Original Article

Does Time of Sampling or Food Intake Alter Thyroid Function Test?

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Abstract

Context: A common question from most patients or laboratories is whether blood sample for thyroid-stimulating hormone (TSH) and free T4 (fT4) needs to be collected in a fasting state and whether time of the day when sample is collected matters. **Aims:** The aim of the study was to study the impact of the time of day and food intake on levels of TSH and fT4. **Settings and Design:** Cross-sectional prospective data collection. **Subjects and Methods:** We prospectively collected data from 52 volunteers who were not known to have any thyroid disorder and were not on any thyroid-related medication. Blood samples for TSH and fT4 were collected on day 1 at 8 am and 10 am with the patient remaining in the fasting state till the collection of the second sample at 10 am. On day 2, samples were collected at 8 am (fasting state) and at 10 am (2 h postprandial state). In 22 volunteers from the group, the tests were performed in three common assay techniques including chemiluminescent assays (chemiluminescent immunoassay [CLIA] and chemiluminescent microparticle immunoassay [CMIA]) and enzyme-linked fluorescence assay. **Results:** The mean (standard deviation) and median (interquartile range) TSH during the extended fast on day 1 were 2.26 ± 1.23 and 2.19 (1.21–3.18), which was significantly lower than the fasting TSH performed on day 1 ($P < 0.001$). Similarly, the values of TSH 2 h postmeal on day 2 of the testing (mean 1.93 ± 1.12; median 1.64 [1.06–2.86]) were significantly lower than TSH performed in the fasting state on day 2 ($P < 0.001$). The mean fT4 value was 1.01 ± 0.15 with median of 0.99 (0.91–1.11) in the fasting state and there was no significant difference between the fT4 values performed during fasting, extended fasting, and postmeal state. Among the volunteers in whom the test was performed in the three different assay techniques, the TSH was not statistically different either in the fasting ($P = 0.801$), extended fasting ($P = 0.955$), and postprandial samples ($P = 0.989$). The fT4 values did not vary significantly when done by the same assay method. However, the fT4 levels varied significantly ($P < 0.001$) when done by another assay method. **Conclusions:** We conclude stating that the timing of the test affects TSH values and this should be factored in making decisions in diagnosis of subclinical hypothyroidism.

Keywords: Fasting, postprandial, timing of test, thyroid-stimulating hormone

Introduction

The question on whether one should fast for a routine thyroid testing (thyroid-stimulating hormone [TSH] and free T4 [fT4]) is a common inquiry by most patients, health-care providers, and laboratories. A strong scientific evidence to support an answer is often lacking. Circulating TSH shows a normal circadian rhythm with a peak between 11 pm and 5 am and a nadir between 5 pm and 8 pm.[1] Secretory pulses occur every 2–3 h and are interspersed with periods of tonic nonpulsatile TSH secretion.[1] A large laboratory data-based study by Ehrenkranz *et al*. showed that there is a significant circadian variation in the TSH levels with peak levels occurring between midnight and 8 am and nadir levels between 10 am–3 pm and 9–11pm.[2] Although the TSH secretion is pulsatile, the low amplitude of the pulses and the long half-life of TSH result in only modest variations in blood levels.[3] Clinical guidelines for thyroid function testing or laboratory guidelines for fT4 and TSH estimation do not emphasize the time of phlebotomy or the fasting/nonfasting status of the patient. An entity like subclinical hypothyroidism (SCH) which heavily relies on TSH values may be under- or over-diagnosed based

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on a single value.[4] Further, in the recent past, narrower and stricter cutoffs for TSH have been advocated for defining euthyroidism in special situations such as pregnancy and prepregnancy counseling.[5] Hence, uniformity in testing under standard conditions is necessary. We had earlier shown that TSH was suppressed in all subjects after food irrespective of the fasting levels and fT4 values did not change significantly.[6] However, 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. In this background, we proposed this study to evaluate whether TSH measured in fasting state or postmeal would make a difference and whether this difference was related to the time of blood draw or the meal intake.

