

Original Article

Co Relation of Thyroid Function Test with the Clinical Presentation

1. Tariq Saeed 2. Shahid Mahmood 3. Muhammad Taimur 4. Sadaf Faisal Bhopal

1. Consultant Surgeon, FFH, Rawalpindi 2. Assoc. Prof. of Surgery, FUMC, Rawalpindi 3. Registrar of Surgery, FUMC, Rawalpindi 4. Medical Student, Wah Medical College, Wah Cantt., Rawalpindi

ABSTRACT

Objective: To correlate the biochemical thyroid profile with the clinical presentation of the patient and decision about the time of surgery.

Study Design: It is an analytical cross sectional study.

Place & Duration of Study: This study was carried out in the Department of Surgery, Fauji Foundation Hospital, Rawalpindi from 1st January 2010 to 31st March 2011

Patients & Methods: Thirty patients were included in this study after taking consent & approval from the ethical committee of the hospital. All of them were females. Age ranges between 13 to 45 with mean of 22.26 years. These patients presented with a swelling in front of neck with or without signs of hypothyroidism or hyperthyroidism. Trial of 6 to 12 months given to every patient to bring the TFT's within normal range. Only those patients were included in the study who took the medicines regularly. Mode of presentation was out door department of Fauji Foundation Hospital Rawalpindi. Patients were examined clinically by surgeon and anesthetist for risk assessment. Routine laboratory investigations including thyroid function test were requested and analyzed by operating surgeon. TFT's were co-related with the clinical signs and symptoms of the patients. Patients were divided into two groups. Group one includes clinically euthyroid patients with TFT's within normal range. Group two again include clinically euthyroid patients but abnormal TFT's.

Results: A total of 30 patients were included in this study. All of them were females & clinically euthyroid. Mode of presentation was the outdoor patient department of Fauji Foundation hospital. Presenting complaint was swelling in front of neck. 23 out of 30 patients (66.6 %) had normal TFT's & clinically euthyroid. 7 out of 30 Patients (33.3%) shows variation between their thyroid profile and clinical presentation. Sub or near total thyroidectomy was done in all the patients. Recovery was un-eventful.

Conclusion: Operation on thyroid gland is a major undertaking & decision should be taken by senior surgeon. Ideally TFT's should be within normal range as well as patient should be euthyroid clinically in order to avoid post operative complications. In those cases where patient is clinically euthyroid but biochemically status is either hyper or hypo thyroid, surgery can be done after clinical trial of at least six months with thyroxin or anti thyroid drugs with a view to bring the TFT's within normal range. We can conclude that although the biochemical profile of the patients with thyroid disease is important but in country like Pakistan where thyroid hormonal assay is not easily available the surgery can be done by careful clinical assessment, keeping in view compliance of patient, regularity of taking medicine, clinical status & side effects of medical treatment.

Keywords: Thyroidectomy, thyroid function test, Hyperthyroidism, hypothyroidism.

INTRODUCTION

The mountain regions in north-west of Pakistan & Kashmir are probably the worst affected areas in the World¹⁻². These areas are labeled as goiter belt due to high incidence of the disease in the area³. Through the incidence of goiter is remarkably decreased all over the world in the last 30 years due to introduction of iodinated salt but the situation is otherwise here. Commonest source of water in the hilly areas of Pakistan is obtained from fountains which is very deficient in iodine & fails to meet the daily requirements. The recommended daily allowance of iodine is about 100 nanogram per day². The deficiency of iodine can cause a lot of complications like goiter,

mental retardation, cretinism, high infant mortality rate, decreased fertility rate & increased perinatal death rate⁴. The iodine deficiency goiter starts as diffuse involvement of the gland due to raised levels of TSH. Later on, the diffuse enlargement develops nodularity due to fluctuating level of TSH & unequal sensitivity of thyroid cells to the stimulating hormone. Multinodular goiter is the most common presentation of thyroid disease in these areas. The female preponderance is well known & is due to increase requirement of iodine at the age of puberty (puberty onset goiter). Another situation when females require extra iodine is during pregnancy as discuss in detail by M A Zahid et al in Annals of PIMS (January 2006).

