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Cytomorphology of Thyroid Lesions in a Sub Himalayan Tertiary Hospital after More Than Two Decades of Iodization

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Original Research Article

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Abstract: Thyroid disorders are one of the commonest endocrinal disorders in the general population. They present with palpable swelling/nodule or may be non-palpable. In the Himalayan goitre belt it is been more than two decades since the Indian Government launched the iodization program in 1986 with the goal of eradicating goitre and Iodine deficient disorders (IDD). In the present study we reviewed 1738 thyroid aspirations performed over a decade .The Bethesda system for reporting thyroid cytology (TBSRTC) was used for categorizing the aspirates. Results showed 76.75% cases in category 2 of Bethesda system. Out of these 69.49% (n= 927) were benign nodules, 29.68% (n=396) were of autoimmune thyroiditis. Out of 927 cases of benign nodule, 62 cases had co-existing thyroiditis. The results clearly show that goitre has not been eradicated contrary to the expectations of the government. FNAC is a cost effective & simple investigation for diagnosing thyroid lesions. Iodine may not be the sole factor in the pathophysiology of goitre. Other goitrogenous food may have a part to play in it. Iodine supplementation as a prophylactic measure for goitre has its own demerits. The substantial number of cases of thyroiditis that emerged in our study clearly indicates that a thorough research regarding any anticipated detrimental side effects must be carried out prior to the implementation for such programs to achieve maximum benefits for the targeted population.
Keywords: Goitre, Iodinization, Thyroiditis.

INTRODUCTION

Thyroid diseases are among the commonest endocrine disorders worldwide. India too, is no exception. According to a projection from various studies on thyroid disease, it has been estimated that about 42 million people in India suffer from thyroid diseases [1]. Early diagnosis and treatment remains the cornerstone of management. Recent population studies have shown that about 12% of adults have a palpable goitre [2]**.** Mountain slopes of the Himalayas, Alps, Pyrenees and Andes have been the most known regions for endemic goitre. Goitre has been recognized in the sub Himalayan region since ancient times. It has been referred in the Atharveda dating back to 2000 B.C. The "Himalaya goitre belt", extending over 2400 kms, is world's biggest goitre belt stretching from Jammu & Kashmir, Himachal Pradesh, Punjab, Haryana, Delhi, Uttar Pradesh, Bihar, West Bengal, Assam, Arunachal Pradesh, Nagaland, Mizoram, Meghalaya, Tripura and Manipur. In the early part of the century late Sir Robert McCarrison carried out pioneering work regarding Himalayan endemic goitre and he focussed not only on the cause but also the reaction of the thyroid to other influences like nutritional, toxic and infective factors [3]. However studies have revealed more areas of goitre prevalence in the Indian subcontinent. Due to the extensive network of rivers in India iodine deficiency affects other parts as well. Several Indian rivers get flooded annually which washes away the soil and leaches away the iodine content. To tackle the problem, the Indian Government in 1983 took a policy decision to iodize edible salt by the year 1992 in the entire country. The programme was started in a phased manner in April 1986. It is now over two decades since the programme was implemented yet only 15% or less of the endemic area has been covered by iodization [4].

Operational difficulties such as inadequate production and difficulty in prevention of sale of uniodized salt in endemic areas resulted in having a little impact on the goitre problem in the country.Thyroid swellings are a significant clinical

problem in the general population but majority of them are non-neoplastic and do not require surgery. Less than 5 % of thyroid nodules are malignant [5]**.** Thyroid surgeries are associated with lifelong thyroid hormones replacement, hypothyroidism and various intra-operative & post-operative risks. If an accurate preoperative diagnosis is made, unnecessary surgery can be avoided in benign conditions. The Bethesda system of thyroid cytology reporting makes the reports clinically relevant and helps the clinicians to take appropriate therapeutic interventions [6]**.** Although a number of tests are now available for thyroid diseases, FNAC in conjugation with ultrasonography is considered as the best initial diagnostic test. It helps to identify the various thyroid lesions with high degree of accuracy. FNAC procedure has an advantage of being simple, safe, speedy, minimally invasive and cost effective and in majority of the cases, it can differentiate neoplastic from nonneoplastic lesions [7]**.**

Our hospital is the only government tertiary care centre offering affordable health care in the Kumaon region. Being ideally located in the foothills of the Himalayas, we have the opportunity of investigating patients presenting with thyroid disorders with and/or without palpable thyroid swelling. This study was conducted to study the cytomorphology of thyroid lesions, according to the Bethesda system, over a period of ten years at our centre.

AIMS & OBJECTIVES

To study the cytomorphology of thyroid lesions according to Bethesda system in a sub Himalayan tertiary care centre of kumaon region of Uttarakhand.

