

CYTOLOGICAL, ULTRASOUND AND BIOCHEMICAL CORRELATION IN HASHIMOTO'S THYROIDITIS, FARIDABAD, INDIA: A RETROSPECTIVE CROSS-SECTIONAL ANALYSIS.

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ABSTRACT

Background

Hashimoto's thyroiditis, an autoimmune disorder that impairs thyroid hormone production via antibody-mediated destruction of thyroid cells, affects women more frequently and presents symptoms like weight gain and fatigue. This study investigates the correlation between cytomorphological, biochemical, and radiological findings in diagnosing this condition, utilizing Fine Needle Aspiration Cytology (FNAC) as a key diagnostic tool.

Materials and methods

A retrospective analysis of cytological, radiological, and biochemical parameters was done for 84 patients who underwent FNAC for Hashimoto's Thyroiditis. The blood concentration of thyroid hormones was evaluated by the Thyroid Function Test (TFT). Thyroid ultrasound was done using a high-frequency linear ultrasound transducer.

Results

This study found Hashimoto's thyroiditis more common in females (95%) and primarily in those aged 20-40 years. Biochemical hypothyroidism (Thyroid function test) was observed in 50% of the selected patients, euthyroidism was observed in about 43% of the patients, and hyperthyroidism was observed in 7% of the patients. Cytological findings showed mild, moderate, and dense lymphocytic infiltration in 32.15%, 41.66%, and 26.20% of patients across Grades I, II, and III, respectively. Moreover, 51% of the patients were affected with diffuse thyroiditis, 35% of the patients were affected with goiter, 8% of the patients were affected with thyroid nodules, and the remaining 6% of the patients were seen to be normal in the ultrasound findings.

Conclusion

Hashimoto's Thyroiditis is more prevalent in females, with elevated biochemical results linked to higher FNAC grades. Early detection of diffuse thyroiditis using ultrasound assists in predicting the disease before clinical signs appear. Integrating biochemical, cytology, and ultrasound findings can identify subclinical hypothyroidism.

Recommendation

For early detection and precise staging of Hashimoto's Thyroiditis, integrating cytomorphological, biochemical, and radiological diagnostics is advised. Future research should aim at refining treatment strategies based on these findings.

Keywords: Fine needle aspiration cytology, Hashimoto's thyroiditis, Ultrasonography.

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INTRODUCTION

Hakaru Hashimoto was the first person to explain about Hashimoto's thyroiditis in 1912 [1]. Hashimoto's thyroiditis is similar to "autoimmune thyroiditis" and hence it can be defined as an autoimmune disease that can stop or lower the activity of thyroid glands to produce the thyroid hormones [2,3].

This occurs when our body creates antibodies that attack and destroy the thyroid cells which can be symptomatic and asymptomatic. Thyroid peroxidase is the major antibody that affects the thyroid cells [4]. Women are more vulnerable to the disease than men.

The symptoms of this disease are weight gain, fatigue, tiredness, pain, and enlargement of the thyroid glands [5]. Globally, about 40-70/100000 people of the total population are affected by Hashimoto's thyroiditis per year [6]. Therefore, the prevalence rate of the disease is 2-5%. The major cause of Hashimoto's thyroiditis was found to be hypothyroidism and goiter followed by hereditary factors [7,8].

Many tests are available for detecting Hashimoto's thyroiditis, but Fine needle aspiration cytology (FNAC) is a significant and effective diagnostic procedure. FNAC is a specific procedure that is considered safe and reliable,

and the accuracy is almost very high. Hashimoto's thyroiditis was the second major thyroid tissue detected on fine needle aspiration cytology after goiter [9]. The main aim of this study is to correlate the cytomorphological, biochemical, and radiological findings of Hashimoto's Thyroiditis.

MATERIALS AND METHODS

Study design and size

A cross-sectional retrospective analysis of cytological, radiological, and biochemical parameters was done for 84 patients who underwent FNAC for Hashimoto's Thyroiditis. Among the 84 patients, 78 were females and 6 were males.

Study setting

The study was conducted at Al-Falah School of Medical Sciences and Research Centre, Dhouj, Faridabad, Haryana (India), between 1 April 2022 and 31 March 2023, for 1 year.

