WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 6, Issue 16, 1019-1028. Research Article ISSN 2277– 7105

STUDY OF THYROID FUNCTION TESTS IN AGING MEN OF RURAL AND URBAN AREAS OF JAMMU REGION

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Article Received on
14 October 2017,

Revised on 05 Nov. 2017,
Accepted on 25 Nov. 2017

DOI: 10.20959/wjpr201716-10262

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ABSTRACT

Aging is the progressive universal decline, first in functional reserve and then in function that occurs in organisms over time. It is heterogeneous and varies widely in different individuals and in different organs within a particular individual. The two most important clinical changes in endocrine activity during aging involve the pancreas and the thyroid gland. There may be impaired glucose tolerance or diabetes mellitus. Several changes in thyroid functions occur during aging. Normal aging is associated with changes in thyroid hormone production and metabolism. This results in an increased prevalence of subclinical thyroid disease in the elderly. In general subclinical thyroid disease is associated with an increased risk of overt thyroid dysfunction and different negative clinical parameters. The present study was undertaken to study the rural-urban difference in the thyroid function tests in healthy aging men of Jammu. The present prospective, one-year study was conducted on 100 healthy male subjects aged 50 years and above each from urban and rural areas of Jammu region. Subjects with any thyroid disorder or intake of drugs known to affect thyroid function, persons with chronic illness such as renal failure, malignant neoplasm, hepatic cirrhosis and diabetes mellitus were excluded from the study. In the present study, the mean T_3 value was found to increase slightly in age group D both in rural and urban subjects but the difference in the mean values was statistically insignificant. the mean T_4 values were within normal range for laboratory, in all the age groups both in rural as well as urban subjects. The difference in the mean values of T_4 in all age groups among rural and urban subjects was also statistically non-significant and the difference in the mean values of TSH in all the age groups among rural and urban subjects was statistically non significant.

KEYWORDS: Thyroid functions, Age, Thyroid hormone, Serum T_3, Serum T_4, Serum TSH.

INTRODUCTION

Aging is a general physiologic process that affects cells and the systems made up of them as well as tissue components.[1] There is a considerable variation in the effects of aging on healthy individuals, with some persons exhibiting extensive alteration in physiological functions with age, others little or none. Genetic factors, life style and societal investments in a safe and healthful environment are important aspects of successful aging.[2] The two most important clinical changes in endocrine activity during aging involve the pancreas and the thyroid gland. There may be impaired glucose tolerance or diabetes mellitus. These adults are at risk for development of secondary complications, mainly macrovascular, at an accelerated rate.[3] Several changes in thyroid functions occur during aging. Normal aging is associated with changes in thyroid hormone production and metabolism. Circulating total and free T_3 concentration demonstrate a clear, age dependent decline because of both reduced secretion and reduced peripheral conversion from T_4. Serum reverse T_3 (rT_3) seems to increase with age.[4] Serum T_4 usually remains the same or decreases in females. Serum thyroid stimulating hormone (TSH) has been reported to increase, decrease or remains unchanged with aging.[5] With an increase in age, marked changes in thyroid hormone production, metabolism and action occur. This results in an increased prevalence of subclinical thyroid disease in the elderly. In general subclinical thyroid disease is associated with an increased risk of overt thyroid dysfunction and different negative clinical parameters.[6] The present study was undertaken to study the rural-urban difference in the thyroid function tests in healthy aging men of Jammu.

MATERIALS AND METHODS

The present prospective, one-year study was conducted on healthy male subjects aged 50 years and above of Jammu region. One hundred subjects were taken from urban areas located in the Jammu city and 100 subjects were taken from rural areas located in the outskirts of Jammu city. After explaining the purpose of the study to all the subjects, they were requested to participate in the study with a written consent. 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 function. Care was taken to exclude persons with chronic illness such as renal failure, malignant neoplasm, hepatic cirrhosis and diabetes mellitus and other diseases known to affect thyroid function.

The subjects were distributed into four groups according to their age:

Age group	Age in years	No. of subjects		Total subjects
		Urban	Rural	
A	50 – 60	52	38	90
B	61 – 70	32	29	61
C	71 – 80	9	19	28
D	≥ 81	7	14	21
Total		**100**	**100**	**200**

The subjects included in the study were ambulatory and in normal nutritional state without any abnormality on routine physical examination. The physical and clinical examinations were performed in the Postgraduate Department of Medical Physiology and thyroid function tests were performed in the Radioimmunoassay (RIA) Section of Government Medical College, Jammu.

All the eligible subjects were interviewed by the investigator himself and details of information like age, respiratory rate, pulse rate, blood pressure and any significant recent or past illness was recorded.