MATERIAL & METHODS

This retroprospective study was carried out in the Department of Pathology, Government Medical College Haldwani (Nainital District) for a period of ten years from 2006-2016. The clinical history and examination were taken from the requisition forms of the patients retrieved from the records of our department. Cases where the reporting had not been done according to the Bethesda system were reviewed and categorized according to the Bethesda system (Table 1).

Table–1: Bethesda reporting system for thyroid lesions

The Bethesda System for Reporting Thyroid Cytopathology:
Recommended Diagnostic Categories*
I. Non-diagnostic or Unsatisfactory-
• Cyst fluid only
• Virtually acellular specimen
• Other (obscuring blood, clotting artifact, etc)
II. Benign-
• Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc)
• Consistent with lymphocytic (Hashimoto) thyroiditis in the proper clinical context
• Consistent with granulomatous (subacute) thyroiditis
• Other
III. Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance
IV. Follicular Neoplasm or Suspicious for a Follicular Neoplasm-
• Specify if Hürthle cell (oncocytic) type
V. Suspicious for Malignancy-
• Suspicious for papillary carcinoma
• Suspicious for medullary carcinoma
• Suspicious for metastatic carcinoma
• Suspicious for lymphoma
• Other
VI. Malignant-
• Papillary thyroid carcinoma
• Poorly differentiated carcinoma
• Medullary thyroid carcinoma
• Undifferentiated (anaplastic) carcinoma
• Squamous cell carcinoma Carcinoma with mixed features (specify)
• Metastatic carcinoma
• Non-Hodgkin lymphoma
• Other *

* Adapted with permission from Ali and Cibas [8].

RESULTS

A total of 1738 aspirations of the thyroid were done during the study period. Their distribution according to Bethesda (Table 2) shows maximum number of cases in Category 2.

A predominance (n=1475) of female patients was observed. Regarding the presentation, we observed that maximum patients came with diffuse swelling (n=1254) in our study.Patients between 30-40 yr of age (n=438) contributed the bulk of the study population Further sub categorization of the individual categories was done according to the cytomorphologic features observed.

Table-2: Bethesda categorization of the thyroid aspirates

Categories	Number of cases
Category 1	341
Categoryt 2	1334
Category 3	0
Category 4	21
Caegoryt5	8
Category 6	34

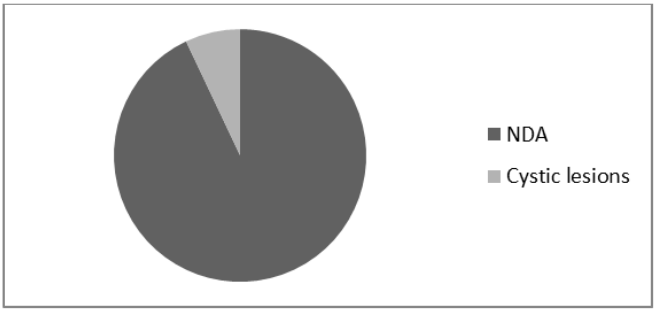

Fig-1: Distribution of lesions in category 1[non diagnostic aspirate (NDA)/unsatisfactory]

In category 1, we had more of non-diagnostic aspirates (n=317) compared to cystic lesions (n=24).

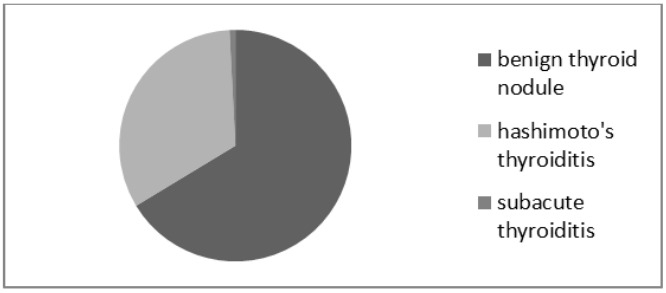

Fig-2: Distribution of lesions in Category 2

In category 2 most of the cases were in the group of benign nodules followed by Hashimoto's thyroiditis (figure 2).

