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EFFECT OF FASTING AND POSTPRANDIAL BLOOD SAMPLES IN RESULTS ON THYROID FUNCTION TEST AMONG EUTHYROID PEOPLE AND PATIENTS WITH THYROID PROBLEM : A SYSTEMATIC REVIEW

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Abstract

The normal 24-hour rhythm of circulating TSH has a maximum between the hours of 11 p.m. and 5 a.m., and a minimum between the hours of 5 p.m. and 8 p.m. Secretory pulses occur approximately every two to three hours, and they are interspersed with periods of tonic, non-pulsatile TSH production. Although TSH secretion is pulsatile, relatively minor circulatory fluctuations are produced as a result due to the low amplitude of the pulses and the prolonged half-life of TSH. In most cases, the TSH levels taken first thing in the morning during fasting situations are found to be much greater than those obtained later in the same day. When compared to the postprandial blood samples, the TSH result value for the usage of blood samples taken while the patient was fasting would be much greater. As a result, this could be useful in the introduction of a new guideline to standardize the blood sample status for the TSH test screening and diagnosis. The food-induced increase in circulating somatostatin and consequent suppression of TSH levels is one idea that may help to explain the acute postprandial decline in serum TSH levels. Varying increases in plasma somatostatin-14 and somatostatin-28, the two primary bioactive forms, have been recorded in normal volunteers after liquid and solid test meals, with the peak occurring 90–120 minutes after ingestion, likely reflecting somatostatin release from the stomach.

Keyword: *Circadian rhythm, Blood samples, Euthyroid, Thyroid*

INTRODUCTION

In clinical practice, hypothyroidism is frequently seen. Subclinical hypothyroidism (SCH), defined as normal Free thyroxine (T4) and increased Thyroid Stimulating Hormone (TSH), is largely diagnosed biochemically, with or without clinical symptoms. SCH is associated with multiple long-term consequences, including as dyslipidemia, hypertension, and subfertility, and may be an independent risk factor for cardiovascular morbidity.[1,2]

Normal circadian rhythm of circulating TSH with a peak between 11 p.m. and 5 a.m. and a minimum between 5 p.m. and 8 p.m. Periods of tonic, non-pulsatile TSH production are interspersed by secretory pulses every two to three hours. Although TSH secretion is pulsatile, the low amplitude of the pulses and the lengthy half-life of TSH result in relatively moderate circulatory fluctuations. In general, TSH levels in early morning fasting states are higher than those measured later on the same day.[1,3–5]

In regular clinical practice, neither the date of the sample nor the fasting/nonfasting status of the patient are accorded a great deal of attention.[1] On the other hand, an entity like SCH that relies primarily on TSH readings may be under- or overdiagnosed based on a single measurement. In addition, in recent years, narrower and more stringent TSH cutoffs for diagnosing euthyroidism in particular circumstances such as pregnancy have been urged.[6]

It has been suggested that diurnal fluctuations and fed status can affect TSH levels, and it has also been suggested that diurnal variation in TSH is a primary component that makes it difficult to evaluate the effect of postprandial state on changes in TSH. As a result, the precise reason for the drop in postprandial TSH levels is still unknown. It has been hypothesized that the drop in postprandial TSH levels is due to the postprandial release of somatostatin.[7,8]

The most plausible reason of postprandial somatostatin release is the rise in plasma glucose that occurs after a meal; however, the data on the association of postprandial TSH change with postprandial change in plasma glucose are limited. An examination of the association between the two could improve our understanding of the pathophysiology underlying the postprandial drop in TSH.[9]

The purpose of this study is to investigate the effect of fasting and postprandial blood samples in results on thyroid function test amongeuthyroid people and patients with thyroid problem.

METHODS

Protocol

The author used the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines to ensure that this research adhered to the cited standards. This is done to ensure the accuracy of this investigation's findings.