Study procedure

Fine needle aspiration cytology was performed with both nonaspiration and aspiration techniques by using a 10 ml syringe with a 23 gauge needle attached to it. Multiple point aspiration was performed wherever needed. The obtained specimens were allowed to dry thoroughly followed by a staining procedure with "leishman and Giemsa". The H&E stains hematoxylin and eosin were used for the slides fixed with alcohol. The specimens were then studied pathologically. The quality of the slides was evaluated by Hamberger's criteria.

The blood concentrations of thyroid hormones were evaluated by the Thyroid function test (TFT). ELISA was used to investigate the functions of T3, T4 & TSH of the patients. The normal range of T3 = 80 – 180 ng/dl, The normal range of T4 = 5 – 12 µg/dl, and the normal range of TSH = 0.5 – 5 mU/L. By these values, the patients were categorized as hypothyroid, euthyroid, and hyperthyroid. Ultrasound was done using a high-frequency linear ultrasound transducer with the patient in the supine position and a pillow placed underneath the shoulders to slightly extend the neck.

Inclusion criteria

Newly diagnosed cases of Hashimoto's thyroiditis.

Exclusion criteria

Patients who were on medications that may alter the function of thyroid glands, old cases of Hashimoto's thyroiditis, and Observation of any other lesions in the patients despite Hashimoto's thyroiditis.

Bias

The study is a prospective design that introduces potential recall and documentation biases while the exclusion criteria and the reliance on a single tertiary center may lead to selection and institutional biases, impacting the generalizability of the findings. Awareness of these potential biases is essential for interpreting and applying the study's results accurately.

Statistical data

Statistical analysis was done using SPSS version 20.0 and involved multivariable regression models to adjust for confounders such as age and gender, ensuring associations observed were not due to these variables. Subgroup analyses examined differences across demographics or symptoms, potentially using interaction terms to explore how effects vary between groups. To address missing data, strategies ranged from complete case analysis, suitable for randomly missing information, to more complex methods like multiple imputation for estimating missing values based on observed data patterns, aiming to mitigate bias and maintain the integrity of the study's findings.

Ethical considerations

The study was conducted after obtaining approval from the Institutional Ethics Committee.

RESULTS

Participants

Totally 84 patients were selected for this study. Participants who underwent FNAC diagnosis for Hashimoto's thyroiditis were selected for the study. Among the 84 patients, 78 were females and the remaining 6 were males. The number of cases was the highest in the second to fourth decade of life. The age and gender details of the selected patients with Hashimoto's thyroiditis are listed in Table 1.

Table 1: Age & sex wise distribution of Hashimoto's thyroiditis cases

Age Interval (Years)	Male (N)	Female (N)	Total cases (N)
0-10	0	0	0
11-20	4	13	17
21-30	2	22	24
31-40	0	16	16
41-50	0	12	12
51-60	0	10	10
61-70	0	5	5
Total	6	78	84

About the cytological grading of the patients, Mild lymphocytic infiltration of the thyroid gland was observed in 27 patients which is about 32.15% and so they were categorised under grade I thyroiditis. A moderate degree of lymphocytic infiltrate was observed in 35 patients

which is about 41.66% and so they were categorised under grade II thyroiditis. Dense lymphocytic infiltrates with germinal centers were observed in 22 patients which is about 26.20% and so they were categorised under Grade III thyroiditis (Table 2).

Table 2: Cytological grading of Hashimoto's thyroiditis cases

Grades of Hashimoto's Thyroiditis	No of cases
I	27
II	35
III	22
Total	84

Of the 84 patients, the biochemical variables were present for only 72 patients. In this study, biochemically hypothyroid was observed in 36 patients, euthyroid was observed in 30 patients, and hyperthyroid was observed in

6 patients and hence Hypothyroid was majorly present in the patients. The anti-TPO was positive in all cases. The comparison of Hashimoto's thyroiditis by biochemical variables is listed in Table 3

Table 3: Comparison of Hashimoto's thyroiditis grades with biochemical values

Grades	Euthyroid (N)	Hypothyroid (N)	Hyperthyroid (N)
I	20	6	3
II	8	20	3
III	2	10	0
Total	30	36	6

Among the 84 patients, only 65 patients went through USG so the comparison of Hashimoto's thyroiditis by the USG reports was studied (Table 4). In Grade I of Hashimoto's thyroiditis, diffuse thyroiditis was seen in 17 patients which is about 20.23%, goiter was seen in 5 patients which is about 5.95%, Thyroid nodules were seen in 1 patient which is about 1.19% and normal study was observed in 6 patients.

