



## Evaluation of Cyto-Morphological Profile of Thyroid Swellings Using Bethesda System for Reporting and its Correlation with Biochemical Parameters in Cases of Autoimmune Thyroiditis: A Sub-Himalayan Tertiary Care Experience

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### Abstract

**Background:** Thyroid disorders are among the commonest endocrine disorders worldwide, including India. FNAC (fine needle aspiration cytology) is used for thyroid swelling as the initial diagnostic test due to its superior diagnostic reliability and cost-effectiveness. Thyroid antibody levels and thyroid function test are among the many other initial tests available for thyroid lesions.

**Objective:** To study the cytomorphological profile of thyroid swelling using the Bethesda system for reporting thyroid cytopathology in a sub-Himalayan tertiary care centre, and assess correlation of biochemical parameters in cytologically diagnosed cases of autoimmune thyroiditis.

**Materials and Methods:** In this retrospective study, departmental records of FNAC performed for thyroid swelling between March 2018 and February 2021 were retrieved and analysed. The Bethesda system was used for reporting of cytology. Biochemical parameters such as antithyroid peroxidase antibody (Anti-TPO) and thyroid stimulating hormone (TSH) of autoimmune thyroiditis were assessed to find out their association with the cytopathology.

**Results:** A total of 303 FNAC of palpable thyroid swelling were included in the present study. 9 (2.97%) cases were nondiagnostic-Bethesda category I, 256 (84.49%) were diagnosed as benign- category II, 4 (1.32%) atypia of undetermined significance or follicular lesion of undetermined significance (AUS/AFLUS)- category III, 10 (3.30%) as follicular neoplasm or suspicious for follicular neoplasm (FN/SFN)- category IV, 2 (0.66%) suspicious for malignancy (SM)- category V and 22 were malignant- category VI. Among the benign cases (category II), the final diagnosis was colloid goitre in 143 (47.19%) and autoimmune thyroiditis in 102 (33.66%). Out of 102 autoimmune thyroiditis cases, biochemical reports (Anti-TPO and TSH) were available in 85 patients. Anti-TPO was raised in 74 out of 85 cases (87.06%). Sixty three of 85 (74.11%) cases were euthyroid, 18 (21.18%) hypothyroid and 04 (4.71%) hyperthyroid. In category VI, papillary carcinoma and anaplastic carcinoma was seen in 20 (6.60%) and 2 (0.66%) cases respectively.

**Conclusion:** Colloid goitre followed by autoimmune thyroiditis, were the most common lesions on evaluating thyroid swelling. Relatively autoimmune thyroiditis was more prevalent in our region.

**Keywords:** Fine Needle Aspiration Cytology; Autoimmune Thyroiditis; Anti-TPO; Sub-Himalayan Region

## Introduction

Thyroid disorders are among the commonest endocrine disorders worldwide, including India. It has been observed that about 42 million people in India suffer from thyroid disorders [1]. Himachal Pradesh, a northern state of India, is also part of world's largest goitre belt, the Himalayan goitre belt [2]. The increased prevalence of goitre could possibly be due the loss of iodine from the soil and the intake of goitrogens (soyabean, sweet potato, broccoli, cabbage and cauliflower) by the inhabitants [3]. In one of the districts of our state, the total goitre rate of 15.8% in the age group of 6-12 years, points out that our population still has mild iodine deficiency even after 60 years of iodine supplementation [4]. This might have led to an increased incidence of thyroid autoimmunity [3]. Additionally, other factors such as infections, life stress, smoking, radiation and environmental toxins) can also trigger the cascade of events resulting in autoimmune thyroiditis in genetically sensitive individuals [5].

FNAC of the thyroid is a cost-effective and time-saving procedure with minimal risk, for early diagnosis, and is considered as the first line of investigation for thyroid swellings in a limited resource country like India [6]. It acts as a good screening test and can prevent needless surgery in benign thyroid conditions. The American Thyroid Association and the National Comprehensive Cancer Network practice guidelines also state that FNAC should be used as the initial diagnostic test because of its superior diagnostic reliability and cost-effectiveness, before thyroid scintigraphy and ultrasonography [7]. Other available initial screening tests for thyroid lesions include ultrasonography, radio nucleotide scan, molecular markers, thyroid antibody levels and thyroid function test [8].

