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ANALYSIS OF APPROPRIATENESS OF THYROID FUNCTION TEST ORDERING IN A TERTIARY CARE HOSPITAL.

Endocrinology

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ABSTRACT

Introduction: Appropriate use of the diagnostic thyroid function tests (T3, T4 & TSH) remains controversial as it is mainly TSH levels which guide treatment.

Aim: To evaluate the appropriateness of ordering of TFT in a public sector hospital.

Methodology: It was a retrospective observational study conducted in a tertiary care public sector hospital. Outcome of TFT was analyzed and correlated with appropriateness of ordering as per the selected guidelines.

Results: During the period of 3 years total 3325 patients were referred for thyroid function test. 78% of the TFT ordering was as per guideline. Our analysis found that proportion of dysthyroid cases being detected in the tests ordered as per guidelines was significantly higher as compared to tests which were not (odds ratio 1.83 (95% confidence interval 1.442 to 2.323). Proportion of dysthyroidism detected was higher in patients having more than one system involved. Serum T3 and T4 were found to be deranged in only 51 out of 633 dysthyroid patients**.**

Summary: In Public sector hospitals resources could be conserved by not only ordering only TSH as a test for primary screening but also when more than one symptomatic indication is present.

KEYWORDS

TSH, dysthyroid, TFT

INTRODUCTION:

Thyroid diseases are among the commonest endocrine disorders worldwide. It has been estimated that in India too, about 42 million people suffer from thyroid diseases[1]. Hence Thyroid function tests (TFT) which are very important for the diagnosis and monitoring of patients with thyroid disorder, are amongst the most widely prescribed laboratory investigations. TFT includes estimation of thyroid stimulating hormone (TSH) along with thyroid hormones, tri iodothyronine (T3) & tetra iodothyronine (T4) either in total or free form. Symptoms of thyroid disease are varied and include cardiovascular, gastrointestinal, autonomic, haematological and metabolic changes amidst others and often TFT is ordered by physicians to rule out thyroid disease in presence of these symptoms which may often be due to other aetiologies.

Appropriate use of these tests remains controversial and various studies have been conducted to evaluate the ordering pattern of thyroid function tests[2,3]. TSH testing is the best method for triaging thyroid dysfunction and for monitoring patients being treated for hypothyroidism[4]. However the habit of prescribing TFT as preliminary test to diagnose or rule out thyroid disorders continues, as observed in a recent Indian study which reported that 47.5% of total samples for thyroid testing were ordered for (TFT) and 46% for TSH [5].The percentage of samples with normal results was around 77% in both thyroid profile and only TSH samples, leading to the conclusion that estimation of thyroid hormones does not offer any additional information in majority of patients. This is leading to an unnecessary cost burden, to the patient and to the government, in public hospitals. With this point of view we decided to evaluate the appropriateness of ordering of TFT in our institute, in a tertiary care hospital.

MATERIALS AND METHODS:

It was a retrospective observational study conducted in a tertiary care public sector hospital. Study related data was collected from the report cards of thyroid function test of patients visiting the thyroid radio-immuno assay clinic in the Department of Pharmacology during the period of 1st January 2013 to 31st December 2015. Report cards were screened and the patient related information was collected from the records of the first visit of the patient as noted below. No follow up visit information was collected.

Demographic data of patient e.g. patient's initials, age and gender was enlisted. Patient OPD/Indoor number and the referring department were noted to maintain exclusiveness of the data entry. Symptoms, clinical history, diagnosis, concurrent medication (if any) and report of the thyroid function test done at first visit were documented.

All the information was recorded on case record form and was entered to the excel sheet for subsequent analysis. Indications for which the patient referred for TFT were compared with the standard guidelines and recommendations for the use of thyroid function tests.

Parameters of TFT analyzed were serum TSH, T3 and T4 levels. These were analyzed by immunoradiometric assay (for TSH) and radioimmunoassay (for T3 and T4) by using the kits bought from Board of Radiation and Isotope Technology, Navi Mumbai and the range of their normal values were standardized as per kit manual reference as follows [6,7,8].

