

# ROLE OF TSH ONLY STRATEGY FOR THE DIAGNOSIS OF THYROID DISEASE

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## ABSTRACT

**Background:** Serum thyroid stimulating hormone (TSH) is advised to assess thyroid function and can be used to replace TFTs. **Objective:** To evaluate the role of TSH only for diagnosis of thyroid dysfunction in tertiary care hospital. **Methodology:** Study design: Cross sectional study. Study setting: Endocrinology, section of Pathology Department and Surgery Department of Sheikh Zayed Medical College/Hospital, Rahim Yar Khan, Pakistan. **Study Subjects:** Patients referred for routine thyroid disease from surgical ward were selected for study. Their history was taken and detailed clinical examination was carried out. **Data Collection:** Data of all the patients in whom TSH, fT<sub>4</sub> and fT<sub>3</sub> tests or TSH and fT<sub>4</sub> were ordered by clinicians during the period of study was collected. fT<sub>3</sub>, fT<sub>4</sub> and TSH were analyzed by fourth generation of ECLIA. Samples were assayed in batches, and sometimes assays were performed in duplicate when necessary. **Results:** This study shows that TSH only strategy has 100% sensitivity in both hyperthyroid and hypothyroid cases when TSH plus fT<sub>4</sub> was taken as golden standard, whereas in hypothyroid cases specificity was 86% and in hyperthyroid cases was 90%. **Conclusion:** This study shows that TSH only strategy can be used as first line test for the diagnosis of thyroid disease and it has good sensitivity and specificity, as many patients with hypothyroidism or hyperthyroidism are diagnosed primarily on the basis of TSH measurement only. **Key words:** TSH only, Diagnosis, TFTs, Reflex testing.

## INTRODUCTION

Thyroid disease, ranges from subclinical to life threatening disease, which can be effectively treated, both under treatment and over treatment of these conditions may have serious consequences for the patient's health, therefore, correct and timely diagnosis and monitoring are important.<sup>1,2</sup>

Thyroid problems have been reported in over 110 countries of the world with 1.6 billion people are at risk. Most of these are in developing countries Asia, Africa and Latin America etc. In Pakistan, the prevalence of hyperthyroidism and subclinical hyperthyroidism was 5.1% and 5.8% respectively. Similarly the prevalence of hypothyroidism and subclinical hypothyroidism was 4.1% and 5.4% respectively.<sup>3</sup> The diagnosis of thyroid disease, however, is difficult due to its non specific symptoms and laboratory findings and these expensive tests are advised too often.<sup>4,5,6</sup>

Thyroid gland secretes two hormones thyroxine or T<sub>4</sub> and T<sub>3</sub>. The thyroid gland synthesis and secretion are controlled by negative feedback system involving (1) TRH from hypothalamus (2) TSH from pituitary (3) Thyroid hormones from follicular cells of thyroid gland.<sup>7-10</sup> Thyrotrophic releasing hormone (TRH) is a tetrapeptide produced in the periventricular nucleus of hypothalamus and drains to pituitary.<sup>11-15</sup> The half-life of TSH is approximately 1 hour, plasma T<sub>4</sub> is 5-7 days and T<sub>3</sub> is 1 day. TSH secretion rhythmically varies between day and night.<sup>16</sup>

Pathological conditions of thyroid broadly divided into two categories; hypothyroidism and hyperthyroidism.<sup>17</sup> Hypothyroidism is a state of deficient thyroid hormone production and its action.<sup>18</sup> Hyperthyroidism is a state of hyper-metabolic condition caused by excessive production of thyroid hormones.<sup>19,20</sup>