For thyroid function tests, blood sample was taken between 9 am and 11 am from non-fasting subjects after obtaining their consent because fasting causes a rapid fall in serum T_3 concentration.[7]

4 ml of venous blood was taken from each subject under aseptic precautions. The blood was collected in a glass test-tube (without anti-coagulant) and allowed to clot at room temperature. The serum samples collected after centrifugation were stored at -20^0C till assay was performed. The samples were thawed prior to assay. The tests were performed by radioimmunoassay method as per the protocol given in the RIAK-4A, RIAK-5A and IRMAK-9 kits for T_3, T_4 and TSH respectively.

The subjects who were found to have altered thyroid function tests values especially higher TSH values, their blood samples were tested for anti-TPO antibodies by using Solid Phase Enzyme Immunoassay Technology.

The data was analyzed using computer software Microsoft Excel and SPSS version 12.0 for Windows. Mean and standard deviation (SD) was calculated and reported for quantitative variables. The statistical difference in mean value was tested using unpaired Student's 't' test. ANOVA (analysis of variance) was performed to evaluate statistical significance in more

than two groups. A p-value of <0.05 was considered a statistically significance. All p-values reported are two-tailed.

RESULTS

The present study was conducted on 100 subjects from urban areas of Jammu city and 100 subjects from rural areas in the outskirts of Jammu city. The mean age (± standard deviation) of rural subjects was 64.74 (± 12.25) years while the mean age (± standard deviation) of urban subjects was 60.99 (± 9.94) years. The difference between rural and urban subjects was statistically significant (t=2.37, p=0.01). Baseline haemodynamic and clinical characteristics of rural and urban subjects are given in Table 1.

The relationship of mean values of serum T_3, serum T_4 and serum TSH between rural and urban subjects according to their age group are given in Tables 2, 3 and 4.

In the age groups 61-70 years, 71-80 years and ≥81 years, the study observed eight subjects who had raised serum TSH. Subsequently, their blood samples were tested for anti-TPO antibodies, which were found to be well within the normal range for laboratory and were considered negative in all eight cases (Table 5).

Table 1: Mean haemodynamic and clinical parameters of rural and urban subjects.

Parameter	Rural area (n=100) Mean ± Standard deviation	Urban area (n=100) Mean ± Standard deviation	Statistical inference
Pulse rate/ minute	77.88 ± 4.54	76.90 ± 4.02	t=1.61, p=4.02*
Respiratory rate/minute	16.81 ± 1.85	16.62 ± 1.90	t=0.75, p=0.45*
SBP (mm Hg)	124.68 ± 6.17	124.12 ± 6.19	t=0.57, p=0.56*
DBP (mm Hg)	80.44 ± 4.17	80.14 ± 4.69	t=0.47, p=0.63*

*Non-significant

Table 2: Relationship of mean values of Serum T_3 (ng/ml) between rural and urban subjects according to their age group.

Age group (in years)	Rural subjects (n=100) Mean ± SD (Range)	Urban subjects (n=100) Mean ± SD (Range)	Statistical inference
Group A (51 – 60)	1.13 ± 0.10 (0.92 – 1.32)	1.09 ± 0.13 (0.68 – 1.38)	t = 1.51 p = 0.13*
Group B (61 – 70)	1.09 ± 0.18 (0.39 – 1.3)	1.05 ± 0.08 (0.94 – 1.28)	t = 1.03 p = 0.30*
Group C (71 – 80)	1.09 ± 0.10 (0.94 – 1.28)	0.98 ± 0.07 (0.88 – 1.12)	t = 2.56 p = 0.01**
Group D (≥ 81)	1.09 ± 0.11 (0.92 – 1.32)	1.12 ± 0.16 (0.94 – 1.42)	t = 0.55 p = 0.58*

Normal serum T_3 value = 0.7-2.0 ng/ml *Non-significant **Significant

Table 3: Relationship of mean values of serum T_4 (ng/ml) between rural and urban subjects according to their age group.

Age group (in years)	Rural subjects (N = 100) Mean ± SD (Range)	Urban subjects (N = 100) Mean ± SD (Range)	Statistical inference
Group A (51 – 60)	87.68 ± 8.98 (72 – 105)	87.73 ± 10.88 (55 – 110)	t = 0.02 p = 0.98*
Group B (61 – 70)	88.48 ± 16.44 (74 – 105)	88.90 ± 10.49 (70 – 110)	t = 0.12 p = 0.90*
Group C (71 – 80)	89.26 ± 9.17 (72 – 107)	90.11 ± 10.81 (70 – 104)	t = 0.21 p = 0.83*
Group D (≥ 81)	85.28 ± 10.11 (70 – 104)	89.85 ± 10.09 (70 – 100)	t = 0.97 p = 0.34*

Normal serum T_4 value = 55-135 ng/ml *Non-significant

Table 4: Relationship of mean values of Serum TSH (µIU/ml) between rural and urban subjects according to their age group.