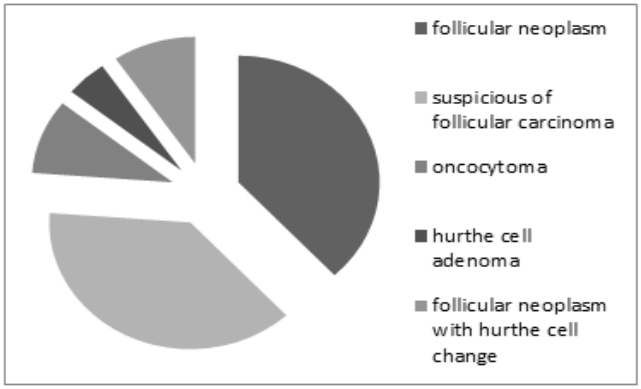

Fig-3: Distribution of lesions in category 4

An equal number of cases were seen of follicular neoplasm and suspicious of follicular neoplasm (n=8) in category 4 (figure 3)

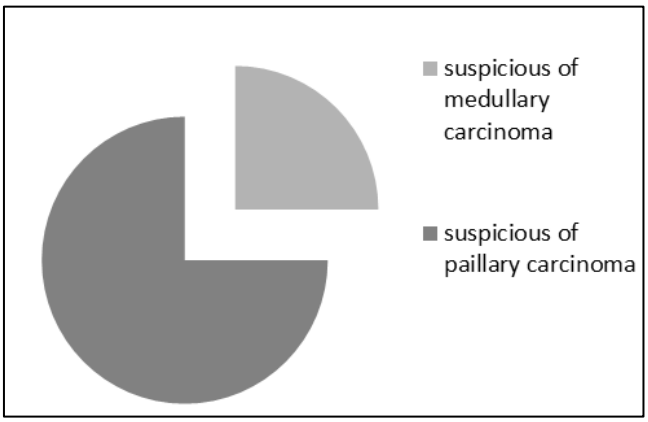

Fig-4: Distribution of cases in Category 5.

Bulk of the cases in category 5 (figure 4) were suspicious of papillary carcinoma (n= 6).

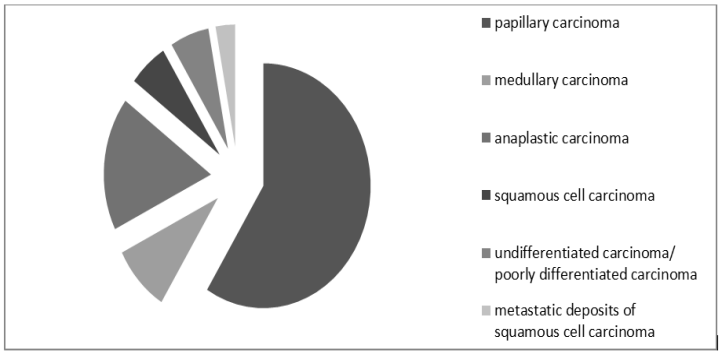

Figure-5: Distribution of cases in Category 6.

In Category 6 again the maximum cases were of Papillary carcinoma (n=20).

Table−3: Cytomorphological Spectrum of thyroid lesions

Category1	Non diagnostic aspirate	317
	Cystic lesions	24
Category2	Nodular goitre	62
	Nodular colloid goitre	184
	Nodular colloid goitre with cystic changes	69
	Nodular colloid goitre with thyroiditis	17
	Nodular goitre with thyroiditis	9
	Nodular colloid goitre with hyperplasia	4
	Nodular colloid goitre with hurthle cell changes	3
	Colloid goitre	271
	Colloid goitre with cystic degeneration	139
	Colloid goitre with thyroiditis	24
	Colloid goitre with adenomatous change	2
	Colloid goitre with cystic degeneration & hurthle cell changes	3
	Multinodular goitre	9
	Multinodular goitre with thyroiditis	4
	Hyperplastic nodule	50
	Solitary nodule	6
	Toxic nodule	2
	Diffuse goitre	35
	Adenomatous goitre	26
	Adenomatous goitre with thyroiditis	8
	Thyroiditis/autoimmune thyroiditis/hashimotos thyroiditis/lymphocytic thyroiditis	396
	Subacute / granulomatous thyroiditis	11
Category 3	-	-
Category4	Follicular neoplasm	8
	Follicular carcinoma	8
	Oncocytoma	2
	Hurthle cell adenoma	1
	Follicular neoplasm with hurthle cell changes	2
Category5	Suspicious for squamous cell carcinoma	2
	Suspicious for medullary carcinoma	2
	Suspicious for papillary carcinoma	4
Category6	Papillary carcinoma	20
	Medullary carcinoma	3
	Anaplastic carcinoma	6
	Squamous cell carcinoma	2
	Undifferentiated/poorly differentiated carcinoma	2
	Metastatic deposits of squamous cell carcinoma	1

DISCUSSION

It has been more than two decades since the Indian government launched the iodization program in 1986. Under the Prevention of Food and Adulteration Act (PFA) 1954, all states and union territories have been advised to ban the sale of unidiozed salt. However, for any community based programme to be successful a prerequisite scientific data base is essential for framing the infrastructure for its effective implementation. The National Goitre Control Board (NGCB) in 1962 launched the National Goitre Control Programme (NGCP) to carry out surveys but they were not successful due to inappropriate and insufficient data. The decision to launch a nationwide iodization programme was seemingly based on conclusions drawn from similar programs launched in other countries with the hope of attaining the same success. Even in the endemic regions there is paucity of data regarding the

actual impact of the program in terms of facts and figures. The prevalence of goitre in India presently is 28.8% [9].