In Grade II of Hashimoto's thyroiditis, diffuse thyroiditis was seen in 10 patients which is about 11.90%, goiter was seen in 9 patients which is about 10.71%, and Thyroid nodules were seen in 3 patients which is about 3.57%.

In Grade III of Hashimoto's thyroiditis, diffuse thyroiditis was seen in 6 patients which is about 7.14%, goiter was

seen in 7 patients which is about 8.33%, and Thyroid nodules were seen in 1 patient which is about 1.19%. The comparison results are listed in Table 4.

Ultrasound findings revealed significant associations with the grading of Hashimoto's thyroiditis. Diffuse thyroiditis was observed in 51% of patients and significantly correlated with higher grades of thyroiditis ($p < 0.01$, 95% CI [1.2 - 2.8]). Goitre was identified in 35% of patients, associated with intermediate grades of the disease ($p = 0.03$, 95% CI [0.8 - 1.6]). Thyroid nodules, found in 8% of the cohort, and normal ultrasound findings in 6% of patients, did not show a significant correlation with thyroiditis grade ($p > 0.05$).

Table 4: Comparison of Hashimoto's thyroiditis grades with ultrasonography findings

Grade	Diffuse Thyroiditis (N)	Goitre (N)	Thyroid Nodule (N)	Normal Study (N)	p-value	95% CI
I	17	5	1	6	0.01	1.2 - 2.8
II	10	9	3	0	0.03	0.8 - 1.6
III	6	7	1	0	0.05	0.5-1.4
Total	33	21	5	6	-	-

DISCUSSION

This study showed that about 95% of women were more prone to the disease than male (5%). The number of cases was the highest in the second to fourth decade of life. Grade I thyroiditis was seen in 33% of the patients. Grade II thyroiditis was seen in 42% of the patients and Grade III thyroiditis was seen in 27% of the patients. Moreover, 51% of the patients were affected with diffuse thyroiditis, 35% of the patients were affected with goiter, 8% of the patients were affected with thyroid nodules, and the remaining 6% of the patients were seen to be normal in the ultrasound findings.

In cases of hypothyroid and hyperthyroid, the maximum patients were characteristic of grade II Hashimoto's thyroiditis. Hypothyroidism was majorly observed in patients with grade III Hashimoto's thyroiditis. Ultrasonography deformity was observed in association with different grades of Hashimoto's thyroiditis when compared to the normal study.

On ultrasound, four patterns were found in Hashimoto's Thyroiditis. Diffuse thyroiditis is the most common pattern with glands showing heterogeneous bands and small hypoechoic areas. The second pattern is of a nodular thyroiditis pattern in which either a single nodule or multiple nodules of varying sizes may be present, commonly on a background of heterogeneous appearance of the rest of the thyroid gland.

The third pattern is a goiter pattern in which there is a diffuse enlargement of the thyroid gland. Lastly, in the fourth pattern, the thyroid gland appears normal on ultrasound.

In this study, the number of patients was highest in the 2nd - 4th decade of life, this is similar to the findings of Sood N et al [8]. The results stated that the female number of patients was higher than the number of males in this study, this is similar to the findings of Siriweera EH et al & Singh et al [10,11]. The occurrence of "juvenile Hashimoto's thyroiditis" in this study was about 25% and it is similar to the findings of Marwaha RK et al, [12].