T3 – 0.7 – 2.0 ng/ml
T4 – 4.5 – 13.5 microgm/dl
TSH – 0.2 – 5.1 microIU/ml

Patient results falling in this range were classified as euthyroid. Subsequently patients with TSH values less than the 0.2 microIU/ml were labelled as hyperthyroid and those with values above 5.1 microIU/ml as hypothyroid. Both these categories together were referred to as dysthyroid.

There are no specific standard Indian guidelines for ordering TFT. Hence collective recommendations from "UK Guidelines for the Use of Thyroid Function Tests", "American Association of Clinical Endocrinologists and American Thyroid Association" and Indian recommendations were used as a reference[9-11]. These were

categorised into systems for the ease of analysis as given in table 1, (henceforth referred to as "guidelines"). Each system was given a number e.g. thyroid 1, other endocrine disease 2, etc. The symptoms and diagnosis on the report card were studied for each patient and the corresponding number was given to the individual cases.

Table 1: Categorisation of indications for thyroid function tests ordering as per UK guidelines, ATA guidelines and Indian suggestions [9-11].

NO	SYSTEM	INDICATIONS
1	Thyroid	1. Monitoring of thyroid function: Treatment of Thyrotoxicosis with Anti-Thyroid Drugs, Patients on thyroxine therapy 2. Congenital hypothyroidism 3. Goitre or thyroid nodule 4. Women with a past history of postpartum thyroiditis 5. Post neck irradiation 6. Following Destructive Treatment for Thyrotoxicosis by either Radioiodine or Surgery
2	Endocrine	1. Type 1 diabetes, type 1Diabetes mellitus 2. Women with Type 1 Diabetes 3. Type 1 diabetes annual review 4. Type 2 diabetes at diagnosis 5. Short stature 6. Adrenal insufficiency 7. Osteoporosis 8. Women on menopausal age
3	CNS	1. Depression 2. Patient with psychiatric disease 3. Dementia
4	CVS	1. Atrial Fibrillation 2. Prolonged QT interval 3. Unspecified Cardiac dysrhythmia 4. Congestive heart failure 5. Hypertension 6. Dyslipidemia 7. Hypercholesterolemia 8. Mixed hyperlipidemia 9. Hyperlipidaemia
5	Dermatology	1. Vitiligo 2. Alopecia 3. Changes in skin texture
6	Pregnancy	
7	Obstetrics & Gynaecology	1. Subfertility 2. Infertility 3. Menstrual irregularity 4. Dysmenorrhea
8	Genetic	Down's and Turner's syndrome
9	Other	1. Constipation 2. Weight gain 3. Malaise and fatigue 4. Unspecified Myopathy 5. Unspecified deficiency Anemia 6. Unexplained hyponatremia 7. Carpal tunnel syndrome
10	Drug induced	Lithium, amiodarone

Patients who were ordered TFT and satisfied one or more indications mentioned in table 1 were termed as a compliant order and those who were not satisfying any of the indication from table 1 but ordered to undergo TFT were called as non-compliant.

Following Percentages were calculated.

- Euthyroid, hypothyroid and hyperthyroid patients
- Guideline compliant and non-compliant orders.

The data entry and analysis was started only after the Institutional Ethics Committee approval for the study was sought. The identity of all the participants was kept confidential.

Statistics: Descriptive statistical analysis was done for the demographic data.

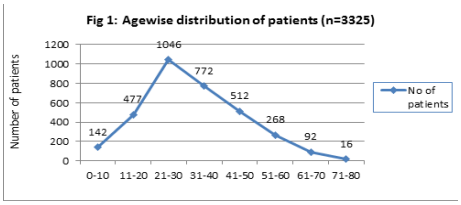
RESULTS:

During the period of 3 years from January 2013 to December 2015 total 3325 patients were referred for thyroid function test. For all the patients parameters ordered in TFT were TSH, T3 and T4. 85.5% of the referred patients were women while 14.5% were men. Gender wise distribution is shown in table 2.