Age group (in years)	Rural subjects (N = 100) Mean ± SD (Range)	Urban subjects (N = 100) Mean ± SD (Range)	Statistical inference
Group A (51 – 60)	2.56 ± 1.39 (0.82 – 5.5)	2.56 ± 3.46 (0.54 – (22.5)	t = 0.003 p = 0.99*
Group B (61 – 70)	5.04 ± 3.47 (0.12 – 70)	2.74 ± 2.56 (0.48 – 12.0)	t = –0.696 p = 0.48*
Group C (71 – 80)	1.96 ± 0.86 (0.51 – 4.1)	2.12 ± 1.73 (0.54 – 6.2)	t = 0.317 p = 0.75*
Group D (≥ 81)	2.38 ± 0.98 (1.2 – 4.9)	2.10 ± 1.41 (0.54 – 4.9)	t = 0.531 p = 0.60*

Normal value of Serum TSH = 0.3-5.0 µIU/ml *Non-significant

Table 5: Status of anti-TPO antibodies in subjects with raised TSH values (n = 8).

S. No.	Serum T_3 (ng/ml)	Serum T_4 (ng/ml)	Serum TSH (µIU/ml)	Anti-TPO Antibodies	
				U/ml	Inference
1.	0.92	95	6.2	6.21	Negative
2.	0.86	84	14.9	14.68	Negative
3.	1.1	82	7.6	19.76	Negative
4.	0.98	74	7.2	11.86	Negative
5.	1.04	90	8.6	22.02	Negative
6.	0.68	55	22.5	31.05	Negative
7.	1.08	82	12.0	13.55	Negative
8.	0.39	74	70.0	36.13	Negative

Normal value of Serum Anti-TPO = <50 U/ml.

Table 5: Status of anti-TPO antibodies in subjects with raised TSH values (n = 8).

S. No.	Serum T_3 (ng/ml)	Serum T_4 (ng/ml)	Serum TSH (µIU/ml)	Anti-TPO Antibodies	
				U/ml	Inference
1.	0.92	95	6.2	6.21	Negative
2.	0.86	84	14.9	14.68	Negative
3.	1.1	82	7.6	19.76	Negative
4.	0.98	74	7.2	11.86	Negative
5.	1.04	90	8.6	22.02	Negative
6.	0.68	55	22.5	31.05	Negative
7.	1.08	82	12.0	13.55	Negative
8.	0.39	74	70.0	36.13	Negative

Normal value of Serum Anti-TPO = <50 U/ml

DISCUSSION

The literature is replete with information concerning the effects of increasing age on different aspects of thyroid hormone economy in seemingly euthyroid individuals.[8] The present study was carried out with the objective of finding out if any age related difference exists in the thyroid functions in normal healthy aging men of rural and urban areas of Jammu region. The thyroid function tests viz. T_3, T_4, TSH were carried out by radioimmunoassay method in non fasting subjects because fasting produces a rapid fall in serum T_3 concentration.[7]

The mean age of rural subjects was 64.74 ± 12.25 years and that of urban subjects was 60.99 ± 9.94 years. The difference in the mean values of age between rural and urban subjects was statistically significant and the reason could be the unequal number of subjects in each age group.

In the present study, the mean T_3 values were higher in group A *i.e.* 1.13 ± 0.10 in rural subjects and 1.09 ± 0.13 in urban subjects, declined in group B *i.e.* 1.09 ± 0.18 in rural subjects and 1.05 ± 0.08 in urban subjects. The values were further low in group C both in rural as well as in urban subjects *i.e.* 1.09 ± 0.10 in rural subjects and 0.98 ± 0.07 in urban subjects.

Similar findings of progressive decrease in T_3 values with advancing age in elderly was reported by Lipson *et al.*,[9] Sawin *et al.*,[10] and Mariotti *et al.*[11] A possible explanation of this decrease in serum T_3 with advancing age could be decreased thyroidal production and release[9] or decrease in peripheral conversion of T_4 to T_3.[9,11]

In the present study, the mean T_3 values in the elderly rural subjects declined from 1.13 ± 0.10 in group A subjects to 1.09 ± 0.10 in group C subjects. In the elderly urban subjects, the mean T_3 values declined from 1.09 ± 0.13 in group A subjects to 0.98 ± 0.07 in group C subjects. The difference in the mean T_3 values in group C among rural and urban subjects was statistically significant and the decline in mean T_3 value was more in urban subjects as compared to rural subjects. The explanation for this could be variations in the dietary habits of urban and rural people. Moreover, the iodine intake of rural population has improved much as a result of awareness being created in the rural masses due to various nutritional and awareness programmes being launched by the government.