Thyroid is a Greek word means "shield" after the shape of the related thyroid cartilage. The most common problem of the thyroid gland is enlargement of gland which is known as goiter. It can be multi nodular, which is the commonest variety seen in our country or diffusely enlarge. Clinically patient can be euthyroid, hyperthyroid or hypothyroid. Graves disease, named after Graves⁵ who first time described it in 1935, is a triad of hyperthyroidism with diffuse enlarge thyroid, ophthalmopathy with exophthalmos & pretibial myxedema. It usually occurs in young females & there is production of auto antibodies that act on TSH receptors. Hypothyroidism may occur as a result of congenital thyroid abnormalities, autoimmune disorders such as Hashimoto's thyroiditis (which is common in females of above 40), iodine deficiency (commonest cause in Pakistan) or the removal of the thyroid following surgery.

A number of studies have sought to determine age related changes in thyroid profile⁶. It was found that lower serum T3 levels and higher rT3 levels were detected in the institutionalized elderly adults. Probably, these changes occur in thyroid profile are due to non thyroidal illness. Two studies that evaluated thyroid hormone profiles in healthy adults have clarified this issue. One study that measured T3 and free T3 levels in healthy adults aged 65 and older determined that while levels of these hormones were lower than in younger adults, they fell well within the limits of reference ranges⁷. Another study of thyroid hormone profiles in a range of healthy adults who were not taking prescribed medications determined that there were no significant differences in T4, free T4, T3 & free T3 levels between groups stratified by age⁸.

Abnormalities in thyroid profile can complicate Hyponatremia, Hyperlipidemia, myopathy with increased creatine phosphokinase levels, hypo chromic microcytic anemia (up to 15% in primary hypothyroidism²⁴) increased homocysteine and lipoprotein levels with primary hypothyroidism, potentially contributing to an increased risk of atherosclerotic disease⁹ are few examples of complicate thyroid physiology.

PATIENTS & METHODS

Thirty patients were included in this study after taking consent & approval from the ethical committee of the hospital. All of them were females. Age ranges between 13 to 45 with mean of 22.26 years. These patients presented with a swelling in front of neck with or without signs of hypothyroidism or hyperthyroidism. Trial of 6 to 12 months given to every patient to bring the TFT's within normal range. Only those patients were included in the study who took the medicines regularly. Mode of presentation was out door

department of Fauji Foundation Hospital Rawalpindi. Patients were examined clinically by surgeon and anesthetist for risk assessment. Routine laboratory investigations including thyroid function test were requested and analyzed by operating surgeon. TFT's were co-related with the clinical signs and symptoms of the patients. Patients were divided into two groups. Group one includes clinically euthyroid patients with TFT's within normal range. Group two again include clinically euthyroid patients but abnormal TFT's.

Inclusion Criteria

Age between 12 to 45, clinically euthyroid with normal or abnormal levels of T3 & T4 and ASA1 were included in the study. Patients who showed poor compliance with irregular medication were excluded from the study.

RESULTS

All 30 patients were females & clinically euthyroid. Youngest patient was 13 years old while oldest one was 49 with a mean of 22.26 years. On admission vitals were noted. Average pulse was 74 beat per minute while blood pressure was 125/85. No other co-morbid factors present & all the patients ranked as ASA 1 by anesthesiologist. 8 out of 30 give H/O dysphagia while 9 out 30 complaint of difficulty in breathing at night. 13 patients were worried about their cosmetic problem.

Table No.1 showing presenting complaints.

Total	30
Dysphagia	8
Difficulty in breathing	9
Cosmetic problem	13

7 (33.3%) patients out of 30 showed variation between their biochemical thyroid profile and clinical presentation. Two (6.6%) patients showed elevated levels of T3 and T4 and decreased levels of TSH. Two (6.6 %) patients had T3 & T4 below normal levels & raised TSH. 2 patient showed normal level of T3, T4 but decreased level of TSH. One patient (3.3%) showed elevated levels of T3 and normal level of T4 and decreased level of TSH. 22 out of 30 patients had subtotal while 8 had near total thyroidectomy. As thyroid surgery is a safe surgery if done by an experienced surgeon. Very few complications were noted which were given in table 2. Hoarseness of voice settles in 2 weeks while symptoms of hypoparathyroidism disappeared within 5 days.

Table No. 2: Showing complications of thyroidectomy.

Total	Hoarseness of voice	Symptoms of hypoparathyroidism	Blood trans-fusion	Skin infection
30	2	1	7	1

Seven patients required blood transfusion pre or post operatively. Nine patients had tachycardia of 96 beat per minute on first post op day which settles completely on second post op day. Tachycardia was attributed to anemia, pain, anxiety & other post op factors. Drain was removed on first or second post op day. Recovery was un-eventful. All the patients discharged on 2nd post op day. Skin stitches were removed on 5th day & TFT's repeated after 1, 3 & 6 months as a policy of the department. Interestingly after 3 months, clear cut correlation was seen between TFT's & clinical status of the patients.