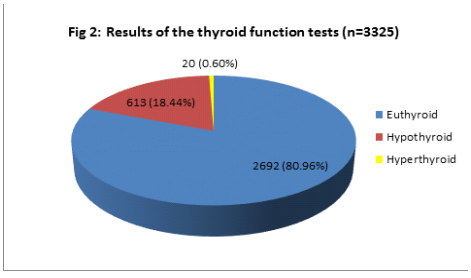
Table 2: Gender wise distribution of patients referred for TFT (n=3325)

	Women	Men
Euthyroid	2300	392
Hypothyroid	524	89
Hyperthyroid	19	1

Patients referred for TFT were ranging from minimum age of 4 days to 80 years with mean 32.88±14.15 standard deviation (Fig 1).



From the TFT reports of the 3325 patients 2692 were diagnosed as euthyroid and 613 were hypothyroid. Only 20 patients were found to be hyperthyroid (Fig 2).



Outpatient departments (OPDs) of various faculties had ordered the TFTs. The maximum ordering was from Medicine OPD (38.07%) followed by Obstetrics and Gynaecology (27.28%) while least referral was from Orthopaedics (0.69%) and Respiratory medicine (0.60%) (Table 3). 93.2% of TFT ordered by Department of obstetrics and gynaecology were compliant with the guidelines while 73.9% of TFT ordered by orthopaedics department were non-compliant with the guidelines (Table 3).

Table 3: Compliance of TFT ordering as per guidelines* and outcome of TFTs ordered by various outpatient departments (OPDs) (n=3325)

Referring OPDs	Total number (%)	Guideline Compliant Ordering Total number (%)		Guideline Non-compliant Ordering Total number (%)	
		Euthyroid	Dysthyroid†	Euthyroid	Dysthyroid†
Medicine	1266 (38.07%)	829 (65.5%)		437 (34.5%)	
		599	230[222/8]‡	390	47[45/2]‡
Obstetrics Gynaecology	907 (27.28%)	845 (93.2%)		62 (6.8%)	
		746	99[98/1]‡	48	14[13/1]‡
ENT	456 (13.71%)	402 (88.2%)		54 (11.8%)	
		272	130[123/7]‡	45	9[9/0]‡
Dermatology	348 (10.47%)	286 (82.2%)		62 (17.8%)	
		255	31[31/0]‡	57	5[5/0]‡
Paediatrics	150 (4.51%)	76 (50.7%)		74 (49.3%)	
		64	12[12/0]‡	61	13[13/0]‡

Psychiatry	97 (2.92%)	89 (91.8%)		8 (8.2%)	
		66	23[23/0]‡	8	0
General Surgery	58 (1.74%)	53 (91.4%)		5 (8.6%)	
		39	14 [13/1]‡	5	0
Orthopaedics	23 (0.69%)	6 (26.1%)		17 (73.9%)	
		4	2[2/0]‡	16	1[1/0]‡
Respirator Medicine	20 (0.60%)	8 (40%)		12 (60%)	
		8	0	9	3[3/0]‡

*Guidelines given as in table 1
† Dysthyroid means either hypothyroid or hyperthyroid.
‡Square bracket in the table, first number denotes hypothyroid results and latter denotes number of hyperthyroid results.

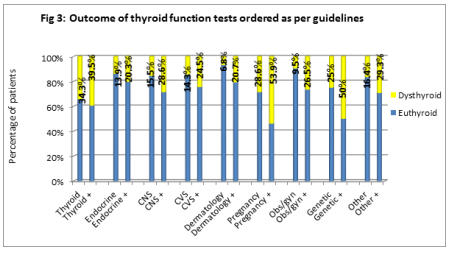
78% of the TFT ordering was guideline compliant. Our analysis supported that proportion of dysthyroid cases being detected in the tests ordered as per guidelines was significantly higher as compared to tests which were not ordered as per guidelines (table 4). ($p < 0.0001$)

Table 4: Effect of compliance to guideline on outcome of Thyroid function test ordering.

