

ASSESSMENT OF T₃, T₄ AND TSH OF GOITROUS FEMALE POPULATION AT BANJOSA, AZAD JAMMU AND KASHMIR

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Abstract: Goiter is a disease physically shown by abnormal enlargement of neck. In such cases, thyroid gland cannot synthesize adequate amounts of tri-iodothyronine (T₃) and thyroxin (T₄) hormones. The blood never carries enough of thyroid hormones to shut off the secretions of thyroid stimulating hormone (TSH) by the hypothalamus. The clinical manifestations are hoarseness, reflex delay, infertility, dry skin, memory and mental retardation. Normal T₃ level in blood is 1.1–2.7 nmol/L, T₄ is 8.0-21.0 pmol/L and TSH ranging from 0.4-4.0 mIU/L. It was measured that the level of thyroidal hormones except TSH becomes high in goitrous patients. The present study was planned to investigate the concentration levels of thyroid hormones (T₃, T₄) and TSH of goitrous female of local population. Total 30 subjects (15 normal and 15 goitrous females) were studied. Biochemical tests were done and the data collected was analyzed statistically. Mean levels of T₃ (3.43±0.15 nmol/L) and T₄ (26.6±1.58 pmol/L) in goitrous were significantly higher as compared to normal while the level of TSH (0.92 mIU/L) was significantly low in goitrous compared to normal subjects. These results suggested that goitrous females have hyperthyroidism.

Keywords: Goiter, iodine, high altitude, hyperthyroidism.

INTRODUCTION

Goiter is a visible swelling in front of neck due to abnormal production of thyroid hormones or any other defect in thyroid gland. It may be due to total or partial enlargement of thyroid gland (Brodowski, 2005). Thyroid size is the main factor influencing the appearance of signs and symptoms, although age and sex are related with

the presence of retrosternal goiter and tracheal deviation. A goiter indicates that there is a condition present which is causing the thyroid to grow abnormally (Ingenbleek and De Visscher, 1979).

The thyroid gland secretes hormones that are involved in human development, growth and metabolism. The follicular cells of thyroid gland secrete hormones called thyroxin (T_4) and tri-iodothyronine (T_3). They enclosed a glutinous material called colloid. Colloid is involved in the formation of T_4 and T_3 . Thyroid stimulating hormone (TSH) is the main regulator of thyroid hormone secretion and synthesis (Bonnema *et al.*, 2002). Disorders in thyroid gland lead to goiter which shows severe clinical manifestation, patient feels hoarseness, depression, memory and mental retardation, infertility, irregular or heavy menses, reflex delay and fatigue (Jabłkowska *et al.*, 2008).

Graves's disease: in which one's own immune system produce protein which stimulate thyroid to produce goiter. Some other causes are production of any nodule, genetic defect, injury in thyroid gland, production tumor, regular and high medication of Lithium Propyl thiouracil, or regular intake of goitrogenic food (Diez, 2005).

Goiter has been sufficiently investigated in many of its manifestations; Williams determined that the goiter is 7-9 times more common in women than in men. Despite the strong implications of differences between females and males in the risk of goiter, gender-specific issues have not been extensively addressed in investigations of goiter prevalence (Bergenfelz *et al.*, 2008). Goiter is common in older people, although the frequency of the different causes of goiter has not been well defined. Gender – specific determinants of goiter are parity and iodine status in females and smoking and increasing age in males (Farahati *et al.*, 2006).

Basically goiter is of three types. More prevalent of these is "Endemic or Diffused goiter" caused by deficiency of iodine found especially in persons living in areas where there is lack of iodine in soil, water and diet (Krysiak, 2006). The second nodular type of goiter is "Idiopathic nontoxic colloid goiter and responsible factors are inflammation in thyroid gland (thyroiditis) and abnormality of enzyme system. Most of the symptoms and signs associated with goiter were dependent on thyroid size and time of evolution. Third rarely occurring type of goiter is "Toxic goiter". Toxic multi-nodular goiters are the main

