



## LEVELS OF SERUM TSH AND ITS IMPLICATIONS IN DEVELOPMENT OF METABOLIC SYNDROME – TIP OF THE ICEBERG: IN YOUNG ADULTS OF GUWAHATI CITY.

### Physiology

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### ABSTRACT

Thyroid Stimulating Hormone (TSH) is a hormone secreted by the anterior pituitary that plays an important role in regulating the function of the thyroid gland. Levels of TSH in the blood - is a reliable index of the functional status of the thyroid gland. At present, TSH levels in serum are estimated by microparticle enzyme immuno assays (MEIA), which are very sensitive. In the current study, serum TSH levels were measured in 100 clinically euthyroid subjects, consisting of 50 males and 50 females. The study found that 12% of the subjects (5 males and 7 females) had TSH values above the normal, the normal range of the TSH assay being 0.35-4.50 m IU/ml. This finding is significant in light of the recent focus on subclinical hypothyroidism being in limelight, particularly the risk of development of overt thyroid dysfunction in persons with high normal values of serum TSH. Furthermore, such kind of studies in general population among young population was done rarely previously, as a reflection of their serum TSH levels in this part of the India who are considered euthyroid till the time they were tested. Moreover, detection of subclinical or overt hypothyroid state helps in the preventive aspects as well as to find out other parameters of metabolic syndrome- which is considered now as just the tip of the iceberg. **Materials and methods:** In the study, serum TSH levels were measured in 100 euthyroid subjects (50 males and 50 females) by microparticle enzyme immune assay. **Results:** After analyzing the values of TSH it was detected that 12% of the subjects (5 males and 7 females) had TSH levels >4.50 m IU/ml (Upper limit of the normal range). **Conclusion:** This finding is significant in light of the recent focus on subclinical hypothyroidism being particularly at the risk of development of overt thyroid dysfunction in young age leading to a gamut of metabolic disorders and mortality & morbidity occurring among such populace at a young age. Further, it is of importance that such type of lifestyle modifiable disorders can be prevented or reverted to normal if detected early.

### KEYWORDS

TSH, euthyroid, subclinical hypothyroidism.

### INTRODUCTION

Thyroid Stimulating Hormone (TSH) as we all know is the major regulator of the functional status of the thyroid gland<sup>(1)</sup>. In normal serum, TSH is present in concentrations between 0.3 – 4.5  $\mu$  U/L; than average plasma level is about 2.5  $\mu$ U/L whereas the biologic half-life of human TSH is about 60 minutes. Circulating TSH shows both pulsatile and circadian variations. The pulsatile nature of the thyroid hormones are characterized by fluctuations at 1- to 2- hour intervals. Fasting, illness and after surgery decreases the magnitude of pulsatile TSH secretion<sup>(2)</sup>. The circadian variation is characterized by a nocturnal surge that precedes the onset of sleep and appears to be independent of the cortisol rhythm and fluctuations in serum T4 and T3<sup>(3,4)</sup>. The secretion of TSH starts to rise at about 9PM, peaks at midnight and then declines during the day. The normal secretion rate is about 110  $\mu$ g/day. When the onset of sleep is delayed, the nocturnal TSH is enhanced and prolonged and the early onset of sleep results in a surge of lesser magnitude and shorter duration<sup>(1,5)</sup>. Compared to other anterior pituitary hormones TSH secretions are modest, in part because TSH has a relatively long plasma half-life. So, single measurements of TSH are adequate for assessing its circulating level<sup>(6)</sup>.