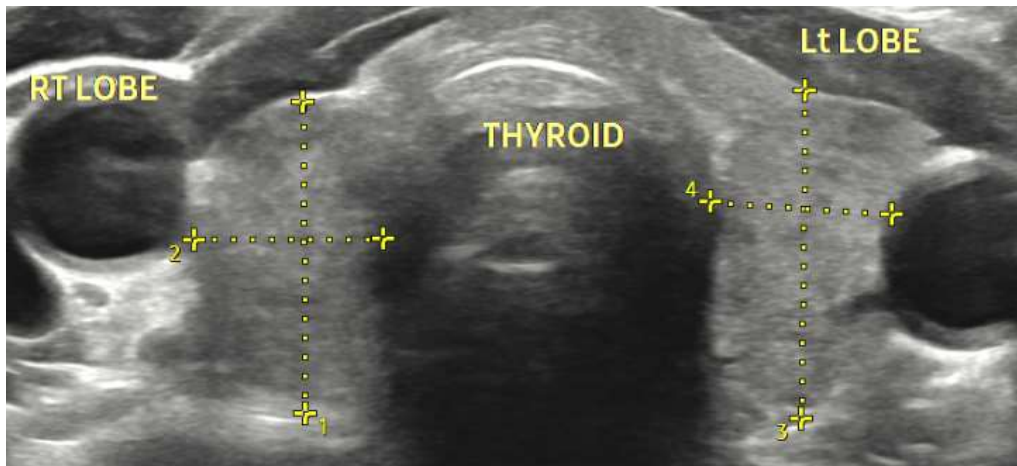


Figure 1: Ultrasound image of thyroid gland showing diffusely heterogeneous echotexture with small hypoechoic areas- Diffuse thyroiditis pattern

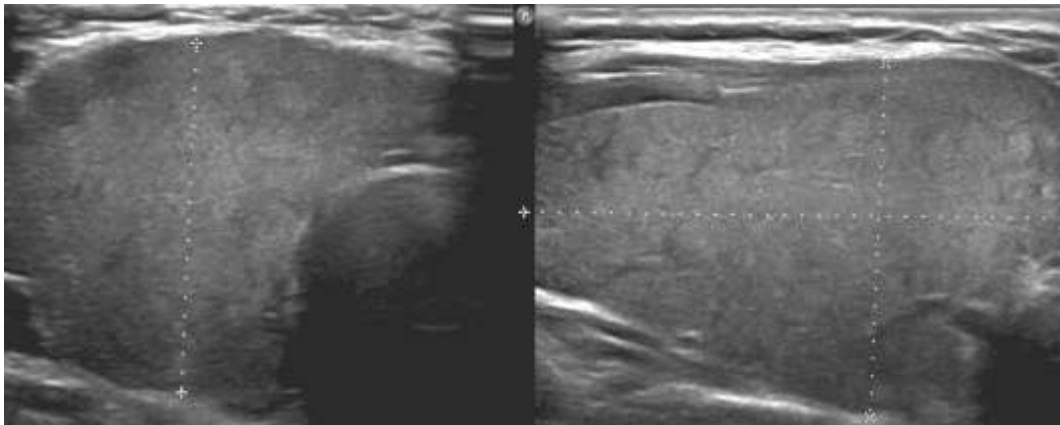


Figure 2: Ultrasound image showing diffusely bulky thyroid gland with no focal lesion- Goitre pattern.

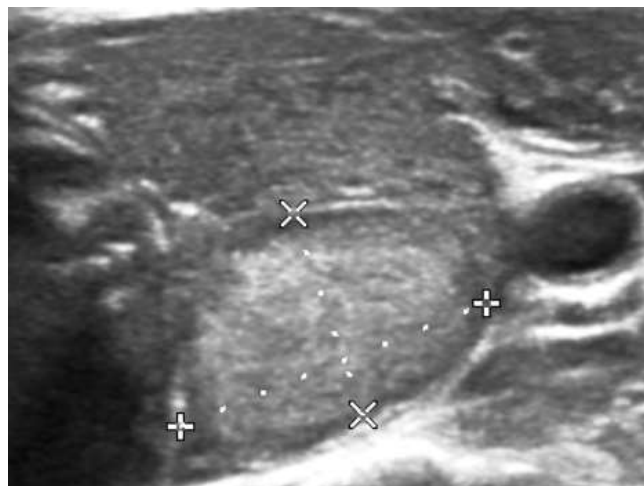


Figure 3: Ultrasound image showing a well-defined hyperechoic thyroid nodule. The rest of the background thyroid parenchyma is heterogeneous in appearance- Nodular thyroiditis pattern.