	Outcome		
Guideline	Dysthyroid	Euthyroid	Total
Competent ordering	541	2053	2594
Non-Competent ordering	92	639	731
Total	633	2692	3325

[df=1, odds ratio = 1.83, confidence interval 1.442 to 2.323]

When patients were categorized according the guidelines it was found that some patients were referred for single primary complaint and others were presenting with complaints affecting more than one system, as given in table 1. Accordingly patients were segregated into primary class with only one system involved e.g. in the group labelled as 'thyroid', patients had symptoms related to only that system. Patients with thyroid related symptoms along with other system involvement were labelled as 'thyroid+'. Difference in the outcomes of TFT for these patient classes are shown in Figure 3. Proportion of dysthyroidism detected was higher in patients having more than one system involvement (e.g. Thyroid+, Endocrine+, etc Fig 3).



Among 613 patients diagnosed as hypothyroid on the basis of serum TSH level, deranged levels of T3 and T4 were seen in only 55 and 49 patients respectively. Out of 20 hyperthyroid patients only six patients had increased serum T3 as well as T4 levels.

Table 4: Details of Thyroid function test in dysthyroid patients.

	TSH microIU/ml	T4 microgm/dl	T3 ng/ml	TSH, T4 & T3 deranged
Hypothyroid	>5.1	<4.5	<0.7	
No of patients (n=613)	613	49	55	45
Hyperthyroid	<0.2	>13.5	>2	
No of patients (n=20)	20	6	6	6

DISCUSSION:

Retrospective analysis of thyroid function test (TFT) ordering for the period of three years was done in a tertiary care hospital. As the study was designed to be a cross sectional analysis of TFT ordering; result of only first TFT of patient were analyzed. Presentation of thyroid gland malfunctioning is varied and can target almost all the organ systems. Diagnosis of thyroid disorder and/or confirmation of this in clinically suspected patients demands for guidelines. In Indian set up such guidelines are still awaited, so to analyze the appropriateness of TFT ordering in this study the guidelines by "American Association of Clinical Endocrinologists and American Thyroid Association" and "UK Guidelines for the Use of Thyroid Function Tests" were utilized along with some recommendations given for the Indian set up [9–11].

TFT reports of 3325 patients referred from various outpatient departments were analyzed. Women preponderance in the thyroid disorders is a known fact [1]. Our study finding of 85.5% of referred patient population being women supports the same. Patients evaluated for TFT were dispersed over wide range of age i.e. from four days to 80 years as ours is a tertiary care centre with multiple disciplines catering to wide range of population. Mean age of patients was 32.87±14.15 years which compares with studies conducted in North India, showing high prevalence of thyroid disorder in third and forth decade of life [5,12].

Maximal references for the TFT were from the outpatient department of medicine followed by obstetrics and gynaecology (OBGY), ENT, dermatology, paediatrics departments. The least referral was from respiratory medicine and orthopaedic department. This result follows the symptomatology of the thyroid disorder [13]. Previous studies have shown similar pattern in this regard though our study has greater referral from dermatology department and none from ophthalmology department [5,12].

When reasons for the referral were analyzed based on guidelines [9-11], it was found that 78% of the TFT orders were guideline compliant. Maximum references from department of OBGY were compliant. This trend of positive compliance was followed by department of psychiatry, surgery and ENT in a descending order. Though medicine department contributed to the maximum TFT ordering, its adherence with guidelines was lower. Varied symptoms of thyroid disorder and its association with other co-morbidities compel physicians to order TFT to rule out presence of dysthyroidism. It was seen that 51% of TFT ordering from paediatric department was compliant with the guidelines. Out of 150 paediatric patients 44 were being managed for thalassaemia. Although thalassaemia Longitudinal Cohort (TLC) recommends TFT to be done annually in these patients[14]; none of our reference guideline mentioned Thalassaemia as an indication for the use of TFT. This is the reason of lower compliance of paediatric department. 15.9% of these patients were hypothyroid and hence patients on treatment for thalassaemia should be included in the guideline for the use of TFT.

Probability of detection of abnormality of thyroid gland function was significantly higher in the cases where tests were ordered according to the guidelines with odds ratio 1.83 (95% confidence interval 1.442 to 2.323). Proportion of dysthyroidism detected was higher in the group of patients having complaints from more than one system.

