e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(1); 1799-1805

Original Research Article

To Study the Different Cytomorphological Patterns of Hashimoto's Thyroiditis (Autoimmune Thyroiditis) on FNAC and its Correlation with Biochemical and Serological Markers like T3, T4, TSH (Thyroid Function Test), Anti TPO, Anti TG Antibody in Patients of Southern Odisha

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Received: 25-11-2023 / Revised: 23-12-2023 / Accepted: 18-01-2024

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Conflict of interest: Nil

Abstract:

Background: In this study, we wanted to define, and sub classify the cytomorphological grading of Hashimoto's Thyroiditis on FNAC smears, and correlate cytological grades with thyroid function and anti-thyroid antibodies.

Methods: This was a hospital-based prospective study conducted among 101 patients presenting with goitrous lesions & on FNAC showing features of autoimmune thyroiditis in the Department of Pathology, MKCG Medical College and Hospital, Berhampur, Odisha, over a period of two years from 2019 to 2021, upon receipt of the study participant's signed informed consent and approval from the institutional ethics committee.

Results: Out of 101 patients, 85.1% had diffuse thyromegaly, multinodular goitres were seen in 11.9% and solitary nodules in 3% patients. FNAC aspirate of these patients showed lymphoplasmacytic infiltration into the thyroid follicles, giant cells, epithelioid cells, hurthle cell change and variable amount of colloid in the background. Biochemically, 15.84% patients were euthyroid, 76.23% were hypothyroid, and 7.9% had features of thyrotoxicosis. In 93% of instances, the thyroid antibody profile showed overall antibody positivity (either Anti-Tg or AMA, or both). Anti-Tg was positive in 66.3% of cases and AMA in 74.3% of patients, whereas a combination of both types of positivity was observed in 49.5% of instances. 6.9% cases were negative for both antibodies. Grade I, II and III thyroiditis was noted in 4%, 77.2% and 18.8% cases, respectively. Cytological grading of chronic thyroiditis statistically correlated with AMA and ATG, and TSH.

Conclusion: Demonstration of lymphocytic infiltration of thyroid follicles is pathognomonic of HT. Significant correlation was seen between lymphocytic infiltrate with ATPO andATG antibodies.

Keywords: Hashimoto's Thyroiditis (Autoimmune Thyroiditis), FNAC, Correlation, Biochemical, Serological Markers, T3, T4, TSH (Thyroid Function Test), Anti TPO, AntiTg.

Introduction

Thyroid diseases are the most common endocrine disorders throughout the world with about 42 million people in India suffering from them. [1] The thyroid disorders are common, disruptive, treatable and preventable. [2]

Thyroid disorders can be easily identified compared to other endocrine disorders because the enlarged gland is easily visible and the approach for the diagnosis is also easy, so the treatment can also be initiated early. [3] Hashimoto's thyroiditis is the most common form of autoimmune chronic thyroiditis observed clinically. [4] It results in destruction of the thyroid gland with gradual and progres-

sive thyroid failure. [5]

The condition known as "struma lymphomatosa," which carries the name of Hakaru Hashimoto, was originally reported to be lymphocytic thyroiditis in 1912. While goitrous thyroiditis is occasionally used to describe Hashimoto's thyroiditis, this condition is more commonly thought of as a synonym for chronic lymphocytic thyroiditis or autoimmune thyroiditis, which includes atrophic and non-goitrous thyroiditis. [6] It is the second most common thyroid lesion diagnosed by cytology, after endemic goitre. HT patients usually present with a diffuse enlargement of the thyroid gland or less frequently with one or two prominent nodules. [7]

The prevalence of this condition is higher in women than in males, with a 10:1 to 20:1 female preponderance. It is a common cause of non-endemic goitre in the paediatric population and can also arise in children. Based on clinical, cytomorphological, and serological characteristics, Hashimoto's thyroiditis is diagnosed. It is a typical type of destructive autoimmune thyroiditis. [8] One well-established technique for obtaining thyroid tissue samples for the diagnosis of various gland-related diseases, including HT, is fine needle aspiration cytology (FNAC). [9]

A dependable and reasonably priced method for diagnosing HT is FNAC. [10] Despite the fact that Hashimoto's thyroiditis has well-established cytomorphologic criteria, many instances remain misdiagnosed because fine needle aspiration (FNA) yields very little material. It has been highlighted that while evaluating HT, a comprehensive approach combining clinical, biochemical, serologic, and cytomorphologic methods is crucial. [11] However, the importance of FNAC in the diagnosis of serologically negative HT is also emphasised, and the method is still considered to be the gold standard in this regard. [12]

Aims and Objectives

1. To define and sub classify the cytomorphological grading of Hashimoto's Thyroiditis on FNAC smears.
2. Correlate cytological grades with thyroid function and anti-thyroid antibodies.

