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Original Research Article

Enhancing Diagnostic Accuracy: The Significance of Color Doppler Imaging Sonography in Thyrotoxicosis Differential Diagnosis

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ABSTRACT

Background and Objectives: The primary culprits behind thyrotoxicosis are either autoimmune-mediated hyperactivity of the thyroid gland, as seen in Graves' disease, or inflammation-induced thyroiditis, including subacute thyroiditis and postpartum thyroiditis. Accurate diagnosis is crucial due to the distinct management approaches based on the underlying cause. While RAIU-radioactive iodine uptake by Thyroid and technetium pertechnetate (99mTc) thyroid scan are considered gold standards, their limited availability and high cost necessitate exploration of alternative diagnostic parameters for hyperthyroidism. This study aimed to assess the diagnostic usefulness of Non-invasive thyroid color flow doppler sonography (CFDS) for distinguishing different etiologies of thyrotoxicosis. **Materials and Methods:** 146 newly diagnosed thyrotoxicosis patients were included. Depending on clinical examination, laboratory parameters, and thyroid scans, patients were categorized in Graves' disease or thyroiditis groups. CFDS assessments were conducted in radiology department. **Results:** 109 cases were diagnosed with Graves' disease, while 37 with thyroiditis. The average peak systolic velocity (PSV) in inferior thyroid artery (ITA) from both thyroid lobes served as indicators of thyroid vascularity. Statistical analysis revealed a significant difference in mean PSV-ITA among Graves' disease vs. thyroiditis cases. ROC analysis demonstrated that a PSV cut-off values of 51 cm/s exhibited 99.2% sensitivity and 97.3% specificity in distinguishing Graves' disease vs. thyroiditis, along with positive and negative predictive values of 98% and 97%, respectively. **Conclusion:** Non-invasive CFDS, characterized by its affordability and accessibility, offers insights into the functionality of thyroid gland. The PSV measurements in ITA present a valuable tool for distinguishing the causes of thyrotoxicosis.

Key Words: Graves’ disease, Goiter, Thyrotoxicosis, Doppler Sonography.

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INTRODUCTION

Thyrotoxicosis, characterized by excess secretion of thyroid gland hormones, namely tetraiodothyronine (T4) and/or triiodothyronine (T3), may stem from autoimmune-mediated hyperactivity of the thyroid gland (Graves' disease) or inflammatory thyroiditis (including lymphocytic "painless" thyroiditis, subacute thyroiditis, and postpartum thyroiditis) [1, 2]. Uncommon causes involve autonomous functioning thyroid nodules (toxic adenomas), multiple toxic multinodular goiter, and factitious ingestion of exogenous thyroxine. The precise etiological diagnosis is crucial for optimal clinical outcomes, given the differing management strategies for Graves' disease and destructive thyroiditis. Challenges arise in distinguishing among Graves' disease or thyroiditis when clinical signs such as ophthalmopathy nail changes, and skin alterations, are absent.

The RAUI-radioactive iodine uptake and technetium pertechnetate (99mTc) thyroid scan stand as gold standards for thyrotoxicosis diagnosis. However, limitations such as availability, cost, and contraindications during pregnancy and lactation exist. While the T3/T4 ratio and anti-TSH receptor antibodies can aid diagnosis, their utility may be compromised by overlapping values and limited availability, emphasizing the need for alternative diagnostic parameters.

Thyroid ultrasonography, a readily available, informative, safe, and cost-effective investigation, offers a viable alternative. Color flow Doppler sonography (CFDS), combining grayscale and colored blood flow, assesses thyroid gland vascularity as an indirect measure of thyroid function. In Graves' disease, thyroid gland vascularity increases, contrasting with the normal or decreased vascularity observed in thyroiditis. Ralls described a distinctive pattern termed "thyroid inferno" in Graves' patients in 1987 [3-4]. The heightened vascularity in Graves' disease may be attributed to the positive impact of TSH-stimulating antibodies on thyroid hormone synthesis and blood flow.

Quantitative analysis of blood flow to thyroid gland involves pulsed wave Doppler study parameters such as peak systolic velocity (PSV) studied in superior and inferior thyroid arteries (ITA), pulsatility and resistivity indices, color pixel density, total thyroid blood flow, or volume flow rate [5-8].

Thyroid ultrasonography, particularly CFDS, emerges as a feasible alternative to scintigraphy (thyroid scan), especially in settings where the latter is unavailable or poses hazards. Thus, our study aimed to evaluate the potential of CFDS, using PSV of inferior thyroid arteries as a diagnostic parameter, to discriminate the causes of thyrotoxicosis.

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MATERIAL AND METHODS

Our investigation was conducted at the Department of Radiology within a tertiary care hospital in India. A total of 146 recently diagnosed and untreated patients with thyrotoxicosis were recruited during the study duration. Comprehensive fasting thyroid function tests, containing serum total T3, T4, TSH, and antithyroid peroxidase levels were measured using enzyme immunoassay.

Graves' disease was diagnosed based on an extended duration of clinical history, physical examination (presence of orbitopathy or dermatopathy), and diffuse uptake observed on thyroid scanning. Conversely, patients with thyroiditis presented a brief clinical history, a tender goiter, and low or no uptake on thyroid scan. Thyrotoxic patients with a prior history of surgery, irradiation, or radioablation were excluded from the study. B-Mode sonography and CFDS were performed using a state-of-the-art ultrasonography machine equipped using a 7 MHz broadband linear probe. Thyroid gland volume and PSV were calculated, with the ITA chosen for quantitative assessment of the thyroid vascularity.