Criteria for Eligibility

This literature review tries to figure out how fasting and post-meal blood samples affect the results of thyroid function tests for both healthy people and people with thyroid problems. It does this by evaluating or analyzing past research on the subject. The main point of this essay is to show how important the issues mentioned are. Researchers who took part in studies met the following requirements: 1) For the paper to be considered for publication, it must be written in English and focus on how blood samples taken before and after a meal affect the results of a thyroid function test in people who don't have a thyroid problem and people who do. 2) This review includes papers that came out after 2017 but before the time period this systematic review looks at. Research that isn't allowed includes editorials, submissions without a DOI, review articles that have already been published, and entries that are almost exactly the same as journal articles that have already been published.

Search Strategy

We used "fasting"; "postprandian" and "thyroid hormone" as keywords.The search for studies to be included in the systematic review was carried out from February, 20th 2023 using the PubMed and SagePub databases by inputting the words: *("fasted"[All Fields] OR "fasting"[MeSH Terms] OR "fasting"[All Fields] OR "fastings"[All Fields] OR "fasts"[All Fields]) AND ("thyroid hormones"[MeSH Terms] OR ("thyroid"[All Fields] AND "hormones"[All Fields]) OR "thyroid hormones"[All Fields] OR ("thyroid"[All Fields] AND "hormone"[All Fields]) OR "thyroid hormone"[All Fields])* used in searching the literature.

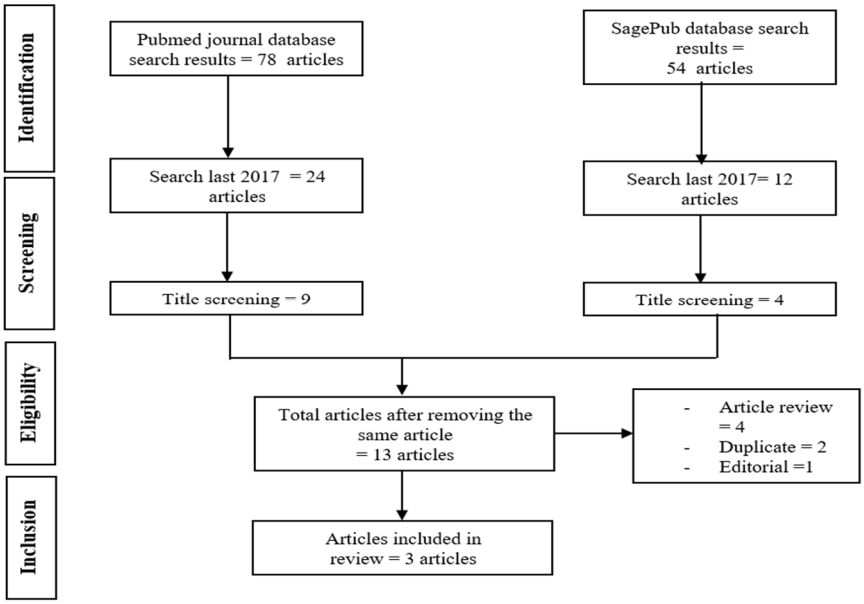

Figure 1. Article search flowchart

Data retrieval

The authors examined each study after reading the abstract and title to see if it met the inclusion criteria. The authors then chose various studies from the past to use as sources in this article. This conclusion was reached after reviewing numerous studies that all revealed the same pattern. All entries must be written in English and never before published.

In the systematic review, only studies that met all of the inclusion criteria were considered. This narrows the search results to only those that are relevant. We do not consider research findings that do not meet our criteria. Following this, the research will be thoroughly examined. During the course of this study's investigation, the following information was discovered: names, authors, dates of publication, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Before deciding which papers to investigate further, each author conducted their own research on the research listed in the publication's title and abstract. Then, we'll look at all papers that meet the review's inclusion criteria and are thus good enough to be included. Then, based on our findings, we'll choose which papers to include in the review. This criterion is used to select manuscripts for evaluation. To make selecting papers to review as simple as possible. Which previous studies were conducted, and what aspects of those studies qualified them for inclusion in the review?

RESULT

Nair, et al (2014)[9] conducted a study and showed TSH levels dropped in all of the individuals after eating, regardless of how high they had been while fasting. The levels of free T4 did not show any significant change. As a consequence of this, 15 out of 20 (75%) of the participants were reclassified as having SCH based on their fasting levels, even though their TSH readings in the postprandial sample were generally within the normal range. This could have an effect on the diagnosis and treatment of hypothyroidism, particularly in situations when even slight variations in TSH could have a clinically significant impact, such as in SCH and during pregnancy.