Materials & Methods

This was a hospital-based prospective study conducted among 101 patients presenting with goitrous lesions & on FNAC showing features of autoimmune thyroiditis in the Department of Pathology, MKCG Medical College and Hospital, Berhampur, Odisha, for two years from 2019 to 2021, upon receipt of the study participants' signed informed consent and approval from the institutional ethics committee.

Inclusion Criteria

- All patients presenting with goitrous lesions & showing features of autoimmune thyroiditis on FNAC.

Exclusion Criteria

- Goitrous lesions which were negative for autoimmune thyroiditis oncytomorphology.
- Patients with neoplastic lesions of thyroid diagnosed on FNAC.
- Inadequate material on FNAC.

Statistical Methods

Data was entered in MS Excel and analysed using SPSS software. Results were resented as tables.

Results

Table 1: Age distribution of Hashimoto's thyroiditis

Age in Years	No. of Cases	Percentage
<10	7	6.9
11-20	20	19.8
21-30	34	33.7
31-40	17	16.8
41-50	14	13.9
51-60	7	6.9
61-70	2	2.0
TOTAL	101	100

In the present study, the peak age group was between 21 – 30 years. The mean age of cases was 30.51. In this study, majority i.e. 94% cases were females.

Table 2

Clinical presentation	No. of Cases	Percentage
Diffuse	86	85.1
Multinodular	12	11.9
Solitary	3	3
Total	101	100

Clinical presentation of Hashimoto's thyroiditis

Cytological Grade	No. of Cases	Percentage
Grade 1	4	4%
Grade 2	78	77.2%
Grade 3	19	18.8%
TOTAL	101	100
Cytological grade of Hashimoto's thyroiditis		

Out of 101 cases, most of the patients presented with diffuse thyroid swelling i.e. 85.1% (86) followed by multinodular thyroid swelling and solitary thyroid nodule in 11.9% (12) and 3% cases respectively.

Grade 2 thyroiditis was observed in 77.2% (78) cases at the time of diagnosis. Rest 18.8% (19) & 4% (4) of the cases werehaving Grade 3 & Grade 1 respectively.

Table 3

Cytological Grade	Euthyroid	Hypothyroid	Hyperthyroid	Total
1	2	1	1	4
2	9	65	4	78
3	5	11	3	19
Total	16	77	8	101
Thyroid function test				
Antibody Profile		**No. of Cases**	**Percentage**	
Overall positive AMA±ATG		94	93	
AMA(Anti-TPO)		75	74.3	
ATG(Anti-Tg)		67	66.3	
AMA+ATG		50	49.5	
Overall negative		7	6.9	
TOTAL		101	100	
Antibody profile				

Out of 4 grade 1 lesions, 2 (50%) cases were biochemically euthyroid, 1 (25%) case was biochemically hypothyroid and 1 (25%) case was biochemically hyperthyroid.

Out of 78 grade 2 lesions, 9 (11.53%) cases were biochemically euthyroid, 65 (83.33%) cases were biochemically hypothyroid and 4 (5.14%) cases were biochemically hyperthyroid.

Out of 19 grade 3 lesions, 5 (26.31%) cases were biochemically euthyroid, 11 (57.89%) cases were biochemically hypothyroid and 3 (15.7%) cases were biochemically hyperthyroid.

In the present study, 75 and 67 cases respectively showed Anti-TPO and Anti-Tg positivity and 7 cases were both AMA and ATG negative.