The rate of TSH secretion is exquisitely sensitive to the plasma concentrations of free thyroid hormones thus providing a precise and specific barometer of the thyroid status of the patient<sup>(5)</sup>. Measurement of TSH by sensitive micro particle enzyme immune assays is currently the most useful first-line test of thyroid function<sup>(7)</sup>. Extremely sensitive (fourth generation) assays can detect TSH levels  $\leq 0.004$  m U/L, but for practical purposes, assays sensitive to  $\leq 0.1$  m U/L are sufficient<sup>(6)</sup>. Micro particle enzyme immune assay technology now makes it possible to define the normal range for serum TSH and hence to ascertain both when thyroid function is inadequate or when hormone supply is excessive. This assay uses the TSH molecule as a link between a TSH antibody bound to an inert surface (e.g. particles, side of a test tube) and a second antibody directed against a different TSH epitope that is labeled with a detectable marker (I125, an enzyme or a chemiluminescent reagent). Thus, the signal generated is proportional to the concentration of TSH in the serum<sup>(8)</sup>.

Plasma TSH concentration is very sensitive to alterations in the levels of free T3 and T4; a 50% decline in the free T4 levels can cause plasma TSH concentration to increase 50-100fold. Alternately, an excess of thyroid hormone leads to a decrease in plasma TSH concentration<sup>(8)</sup>. Whenever the rate of thyroid hormone secretion rises to 1.75 times normal, the rate of TSH secretion falls towards the zero mark<sup>(9)</sup>. There is a linear inverse relationship between the serum free T4 concentration and the log of TSH, making the serum TSH

concentration an exquisitely sensitive indicator of the thyroid state of patients with an intact hypothalamic-pituitary axis<sup>(10)</sup>.

The aim of the present study was to measure the serum TSH levels in a healthy young adult population (of either gender).

### AIMS AND OBJECTIVES

The aim of the present study was to measure the serum TSH levels in a healthy young adult population.

### MATERIALS AND METHODS

The purpose of the study and the study procedure was explained to all participants. Written consent of the participants were obtained prior to starting of the evaluation. The history was taken in detail and general and systemic examination was done. Subjects with present or past history of any thyroid disorder, with family history of thyroid disorder, with history of intake of any medication that might affect the thyroid hormone profile or with history or clinical examination suggestive of any signs or symptoms related to thyroid disorder were excluded from the study.

Also, family history of thyroid disorder and other metabolic diseases amongst first degree relatives were enquired. After taking history and conducting general and systemic examination, a total of 100 students, with no symptoms or signs suggestive of any thyroid disorder, were included in the study. The subjects consisted of 50 males and 50 females. Serum TSH levels of the subjects was estimated by micro particle enzyme assay method.

### Statistical methods:

The data collected was tabulated and subjected to statistical analysis. All data were expressed as Mean  $\pm$  SD. The data was analyzed using MS Excel.

### RESULTS

A total of 100 students aged 18-25 years were included in the study. The mean age of the subjects was 21.05  $\pm$  0.896 years.

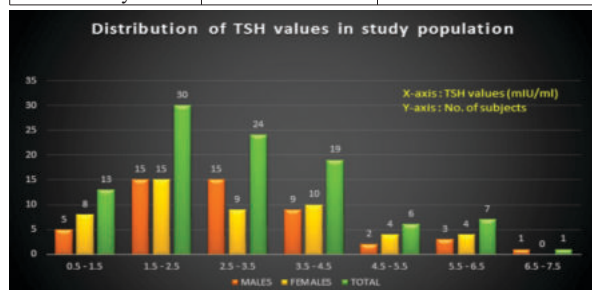
The normal range of TSH assay was 0.35 – 4.5 m IU/ml. The mean TSH of the 100 subjects was 2.99  $\pm$  1.43 m IU/ml with 12 subjects (12%) having TSH value >4.5 m IU/ml. The male subjects had a mean TSH value of 2.96  $\pm$  1.43 m IU/ml with 5 subjects (10%) having TSH value > 4.5 m IU/ml. The female subjects had a mean TSH value of 3.01  $\pm$  1.43 m IU/ml with 7 subjects (14%) having TSH value >4.5 m IU/ml. None of the subjects had TSH value less than 0.35 m IU/ml. Although the mean TSH value in females was higher than that in

males, the difference was not significant. In the present study, the combined male and female range for TSH concentration was found to be 0.74-7.34m IU/ml. The TSH range in females was 0.64-5.90m IU/ml and that in males was 0.56-7.2 2mIU/ml. Figure 1 shows the distribution of TSH values in the study population. The subjects were residents of Guwahati City.

