Diagnosis of Lymphocytic Thyroiditis Based on Grey Scale Evaluation in Correlation with Ultrasound Guided Fine Needle Aspiration Cytology

Authors
Amilu Elsa Varghese\(^1\), Reeba George Pulinikunnathil\(^2\), Beenamol S\(^3\), Natesan Roy\(^4\)

\(^1\)Resident, Govt T. D. Medical College Alappuzha
\(^2\)Assistant Professor, Dept of Radiodiagnosis, Medical College Trivandrum Kerala
\(^3\)Associate Professor, Dept of Radiodiagnosis, Medical College Trivandrum Kerala
\(^4\)Professor and Head of Dept, Dept of Radiodiagnosis, Medical College Trivandrum Kerala

Abstract
Aim: The aim of study was to validate the grey scale sonographic findings in lymphocytic thyroiditis using fine needle aspiration cytology which is taken as reference standard.

Methodology: 89 patients with diffuse neck swelling of the age group 18-80 years who came for sonographic examination of thyroid in the Department of Radiodiagnosis, in Medical college Alappuzha were included in the study, for a period of one year. Grey scale evaluation was done followed by ultrasound guided fine needle aspiration cytology.

Study Design: Descriptive study, with diagnostic test evaluation.

Results: The results indicated that there can be sonographically normal forms of thyroiditis, and also it not associated with thyroid enlargement always. The reduction in echogenicity correlated with reduction in thyroid follicles, which is due to lymphocytic infiltration in lymphocytic thyroiditis. A combination of grayscale parameters, presence of micronodules, fibrotic septations and absence of calcification can diagnose thyroiditis with sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 85%, 70%, 88%, 64% and 80% respectively. New cut off value of 1.2 cm, for anteroposterior diameter of thyroid is obtained from the receiver operator characteristic curve which can diagnose lymphocytic thyroiditis with 70% sensitivity and 60% specificity.

Keywords: Lymphocytic Thyroiditis, ultrasound thyroid.

Introduction
Lymphocytic thyroiditis or autoimmune thyroiditis\(^1\) is the most common cause of subclinical and overt hypothyroidism in an iodine sufficient region. Alappuzha, the coastal terrain of Kerala constitutes the zonal predilection for lymphocytic or autoimmune thyroiditis. The importance of detection of lymphocytic thyroiditis is, because of its increased association with thyroid malignancies like papillary carcinoma and lymphoma. And it is reassuring to know that prognosis is better when papillary carcinoma is associated with lymphocytic thyroiditis. Lymphocytic thyroiditis, is an autoimmune inflammatory disease caused by activation of CD4 helper T-lymphocytes specific for thyroid antigen and characterized by lymphocyte infiltration, fibrosis, and gradual destruction of the thyroid gland. This study is an attempt to characterize and validate the sonological patterns of lymphocytic thyroiditis. Though there are many studies discussing the prevalence of thyroid disorder,
those discussing the imaging appearance of lymphocytic thyroiditis in Kerala are rare.

**Imaging technique and protocol**

The study was designed as a descriptive study, with diagnostic test evaluation, conducted in the Department of Radiodiagnosis, Govt TD medical college, Alappuzha, during the period January 2014 – June 2015. 89 patients, in the age group of 18- 80 years with diffuse neck swelling, who came for sonographic examination of thyroid in the dept. of Radiodiagnosis, were included in the study. Those patients not giving consent and woman detected to have post partum thyroiditis, (within one year after child birth) were excluded from the study.

Sonographic examination was done using a Siemens Acuson sonographic machine with VF 13- 5 MHz linear transducer. Sonographic examinations was performed by the same researcher for all patients. Gray-scale sonography parameters included size of the thyroid gland, echogenicity pattern, presence of micronodules, fibrotic strands and calcification.

The informed consent from patient was obtained and ultrasonography of thyroid was done using a linear transducer in thyroid preset. The patient was examined in supine position with neck extended. A small pad was kept under the shoulder to provide better exposure of neck in patients with short habitus. During the procedure, both lobes of thyroid was examined in at least 2 projections: axial (transverse) and sagittal (longitudinal) planes. To decrease the machine occupancy time and there by utilize the time and resources effectively, anteroposterior diameter of thyroid was measured in this study.