Subjects and Methods

We then proceeded with prospective collection of data from 52 nonpregnant volunteers who were not known to have any thyroid disorder and were not on any thyroid-related medication. Blood samples for TSH and fT4 were collected as follows: on day 1, at 8 am and 10 am (common collection times in most laboratories), respectively, with the patient remaining in fasting state till the collection of the second sample at 10 am. On day 2, samples were collected at 8 am (fasting state) and at 10 am (2 h postprandial state). Values were compared to find out the effects of the time of the blood draw as well as the meal. Additional data were collected in 22 volunteers of the group where the tests were performed in three common assay techniques including chemiluminescent assays (CLIA and CMIA) and enzyme-linked fluorescence assay to assess the degree of differences in TSH and fT4 values related to the technique of measurement. Five patients with overt hypothyroidism (TSH > 10) were excluded from analysis.

Statistical methods

Continuous variables were tabulated and the mean, standard deviation (SD), and median were calculated. Comparison of means was carried out using paired *t*-test to find out significant differences.

Results

The mean (SD) age was 30 ± 10 years (range 14–64) with 67% females. The mean (SD) and median (interquartile range [IQR]) TSH in the fasting state on day 1 were 2.93 ± 1.62 and 2.74 (1.69–3.75) and day 2 were 2.46 ± 1.32 and 2.34 (1.28–3.32) ($P = 0.13$). The mean (SD) and median (IQR) TSH during the extended fast on day 1 were 2.26 ± 1.19 and 2.07 (1.31–3.15), which was significantly lower than the fasting TSH performed on day 1 ($P < 0.001$). Similarly, the values of TSH 2 h postmeal on day 2 of the testing (mean 1.89 ± 1.01; median 1.77 [1.08–2.22]) were significantly lower than TSH performed in the fasting state on day 2 ($P < 0.001$) [Table 1]. The mean difference in TSH values performed during fasting and extended fasting state (Delta 1) was 0.59 ± 0.72 (median 0.38 and range of −1.26 to 2.78). The mean difference in TSH values performed during fasting and 2 h postmeal state (Delta 2) was 0.51 ± 0.44 (median 0.41 and range of −0.4 to 1.68). Difference between Delta 1 and Delta 2 was not statistically significant ($P = 0.61$). The mean fT4 value was 1.14 ± 0.2 with median of 1.14 (0.98–1.26) in the fasting state on day 1 and there was no significant difference between the fT4 values performed during fasting (on day 2), extended fasting, and postmeal state (data not shown).

Among those with testing of TSH in three different assay techniques, there was no significant difference between the TSH either in the fasting ($P = 0.801$), extended fasting ($P = 0.955$), and postprandial samples ($P = 0.989$) as in Table 2. With the same assay method, fT4 values did not vary significantly whether done in fasting, extended fasting, or postmeal, but the values varied statistically significantly between different assay methodologies [Table 2].

Discussion

In our previous study, we observed that TSH values get lowered if estimated postprandially irrespective of the fasting levels.[6] In a previous study by Scobbo *et al*., similar observation of TSH suppression postprandially was shown.[7] TSH secretion is heavily dependent on two factors: thyrotropin-releasing hormone and somatostatin; the former being stimulating TSH and the latter inhibiting TSH.[8] A possible explanation for the acute postprandial decline of serum TSH is food-induced elevation of circulating somatostatin and consequent suppression of TSH. Variable increases in plasma somatostatin-14 and somatostatin-28, the two principal bioactive forms, have been reported in normal volunteers following liquid and solid test meals, the peak occurring 90–120 min after ingestion and presumably reflecting release of somatostatin from the gut.[9] However, 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.

In the current study, we noticed that there was a significant decline in TSH values when the sample was collected at around 10 am regardless of whether it was a fasting (extended

Table 1: Thyroid-stimulating hormone values: Comparison between fasting and extended fasting (day 1) and fasting and postprandial (day 2)

	Day 1			Day 2		
	Fasting	2 h extended fasting	*P* (paired *t*-test)	Fasting	2 h postprandial	*P* (paired *t*-test)
TSH (mIU/L)	2.93±1.62	2.26±1.19	<0.001	2.46±1.32	1.89±1.01	<0.001

Values are mean±SD. TSH: Thyroid-stimulating hormone, SD: Standard deviation

Table 2: Comparison of free thyroxine and thyroid-stimulating hormone values by different assay methods