Table 4

TFT	I (n=4)	II (n=78)	III (n=19)	Significance (P -Value)		
T3	8.5 ± 5.02	14.10 ± 38.27	12.21±31.37	0.33		
T4	10.22±6.74	12.40±36.30	4.30±3.27	0.98		
TSH	1.41±0.92	32.35±31.89	43.42±28.16	0.02		
Correlation between TFT & cytological grading						
Serum Values			**Cytological Grade 1**	**Cytological Grade 2**	**Cytological Grade 3**	**Total**
ATPO Increase, ATG Increase, TSH Increase			0	34	8	42
ATPO Increase, ATG Increase, TSH WNL			0	5	2	7
ATPO Increase, TSH Increase, ATG WNL			0	15	2	17
ATPO Increase, ATG WNL, TSH WNL			0	6	2	6
ATG Increase, ATPO WNL, TSH WNL			3	9	2	12
ATPO Increase, ATG Increase, TSH Decreased			1	4	1	6
ATPO WNL, ATG WNL, TSH WNL			0	5	2	11
Total			4	78	19	100
Correlation between cytological grade and ANTI-TPO, ANTI-Tg, TSH						

Using ANOVA-TEST, statistically significant association was observedbetween cytological grades of thyroiditis and TSH levels (P= 0.02).

There was a statistically significant correlation between cytological grade and antibody titres (P<0.05).

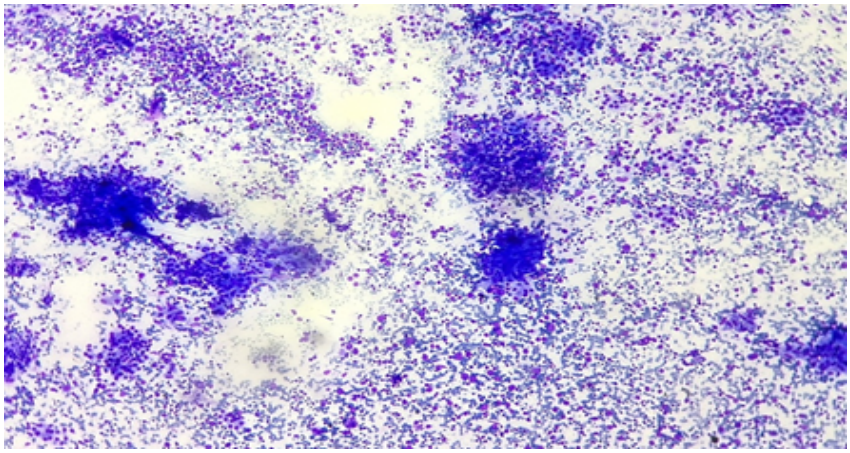

Figure 1: scanner view 40X- Thyroid follicular cells in clusters in background of lymphocytes

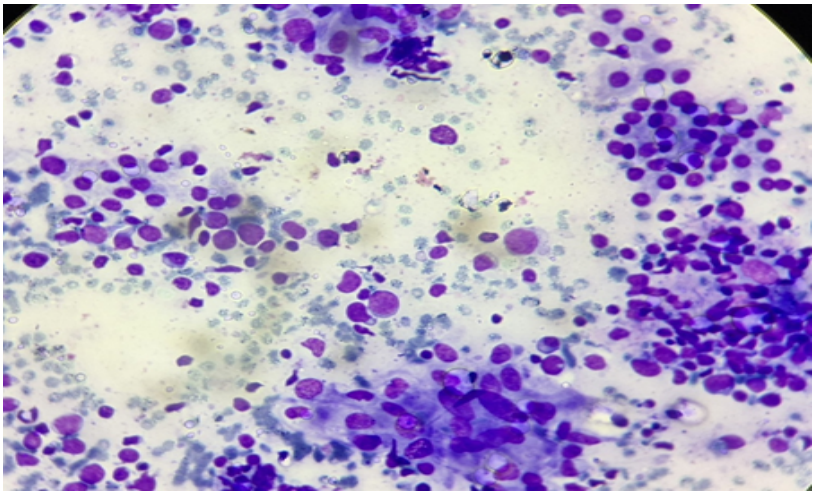

Figure 2:) LP100X- Lymphocytes impinging on thyroid follicular cells destroying the follicular architecture (Folliculolysis)

