Original Article

# Does fasting or postprandial state affect thyroid function testing?

**Rakesh Nair, Shriraam Mahadevan[1], R. S. Muralidharan, S. Madhavan**

*Department of General Medicine, Stanley Medical College, Chennai, [1]Department of Endocrinology, Sri Ramachandra Medical College and Research Institute, Chennai, Tamil Nadu, India*

## ABSTRACT

**Background:** Thyroid stimulating hormone (TSH) levels vary with the time of the day and probably in relation to food. In this study, we addressed the question of whether a fasting or non-fasting sample would make a clinically significant difference in the interpretation of thyroid function tests. **Materials and Methods:** Fifty seven adult ambulatory patients were selected from our laboratory database and were divided into Group A [Normal free thyroxine (T4) and TSH], Group B (subclinical hypothyroid with increased TSH and normal free T4) and Group C (overt hypothyroid with low free T4 and high TSH). Thyroid functions (free T4 and TSH) were done in fasting state and 2 hours postprandially. **Results:** TSH was suppressed in all subjects after food irrespective of the fasting levels. Free T4 values did not change significantly. This resulted in reclassification of 15 out of 20 (75%) subjects as subclinical hypothyroidism (SCH) based on fasting values whose TSH values were otherwise within range in the postprandial sample. This may have an impact on the diagnosis and management of hypothyroidism especially where even marginal changes in TSH may be clinically relevant as in SCH and in pregnancy. **Conclusion:** TSH levels showed a statistically significant decline postprandially in comparison to fasting values. This may have clinical implications in the diagnosis and management of hypothyroidism, especially SCH.

**Key words:** Fasting, subclinical hypothyroidism, thyroid function test, thyroid stimulating hormone

## Introduction

Hypothyroidism is commonly encountered in clinical practice. Subclinical hypothyroidism (SCH) defined as normal Free thyroxine (T4) and elevated Thyroid Stimulating Hormone (TSH) is primarily a biochemical diagnosis with or without clinical symptoms.[1] SCH is associated with several long term effects including dyslipidemia, hypertension, subfertility and may be an independent risk factor for cardiovascular morbidity.[2,3] Circulating TSH shows a normal circadian rhythm with a peak between 11 pm-5 am and a nadir between 5 pm-8 pm.[4] Secretory pulses occur every 2-3 hours and are interspersed with periods of tonic non-pulsatile TSH secretion.[4] Although the TSH secretion is pulsatile, the low amplitude of the pulses and the long half-life of TSH result in only modest circulatory variations.[5] It is generally observed that TSH in early morning fasting states were higher than TSH levels measured later in the same day. In routine clinical practice not much importance is being given to the timing of the sample or the fasting/non-fasting status of the patient. However, an entity like SCH which heavily relies on TSH values may be under or overdiagnosed based on a single value.[6] Further, in the recent past, narrower and stricter cut-offs for TSH has been advocated for defining euthyroidism in special situations like pregnancy.[7] Hence uniformity in testing under standard conditions is necessary. With this background, we proposed this study to evaluate whether TSH measured in fasting state or postprandially would make a difference.

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## Materials and Methods

The study was conducted in the Government Stanley Medical College Hospital, Chennai, Tamilnadu where

**Corresponding Author:** Dr. Shriraam Mahadevan, Department of Endocrinology, Sri Ramachandra Medical College and Research Institute, Porur, Chennai - 600 116, Tamil Nadu, India. E-mail: mshriraam@gmail.com

the thyroid functions are usually done in fasting state only. Fifty-seven adult ambulatory patients were selected from our laboratory database and were divided into Group A (Normal freeT4 and TSH), Group B (SCH with increased TSH and normal free T4) and Group C (overt hypothyroidism with low free T4 and high TSH). The lab reference ranges (given below) were used to define low and high values of freeT4 and TSH. Patients with renal or liver dysfunction, steroid or thyroxine therapy were excluded. The study was approved by the Institutional Review Board, Government Stanley Medical College, Chennai and informed consent was obtained prior to phlebotomy from the patients. Phlebotomy was performed after an 8-12 hour overnight fast between 7:30-8:30 am for free T4 and TSH measurements and the patients returned 2 hours after breakfast for their samples to be rechecked between 10:30-11:00 am on the same day. Samples were analyzed by the Electrochemiluminesence immunoassay intended for use on Eleccsys and Cobas immunoassay analyzers.[8] Machine was calibrated and the serum was collected and processed according to manufacturer's instructions. The methodology had an analytical sensitivity of 0.005 μIU/ml and a functional sensitivity of 0.014 μIU/ml (coeffecient of variation 1.4%).[8-10] Suggested normal values for TSH were 0.27-4.2 μIU/ml and these values correspond to the 2.5 and 97.5% of results obtained from a total of 516 healthy test subjects examined. Suggested normal values for free T4 was 0.80-1.8 ng/ml and the values correspond to the 2.5 and 97.5% of results from a total of 801 healthy test subjects studied.