Assay method	Day 1							Day 2						
	Fasting				Extended fasting			Fasting				2 h postprandial		
	CMIA	CLIA	ELFA	*P*	CMIA	CLIA	ELFA	*P*	CMIA	CLIA	ELFA	*P*	CMIA	CLIA	ELFA	*P*
FT4 (ng/mL)	1.10±0.16	1.24±0.20	1.23±0.29	0.001	1.01±0.16	1.22±0.20	1.23±0.29	0.004	0.96±0.12	1.16±0.19	1.18±0.22	0.003	0.97±0.12	1.22±0.19	1.21±0.29	0.002
TSH (mIU/L)	7.19±12.95	8.30±15.51	12.06±21.63	0.801	6.23±10.26	6.70±11.79	8.06±13.72	0.955	6.37±11.13	7.04±13.96	6.49±8.78	0.889	5.41±9.71	5.57±11.34	4.95±6.23	0.989

CMIA: Chemiluminescent microparticle immunoassay, CLIA: Chemiluminescent immunoassay, ELFA: Enzyme-linked fluorescence assay, FT4: Free thyroxine, TSH: Thyroid-stimulating hormone

fast) or postmeal sample. This finding is consistent with the observations of Ehrenkranz *et al*. that there is a nadir of TSH beginning at 10 am which may be the physiological explanation for TSH suppression seen in our study.

To rule out whether the assay methodology used was responsible for the observation, we did the same assay in three different methods and showed that TSH values did not differ significantly between any of the assay methods [Table 2]. This indicates that the decline in TSH value is most likely due to biological factors alone as discussed above. In contrast, fT4 values varied significantly based on the assay method used [Table 2], but when assayed by the same method, fT4 did not vary with timing or food intake.

Thus, timing of TSH sample is important, especially while dealing with minor variations in TSH. Although the mean TSH difference due to sample timing in our study was around 0.5–0.6 mIU/L (with maximum of 2.78 mIu/L), we believe that even this minor variation could be clinically relevant, especially while diagnosing SCH, prepregnancy counseling, and subfertility. It may be preferable to do an early morning sample for TSH in the latter two settings where narrower and stricter reference ranges for TSH are being advocated recently.

Conclusions

We conclude stating that the timing of the sample regardless of meal intake affects TSH values and this should be factored in making decisions in diagnosis of subclinical hypothyroidism.

Limitations

In our study, we studied the levels of TSH 2 h postmeal. Whether the study results would still be consistent and reproducible if the TSH was checked <2 h after a meal is not known and was not evaluated in this clinical study. However, sample collection after 10 am is common practice clinically and effect of TSH lowering should be borne in mind while interpretation of laboratory data.

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Conflicts of interest

There are no conflicts of interest.

References

1. Brabant G, Prank K, Ranft U, Schuermeyer T, Wagner TO, Hauser H, *et al.* Physiological regulation of circadian and pulsatile thyrotropin secretion in normal man and woman. J Clin Endocrinol Metab 1990;70:403-9.
2. Ehrenkranz J, Bach PR, Snow GL, Schneider A, Lee JL, Ilstrup S, *et al.* Circadian and circannual rhythms in thyroid hormones: Determining the TSH and free T4 reference intervals based upon time of day, age, and sex. Thyroid 2015;25:954-61.
3. Patel YC, Alford FP, Burger HG. The 24-hour plasma thyrotrophin profile. Clin Sci 1972;43:71-7.
4. Surks MI, Ortiz E, Daniels GH. Subclinical thyroid disease: Clinical applications. JAMA 2004;291:239-43.
5. De Groot L, Abalovich M, Alexander EK, Amino N, Barbour L,

Cobin RH, *et al.* Management of thyroid dysfunction during pregnancy and postpartum: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2012;97:2543-65.
6. Nair R, Mahadevan S, Muralidharan RS, Madhavan S. Does fasting or postprandial state affect thyroid function testing? Indian J Endocrinol Metab 2014;18:705-7.
7. Scobbo RR, VonDohlen TW, Hassan M, Islam S. Serum TSH variability in normal individuals: The influence of time of sample collection. W V Med J 2004;100:138-42.
8. Morley JE. Neuroendocrine control of thyrotropin secretion. Endocr Rev 1981;2:396-436.
9. Hildebrand P, Ensinck JW, Buettiker J, Drewe J, Burckhardt B, Gyr K, *et al.* Circulating somatostatin-28 is not a physiologic regulator of gastric acid production in man. Eur J Clin Invest 1994;24:50-6.