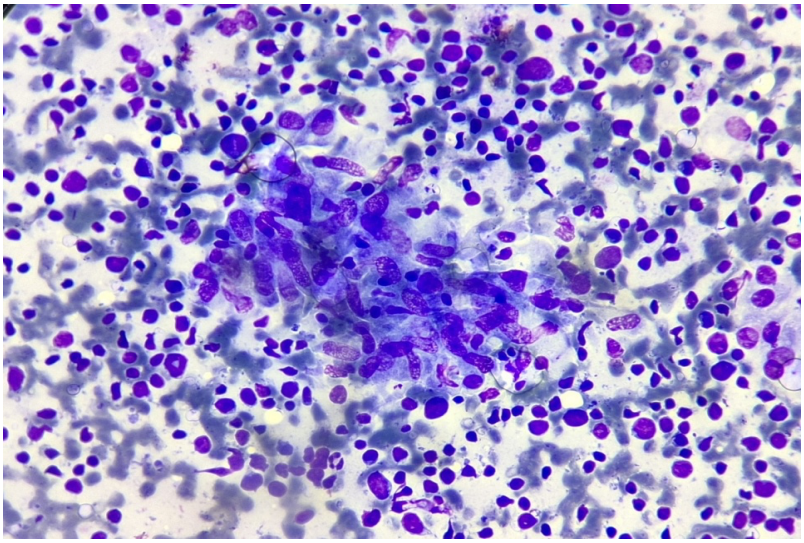

Figure 3: LP100X- Epitheloid cell clusters found as a feature in autoimmune thyroiditis.

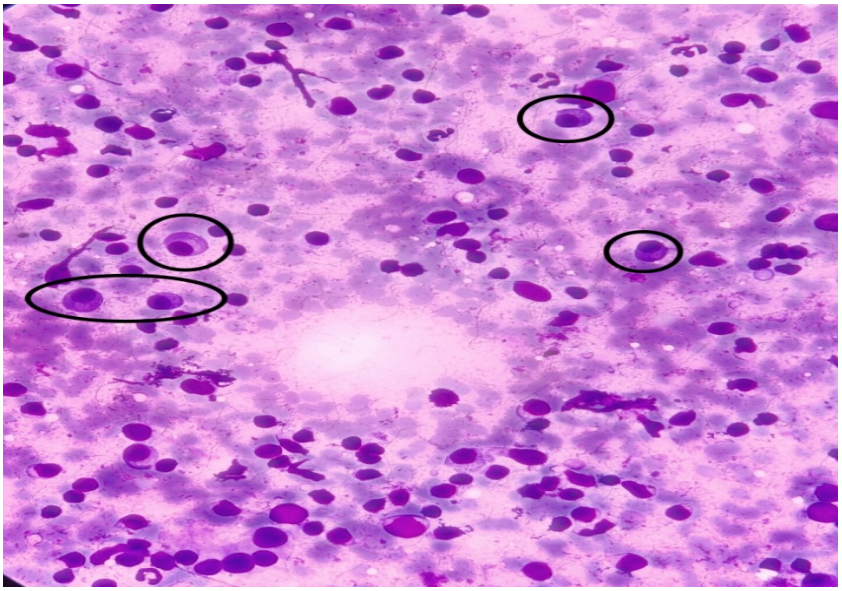

Figure 4: 100x-showing presence of plasma cells confirming the features of autoimmune thyroiditis.

Discussion

When diagnosing autoimmune thyroid disorders on cytology, several writers use the terms chronic lymphocytic thyroiditis (CLT) and Hashimoto's thyroiditis (HT) interchangeably. [13]

The cytomorphologic indicators consist of lymphocytic infiltration of the interfollicular area, lymphocyte invasion of the follicles, and ultimately, complete follicle death. Over the time, fibrosis completely replaces the lost follicular architecture. While subclinical or overt hypothyroidism is a symptom of the disease's progression and destructive phases, thyrotoxicosis is the clinical manifestation of the early, brief active phase of the illness [14]

According to Bhatia et al.'s postulated cytological grades of thyroiditis, 101 instances of HT were associated with TFT, Anti TPO, and ATG levels in this investigation.

In the current study, females made up 94.1% of the patient population. The male to female ratio was 16:1, with just 6 patients being male. The majority of the research published in the literature showed a preponderance of women. [15,16, 17]

The age ranged from 7-67 years, with a mean age of 30.51. The commonest age group was 21-30 years. So most cases documented in this study are of younger age group. As observed by Bhatia et al[18] the common age group was 31-40 yrs. Some authors claim that the difference in age distribution between India and other countries is caused by iodine deficiency, which causes thyroiditis to develop in India at a younger age. [19]

There are also opinions on how high iodine consumption, especially in coastal locations, contributes to the increased prevalence of HT. [20] High iodine consumption was found to be a risk factor for hypothyroidism development in antibody-positive participants in a research by Li et al. [21] Where iodine levels are adequate, HT is thought to be a prevalent cause of hypothyroidism. [22]

Clinically, most of the patients in the present study manifested with diffuse thyromegaly (85.1%) although multinodular enlargement and solitary thyroid nodule in 11.9% and 3% respectively which is compatible with Bhatia et al (89.47%), Singh et al (86%), KIni et al [23] (78.16%). However, Friedman et al [24] got 20% diffuse thyroid enlargement only.