Our study has underlined the redundancy of TFT in the form of ordering all T3, T4 and TSH for a single patient. When 613 (18.33%) patients were diagnosed to have hypothyroidism, only 45 patients (1.35%) had all three parameters of TFT (T3, T4 and TSH) deranged. Previous studies have shown similar fact [5,12,15]. Decision about the thyroid supplementation is generally taken on the basis of TSH levels. In such scenario ordering of all three parameters for primary screening is leading to wastage of resources. This result of our study is in line with the findings of study done by Kluesner et al. i.e. restriction of overutilization of the laboratory could save the public sector funds enormously [16].

CONCLUSION:

In our set up 78% TFT were ordered appropriately according to the guideline. In Public sector hospitals resources could be conserved by not only ordering only TSH as a test for primary screening but also when more than one symptomatic indication is present.

REFERENCES:

1. Unnikrishnan A, Menon U. Thyroid disorders in India: An epidemiological perspective. Indian J Endocrinol Metab [Internet]. 2011;15(6):78–81. Available from: http://www.ijem.in/text.asp?2011/15/6/78/83329
2. Roti E, Gardini E, Magotti MG, Pilla S, Minelli R, Salvi M, et al. Are thyroid function tests too frequently and inappropriately requested? J Endocrinol Invest. 1999;22(3):184–90.
3. 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(6):605–10.
4. Carvalho GA de, Perez CLS, Ward LS. Utilização dos testes de função tireoidiana na prática clínica. Arq Bras Endocrinol Metabol [Internet]. 2013;57(3):193–204. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-27302013000300005&lng=pt&tlng=pt
5. Gupta S, Verma M, Gupta AK, Kaur A, Kaur V, Singh K. Are we using thyroid function tests appropriately? Indian J Clin Biochem. 2011;26(2):178–81.
6. Immunoradiometric assay (IRMA) kit for human thyroid stimulating hormone. IRMAK – 9. Board of radiation and isotope technology, Navi Mumbai. www.britatom.gov. in.
7. BRIA MAG 3. Radioimmunoassay kit for total triiodothyronine. Board of radiation and isotope technology, Navi Mumbai. www.britatom.gov.in.
8. BRIA MAG 4. Radioimmunoassay kit for total thyroxine. Board of radiation and isotope technology, Navi Mumbai. www.britatom.gov.in.
9. British Thyroid Association. UK Guidelines for the Use of Thyroid Function Tests July 2006 1. Consultant. 2006;(July):1–86.
10. Garber JR, Cobin RH, Gharib H, Hennessey J V., Klein I, Mechanick JI, et al. Clinical Practice Guidelines for Hypothyroidism in Adults: Cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. Thyroid [Internet]. 2012;22(12):1200–35. Available from: http://online.liebertpub.com/doi/abs/10.1089/thy.2012.0205
11. Unnikrishnan AG. Treatment of Primary Hypothyroidism: Towards an Indian Consensus. Med Updat. 2005;314–7.
12. Mahajan RD, Yasmin T. Research and Reviews : Journal of Medical and Health Sciences Thyroid Function Test Ordering Pattern in a Tertiary Care Hospital in Western Uttar. 2013;2(4):7–11.
13. Lazarus JH, Obuobie K. Thyroid disorders - An update. Postgrad Med J [Internet]. 2000;76(899):529–36. Available from: http://www.embase.com/search/results?subaction=viewrecord&from=export&id=L30696806\nhttp://dx.doi.org/10.1136/pmj.76.899.529\nhttp://sfx.library.uu.nl/utrecht?sid=EMBASE&issn=00325473&id=doi:10.1136/pmj.76.899.529&atitle=Thyroid+disorders+-+An+update&stit
14. Tubman VN, Fung EB, Vogiatzi M, Alexis A, Rogers ZR, Neufeld EJ, et al. Thalassemia : Report of the Thalassemia Longitudinal Cohort. J Pediatr Hematol Oncol. 2016;37(3):1–16.
15. Shrivastava RK, Meena M, Varma M, Jha RK, Kosta S KR. Is TSH alone can be a treated as diagnostic marker for thyroid disorders. Indian J Appl Res. 2013;3(11):361–3.
16. Kluesner JK, Beckman DJ, Tate JM, Beauvais AA, Kravchenko MI, Wardian JL, et al. Analysis of current thyroid function test ordering practices. J Eval Clin Pract. 2017;1–6.