RESEARCH PAPER | Medical Science | Volume : 3 | Issue : 11 | Nov 2013 | ISSN - 2249-555X

Is TSH Alone Can be A Treated as Diagnostic Marker for Thyroid Disorders

KEYWORDS: Thyroid function tests (TFT), Thyroid stimulating hormone (TSH), Tri iodothyronine (T3), Tetra iodothyronine(T4)

Rajesh Kumar Shrivastava	MukeshMeena	MeenaVarma
Department of Biochemistry, Sri Aurobindo Medical College and PG Institute, Indore, Madhya Pradesh, India	Department of Biochemistry, Sri Aurobindo Medical College and PG Institute, Indore, Madhya Pradesh, India	Department of Biochemistry, Sri Aurobindo Medical College and PG Institute, Indore, Madhya Pradesh, India
Rajesh Kumar Jha	**SusmitKosta**	**Ravindra Kumar**
Department of Medicine, Sri Aurbindo Medical College and PG Institute, Indore, Madhya Pradesh, India	Central Research Laboratory, Sri Aurobindo Medical College and PG Institute, Indore, Madhya Pradesh, India	Central Research Laboratory, Sri Aurobindo Medical College and PG Institute, Indore, Madhya Pradesh, India

ABSTRACT *The objective of the study was to examine thyroid dysfunction as a measurement of viability and the cost-effectiveness of universal screening in Central India. It is a first study in the Central India to analyze the ordering pattern of thyroid related tests referred by clinicians to the Department of Medicine SAIMS, from March 2012 to July 2013. The thyroid function tests were analyzed for four different screening strategies. Thyroid stimulating hormone, T3, T4, FT4 and FT3 estimation was doneon automated immunoassay analyzer.*

The findings of this study sustain to theTSH measurement as the gold standard when do screening for thyroid disease, a normal sensitive TSH test alone is sufficient to rule out thyroid dysfunction in patients. It is possible that thyroid screening may present with transient abnormalities of no particular clinical significance, and would therefore be a cost effective practice.

Introduction

Thyroid diseases are common,non-specific, clinical consequences of many medical, neurological and psychiatric conditions and tend to affect women disproportionately. Disorders of the thyroid gland include clinical and subclinical hyperthyroidism, hypothyroidism, goiter and thyroid cancer [1]. Thyroid dysfunction can be diagnosed accurately and is amenable to treatment. Due to the wide range of specific and non-specific symptoms of thyroid diseases, thyroid function tests (TFT) are among the most frequently prescribed laboratory procedures [2].

Commonlydone tests to diagnose thyroid disorders include estimationof thyroid stimulating hormone (TSH) along with thyroidhormones, tri iodothyronine (T3) & tetra iodothyronine(T4) either in total or free form.The guidelines ofAmerican thyroid association and American Associationof Clinical Endocrinologists recommend serum TSHmeasurement as the single most reliable test to diagnoseall common forms of hypothyroidism and hyperthyroidismparticularly in the ambulatory setting [3,4]. Thyroidstimulating hormone confirms or excludes the diagnosis inall patients with primary hypothyroidism, an elevatedconcentration being present in both overt and mild hypothyroidism [5].Patients with hyperthyroidism have serum TSH concentration less than 0.1mIU/ml and usually less than 0.05mIU/ml. A serum TSH within the euthyroid reference interval almost always eliminates adiagnosis of hyperthyroidism [6]. Free T4 levels can beordered when TSH level is abnormally high or low. ThisTSH centered strategy for initial evaluation of thyroid function is both cost effective and medically efficient[7,8].The appropriate use of these tests remains controversialand medical practice may vary from the guidelines.The various studies done to evaluate the orderingpattern of thyroid function tests indicate that frequencyof order of TFT is much higher than that of onlyTSH [9,10]. So the aim of our study is to analyze the ordering pattern ofthyroid related tests so that it can be cost effective.