etiologies of goiter in patients aged 55 years and older (Meller *et al.*, 2006). Iodine is a key element in the synthesis of thyroid hormones and severe iodine deficiency results in hypothyroidism, goiter, and cretinism (Verheesen and Schweitzer, 2008). It is essential to study the influence of water source with high iodine on human health for the purpose of reasonable supplementary of iodine. Both inadequate and high intakes of iodine are associated with thyroid disease and associated abnormalities. Iodine deficiency causes impairment of thyroid hormonogenesis resulting in goiter (Struma), cretinism which is associated with increased prenatal and infant mortality, deafness, motor disabilities and mental retardation due to the damage during fetal and neonatal brain development (Hashemipour *et al.*, 2007). Treatment given is normally hormone suppression therapy, radioactive iodine and surgery (Jabłkowska *et al.*, 2008).

To understand the effect of high iodine in the people was conducted by investigating goiter state. After ten years of Universal Salt Iodization (USI) in Shanxi province the Children's goiter rate was measured by palpation, iodine concentration in urine was tested by ammonium persulfate, IQ (intelligence quotient) was evaluated by combine Ravens Test in China. It has no significant effect on IQ. It is suggested that supplying of iodized salt be stopped in high iodine areas immediately (Azizi *et al.*, 2001).

Despite the strong implications of differences between females and males in the risk of goiter, gender specific issues have not been extensively addressed in investigations of goiter prevalence. The objective of analysis was to investigate the gender-specific determinants of goiter between April, 2001 and April, 2002 (Farahati *et al.*, 2006).

To sum up the experience with resecting the endemic goiter all the patients received bilateral subtotal thyroidectomy without drainage except few patients kept infrahyoid muscles integrated due to their huge size of thyroid gland. The largest average size was 8.5 cm. It is feasible to deep infrahyoid muscles integrated without drainage in patients of endemic goiter of mild to moderate status (Kotwal *et al.*, 2006). It is essential to investigate the status of iodine nutrition of pregnant or lactating woman, infants and children in the coastal area after implementing Universal Salt iodization (USI) (Tang *et al.*, 2005).

In pregnant women with past-occurred Grave's disease, ultrasonography of the fetal thyroid gland by an experienced ultrasonographer is an excellent diagnostic tool (Luton *et al.*, 2005). The high incidence of hypothyroidism and nodular goiter in goitrous patients shows that screening for thyroid dysfunction, using appropriate laboratory tests and ultrasonography (Kutlay *et al.*, 2005). Abnormal glycosylation of cell structures, including changes in sialylation, cause euplastic changes in thyroid gland and causes goiter formation (Babal *et al.*, 2006).

MATERIALS AND METHODS

Subjects

A comprehensive study on goiter incidence was done on 30 female subjects (15 normal and 15 goitrous) in Banjosa hilly area of Azad Jammu and Kashmir, at the altitude of 6294 feet. These females were under medication.

Thyroidal hormone measurements

Primary measurement test of interest in the present study were thyroidal hormones (T₃, T₄ and TSH) tests of blood. Blood of all subjects was taken in a peaceful and calm environment. All samples of blood were examined and levels of T₃, T₄ and TSH were measured respectively.

Method of thyroid hormones tests

Blood samples were taken and saved in nominated test tubes without any external interruption. Then serum of each sample was prepared and taken under the biochemical test in "Thyroidal hormone testing apparatus". Biochemical tests were performed for determination of the levels of the thyroidal hormones. After completion of tests the whole data was put into related questionnaires.

The level of T₃, T₄ and TSH were determined in each sample. After this procedure, the data of each sample was calculated and analyzed individually. The mean of data was calculated into groups separately, normal subjects group and goitrous subject groups. The analyzed data was set in tables. Successful readings of thyroid hormones were compared between both groups. Mean values of T₃, T₄ and TSH was also analyzed and arranged according to the requirement of research. All clinical and

laboratory work and investigations including thyroid hormones tests were completed.