The Bethesda system for reporting thyroid cytopathology has standardized the reporting of thyroid cytology and has improved communication between cytopathologists and clinicians, thereby leading to more consistent management approaches. It consists of 6 diagnostic categories and each category is associated with an implied risk of malignancy that directly influences the clinical management algorithm [9].

Our hospital, being a government tertiary care centre provides health services to approximately one-third of the population of

state of Himachal Pradesh, which is around 2.5 million. In view of the paucity of cytomorphological studies of thyroid lesions, particularly using the Bethesda system for reporting, the present study was planned. The objective of the study is to evaluate the cytomorphological profile of thyroid lesions with FNAC using the Bethesda system for reporting and assessing its correlation with biochemical parameters in autoimmune thyroiditis. The findings of this study will generate valuable data about thyroid lesion in this area.

## Materials and Methods

The data of patients who underwent FNAC for palpable thyroid lesions were retrieved from the cytology record in the Department of Pathology from March 2018 to February 2021. All patients with clinically palpable thyroid swelling were referred to our department for FNAC as part of the required (initial routine) investigation. FNAC was done using a 23 Gauge needle. Only in 18 patients with thyroid swellings but difficult to perform FNAC, ultrasound guided FNAC was required. Smears were prepared and stained with both Giemsa and Papanicolaou stains. The Bethesda system of thyroid cytomorphology reporting was used due to its relevant reporting system and as it helps clinicians to take appropriate therapeutic interventions [9]. The cases were categorized mainly into non-neoplastic and neoplastic lesions. Non-neoplastic lesions include goitre, autoimmune thyroiditis and others. Biochemical parameters like TSH levels and Anti-TPO were also collected for patients diagnosed with autoimmune thyroiditis on cytomorphology. The serological tests were done by an Immunoassay analyser based on ElectroChemiLuminescence (Cobas e-411 Roche Hitachi).

## Results

A total of 303 patients had FNAC and there was female dominance with 271 women and 32 men with a male-female ratio of 1:8.5. The age of the patients ranged from nine to ninety-six years with a median age of 46 years. The majority of them were in the fifth and sixth decade (42.90%), followed by the fourth decade (19.47%), of life (Table 1). On cytomorphologic examination of 303 cases, 9 (2.98%) cases were Non-diagnostic, 256 (84.48%) benign, 4 (1.32%) AUS/FLUS, 10 (3.30%) FN or SFN, 02 (0.66%) SM and 22 (7.26%) malignant (Table 2).

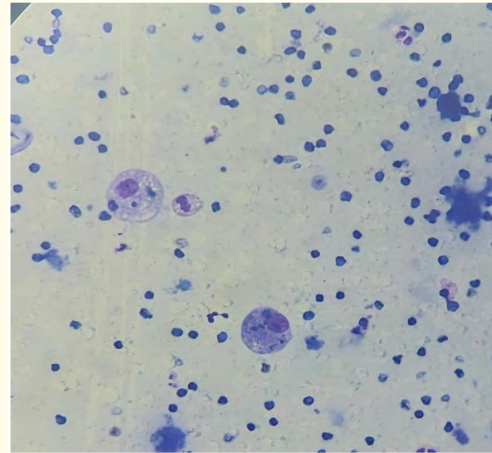
Age in (years)	No. of patients	Percentage
<20	12	3.96
21-30	32	10.56
31-40	59	19.47
41-50	65	21.45
51-60	65	21.45
61-70	42	13.86
71-80	24	7.93
>80	4	1.32
Total	303	100