Given the rise in thyroid test requests,<sup>12,13</sup> which is disproportionate to thyroid disease burden and the fact that these tests requests are significant proportion of all laboratory tests ordered there is a need to help clinicians to follow reflex testing.<sup>14</sup> Reflex testing occurs when some initial test like TSH is abnormal i.e beyond normal limits and it is non conclusive without a follow up test like T<sub>4</sub> and T<sub>3</sub> and it is performed without further ordering by physician.<sup>8,9,10</sup> A serum TSH within the euthyroid reference interval usually excludes a diagnosis of hyperthyroidism.<sup>10</sup> Free T<sub>4</sub> levels can than be requested when TSH level is abnormally high or low. This strategy for initial evaluation of thyroid disease is both cost effective and efficient.<sup>9,11</sup> This is labeled as reflex testing. The objective of this study was to access the role of TSH only strategy for the diagnosis of thyroid dysfunction in tertiary care hospital.

## METHODOLOGY

Study design: Cross sectional study. Setting: This study was conducted in Endocrinology, section of Pathology department Sheikh Zayed Medical

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College/Hospital, Rahim Yar Khan, Pakistan. Duration: 1<sup>st</sup> October 2016 to 31<sup>st</sup> January 2017 Study subjects: All those patients who had been suspected having any thyroid dysfunction, referred from OPD and indoor sections of surgery department and surgery department of patients, were included in this study.

#### Inclusion criteria:

- Patients age 20-80 years .

#### Exclusion criteria:

- Pregnancy (especially first trimester).
- Patients taking any medication that temporarily disrupt the normal hypothalamic-pituitary-thyroid axis.
  - Lithium carbonate and amiodarone etc. (these drugs may lead to transient increased of TSH).
  - Glucocorticoids and dopamine. ( transient suppression of TSH)

**Sample size:** A total of 350 samples were collected. Data was collected with the help of a predesigned questionnaire. Variables included in questionnaire were age, gender, clinical history, sign, symptoms TSH and  $fT_4$ . **Specimen handling and storage:** The type of specimen that required for analysis was blood sample. The blood sample was taken at any time of the day, and most samples were centrifuged within 2 hours.

Serum was separated from the cells and stored at 4°C until all assays were completed, within 24 hours, and then stored it at -20°C for further analysis. Samples were assayed in batches, and sometimes assays were performed in duplicate when necessary.

Electrochemiluminescence assay fourth generation was used that is ten folds more sensitive than most other immunometric assays.

The TSH was performed using fourth generation immunometric assay by Electrochemiluminescence (ECLIA) [COBASE e 04],  $fT_4$  tests was performed by competitive analog assay chemiluminescence. The reference ranges were 0.27 - 4.2 mIU/L for TSH and 0.93 – 1.7 ng/dL for  $fT_4$ . Hyperthyroidism was labelled when TSH was lower than normal and  $fT_4$  were higher than normal ranges. Hypothyroidism was labelled when the TSH was higher than normal and  $fT_4$  was lower than normal range. Data was analyzed by SPSS version 16. TSH and  $fT_4$  was taken as gold standard and sensitivity and specificity was calculated for TSH only strategy in hypothyroid and hyperthyroid status.

## RESULTS

A total of 350 patients 256, females and 94 males were included in this study, with mean age of  $39 \pm 11$  years.

**Table I: TSH alone status versus TFTs status in hyperthyroid and hypothyroid state**

TSH only versus TFTs in hyperthyroid status			
TSH only status	Status of TFTs (Combine TSH+ $fT_4$ )		Total
	Hyperthyroid	Not Hyperthyroid	
Hyperthyroid	74	25	99
Not Hyperthyroid	0	251	251
<b>Total</b>	<b>74</b>	<b>276</b>	<b>350</b>
TSH only versus TFTs in hypothyroid status			
TSH Alone status	Status of TFTs (combine TSH+ $fT_4$ )		Total
	Hypothyroid	Not Hypothyroid	
Hypothyroid	63	40	103
Not Hypothyroid	0	247	247
<b>Total</b>	<b>63</b>	<b>287</b>	<b>350</b>

Table I shows that TSH only strategy, had 99 patients in hyperthyroid category, according to combined status of TFTs, only 74 persons were diagnosed as primary hyperthyroidism. This shows the specificity of TSH only for the detection of hyperthyroidism (thyroid dysfunction) was 90% and a sensitivity of 100%.