Material and Method

This study was designed to analyze the ordering pattern of thyroid related tests referred by clinicians of the department of Medicine SAIMS, from March 2012 to July 2013. The thyroid function tests were analyzed for fourdifferent screening strategies. (a. According to age and sex b.Combinations of thyroid related tests ordered c. Different combinations of thyroid related tests ordered d.Overall cost utility). Analysis of results was done to find out the percentage of abnormal reports. The criterions for abnormal reports were results higher orlower than the reference interval and thus included subclinicalcases also.Thyroid stimulating hormone, T3, T4, FT4 and FT3were the assays performed in our lab. Estimation was done on automated Analyser (Elcysis 2010, Hitachi).

Results and Discussion

The incidence and pattern of changes in thyroid function tests were studied in patients and the cost effectiveness of a systematic screening program for thyroid dysfunction was estimated. Thyroid testing was screened on 3169 of which 172 (5.4%) contained missing or incomplete clinical data therefore excluded from the study. Out of remaining 2997, 2616 (87.2%) were female and 381 (12.8%) were male patients. This significant difference may be due to the bias of clinician in suspecting thyroid disorder in female patients as these are common in females as compared to males [11]. Higher rate of testing of thyroid hormones in females has been reported in previous studies also [12, 13]. Analysis of age wise distribution of samples was done to know about the susceptibility to thyroid disease among people of different age groups. High prevalence of thyroid disorders has been found in age groups of 21–50 respectively (Table 1). High prevalence of thyroid disorders hasbeen reported in age groups of 21–35 and 20–55 respectivelyin previous studies from India [12, 14].

Volume : 3 | Issue : 11 | Nov 2013 | ISSN - 2249-555X

Table 1: Distribution of patients according to age and sex

	10-20	21-30	31-40	41-50	51-60	61-70	71-80
Male	2 (0.5%)	158 (41.4%)	108 (28.3%)	73 (19.2%)	21 (5.6%)	14 (3.7%)	5 (1.3%)
Female	145 (5.5%)	867 (33.1%)	721 (27.6%)	591 (22.6%)	241 (9.2%)	39 (1.4%)	12 (0.6%)
Total	147 (5%)	1025 (34.3%)	829 (27.6%)	664 (22.1%)	262 (8.7%)	53 (1.7%)	17 (0.6%)

The case-finding strategies for thyroid dysfunction as a first-level measurement, the viability of such prescribed laboratory procedures and the cost entailed in administering TFTs. On the whole, the present study has demonstrated that there is a temporal relationship between first-level measurement and eventual diagnosis [15]. There was also a discrepancy between initial diagnosis and subsequent diagnosis confirmed by using TFT. With a few exceptions, the results of the TFT were not remarkable. It is worthwhile noting that most of the cases could have been diagnosed by clinical impression only. The samples were ordered for different combinations of thyroid function tests. 48.9% of total samples were ordered for complete thyroid profile which includes T3 + T4 + TSH. Thyroid stimulating hormone was the investigation requested in 35.8% of samples. FT3 + FT4 + TSH were the investigations marked in 6.4%of samples. 3.3% of samples required FT4 + TSH (Table 2).

Among the TFT profile samples, 1969(65.7%) had same results within reference interval for all the three parameters and thus excluded thyroid disorder. Typical biochemical picture suggestive of hypothyroidism was observed in 11 (0.3%) had high and 13(0.4%) low TSH but T3 or T4 found normal. Typical biochemical picture suggestive of hypothyroidism was observed in 4.1% of samples. Raised concentration of thyroid hormones with low TSH levels suggestive of hyperthyroidism was seen in 3.2% of samples.

Table 2: Analysis of different combinations of thyroid related tests ordered

Investigations ordered	No of samples (2997)
T3 + T4 + TSH	1468(48.9%)
TSH	1074(35.8%)
FT3 + FT4 + TSH	189(6.4%)
FT4 + TSH	99(3.3%)
T3 + T4	74(2.5%)
T4 + TSH	39(1.3%)
Other (T4/FT4/T3/T3 + TSH/ FT3+ TSH)	54(1.8%)

In 516(17.3%) found high TSH with normal value for thyroid hormones which may be suggestive of subclinical hypothyroidism and low T3 or T4. Four hundred and thirty three (14.5%) subjects have low TSH and high T3, T4.