**Table 1:** Age distribution of the patients.

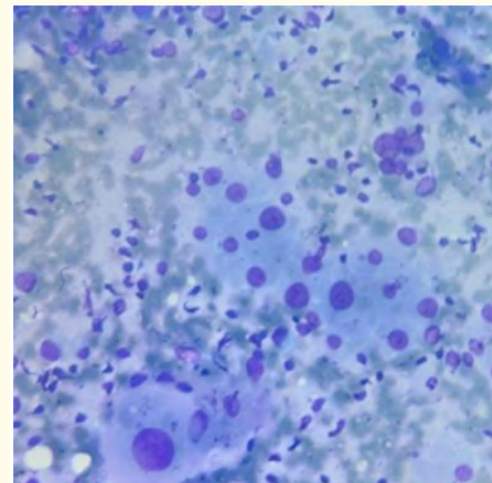
Category	FNA Diagnosis	No. of patients	Percentage
I	Non-diagnostic or Unsatisfactory		
	Cyst fluid only	04	1.32%
	Acellular/obscuring blood	05	1.66%
II	Benign		
	Colloid nodule/goitre	143	47.19%
	Hyperplastic nodule	07	2.31%
	Autoimmune thyroiditis	102	33.66%
	Granulomatous lesion	02	0.66%
	Tubercular Abscess	02	0.66%
III	Atypia of Undetermined Significance (AUS) or Follicular lesion of Undetermined Significance (FLUS)	04	1.32%
IV	Follicular Neoplasm (FN) or Suspicious	10	3.30%
V	Suspicious for Malignancy	02	0.66%
VI	Malignant		
	Papillary thyroid carcinoma	20	6.60%
	Undifferentiated (anaplastic) carcinoma	02	0.66%
Total		303	100

**Table 2:** Distribution of thyroid lesions according to Bethesda system.

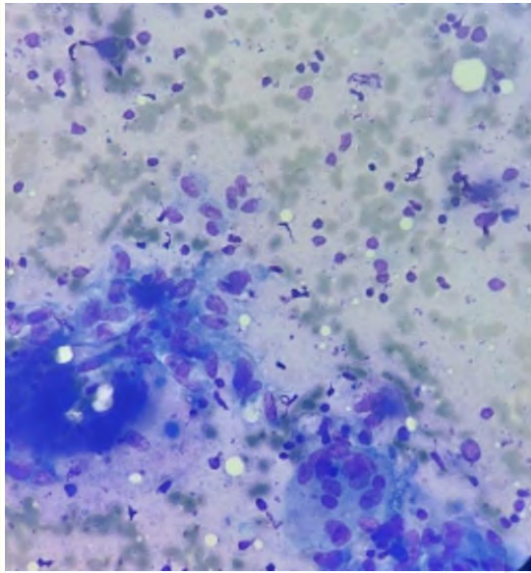
Among these 256 (84.48%) benign lesions, 143 (47.19%) cases were of colloid goitre (Figure 1), 102 (33.66%) autoimmune thyroiditis (Figure 2, 3 and 4), 07 hyperplastic nodule, 02 tubercular, and 02 were granulomatous thyroiditis. Similarly, out of 22 (7.26%) malignant cases, 20(6.60%) cases were papillary carcinoma (Figure 5) and 2 were anaplastic carcinoma.



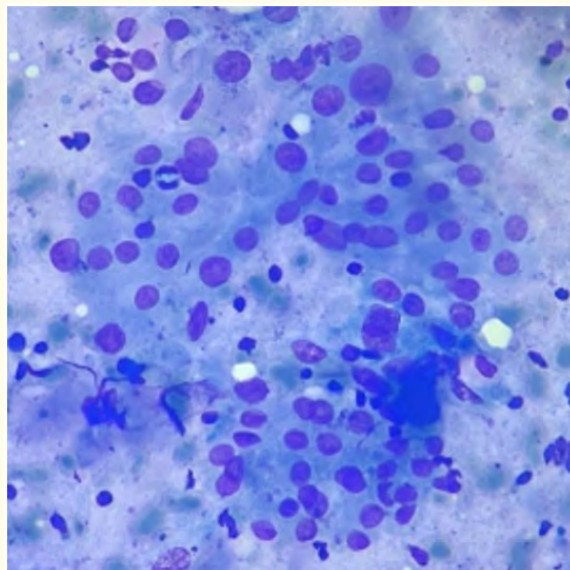
**Figure 1:** Colloid goitre with cystic change: smear showing cyst macrophages with colloid material and scattered follicular cells (Giemsa, x40).