Sonographic picture of lymphocytic thyroiditis is defined as diffusely heterogeneous hypoechoic pattern, fibronodules and fibrotic septations. In auto immune thyroiditis, lymphocytic infiltration and disruption of tissue architecture cause a reduction in thyroid echogenicity. Reduced thyroid echogenicity detected by thyroid ultrasonography is a strong predictor of auto immune thyroiditis even when these disorders have not been suspected clinically.

The echogenicity pattern of thyroid was divided into three patterns in the present study

| Pattern     | Compared to submandibular gland | Compared to neck muscles |
|-------------|---------------------------------|--------------------------|
| Pattern 1   | normal                          | hyperechoic              |
| Pattern 2   | hypoechoic                      | Hyperechoic              |
| Pattern 3   | iso-/hypoechoic                 | hypoechoic               |

Micronodules were defined as discrete hypoechoic nodules of 1-6mm in diameter. Echogenic fibrotic septations are noted in the lymphocytic thyroiditis, which are considered to be result of fibrosis within the parenchyma.

Fine needle aspiration cytology is done in supine position, immediately after the sonographic examination. A small pad may be placed under the shoulder to provide better exposure of neck in patients with short habitus. The thyroid gland is visualized with linear transducer in thyroid setting. The site for aspiration cytology is marked and the transducer is placed over the site. A 23 gauge needle is placed on the site of interest by adjusting the transducer so that the site is not changed. The needle is pushed forward and the aspirate is obtained using a 10 cc syringe. The patient is observed for half an hour for any complications.

The data collected was entered and assessed in Microsoft excel sheet. Analysis of data was done in SPSS version 17.0 and DAG Stat software package. Frequency of variables, correlation between variables, sensitivity, specificity, positive predictive value , negative predictive value, accuracy, likelihood ratios were calculated after plotting 2X2 table. A ROC curve was plotted and a cut off for anteroposterior diameter and RI value was calculated.

**Results**

A total of 89 patients were studied, as the cytology results of 7 patients came as inconclusive they were excluded from the study. Out of the 82 patients, 52 patient were diagnosed as lymphocytic thyroiditis in the study sample.
It was observed that taking a cut off value of 1.25 cm for anteroposterior diameter of thyroid has a sensitivity of 80% and specificity of 70%, suggesting that lymphocytic thyroiditis is not essentially goitrogenic.

Table 1

| Variables                                      | Sensitivity | Specificity | PPV  | NPV  | Accuracy |
|------------------------------------------------|-------------|-------------|------|------|----------|
| 1 Enlargement of thyroid                       | 27.12       | 78.2        | 76.10| 29.5 | 41.7     |
| 2 Pattern 2 or 3 echogenicity                   | 81.3        | 65.2        | 85.6 | 57.6 | 76.8     |
| 3 Pattern 3 echogenicity                        | 67.8        | 82.6        | 90.9 | 50   | 71.9     |
| 4 Presence of micronodules                      | 66          | 78          | 88.6 | 47.4 | 69.5     |
| 5 Presence of fibrotic strands                  | 81          | 65          | 85   | 57   | 76.8     |
| 6 Absence of calcification                      | 86          | 43.4        | 79.6 | 55.6 | 74.3     |
| 11 Grey scale combinations (pattern 2 or 3      | 54          | 86          | 91.4 | 42.5 | 63.4     |
| echogenicity, presence of micronodules and      |             |             |      |      |          |
| fibrotic septa-3 parameters)                    |             |             |      |      |          |

Discussion

In this study involving 82 patients with diffuse thyroid swelling, 52 patients were diagnosed as having lymphocytic thyroiditis by cytology. Most of the patients, were females belong to the age group 30-50, consistent with the studies conducted by deshmukh et al¹ and hemalata et al². The median age in this study is 39 age, younger when compared to the western population, where median age is 49 years³. The 80% of the study sample were females, consistent with studies by the Deshmukh et al¹, Usha et al⁴ and Anderson et al⁵.
From the analysis it is observed that the positive predictive value of abnormal echogenicity (pattern 2 or 3) in detecting lymphocytic thyroiditis is 85.6, and that of pattern 3 echogenicity is 90.9 - both values are similar to the results obtained (87% and 96%) by raber et al.

Micronodulation is considered as a sensitive sign for lymphocytic thyroiditis, with positive predictive value of 94% and 93.9% in a study conducted by Yeh et al. and Acar et al. respectively.

In the present study it is observed that positive predictive value of micronodules in diagnosing lymphocytic thyroiditis is 88.6.