If few cases, T₄ mildly increased and were stabilized on the symptoms such as swelling in front of neck was chief complaint in all the cases followed by symptoms of hyperthyroidism, pain and hoarseness in throat and difficulty in swallowing. The risk of malignancy in MNG should not be under estimated and the dominant nodule in MNG should be regarded as a solitary nodule in a normal gland so that a more radical procedure could be adopted. Results suggest that near total thyroidectomy with minimal residual tissue is a versatile surgical procedure for patients with multi-nodular goiter with low risk of complications.

The maximum postoperative stay in hospital was 48 hours and recorded. Histopathology of the excised specimen was received in 20 days. While further management in the form of either completion thyroidectomy or radioiodine ablation was carried out within a month, after one informed and written consent from patients. All the patients were underwent near total thyroidectomy, with preservation of recurrent laryngeal nerves and parathyroid gland.

Statistical analysis

Statistical analyses were performed using GraphPad Prism for Windows (version 6.01) and graphs were made in Microsoft Excel 2007. To compare the concentrations of T₃, T₄ and TSH in normal and the goitrous females, we used one-way analysis of variance (ANOVA) and Dunnett's Multiple Comparison tests with probability level of 5% as the minimal criterion of significance.

RESULTS

Total 30 females subjects (15 normal and 15 goitrous) age > 20 years were studied.

T₃, T₄ and TSH level in normal female subjects aging >20 years

The normal level of T₃ in different subjects was ranging from 1.4-2.2 nmol/L. It was significantly low in normal subjects as compared to goitrous subjects. Thyroxin in normal subjects was ranging from 10.9-16.0 pmol/L and was significantly low than the goitrous subjects. TSH level in

normal subjects was ranging from 1.07-3.21 mIU/L which was slightly higher than goitrous TSH level.

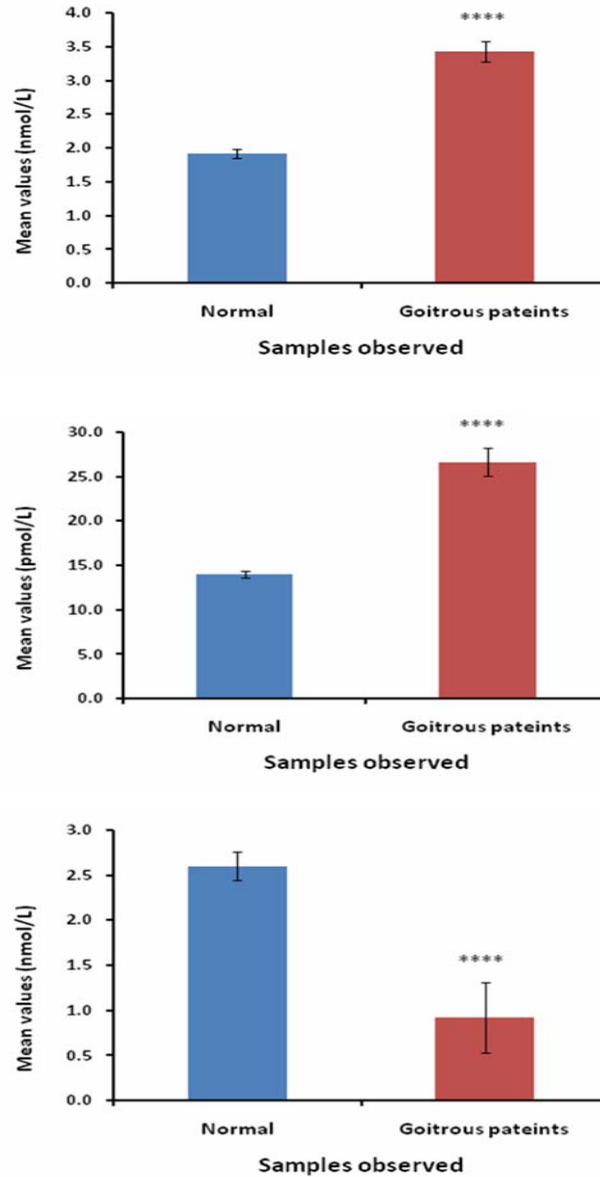


Figure 1: The Mean±SEM values (N=15) of (a) T₃, (b) T₄ (c) TSH in normal and goitrous females. ** indicating $p < 0.0001$**



Figure 2. Representative examples of goitrous females in high altitude area.