T4 toxicosis (T4 raised, T3 normal, TSH low) was seen in 23(0.8%) of cases referred. Another important category was of results which had T4 as the only abnormal parameter with other two lying within reference interval. 32(1.0%) of the samples had this type of result. This may be due to rise in levels of thyroxine binding globulin which may occur due to pregnancy, neonatal age, infection, chronic active hepatitis, genetic factors and use of drugs e.g. estrogen, oral contraceptive pills and tamoxifen [16]. Pregnancy and neonatal age have already been excluded as the causative factor for rise in total T4 levels.

Table 3: Analysis of results for thyroid profile samples

T3/T4/ TSH Normal	T3 & T4N, TSH	T3 & T4N, TSH	T3 & T4 TSH	T3 & T4 ; TSH	T3N,T4, TSH (T4 toxicosis)	T4, T3 & TSH N
1969 (65.7%)	11 (0.3%)	13 (0.4%)	516 (17.3%)	433 (14.5%)	23 (0.8%)	32 (1.0%)

Analysis of results for TSH requests showed that the results of 71.2% samples were within the reference interval. 24.6% of samples had TSH results higher and 4.2% had values lower than the reference range (Table 4). Since the percentage of samples with normal results was around 77% in both thyroid profile and only TSH samples, it can be concluded that estimation of thyroid hormones does not offer any additional information in majority of patients. Percentage of normal results did not have much difference when results for all the TSH tests done during this period were taken into account (only TSH + TSH included in thyroid profile or in other combinations). Out of total 2923 TSH done, 2426 (82.9%) had results within the reference interval.

Table 4: Analysis of results of TSH samples

	TSH normal	TSH	TSH
TSH= 1074	764 (71.2%)	264 (24.6%)	46 (4.2%)
Total TSH = 2923 (included in all combinations)	2426 (82.9%)	399 (13.7%)	98 (3.4%)

The costs per test are summarized in Table 5. There were 2426 test requests for TSH, whilst T3 (n=1785) and T4 (n=1923) tests were also requested. Based on the ordering of the thyroid function tests or results indicate that in most cases 2997 of 2918 (97.3%) we found same result in all three tests (THS+T3+T4), simultaneous measurement of T3 and T4 is unnecessary. 79(2.7%) cases found different results this may be due to infection, genetic factors and use of drugs (Table 5). TSH screening of thyroid tests may be helpful to assesscertain categories of patients. The simple cost analysis described earlier, significant cost savings will result if TSH tests are only performed when T3 oT4 results are abnormal. Clinicians use the Thyroid Stimulating Hormone (TSH) measurement as the gold standard when screening for thyroid disease [7,17]. In most studies, the yield of abnormal thyroid testresults however remains low. Psychiatric clinicians should beaware that thyroid test abnormalities do not always denotethyroid disease and that the proper interpretation of testresults is dependent on a good basic understanding of thyroidphysiology and the methodology of the test [18].

Table 5: Review of test result

Test	No. of Samples	Same Result	Different Result
TSH	2426	2918 (97.3%)	79(2.7%)
T3	1785		
T4	1923		

Conclusion

This, to our knowledge is the first study in the Central India; to examine thyroid dysfunction as a measurement of viability and the cost entailed in administering TFTs in assumed patients. Despite the availability of TFTs in laboratories, the appropriate use of these tests, to detect thyroid dysfunction remains controversial. The probability of thyroid dysfunction is approximately one in every seven suspected patients. An important conclusion from this study is that, though the guidelines favour TSH as the screening test for thyroid dysfunction, a normal sensitive TSH test alone is sufficient to rule out thyroid dysfunction in patients.TSH not only improves the suitability of ordering the tests related to thyroid function it will be definitely more cost effective and help in achievingbetter patient satisfaction.