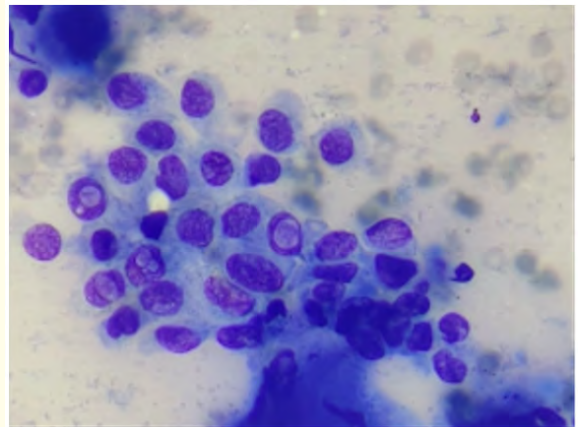
**Figure 2:** Autoimmune thyroiditis: Smear showing lymphoid cell population along with follicular cells and Hurthle cell (Giemsa, x40).



**Figure 3:** Autoimmune thyroiditis: Smears showing giant cell, epithelioid cell aggregates along with follicular cells and lymphoid cells (Giemsa, x40).



**Figure 4:** Autoimmune thyroiditis: Smears showing lymphoid cell population along with follicular cells and Hurthle cell (Giemsa, x40).



**Figure 5:** Papillary carcinoma thyroid: smears showing intra nuclear cytoplasmic pseudo inclusion in tumor cells (Giemsa stain, x40).

We could collect biochemical reports (Anti-TPO and TSH) of only 85 out of 102 cases of autoimmune thyroiditis from the biochemistry laboratory. Out of these 85 cases of autoimmune thyroiditis 74 (87.06%) had raised Anti-TPO. TSH level showed 63 (74.11%) cases were euthyroid, 18 (21.18%) hypothyroid and 04 (4.71%) were hyperthyroid (Table 3).

S. No.	Anti TPO	TSH	No. of patients Of Autoimmune thyroiditis	Percentage
1	Increased	WNL	52	61.17
2	Increased	Increased	18	21.18
3	Increased	De-creased	04	4.71
4	WNL	WNL	11	12.94
Total			85	100

**Table 3:** Serum values of ATPO (Anti Thyroid Peroxidaes) and TSH (Thyroid Stimulating Hormones) in Auto Immune Thyroiditis.

**Discussion**

Thyroid disorders are the commonest endocrine disorder worlds over, and one of the commonest presentations is thyroid swelling. FNAC has been a very important part of diagnostic tools

in the investigation of thyroid swellings. In the present study, FNAC of palpable thyroid lesion was performed in 303 patients. The age of patients ranged from 9 years to 96 years, with a peak incidence in the 5<sup>th</sup> and 6<sup>th</sup> decade which was in concordance with previous studies [10,11]. In a study by Shrivastava, *et al.* most of the patients were in the age group of 51-60 years followed by 41-50 years and in a study by Sharma, *et al.* the mean age was 43 years and most of the patients were in the age group of 30-49 years.

Thyroid diseases are more commonly seen in females than in males. In our study, there was a female predominance with males to females ratio of 1:8.5. An almost similar pattern of female preponderance was observed by other studies [12-14].

The cytomorphologically benign thyroid lesions were most common finding in studies done by Tamta, *et al.* from Haldwani (76.75%), Sharma, *et al.* from Shimla (74%), Dharrao, *et al.* from Maharashtra (81.25%) and Chakraborty, *et al.* from Malwa (86.56%) [2,11,14,15]. Our finding (84.48%) is also consistent with these studies.

Among the benign lesions, the most common lesion was colloid goitre found in 143(47.19%) cases, followed by autoimmune thyroiditis in 102 (33.66%). In most previous studies too colloid goitre has been observed to be the most common lesion. Possible factors contributing to colloid goitre could be that iodine gets washed away from soil as a result of erosions in our mountainous area due to rain, dietary habits like consumption of naturally occurring goitrogens, and lack of awareness among the general public resulting in non-implementation of the iodization programme [3].