T₃, T₄ and TSH level in female goitrous subjects aging > 20 years

The value of T₃ in goitrous subjects was varied between 2.81-4.28 nmol/ L., while T₄ was ranging from 12.2-38.0 pmol/L. whereas the level of TSH in goitrous subjects was fluctuating between 0.01-4.56 mIU/ L.

Mean values of T₃, T₄ and TSH in normal subjects

Mean value and SEM of T₃ in normal subjects was 1.91 nmol/L ± 0.07 while T₄ was 13.99 pmol/L ± 0.37 and TSH was 2.6 mIU/L ± 0.15.

Mean values of T₃, T₄ and TSH in goitrous subjects

Mean value of T₃ in goitrous was 3.43 nmol/L ± 0.15 while T₄ was 26.6 pmol/L ± 1.58 and the mean value of TSH was 0.92 mIU/L ± 0.39 (SEM).

DISCUSSION

Goiter development occurs due to particular disruption in the production of thyroidal hormones (T₃, T₄ and TSH). Goiter causes clinical manifestations such as mental impairment, memory loss, infertility, heavy menses, constipation, hoarseness in throat and several other disorders appeared. Some time goiter leads to severe condition such as malignancy (cancer). Goiter production is significantly caused by “Hashimoto’s disease”, thyroiditis, hypothyroidism, hyperthyroidism, Grave’s disease, genetic defect and any injury in the thyroid gland.

The present study suggested that T₃ and T₄ produced by the thyroid gland were involved in growth, development and metabolism. These were produced from thyroglobulin attached to iodine. Iodine obtained from the diet converted to iodide which combined with thyroglobulin to form mono-iodo-tyrosine (MIT). Due to excess consumption of iodine resulted in excess of hormones caused hyperthyroidism, and deficiency in these hormones caused hypothyroidism. Group data suggested an inverse correlation between TSH suppression of the thyroid function. Group data also suggested that TSH suppression was significantly correlated to the basal TSH.

The hypothalamic pituitary feedback system is one of most complex regulation systems and it has intrigued researchers for more than 50 years. Group data suggested an inverse correlation between TSH suppression and suppression of thyroid function. Group data suggested

TSH suppression was significantly correlated to the basal TSH (Vadstrup, 2006).

In a recent report a young woman with goiter and hearing impairment with an impaired per-chlorate washout test. Genetic test confirmed the diagnosis of Pendred Syndrome with a mutation in Pds gene. She was treated with potassium iodine. After starting the therapy the goiter decreased in size (Arwert and Sepers, 2008). Near total thyroidectomy is a versatile surgical procedure for patients with multi-nodular goiter, keeping in view the risk of associated occult malignancy. Furthermore the risk of damage to recurrent laryngeal nerve and parathyroid is low in patients undergoing completion thyroidectomy. Hence, a more radical procedure should be adopted for surgical treatment in MNG (Baloch *et al.*, 2007).

Iodine deficiency may give rise to the clinical symptoms of hypothyroidism without any abnormality of thyroid hormone (Verheesen and Schweitzer, 2008). Hyperplastic goiter is also a thyroid disorder. In this goiter thyroid enlargement occur but after a few months TSH skeletal lesions appeared. The plasma thyroid hormone concentration (T₄) was normal all the time (Mausberg *et al.*, 2007). Despite long standing iodine supplementation in Iran the prevalence of goiter remain high in some areas. This may suggest that there are some other causes also responsible of goiter other than iodine deficiency. Such as autoimmune thyroid disease should also be considered (Hashemipour *et al.*, 2007).

It was estimated that the country wide incidence of nodular goiter is close to 17%. Incidence of malignancy in goiter is 6.6% in multi-nodular goiter (Grussendorf *et al.*, 1990). The incidence of solitary nodular goiter is 1% and 10-25% nodularity ratio (Erbil *et al.*, 2008). The results of present study highlight the successful implementation of the salt iodization program. Government improving the quality of salt and information and awareness also developed through communication activities and media (Kapil *et al.*, 2005).

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