Table 1. The litelature include in this study

Author	Origin	Method	Sample Size	Result
Nair, 2014[9]	India	Case control	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 (SCH with increased TSH and normal free T4) and Group C (overt hypothyroid with low free T4 and high TSH)	When compared to the numbers obtained while fasting, the TSH levels dropped significantly after eating, as shown by statistical analysis. This might have some consequences for the clinical diagnosis and treatment of hypothyroidism, particularly SCH.
Mahadevan, 2017[10]	India	Cross-sectional prospective study	52 volunteers who were not known to have any thyroid disorder and were not on any thyroid-related medication	They come to the conclusion that the timing of the test has an effect on the TSH results, and this is something that should be taken into consideration when making decisions regarding the diagnosis of subclinical hypothyroidism.
Pradeep, 2018[11]	India	Prospective, cross-sectional study	200 participants: 75 healthy volunteers without known thyroid dysfunction (Group A), 65 healthy pregnant women (Group B), and 60 patients who were known hypothyroid (clinical and subclinical hypothyroid) on levothyroxine therapy (Group C)	According to the findings of this study, after a meal there is a considerable drop in TSH levels, however there is no significant association between postprandial changes in plasma glucose and TSH levels.

Mahadevan, et al conducted a study and they showed 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).[10]

There was no significant difference in the fT4 values obtained during fasting, extended fasting, and the post-meal condition. TSH was not statistically different in the fasted or nonfasted states among the subjects on whom the test was conducted using three distinct assay methodologies (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.[10]

Other wtudy conducted with three groups. They showed serum TSH was significantly lower in the postprandial state than in the fasting state, whereas the levels of free triiodothyronine and free thyroxine were not significantly different between the fasting and postprandial states. In no group was there a correlation between the change in plasma glucose and the change in TFT. In pregnant women (Group B), the prevalence of hypothyroidism was significantly higher in the fasting state than in the postprandial state when using a cutoff of 2.5 IU/ml (41.5% vs. 18.4%, P = 0.004) and 4 IU/ml (12.3% vs. 1.5%, P = 0.03), but not in other groups (Group A and Group C).[11]

DISCUSSION

The thyroid gland is the largest endocrine gland in the human body. In the thyroid gland it is quite common to find nodules in it. About 4-8% of thyroid nodules can be found on physical examination (palpation of the neck area) and about 13-67% can be found on ultrasound examination, generally found in women. Thyroid gland disorders can be classified into two major groups, namely diseases that cause changes in function, such as hyperthyroidism and diseases that cause changes in tissue and shape of the gland, such as nodular goiter.[5,12,13]

There are three possible states for thyroid function: decreased, normal, or elevated. Diseases of the hypothalamus, injury to the pituitary gland, an iodine deficit, a lack of antithyroid medication, and thyroiditis are all potential causes of reduced thyroid function or hypothyroidism. Iatrogenic hypothyroidism is a disorder that can develop after a thyroidectomy or after therapy with radioactive iodine. This type of hypothyroidism is caused by medical intervention.[12,13]

Hyperthyroidism may occur in diffuse toxic goiter (Graves' disease), toxic goiter nodosa, overmedication with thyroxine, thyroiditis, ovarian goiter (rare), and extensive metastases of differentiated thyroid carcinoma. Autoimmune disorders with or without an inflammatory reaction can cause Graves' goitre which is symptomatic of hyperthyroidism and Hashimoto's goiter which eventually results in hypothyroidism. Examples of hyperplastic disorders are colloidal goiter and endemic goiter. Malignancy is mainly caused by adenocarcinoma. Malignant tumors of the thyroid gland can be divided according to the degree of malignancy.[12,13]