An important observation in our study is that relatively higher frequency of the autoimmune thyroiditis (33.66%; 102/303) in comparison to other studies [16-18]. A similar trend of a higher proportion of autoimmune thyroiditis was described by a recent study carried out in a neighbouring state [19]. This may be partly attributed to the ongoing iodine supplementation programme in our state. It has been found that iodine supplementation in iodine-deficient populations may lead to an increase in numbers of cases of thyroid autoimmunity [20-22]. Similarly, it has been observed that lymphocytic infiltration in the thyroid increases by 3 fold with iodine supplements in an area previously deficient in iodine [21].

Boukis, *et al.* showed that the prevalence of thyroid autoantibody positivity rises to over 40% within 5 years of initiating the iodine supplementation [23]. Possible loss of regulatory mechanisms due to pre-existing iodine deficiency followed by iodine repletion, rather than iodine excess, is an etiological factor in the development of thyroid autoimmunity. Iodine deficiency causes thyroid dysfunction in genetically predisposed individuals, which leads to oxidative damage, inflammation, and immune stimulation upon supplementation. Therefore, iodine supplementation in previously iodine deficient areas may be a double edged sword resulting in an increase in autoimmune thyroiditis [24]. Moreover there is increased risk of malignancy in patients of autoimmune thyroiditis. Hence such patients may require long term follow-up [25].

In 87.06% of our patients with autoimmune thyroiditis Anti-TPO was raised. Nearly similar proportion of cases had reported increased Anti-TPO in previous studies [5,16]. Increased Anti-TPO in these patients is serologically indicative of autoimmunity and has good correlation with cytomorphology. Hormonally, most of them (74.11%) were euthyroids, hypothyroidism was present in 21.18%, and hyperthyroidism was observed in only 4.71%. The finding of raised Anti-TPO and euthyroid cases in this study suggests that these cases were towards the early stage of the autoimmune disease [27]. In late phase of autoimmune thyroiditis most of the patient present with hypothyroidism [16]. A community survey also had a similar findings, that 50-75 % of cases with thyroid antibodies were euthyroid biochemically [21].

Only 2.98% of our patients were classified as non-diagnostic or unsatisfactory in present study which is similar to the observations of studies by Chakrabarti PR, *et al.* (1.07%) and Bagg PK, *et al.* (1.6%) [15,27]. Findings of the present study and that of previous studies where cytopathology was also correlated with histopathology indicate that FNAC is a good initial diagnostic test for thyroid swelling.

One of the limitations of our study is that the histopathological finding was not included where surgical intervention was required such as in Bethesda categories III, IV, V and VI.

## Conclusions

The most common observation in this study was colloid goitre, followed by autoimmune thyroiditis. Autoimmune thyroiditis

appears to be more prevalent in this region than in many other states, this may possibly be due to iodine supplementation in previously iodine deficient condition and increased immunogenic predisposition of our population. Serologically Anti-TPO correlated well with cytology in autoimmune thyroiditis. Papillary thyroid carcinoma was the most frequent malignant tumour in this study.