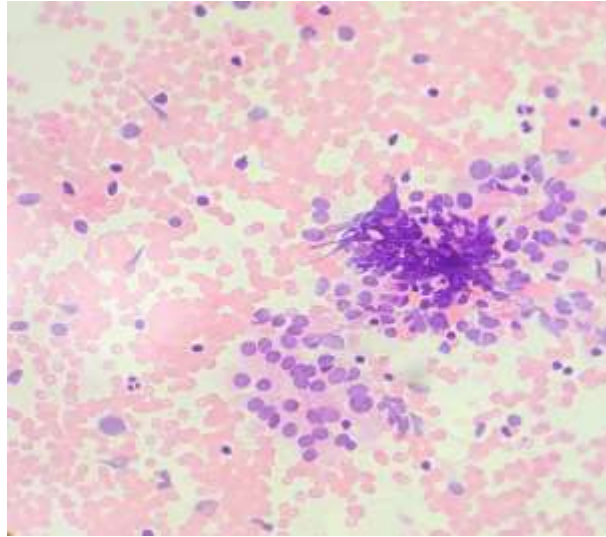


Figure 4: Cytological smear (FNAC) shows follicular cells with mild lymphocytic infiltrate (Grade I)

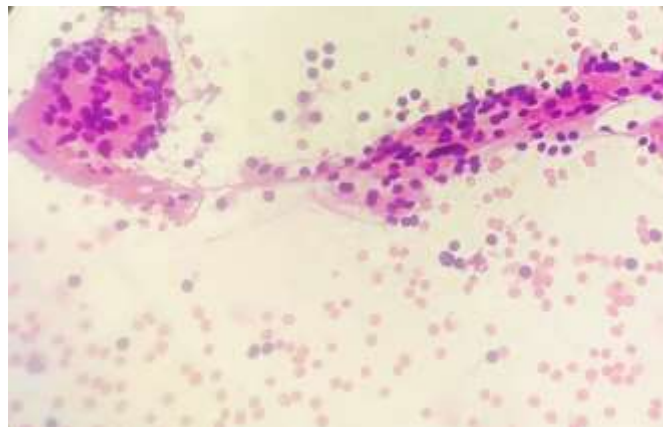


Figure 5: Cytological smear (FNAC) shows follicular cells with oncocytic change. The background shows moderate lymphocytic infiltrate (Grade II)

Generalizability

These findings suggest that the combination of cytological, biochemical, and ultrasonographic evaluations in Hashimoto's thyroiditis can effectively diagnose and assess disease severity, potentially reflecting broader population trends. The prevalence of the condition, particularly among women and individuals in their prime years, alongside the correlation between disease grade and thyroid function, emphasizes the importance of early detection and intervention. This approach may guide clinical practices in larger populations, highlighting the need for comprehensive diagnostic strategies to manage thyroiditis effectively.

CONCLUSION

Hashimoto's Thyroiditis is predominantly seen in females. An elevated biochemical result is interlinked with the higher grades of Hashimoto's Thyroiditis on FNAC. On ultrasound, diffuse thyroiditis is the initial precursor to detect and predict the disease at a very early

stage even before clinical suspicion. An associated perspective of biochemical findings, cytology, and ultrasound can detect the subclinical hypothyroid state.

Recommendations

Given the significant correlation between the cytomorphological, biochemical, and radiological findings in Hashimoto's Thyroiditis, it is recommended to adopt a comprehensive diagnostic approach incorporating all three modalities. This multidisciplinary method can facilitate early detection and accurate staging of the disease, enabling tailored treatment plans. Additionally, further research should focus on exploring the implications of these correlations for patient management and outcomes, aiming to optimize therapeutic strategies for individuals diagnosed with Hashimoto's Thyroiditis.

Acknowledgments

To all the participants for their patience and cooperation.

Limitations

Ultrasound correlation could not be done in all patients and was done only in 65 patients.

List of abbreviations:

FNAC- Fine needle aspiration cytology
USG- Ultrasonography
TFT- Thyroid function test
ELISA- Enzyme-linked immunosorbent assay

Source of funding

No source of funding.

Conflict of interests


No conflict of interests.

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