Data analyses were done using SPSS-20. Biochemical and sonographic parameters were compared among Graves' disease vs. thyroiditis patients utilising the paired Student’s-t test. ROC curve was employed to decide the cut-off value of PSV for distinguishing among Graves’ disease vs. thyroiditis patients, and to ascertain the sensitivity and specificity of the test. A significance threshold of $P < 0.05$ was deemed statistically significant.

RESULTS

Total 146 patients satisfied the predefined inclusion criteria, presenting with reduced levels of TSH. Technetium-99 (Tc-99m) thyroid scans were conducted for all enrolled patients. Following a comprehensive assessment based on both thyroid scans and clinical features, 109 individuals received a clinical diagnosis of Graves’ disease, whereas 37 patients were identified with thyroiditis. Detailed demographic, biochemical, and sonological characteristics of untreated, newly diagnosed thyrotoxic patients are outlined in Tables 1-3.

Comparative analysis revealed significantly elevated thyroid gland volume and peak systolic velocity in the inferior thyroid artery (PSV-ITA) in individuals with Graves’ disease in comparison to those with thyroiditis.

The accuracy of PSV was evaluated using receiver operating characteristic (ROC) analysis. Setting PSV threshold at greater than 51 cm/s, area under curve demonstrated a value of 0.998, yielding 99.2% sensitivity and 97.3% specificity in effectively discriminating among

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Graves' disease vs. thyroiditis with positive and negative predictive values of 98% and 97%, in that order.

Table 1: Demographic parameters of study patients

Variables	Graves' Disease (mean±SD)	Thyroiditis (mean±SD)	p-value
Age in years	35.25 ± 6.20	33.50 ± 6.20	0.92
Gender			
Male	24	15	0.21
Female	85	22	

Table 2: Biochemical variables of study patients

Parameter	Graves' Disease (mean±SD)	Thyroiditis (mean±SD)	p-value
T3 ng/dL	590.80 ± 152.75	247.80 ± 59.80	<0.05
T4 µg/dL	20.85 ± 4.20	17.25 ± 3.20	<0.05
AntiTPOab µIU/mL	487.75 ± 220.75	151.20 ± 129.50	<0.05

Table 3: CFDS findings in newly diagnosed thyrotoxicosis patients

Parameter	Graves' Disease (mean±SD)	Thyroiditis (mean±SD)	p-value
Volume of Thyroid Gland, ml	24.30 ± 3.10 mL	14.80 ± 2.30	<0.05
PSV-ITA, cm/s	93.75 ± 32.10	28.750 ±10.50	<0.05

DISCUSSION

It is imperative to ascertain the etiological diagnosis of thyrotoxicosis, distinguishing among Graves' disease vs. thyroiditis due to the divergent management approaches required for each. Although scintigraphy of thyroid is conventionally deemed the "gold standard" investigation of thyrotoxicosis, it has inherent limitations [9]. In our investigation, we utilized the vascular (thyroid inferno) pattern and the mean PSV of the ITA from the two lobes of the thyroid glands as indicators of thyroid vascularity.

The disparity in average PSV-ITA among patients with Graves' disease vs. thyroiditis demonstrated statistical significance upon ROC analysis. Our findings indicated that a cutoff PSV of 51 cm/s exhibited 99.2% sensitivity and 97.3% specificity in discriminating Graves'

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disease and thyroiditis, with a positive predictive value (PPV) of 98% and a negative predictive value (NPV) of 97%. The distinctive vascular pattern described by Ralls et al. was initially observed exclusively in Graves' disease cases [3]. While Bogazzi et al. noted an elevated PSV in the ITA in Graves' disease; this increase was not observed in cases of subacute thyroiditis and thyrotoxicosis factitia [10].

CFDS demonstrated 84% sensitivity and 90% specificity in discerning the causes of hyperthyroidism [11]. A study conducted by Hari Kumar et al. in India, utilizing color flow sonography, reported 96% sensitivity and 95% specificity for differentiating thyroiditis from Graves' disease [12]. Previous methods employed to assess thyroid blood flow, such as high-resolution Doppler, vascularization index, and area of thyroid blood flow, aimed to enhance differentiation [13-15]. Notably, our study indicated a higher cut-off value for PSV of ITA at 51 cm/s to discriminate Graves' disease vs. thyroiditis, in contrast to the 40 cm/s reported in various literature [16-18].

In summary, CFDS emerges as a non-invasive, readily available, and cost-effective investigative tool. It holds potential utility in the clinical assessment of thyrotoxic patients. The PSV proves to be a pivotal factor in distinguishing among Graves' disease or subacute or autoimmune thyroiditis. Consequently, color doppler sonography can be deemed an alternative in scenarios where nuclear scanning is unavailable or contraindicated.

CONCLUSION

Thyrotoxicosis is characterized by a state of elevated thyroid hormone secretion, encompassing FT4 and/or FT3. Accurate diagnosis of thyrotoxicosis is crucial, given the varying management approaches based on its etiology. The RAIU and 99mTc thyroid scan, while considered gold standards in diagnosis, are constrained by limited availability and high costs. In contrast, non-invasive thyroid CFDS stands out as an easily accessible, highly informative, safe, and cost-effective investigative tool for the clinical assessment of individuals with thyrotoxicosis.

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