### Statistical methods

Differences in free T4 and TSH levels between fasting and non-fasting state were analyzed by paired student-*t* test. *P* value below 0.05 was considered statistically significant.

## Results

TSH values were lowered after food when compared to fasting in a statistically significant manner in all the three groups as shown in [Table 1]. Free T4 values did not significantly alter after food in all the three groups.

**Table 1: Fasting and 2 hour post-prandial values (mean±standard deviation) of free T4 and TSH among the three groups**

| | Fasting | 2 hour-postprandial | *P* value |
|---|---|---|---|
| Group A: (*n*=19) | | | |
| Free T4 (ng/ml) | 1.06±0.11 | 1.05±0.11 | 0.07 |
| TSH (mIU/L) | 2.42±1.49 | 1.79±1.10 | 0.00* |
| Group B: (*n*=20) | | | |
| Free T4 (ng/ml) | 0.89±0.20 | 0.88±0.21 | 0.35 |
| TSH (mIU/L) | 7.53±1.50 | 5.35±1.40 | 0.00* |
| Group C: (*n*=18) | | | |
| Free T4 (ng/ml) | 0.57±0.18 | 0.56±0.17 | 0.75 |
| TSH (mIU/L) | 66.93±17.83 | 61.22±16.41 | 0.00* |

Group A: Normal free T4 and TSH, Group B: Subclinical hypothyroidism with increased TSH and normal free T4, Group C: Overt hypothyroidism with low free T4 and high TSH, (*$P$<0.05), T4: Thyroxine; TSH: Thyroid stimulating hormone

## Discussion

In our study we addressed a clinically relevant question: Whether thyroid function tests (Free T4 and TSH) should be estimated in fasting state or not? We observed that TSH values get lowered if estimated postprandially irrespective of the fasting levels. The reason for the above observation is not clear. TSH is a glycoprotein hormone secreted in a pulsatile fashion.[5] But due to its low pulse amplitude and long half-life the circulating variations is only modest.[5]

Previous studies by Scobbo *et al*.[11], Kamat *et al*.[12] and Bandhopadhyay *et al*.[13] have shown postprandial TSH decline similar to our study. TSH secretion is heavily dependent on two factors namely Thyrotropin Releasing Hormone (TRH) and somatostatin; the former stimulating and the latter inhibiting TSH.[14] A possible explanation for the acute postprandial decline of serum TSH is food induced elevation of circulating somatostatin and consequent suppression of TSH.[12] Further, the TSH variation is unlikely to have been due to assay differences. The three previous studies[11-13] addressing this issue have used different assays for TSH viz. Microparticle Enzyme Immuno Assay (second generation)[11], Radioimmunoassay[12], immunofluorescence assay[13] but observed results similar to our study. In a recent study by Sarkar comparing two third generation TSH assay methods, [chemiluminescence (Architect) vs electrochemiluminescence (Cobas)], the inter assay variations were well within the limits of agreement.[9]

Timing of sampling was considered as one of the factors which might have influenced the decline in TSH in the previous studies.[13,14] Hence, whether the TSH suppression in our study was due to food related alteration in blood chemistry or timing of sample or both could not be clarified. Clinical guidelines for thyroid function testing or laboratory guidelines for free T4 and TSH estimation do not emphasize the time of phlebotomy or the fasting/non-fasting status of the patient.[15] Clinically, in our study, the lowering of TSH postprandially led to reclassification of 15 out of 20 subjects (75%) as euthyroid who would have otherwise been labelled as SCH based on fasting TSH alone. This may have a significant impact not only on the diagnosis but also monitoring of hypothyroidism, especially in situations where even marginal variations in TSH may be important like in pregnancy or sub-fertility. With recent guidelines for management of hypothyroidism during pregnancy stressing a target TSH of 2.5 mIU/L or less, the findings of our study may have more 0.[7] Further, lack

of uniformity in the time of sampling for TSH may lead to unnecessary repetition of tests especially in a resource limited setting. With the above observations, we propose that a fasting TSH sample may be preferred to random or postprandial estimations as normal fasting values would obviate the need for retesting.

## Limitations

Factors other than food or timing of sample have not been addressed in our study. Larger sample size may be required to confirm our findings.

## Conclusion

TSH levels showed a statistically significant decline postprandially in comparison to fasting values. This may have clinical implications in the diagnosis and management of hypothyroidism, especially SCH.

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