DISCUSSION

Most of the studies published all over the world shows that thyroid disease is a predominant disease of female gender¹⁰⁻¹¹. In our study, all the 30 patients were female.

Another point noted by the team of surgeons in our department is 7 patients (33 %) presented with abnormal TFT's but they were euthyroid clinically. The interpretation of thyroid function test profiles in hospitalized patients must be tempered by an understanding of how non thyroidal illnesses may produce changes in TSH and thyroid hormone levels. The direction and extent of changes observed may depend on the severity of an underlying illness and the point in the course of recovery at which thyroid function tests are measured¹². Longitudinal studies have demonstrated that early on in the course of severe illnesses or protracted procedures, TSH levels in euthyroid patients may decline to levels that fall below the lower limits of normal reference ranges¹³. This change may be paralleled by a decline in T4 and T3 levels that may be particularly pronounced in elderly patients. One study demonstrated that 59% of elderly patients known to be euthyroid had documented low T3 levels measured during a course of hospitalization, whereas another demonstrated that changes in T3 levels detected in elderly hospitalized patients were more closely correlated with the severity of each underlying illness than with advanced age itself¹⁴. In our study, 6.6 % of patients had below normal T4 levels with raised TSH though T3 was normal. Another 6.6 % had both below normal T4 & T3 levels with raised TSH.

Although data from the NHANES III study has established that median TSH levels appear to increase with advancing age, the normal upper limit of established reference range may still be used as a cutoff to confirm the diagnosis of primary hypothyroidism in most elderly patients. While a blood spot TSH level has been shown to be an adequate screening test for the detection of overt primary hypothyroidism in the elderly, it may not be sensitive enough to detect cases of subclinical hypothyroidism characterized by elevated

serum TSH levels with normal T4 or free T4 levels¹⁵. One study has determined that there may be a negative correlation between age and the degree to which TSH levels are elevated in elderly patients presenting with primary hypothyroidism¹⁶. In cases of suspected secondary hypothyroidism that may result from disruption of the anatomy or function of the hypothalamic-pituitary axis, the TSH level may not be relied upon as an accurate index of thyroid function. In this setting the free T4 level may serve as more reliable measure of thyroid hormone production.

Current data indicates that the normal or low TSH levels found in the presence of low T4 and T3 levels in the setting of nonthyroidal illness likely reflect the combined effects of central hypothyroidism and reduced peripheral generation of T3, effectively representing a deficiency of thyroid hormone. Whether this condition should be treated with administration of thyroid hormone preparations remains controversial. Some observers argue in favor of thyroid hormone replacement, while others weigh against it, without conclusive data to support either viewpoint¹⁷.

In cases where changes in TSH and thyroid hormone levels may be plausibly ascribed to nonthyroidal illness, the patient's thyroid function tests should be reassessed one to two weeks later to see if observed changes are resolving. One study completed 24 years ago that tracked thyroid function test profiles in hospitalized elderly female patients showed that while 14% of the subjects had increased TSH levels and decreased T4 and T3 levels on initial assessment, only 2% were proven to have evidence of underlying primary hypothyroidism in follow up¹⁸.

Estimates of subclinical hypothyroidism range between 3–8%. Incidence is more common in women than in men¹⁹. A 2007 meta-analysis by the Cochrane Collaboration found no benefit of thyroid hormone replacement except in some parameters of lipid profiles and left-ventricular function

We can see that there are many factors in the body which can change the levels of T3, T4 & TSH levels and it is not easy to interpret the thyroid profile correlating with the clinical status of the patient. So clinical thyroid status is very important to decide about the time of surgery in conditions where ambiguity exists and hormonal assay does not relate with the clinical status of the patient. The physiology of thyroid gland is very complex. The production, conversion and uptake of thyroid hormone in the body involve several steps. A malfunction in any of these steps can cause hypothyroid symptoms, but may not show up on standard lab tests²⁰. It's incorrect and even negligent to assume that all cases of hypothyroidism share the same cause and require the same treatment. Subclinical hypothyroidism occurs when thyrotropin (TSH) levels are elevated but thyroxine (T4) and triiodothyronine (T3) levels are

normal. The levels of the active hormones will be within the laboratory reference range. About three percent of the general population has hypothyroidism¹¹.

