford Textbook of Medicine, 4th Edn, Vol.2. Oxford University Press 2003: pp 209-23
2. Larsen PR, Davies FT and Hay ID. The thyroid gland. In: Wilson, Foster, Kronenberg et al (eds).Williams Textbook of Endocrinology, 9th Edn. Saunders Company, Philadelphia 1998: pp 390-10
3. Laurberg P, Pederson KM, Hreidarsson A et al: Iodine intake and the pattern of thyroid disorders: A comparative epidemiological study of thyroid abnormalities in the elderly in Iceland and in Jutland, Denmark. J Clin Endocrinol Metab 1998; 83: 765-69
4. Van den Beld AW, Visser TJ, feelders RA, Grobbee DE, Lamberts SW. Thyroid hormone concentrations, disease, physical function and mortality in elderly men. J Clin Endocrinol Metab. 2005; 90(12):6735-37
5. Lipson A, Nickoloff LE, Tah HH et al: A study of age dependent changes in thyroid function tests in adults. J Nuclear Medicine 1979; 20: 1124-30
6. Westgren U, Burger A,Ingemansson S et al: Blood levels of 3,5,3'-triiodothyronine and thyroxine: Difference between children, adults and elderly subjects. Acta Med Scand 1976; 200: 493-95
7. Fleury Y, Van Melle G, Woringer V et al. Sex dependent variations and timing of thyroid growth during puberty. J Clin Endocrinol Metab 2001; 86:750-54
8. World Health Organization, International Council for control of Iodine Deficiency Disorders. Recommended normative values for thyroid volume in children aged 6-15 years. Bull World Health Organ 1997; 75:95-97
9. Michand P, Foradori A, Rodriguez-Portales JA et al: A prepubertal surge of thyrotropin proceeds an increase in thyroxine and 3',5',3'-triiodothyronine in normal children. J Clin Endocrinol Metab. 1991;72:976-81
10. Ganang WF. The thyroid gland. In: Ganong WF (ed).Review of Medical Physiology, 22nd Edn. The McGraw-Hill Companies. Inc.2005; PP 317-32
11. Nishikawa M, Inada M, Naito K et al. Age related changes of serum 3,3' - iiodothyronine, 3, 5'-diiodothyronine and 3, 5 - diiodothyronine concentrations in man. J Clin Endocrinol Metab 1981: 52; 517-22
12. Anderson S, Pederson KM, Bruun NH, Laurberg P. Narrow individual variations in serum T_4 and T_3 in normal subjects: a clue to the understanding of sub clinical thyroid disease. J Clin Endocrinol Metab. 2002;87:1068-72
13. Dunger DB, Perkins JA, Jowett TP et al. A longitudinal study of total and free thyroid hormones and thyroxine binding globulin during normal puberty. Acta Endocrinol (Copenh)1990; 123:305-10
14. Dalla Valle L, Ramina A, Vianello S et al. Potential for estrogen synthesis and action in human normal and neoplastic thyroid tissues. J Clin Endocrinol Metab 1998;83:3702-09
15. Rossi R, Franceschetti P, Maestri I et al. Evidence for androgen receptor gene expression in human thyroid cells and tumours. J Endocrinol 1996; 148:77-85
16. Mariotti S et al. Complex alteration of thyroid function in healthy centenarians. J Clin Endocrinol Metab 1993;77: 1130-34
17. Shetty, Duthie: Anterior pituitary function and GH use in the elderly. Endocrinol Metab Clin Nor Am 1995; 24: 218.