Volume : 3 | Issue : 11 | Nov 2013 | ISSN - 2249-555X

REFERENCE

1. Vanderpump MPJ, Tunbridge WMG, French JM, Appleton D, Bates F, Clark J, et al. The incidence of thyroid disorders in the community; a twenty-year follow up of the Whickham survey. Clin Endocrinol 1995; 43:55–68. | 2. Toubert ME, Chevret S, Cassinat B, Schlageter MH, Beressi JP, Rain JD. From guidelines to hospital practice: Reducing inappropriate ordering of thyroid hormone and antibody tests. Eur J Endocrinol 2000; 142:605–10. | 3. Ladenson PW, Singer PA, Ain KB, Bagchi N, Bigos ST, Levy EG, Smith SA, Daniels GH, Cohen HD. American thyroid association guidelines for detection of thyroid dysfunction. Arch Intern Med. 2000; 160:1573–5. | 4. Baskin HJ, Cobin RH, Duick DS, Gharib H, Guttler RB, Kaplan MM, Segal RL; American Association of Clinical Endocrinologists.American association of clinical endocrinologists medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. Endocr Pract. 2002; 8(6):457–69. | 5. Klee GG, Hay ID. Biochemical testing of thyroid function. Endocrinol Metab Clin N Am. 1997; 26:763–75. | 6. Rodriguez EJ, Montanes BR, Ordonez LJ, Cortes RM, Gonzalez SF. Evaluation of a new strategy for detecting thyroid dysfunction. Med Clin (Barc). 1990; 94(11):406–13. | 7. Roti E, Gardini E, Magotti MG, Pilla S, Minelli R, Salvi M, Monica C, Maestri D, Cencetti S, Braverman LE. Are thyroid function tests too frequently and inappropriately requested? J Endocrinol Invest. 1999; 22(3):184–90. | 8. Tubert ME, Chevret S, Cassinat B, Scahlageter MH, Beressi JP,Rain JD. From guidelines to hospital practice: reducing inappropriate ordering of thyroid hormone and antibody tests. Eur J Endocrinol. 2000; 142(6):605–10. | 9. Cohen KL, Swigar ME. Thyroid function screening in psychiatricpatients. JAMA 1979; 242:254-257. | 10. Levy RP, Jensen JB, Laus VG, Agle DP, Engel IM. Serum thyroid hormone abnormalities in psychiatric disease. Metabolism1981; 30:1060-1064. | 11. Brent GA, Larsen PR, Davis TF. Hypothyroidism and thyroiditis. In: Melmed S, Polonsky KS, Larsen PR, Korenberg HM, editors. Williams textbook of endocrinology. 11th ed. Noida: Saunders; 2009. p. 377–409. | 12. Chauduri S, Roy A, Mukherjee A, Biswas AB. An analysis of cases refereed for thyroid function disorder in a teaching hospital of Calcutta. Indian J Public Health. 1996;40(2):50–1. | 13. Gibbons V, Lillis S, Conaglen JV, Lawrenson R. Do general practitioners use thyroid stimulating hormone assay for opportunistic screening? N Z Med J. 2009;122(1301):25–30. | 14. Sinha KK, Ekka BR. Thyroid status in hospital based cases from Rajendra institute of medical sciences, Ranchi. Indian J ClinBiochem. 2009; 24:S248–9. | 15. Wong ET. Improving laboratory testing: can we get physicians to focus on outcome? ClinChem 1995; 41:1241–7. | 16. Larsen PR, Davies TF, Schlumberger MJ, Hay ID. Thyroid physiology and diagnostic evaluation of patients with thyroid disorders. In: Kronenberg HM, Melmed S, Polonsky KS, Larsen PR, editors. Williams textbook of endocrinology. 11th ed. Canada: Saunders Elsevier; 2008. p. 299–332. | 17. Viera AJ. Thyroid funtion testing in outpatients: Are both sensitive thyrotropin (sTSH) and free thyroxine (FT4) necessary? Fam Med 2003; 35:408-410. | 18. Spencer CA. Clinical utility and cost effectiveness of sensitive thyrotrophin assays in ambulatory and hospitalised patients. Mayo ClinProc 1988; 63:1214-1222. |