The TSH values of 12 subjects were found to be >4.5 m IU/ml. They were detected to be cases of subclinical hypothyroidism. On further evaluation it was found that these subject of the populace who had subclinical hypothyroidism had definitely one or the other types of metabolic disorders like some fell in the group of prehypertension or pre diabetes alongwith derangement of the lipid profile or PCOD in case of girls with obesity/ overweight being a common factor with almost 100% favoring or likeness towards junk food. In the study, the prevalence of subclinical hypothyroidism was found to be 12% with a male: female ratio of 1:1.5. The mean TSH among the subclinical hypothyroid subjects was  $5.05 \pm 0.55$  m IU/ml ( $6.02 \pm 0.85$  m IU/ml among the males and  $5.75 \pm 0.33$  m IU/ml among the females). The remaining 88 subjects, who were euthyroid, had a mean TSH value of  $2.51 \pm 1.34$  m IU/ml ( $2.32 \pm 1.2$  m IU/ml in males and  $2.58 \pm 1.10$  m IU/ml in females)

**Table 1: Comparison Of The Tsh Range Among Different Studies**

STUDY	TSH RANGE (COMBINED MALE + FEMALE) in micro IU/ml	
Present Study	0.56-7.2	
Hubl W et al	0.17-4.23	
Gonzalez-Sagrado M & Martin-Gil FJ	0.51-5.95	
Dhatt GS et al	0.32-4.32	
Taimela E et al	0.6-4.3	
Alqahatani M et al	0.48-6.30	
Angel OK Chan et al	0.68-3.70	
	TSH RANGE (MALES)micIU/ml	TSH RANGE (FEMALES)micIU/ml
Present Study	0.56-7.2	0.64-5.90



**Fig:1 Bar diagram showing distribution of TSH values in study population**

## CONCLUSION

It was found that even among healthy young adults, whose history and clinical examination is not suggestive of the presence of any thyroid disorder and who have no family history of thyroid disease also and no history of any medication in the past which might interfere with thyroid function, there were a number of cases whose TSH levels were above normal. On further endocrinological evaluation, they were all found to be cases of subclinical hypothyroidism- which is defined as the serum TSH concentration above the statistically defined upper limit of the reference range when serum free thyroxine (FT4) concentration is within the reference range (Ross Ds et al). Presently, the interest as well as early determination of subclinical hypothyroidism has come into limelight because it has an impact on morbidity and mortality especially of the young population.

The complications occurring due to subclinical hypothyroidism are dyslipidemia, diabetes mellitus (Type-2), hypertension & increased incidence of cardiovascular diseases occur in subclinical hypothyroidism as well as coronary artery disease and depression and most importantly infertility amongst the most fertile group of people. Detrimental effects on the cardiovascular system have been reported for suppressed and particularly, elevated serum levels of TSH and follow-up studies have shown an increase in the risk of development of overt thyroid dysfunction in subjects with high normal serum TSH

levels<sup>(26,27,28,29)</sup>. Subclinical hyperthyroidism is also a risk factor for atrial fibrillation<sup>(30,31)</sup>.

The early identification and follow-up of such cases of subclinical hypothyroidism among young adults will aid in early diagnosis of overt hypothyroidism and prompt institution of appropriate treatment measures.

## Limitations of the study:

Due to small sample size, self-funding adding to it the high cost of the test for doing TSH estimation was the primary limitation as also the time binding factor ensuing the ongoing epidemic of Covid-19 was a limiting factor as only one parameter of TFT was done, TSH. Prospective studies involving the total thyroid function tests in a large sample size is surely within the ambit of doing further research in this rapidly occurring aspect of silent or overt subclinical hypothyroidism in young population leading to a barrage of metabolic disorders in them in future would surely have a long lasting impact on the health of the young population who can contribute actively to the society.

**Conflict of Interest:** There is no conflict of interest with any person or organization.

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