CONCLUSION

We concluded that although the biochemical profile of the patients with thyroid disease is very important factor but clinical signs and symptoms of the patients have come out to be other important criteria. 33.3 % of the total patients had clinical presentation different from biochemical profile and decision about the time of surgery was planned on their clinical status. Patient remained well during and after the surgery. So it is recommended in country like Pakistan where thyroid hormonal assay is expensive, not easily available, laboratory error, compliance of patients e.t.c, the decision about surgery should be taken as last step if clinically patients are euthyroid & no other risk factors are present.

REFERENCES

1. Sooch SS, Deo MG, Karmarker MG. Prevalence of endemic goiter with iodized salt. Bull WHO 1973; 49:307
2. Zafar A. Survey of school going children in Murree for prevalence of goiter. J Surg PIMS 1993;(3): 62-5
3. Zahid MA. Role of thyroid scan in the management of thyroid disorders. Annals of PIMS 2006;2(1).
4. Delang F. The disorders induced by iodine deficiency thyroid. 1994;4(1):107-28.
5. Robbins and Cotran. Pathologic Basis of Disease. 8th ed. Philadelphia: W B Saunders; 2011.p.1117.
6. Yalcin B, Ozan H. "Detailed investigation of the relationship between the inferior laryngeal nerve including laryngeal branches and ligament of Berry". J Am College of Surgeons 2006;202(2): 291-6.
7. Venturi S, Donati FM. "Environmental iodine deficiency: A challenge to the evolution of terrestrial life?" Thyroid. J American Thyroid Association 2000;10 (8): 727-728
8. Küpper FC, Carpenter LJ, McFiggans GB, et al. "Iodide accumulation provides an inorganic antioxidant impacting atmospheric chemistry" Proceedings of the National Academy of Sciences of the United States of America 2008;105(19): 6954-8.
9. Venturi S; Bégin ME. "Thyroid Hormone, Iodine and Human Brain Evolution". Environmental Influences on Human Brain Evolution. John Wiley & Sons 2010.p.105-124.
10. Klofanda J. Thyroid surgery at the first surgical clinic of the first medical school of Charles University and Genetic Medical School Hospital in Prague; Review of Problems.1998;77(10):435-40.
11. Korcen N, Asci C, Yilmazlem T. Total thyroidectomy or lobectomy in benign nodular disease of thyroid. Int Surg 1997;82 (4):417-9
12. Brown-Grant. "Extrathyroidal iodide concentrating mechanisms". Physiol Rev 1961;41:189.
13. Spitzweg C, Joba W, Eisenmenger W, Heufelder AE. "Analysis of human sodium iodide symporter gene expression in extrathyroidal tissues and cloning of its complementary deoxyribonucleic acid from salivary gland, mammary gland, and gastric mucosa". J Clin Endocrinol Metab 1998;83:1746.
14. Banerjee RK, Bose AK, Chakraborty TK, Datta AG. "Peroxidase catalysed iodotyrosine formation in dispersed cells of mouse extrathyroidal tissues". J Endocrinol 1985;2:159.
15. Eugster, Erica A, Pescovitz, Ora Hirsch. Pediatric endocrinology. Mechanisms, manifestations and management. Lippincott Williams & Wilkins 2004. ISBN 0-7817-4059-2.
16. Zoeller RT. "Transplacental thyroxine and fetal brain development". J Clin. Invest 2003;111 (7): 954-956
17. Berbel P, Navarro D, Ausó E, Varea E, Rodríguez AE, Ballesta JJ, et al. Role of late maternal thyroid hormones in cerebral cortex development, an experimental model for human prematurity. Cereb Cortex 2010;20(6):1462-75.
18. Don F, Ronald J. Bloom & Fawcett's Concise Histology. New York: Arnold Publishers; 2002.p.257-258.
19. Yamamoto M, Shibuya N, Chen LC, Ogata E. "Seasonal recurrence of transient hypothyroidism in a patient with autoimmune thyroiditis". Endocrinol. Jpn 35 (1):135-42.
20. Hidaka Y, Amino N, Iwatani Y, Itoh E, Matsunaga M, Tamaki H. "Recurrence of thyrotoxicosis after attack of allergic rhinitis in patients with Graves' disease". J Clin Endocrinol Metab 77 (6):1667-70.
21. Nussey S, Whitehead S. Thyroid Gland Endocrinology: An Integrated Approach. Published by BIOS Scientific Publishers Ltd. 2001.

Address for Corresponding Author:

Dr Tariq Saeed,
Consultant Surgeon,
Fauji Foundation Hospital Rawalpindi
Mobile: 0321-5871036
E- mail: surgeontariq@ yahoo.com