Echogenic fibrotic septations are noted in the lymphocytic thyroiditis, which are considered to be the result of fibrosis within the parenchyma as per studies of Yeh et al. and Pedersen et al.

In the present study it is observed that the sensitivity, specificity, PPV, NPV of fibrotic strands in diagnosing lymphocytic thyroiditis is 81%, 65%, 85%, and 57% respectively which is consistent with findings of Ceylan et al.

Various patterns of calcifications were observed in the study sample was analyzed. It was then observed that absence of calcification is sensitive for diagnosing lymphocytic thyroiditis in the study sample but less specific. Similar finding was observed by Sena hwang et al. in their study to differentiate focal lymphocytic thyroiditis from papillary carcinoma

Conclusion
- Lymphocytic thyroiditis was seen mostly in people with age group 30-50.
- The mean age of study sample with diagnosis as lymphocytic thyroiditis was 39 years.
- Females are commonly associated with lymphocytic thyroiditis.
- 15% lymphocytic thyroiditis was found to have no sonographic abnormality in the present study.
- A new cut off value for anteroposterior diameter of 1.2 cm is obtained from the receiver operator characteristic curve which can diagnose lymphocytic thyroiditis with 70% sensitivity and 60% specificity.
- The combination of the greyscale parameters, and absence of calcification can diagnose lymphocytic thyroiditis with sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 85%, 70%, 88%, 64% and 80% respectively

References
1. Vaishali Deshmukh, Anish Behl, Vagesh Iyer, Harish Joshi, Jayashree P. Dholye, Prema K. Varthakavi. Prevalence, clinical and biochemical profile of subclinical hypothyroidism in India. Indian Journal of Endocrinology and Metabolism. 2013 may-June; 17(3).
2. Hemlata T Kamra1, Ruchi Agarwal2, Parveen Rana3, Rajnish Kalra4, Swarn Kaur5. Evaluation Profile of Thyroid Nodule by FNAC in the Rural Population of Khanpur Kalan, Sonepat, Haryana. Journal of Clinical and Diagnostic Research. 2014 oct; 8(10)(FC16-FC18).
3. Anderson L, Middleton WD, Teefey SA, Reading CC, Langer JE. Part 2, sonographic analysis of benign and malignant nodules associated with lymphocytic thyroiditis. 2010;(195).
4. Marcocci C, Vitti P, Cetani F, Catalano F, Concetti R. Thyroid ultrasonography helps to identify patients with diffuse lymphocytic thyroiditis who are prone to hypothyroidism. J Clin Endocrinol Metab. 1993; 72(209-213).
5. Anderson L, Middleton W, Teefey SA, Reading CC, Langer JE et al. Hashimoto Thyroiditis: Part 1, sonographic analysis of the nodular form of Hashimoto thyroiditis. 2010; 195.
6. Yeh H C, Futterweit W, Gilbert P. Micronodulation: ultrasonographic sign of Hashimoto’s thyroiditis. j ultrasound med. 1996; 15(813-819).
7. Bogazzi F, Bartalena L, Brogioni S, Burelli A, Manetti L, Tanda ML, et al. Thyroid vascularity and blood flow are not dependent on serum thyroid hormone levels: studies in vivo by color flow Doppler sonography. 1999; 140(5).

8. Pedersen OM, Aardal NP, Larssen TB et al. The value of ultrasonography in predicting autoimmune thyroid disease. eur thyroid j. 2000; 10(251-259).

9. Isin Ceylan, Serkan Yener, Firat Bayraktar, Mustafa Secil. Roles of ultrasound and power Doppler ultrasound for diagnosis of Hashimoto thyroiditis in anti-thyroid marker-positive euthyroid subjects. Quantitative Imaging in Medicine and Surgery. 2014 august; 4(4)(232-238).

10. Sena Hwang1, Dong Yeob Shin, Eun Kyung Kim, Woo Ick Yang, Jung Woo Byun. Focal Lymphocytic Thyroiditis Nodules Share the Features of Papillary Thyroid Cancer on Ultrasound. Yonsei Med J 2015 Sep;56(5):1338-1344. 2015 sep; 56(5)(1338-1344).

11. Türker Acar, Süha Süreyya Özbek, Mehmet Erdoğan, Ahmet Gökhan Özgen, Selçuk Orhan Demirel. US findings in euthyroid patients with positive antithyroid autoantibody tests compared to normal and hypothyroid cases. Turkish society of radiology. 2013; 19(265-270).