Symptoms of hyperthyroidism can include hypermetabolism and increased sympathetic activity such as patients complaining of fatigue, tremors, heat intolerance, excessive sweating, decreased body weight while increasing appetite, palpitations, tachycardia, diarrhea, and muscle weakness or atrophy. Extrathyroidal manifestations may be present such as ophthalmopathy and localized skin infiltration confined to the lower extremities usually.[3,14]

The symptoms of hypothyroidism are often unrecognized and nonspecific and are often related to aging. Patients with mild hypothyroidism may have no signs or symptoms. Symptoms generally become more pronounced as the condition worsens and the majority of these complaints are associated with a slowing of the body's metabolism. Common symptoms are fatigue, depression, moderate weight gain, cold intolerance, excessive sleepiness, dry, coarse hair, constipation, dry skin, muscle cramps, increased cholesterol levels, decreased concentration, vague aches and pains, and edema on the legs.[3]

Investigations that can help establish the diagnosis are T4 and T3 levels, free T4 or FT4i (free thyroxine index), thyroid antibody tests which include anti-thyroglobulin and antimicrosomes, decreased serum TSH levels, radioactive iodine uptake test and thyroid scans. . The gold standards used clinically are serum TSH and FT4.[3,14,15]

Time of sampling was regarded to be one of the variables that may have influenced the decrease in TSH in prior investigations. However, it was unclear if the TSH suppression in our study was attributable to a food-related change in blood chemistry, the time of the sample, or both. Clinical guidelines for thyroid function tests or laboratory guidelines for free T4 and TSH estimates do not stress phlebotomy time or the patient's fasting/nonfasting status.[16,17]

Nair study showed the postprandial reduction of TSH reclassified as euthyroid 15 out of 20 participants (75%) who would have been classified as SCH based on fasting TSH alone.[9] Other study observed a significant decrease in TSH levels when the sample was collected at approximately 10 a.m., regardless of whether it was a fasting (extended fast) or post-meal sample.[10]

This conclusion is consistent with Ehrenkranz et alobservation .'s that TSH levels began to decline after 10 a.m., which may be the physiological basis for the TSH suppression observed in our investigation.

This may have a significant impact not only on the diagnosis but also on the monitoring of hypothyroidism, particularly in situations where even minor fluctuations in TSH, such as during pregnancy or subfertility, may be crucial. This may have an impact on both the diagnosis and the monitoring of hypothyroidism. Considering recent recommendations for the care of hypothyroidism during pregnancy emphasizing a TSH target of 2.5 mIU/L or less, the results of our study may have greater 0.[16–18]

Food-induced rise of circulating somatostatin and subsequent suppression of TSH levels is one hypothesis that could help to explain the acute postprandial fall in serum TSH levels. Variable increases in plasma somatostatin-14 and somatostatin-28, the two principal bioactive forms, have been reported in normal volunteers after liquid and solid test meals, with the peak occurring 90–120 minutes after ingestion and presumably reflecting release of somatostatin from the gut. These increases have been observed following both liquid and solid test meals.[15,19]

The condition of the thyroid hormones can be significantly influenced by the origin of the protein that is consumed. It was demonstrated that some of the sulfurous and aromatic amino acids that were produced from acidic hydrolysis of casein were able to block in vitro the iodide oxidation reaction that was catalyzed by thyroid peroxidase. This was done by using a model system consisting of iodide ions (TPO).[20]

Study showed, both the amount of protein consumed and the kind of protein that is consumed affect the activity of the HPT axis. Protein restriction is dangerous for both humans and animals, but it is especially dangerous during pregnancy and/or lactation, because it has long-term effects on the development, growth, metabolic state, and hormonal status of progeny.[21]

Protein restriction is especially dangerous for pregnant women. In spite of the fact that it was demonstrated that isoflavones are capable of inhibiting TPO activity in vitro, the in vivo study found no direct connection between them and hypothyroidism. It appears that additional conditions, such as a shortage in iodine or other goitrogenic dietary variables, are required for soy protein to change the activity of the thyroid axis.[21]

CONCLUSION

When compared to the postprandial blood samples, the TSH result value for the usage of blood samples taken while the patient was fasting would be much greater. As a result, this could be useful in the introduction of a new guideline to standardize the blood sample status for the TSH test screening and diagnosis.

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