Even minor differences in iodine intake between populations are associated with differences in the occurrence of thyroid disorders. Both iodine intake levels below and above the recommended quantity are associated with an increase in the risk of disease in the population.[12]

In the present study, the mean T_3 value was found to increase slightly in age group D both in rural and urban subjects but the difference in the mean values was statistically insignificant.

Gupta *et al.*,[5] failed to show any decrease in serum T_3 values in older persons. The authors observed that in studies showing opposite results, it could be the inclusion of hospitalized patients with non-thyroidal illness, which resulted in varying reports of age related changes in thyroid function in the literature.

In the present study, the mean T_4 values were within normal range for laboratory, in all the age groups both in rural as well as urban subjects. The mean T_4 values in group A were 87.68 ± 8.98 in rural subjects and 87.73 ± 10.88 in urban subjects; in group B the mean T_4 values were 88.48 ± 16.44 in rural subjects and 88.90 ± 10.49 in urban subjects; in group C the values were 89.26 ± 9.17 in rural subjects and 90.11 ± 10.81 in urban subjects; and in group D the values were 85.28 ± 10.11 in rural subjects and 89.85 ± 10.09. The difference in the mean values of T_4 in all age groups among rural and urban subjects was also statistically non-significant.

Similar findings of normal range of T_4 values in elderly subjects were reported by Lipson *et al.*[9], Sawin *et al.*[10] and Mariotti *et al.*[11] Slight increase in the mean values of T_4, though in

normal range, had been reported in few percentages of subjects in their studies on elderly people by Kalmijn S *et al.*[13], Gussekloo *et al.*,[14] and Van den Beld *et al.*[15]

A similar slight increase in mean T_4 values with increasing age up to group C subjects (age group 71-80 years) followed by a decline thereafter, though the values were within normal range for laboratory were observed in the present study also. The values were higher in group C subjects (age group 71-80 yrs) *i.e.* 89.26 ± 9.17 in rural subjects and 90.11 ± 10.81 in urban subjects, but the difference in the mean values of T_4 in rural and urban subjects were statistically non-significant.

Van den Beld *et al.*[15] in their study on 403 elderly men aged 73-94 years reported increased mean values of T_4, though in normal range in the subjects and they explained that the changes in thyroid hormone concentrations may be due to a decrease in peripheral (hepatic) thyroid hormone metabolism with aging and also probably reflecting the effect of subtle NTI (non-thyroidal illness) and/or an increased catabolic state.

In the present study, the mean TSH values were within normal range for laboratory, in all the age groups in rural and urban subjects. In group A, the mean TSH values were 2.56 ± 1.39 in rural subjects and 2.56 ± 3.46 in urban subjects. In group B, the mean TSH values were 5.04 ± 3.47 in rural subjects and 2.74 ± 2.56 in urban subjects. In group C, the mean TSH values were 1.96 ± 0.86 in rural subjects and 2.12 ± 1.73 in urban subjects and in group D, the mean TSH values were 2.38 ± 0.98 in rural subjects and 2.10 ± 1.41 in urban subjects. The difference in the mean values of TSH in all the age groups among rural and urban subjects was statistically non significant.

Gupta *et al.*,[5] in their study of subjects ranging in age from 40-70 years, observed high values of TSH in elderly group but these were statistically insignificant. In the present study also there was no significant difference between TSH values of rural and urban subjects.

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 in younger individuals would be required to elicit hypersecretion of TSH.[8]

Surks and Hollowell[16] reported positive antithyroid antibodies (ATA) in few percentages of their subjects and the positivity of ATA was more in women than men. In the present study, ATA (Anti-TPO) performed in subjects with raised TSH values were negative as the values

were well within the normal range for laboratory. The explanation for this could be the less number of subjects with raised TSH and less prevalence of autoimmunity in the male subjects of the region.

CONCLUSION

In conclusion, in the present study serum T_3 levels decreased progressively with age in both rural and urban subjects up to age group 71-80 years with a slight but insignificant increase in age group ≥ 81 years. The mean serum T_3 concentrations in rural and urban subjects were significantly different from each other in age group 71-80 years but values did not differ significantly in other age groups.

Serum T_4 levels increased slightly in the age group 71-80 years, though in normal range and the increase was statistically non-significant. Also a non-significant decrease in the levels was observed after the age of 81 years. Moreover, mean serum T_4 values in rural and urban subjects did not differ significantly in any age group.

Serum TSH values increased with age up to age group 61-70 years followed by a decrease in other groups in urban subjects and group C in rural subjects and a slight increase in the level was observed in age group ≥81 years of rural subjects but the changes were statistically non-significant. Moreover, mean serum TSH values in rural and urban subjects did not differ significantly in any age group.

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