## Bibliography

1. Unnikrishnan AG and Menon UV. "Thyroid disorders in India: An epidemiological perspective". *Indian Journal of Endocrinology and Metabolism* 15 (2011): 78-81.
2. Tamta P, et al. "Cytomorphology of Thyroid Lesions in a Sub Himalayan Tertiary Hospital after More Than Two Decades of Iodization". *Scholars Journal of Applied Medical Sciences* 5.10A (2017): 3872-3879.
3. Bhatia S, et al. "Thyroid swellings- A Common Problem in Hilly Areas". *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)* 13 (2014): 88-90.
4. U Kapil, et al. "Status of iodine deficiency in district Kangra, Himachal Pradesh after 60 years of salt iodization". *European Journal of Clinical Nutrition* 67 (2013): 827-828.
5. Sharma M, et al. "Clinical, biochemical, and cytomorphological profile of lymphocytic thyroiditis: A study from a medical college in the Kangra Valley, India". *Thyroid Research Practice* 16 (2010): 66-70.
6. La Rosa GL, et al. "Evaluation of fine needle aspiration biopsy in preoperative selection of cold thyroid nodules". *Cancer* 67 (1991): 2137-2141.
7. Sclabas GM, et al. "Fine Needle Aspiration thyroid and correlation with histopathology in a contemporary series of 240 patients". *American Journal of Surgery* 186 (2003): 702-710.
8. Hegedus L. "Clinical practice. The thyroid nodule". *The New England Journal of Medicine* 351 (2004): 1764-1771.
9. Cibas ES and Ali SZ. "The Bethesda system for reporting thyroid cytopathology". *American Journal of Clinical Pathology* 132 (2009): 658-663.
10. Srivastava CS and Saxena A. "Study of clinical and epidemiological profile of thyroid swelling". *International Journal of Medical Research and Review* 3.8 (2015): 783-788.
11. Sharma R, et al. "Diagnostic accuracy of fine-needle aspiration cytology of thyroid gland lesions: A study of 200 cases in Himalayan belt". *Journal of Cancer Research and Therapeutics* 13.3 (2017): 451-455.
12. Chandanwale S and Singh N. "Clinicopathological correlation of thyroid nodules". *International Journal Of Pharmaceutical And Bio-Medical Science* 3.3 (2012): 97-102.
13. Likhar KS and Hazari RA. "Diagnostic accuracy of fine needle aspiration cytology in thyroid lesions: A hospital-based study". *Thyroid Research and Practice* 10.2 (2013): 68-71.
14. Dharrao SS and Mahajan SV. "Fine Needle Aspiration Cytological Study of Various Thyroid Lesions and its Clinical Correlation in a Tertiary Health Care Centre - A Prospective Study". *MVP Journal of Medical Sciences* 4.2 (2017): 152-155.
15. Chakrabarti PR, et al. "Trends in Cytomorphological Study of Thyroid lesions: A two year prospective study in the malwa region of central India". *International Journal of Medical Research and Review* 4.3 (2016): 450-455.
16. Anila KR, et al. "Cytomorphologic spectrum of lymphocytic thyroiditis and correlation between cytological grading and biochemical parameters". *Journal of Cytology* 33 (2016): 145-149.
17. Kanukuntla S, et al. "Evaluation of fine needle aspiration cytology of thyroid lesions by Bethesda system and its histopathological correlation". *Indian Journal of Pathology and Oncology* 7 (2020): 273-278.
18. Thakor T, et al. "Cytomorphological study of thyroid lesions using the bethesda system for reporting thyroid cytology and its correlation with Thyroid Function Test". *Journal of Evolution of Medical and Dental Sciences* 9 (2020): 949-952.
19. Kamra HT, et al. "Evaluation profile of thyroid nodule by fnac in the rural population of khandpur kalan, sonapat, Haryana". *Journal of Clinical and Diagnostic Research* 8.10 (2014): FC16-18.
20. Harach HR, et al. "Thyroid carcinoma and thyroiditis in endemic goiter region before and after iodine prophylaxis". *Acta Endocrinology (Copenh)* 108 (1985): 55-60.

21. Dayan CM and Daniels GH. "Chronic autoimmune thyroiditis". *The New England Journal of Medicine* 335 (1996): 99-107.
22. Oechslin E and Hedinger C. "Hashimoto's lymphomatous thyroiditis and endemic struma". *Schweiz Med Wochenschr* 115 (1985): 1182-1191.
23. Boukis MA, et al. "Thyroid hormone and immunological studies in endemic goiter". *The Journal of Clinical Endocrinology and Metabolism* 57 (1983): 859-862.
24. Murphy R, et al. "The Role of Iodine Deficiency and Subsequent Repletion in Autoimmune Thyroid Disease and Thyroid Cancer". *Journal of Restorative Medicine* 5 (2016): 32-38.
25. Gayathri BN, et al. "Fine needle aspiration cytology of Hashimoto's thyroiditis - A diagnostic pitfall with review of literature". *Journal of Cytology* 28 (2011): 210-213.
26. Sood N and Nigam JS. "Correlation of Fine Needle Aspiration Cytology Findings with Thyroid Function Test in Cases of Lymphocytic Thyroiditis". *Journal of Thyroid Research* 2014 (2014): 430510.
27. Bagga PK and Mahajan NC. "Fine needle aspiration cytology of thyroid swellings: How useful and accurate is it?" *Indian Journal of Cancer* 47.4 (2010): 437-442.