Diffuse enlargement at the time of presentation may be due to patients coming to the hospital in the later stage of HT where the clinical and hormonal changes have become established.

11.9% of cases presented with multinodular disease. This is higher when compared to Bhatia et al, Singh et al and Kini et al as 2.63%, 8.7% and 8% respectively. However, there are other studies in literature where 26%of patients presented with nodular disease. [25]

HT can present as solitary nodule. In this study, only 3% of cases presented with solitary nodule. One may confuse nodular illness for a tumour. Making the right diagnosis requires a multimodal approach that includes hormone status, antithyroid antibody levels, and clinical, radiographic, and cytological modalities.

Grading of thyroiditis was done according to the predefined criteria by Bhatia et al. 4% of the patients had shown mild lymphocytic infiltration of thyroid gland. 77.2% of the patients had shown moderate degree of lymphocytic infiltrate or mild lymphocytic infiltration with Hurthle cell change,

giant cells, anisonucleosis. Grade 3 thyroiditis was observed in 18.8% of cases that showed dense infiltration with germinal centres and follicular atrophy. In our study, majority of the patients presented with Grade 2 disease which is correlated withJayaram et al [26] and Bhatia et al where they found Grade 2 thyroiditis in 62.16% and 44% of the patients respectively. But 40% of the patients in Sood and Nigam's research had Grade 3 thyroiditis.

On hormonal assay, majority of the patients were hypothyroid (76.23%) and 15.84% patients were euthyroid and the rest 7.9% cases were hyperthyroid. The mean T3, T4, TSH levels were 13.52 ng/ml, 10.79 ug/ml and 33.21 mlIU/ml respectively with a standard deviation of 36.16, 32.06 and 31.41 respectively.

In this study, hormonal status of higher hypothyroidism is compared with studies by Singh et al and Bagchi et al [27] Uma P et al.

In this study, normal TSH value was observed in 12.9 % cases and elevated in 82.2% cases. In 5% cases, low TSH was observed. Measurement of serum TSH levels is generally considered the best screening test for thyroid disease. [28] Increased value usually indicates hypothyroidism and decreased value indicates hyperthyroidism. According to the study by Bhatt et al, TSH was elevated in 15% cases and normal in 31 cases.

In this study, no significant correlation was seen between T3, T4 status and severity of the cytological grading, but TSH correlated well with the cytological grading (p value=0.02)

The Anti- TPO titres ranged from 0.43 to 1968.10. Raised Anti-TPO level was observed in 74.3% cases. Anti-Tg titres ranged from 0.67 to 1008.40. Raised Anti-Tg was observed in 66.3% cases. In this study, 7 patients showed higher ATPO values with normal hormone status. This is because patients who appeared early had elevated ATPO values, even in the absence of serological proof of a hormonal imbalance. Significantly sooner than any observable serological evidence, intrathyroidal immune destruction takes place. [29] Grade 3 thyroiditis affected one patient, grade 2 thyroiditis affected four, and grade 1 thyroiditis affected one. This phenomenon, in which thyroid follicular cells are acutely destroyed by autoantibodies, is observed in the active early stages of the illness.

The cytological grades correlated significantly with Anti-TPO and Anti-TG levels among the patients in our study which was comparable with studies by Ahluwalia et al. [30] Similar grading was done by Bhatia et al, but they did not find any statistically significant correlation between the grades and any of the serological parameters.

A study by Sharma et al [31] showed Anti-TPO positivity in 94. % cases and got a strong correlation between cytological grading and antibody. The results are consistent with other studies from India. [32]

However, discrepancy between cytological finding and antibody titre has been well recognized in other studies. [33]

Conclusion

In conclusion, a multidisciplinary approach incorporating clinical, cytological, serological, biochemical, and radiographic characteristics should be used to diagnose HT. However, demonstration of lymphocytic infiltration of thyroid follicles is pathognomonic of HT. Significant correlation was seen between lymphocytic infiltrate with ATPO andATG antibodies.

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