Table I shows that TSH only strategy, has 103 patients in hypothyroid category, according to combined status of TFTs, only 63 persons were diagnosed as primary hypothyroidism. The specificity of TSH for the detection of hypothyroidism (thyroid dysfunction) was 86% and sensitivity of 100%. Thyroid function tests are frequently advised by clinicians, however, systematic use of this test is required to reach the same diagnosis resulting in low cost and efforts. TSH screening with fourth generation assay reduced the need of complete thyroid profile for screening.<sup>18,21</sup>

Current study was conducted, to evaluate the unity of TSH only strategy for the diagnosis of thyroid disease. In our study TSH alone was compared with Thyroid profile on 350 study subjects. Out of 350 person, 94 (26.8%) were males and 256 (73.2%) were females. In study subjects male to female ratio were 1:2.7. Age criteria of these persons were 20-80 years.

A previous study also concluded that if TSH is dearranged, its necessary to differentiate the hypo/hyperthyroidism by reflex testing  $fT_4$  assay. The sensitivity of TSH only strategies for diagnosis of thyroid disease was 100% in our study. A fourth generation TSH assay with the sensitivity of at least 0.001mU/l may help to distinguish patient with

undetectable TSH with real thyroid disease. Furthermore, many patients with subclinical hypo/hyperthyroidism was diagnosed primarily on the basis of TSH measurement. Our study showed good specificity (86%) for hypothyroid disease and even better (90%) for hyperthyroid disease. White GH et al<sup>19</sup> and Hopton MR et al,<sup>20</sup> demonstrated that TSH can be used as a first line test of thyroid function in non selected out patients. It is more sensitive and specific marker than fT<sub>4</sub> measurement for the assessment of thyroid status.

Recent study in Karachi,<sup>21</sup> suggested that the fourth generation ECLIA expands the utility of TSH measurements used as single line test of thyroid function by providing wider range up to 0.001mU/l. TSH screening of newborn is carried out in developed countries. Better clinical knowledge and technology clinical utility of this assay can be enhanced. Although various guidelines were available, however; in most studies, TSH as a single first-line test for suspected thyroid dysfunction and monitoring patients are followed now a days.<sup>16</sup>

Most of the hospitals and laboratories has own protocol for reflex testing; if the TSH is abnormal, a reflex fT<sub>4</sub> and/or fT<sub>3</sub> is requested. Studies have found that reflex testing allows clinicians to obtain right diagnosis faster and at less cost. Thyroxine replacement therapy can effect diagnosis, like a patient with high TSH and normal fT<sub>4</sub> can be wrongly labeled as a case of subclinical hypothyroidism, which in fact be a case of non-compliance or inadequate dosage.

It is suggested in thyroid crisis or in emergency indoor patients complete thyroid function tests may be appropriate otherwise in routine cases, screen with TSH alone, followed by fT<sub>4</sub> or fT<sub>3</sub> in selected cases. This would decrease the cost and workload. In cases of abnormal TSH values, nature of thyroid disease investigated according to severity of the condition.

## CONCLUSION

This study shows that TSH only strategy can be used as first line test for the diagnosis of thyroid disease and it has good sensitivity and specificity, as many patients with hypothyroidism or hyperthyroidism are diagnosed primarily on the basis of TSH measurement only.

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## **CORRIGENDUM**

### **Evaluation of serum ferritin as predictor of HbA1c in patients with type-2 diabetes mellitus**

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In the version of this article initially published, Farheen Aslam's affiliation was incorrect. Her correct affiliation is Department of Pathology, Quaid-e-Azam Medical College/BVH, Bhawalpur, Pakistan. The error has been corrected in PDF versions of this article.

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