In the present study, 1738 thyroid aspirations were studied. Results showed 76.75% cases in category 2 of Bethesda system which includes benign follicular nodule (adenomatiod nodule, colloid nodule, etc), lymphocytic thyroiditis, granulomatous (subacute) thyroiditis and others. Out of these 69.49% (n= 927) were benign nodules, 29.68% (n=396) were of autoimmune thyroiditis. Out of 927 cases of benign nodule, 62 cases had co-existing thyroiditis. The results clearly show that goitre has not been eradicated contrary to the expectations of the government. The role of cyanogenic food acting as goitrogens which can interfere with iodine nutrition as proposed by Chandra AK may be reason for high number of cases of goitre in our study. Industrial & agricultural contaminants which act as thyroid disruptors may also play a role in etiology of goitre in this region. Farswan A [10] studied the incidence of goitre & other iodine deficient disorders (IDD) in Chamoli district of Garhwal & the results showed less than 0.2% incidence of goitre in the surveyed population which included 11 villages of that region. This is dramatically lesser than the figures reported in other endemic regions, 50% in Shimla, Himanchal Pradesh & North Western Himalaya [11]. 17-73% from school children in Champaran [12]. 25.93% in West Bengal [13] & 34.96% in North East India [14]. The most astonishing fact in the study was that there was no iodine prophylaxis in that region of Garhwal which could explain the low figures. The local inhabitants still continue to consume the crude crystalline non iodized salt. The only explanation that could be given for such an observation is that either they are getting adequate iodine from other food sources or that iodine deficiency is not the only culprit in causing goitre.

We also observed a substantial number of cases of autoimmune thyroiditis. Autoimmune thyroiditis can manifest either as goitrous or non goitrous (atrophic variant). Goitrous autoimmune thyroiditis can itself be a focal or diffuse thyroiditis. Hashimotos thyroiditis reflects the pathological modifications of the gland over a period of time. A cytomorphological diagnosis of Hashimoto thyroiditis is based on the evidence of inflammatory destruction of follicular epithelial cells by the lymphoid cells accompanied with varying degrees of hurthle cell change. Small lymphocytes either isolated or intermingled with the follicular cells are seen along with histiocytes & occasional plasma cells. Stretched lymphocytes may also be seen. The other population of cells are larger lymphocytes & germinal centre cells. Such smears give a “lymph node like” appearance. The population of hurthle cells is variable. In some cases a predominant population of hurthle cells may lead to a false diagnosis of Hurthle cell neoplasm. In such cases the polymorphous population of cells along with the presence of lymphocytes supports the diagnosis of Hashimotos thyroiditis. The lymphoid aggregates may remain as tight groups of cells mimicking a tissue fragment of follicular cells. In such cases the findings may be misinterpreted. The presence of discrete lymphocytes is helpful in such cases. It is important to diagnose Hashimotos thyroiditis as these patients will become hypothyroid over a period of time, as the disease progresses & would therefore require thyroxine supplementation lifelong. Secondly such patients are at a risk to develop extranodal marginal B cell lymphoma & carcinoma, therefore keeping them in follow up is important. A correct cytomorphological diagnosis can avoid unnecessary surgeries under the suspicion that the nodule/swelling maybe malignant. Harach, Dayan, & Oecslin [15-17] have argued in their respective studies that iodine supplementation in iodine deficient population may lead to thyroid autoimmunity. Harach HR [15] also showed in his study that lymphocytic infiltration in thyroid increases 3 folds with iodine supplementations in previously iodine deficient areas. Boukis MA [18] showed that the prevalence of thyroid auto antibody positivity rises to over 40% within 5 years of initiating iodine supplementation. Therefore iodine supplementation in previously iodine deficient areas may be double edged sword.

The difference between the serological & cytomorphological criteria for diagnosis of Hashimotos thyroiditis has frequently been the topic of controversy. It has been observed that the TMA positivity may differ in goitrous & non goitrous subjects both in terms of titre & prevalence [9]. The possible explanation for the discrepancy between the cytomorphological features & serological titres was that the antibody production is limited to the intrathyroid lymphocytes only [19]. Roth *et al*, Dorose et al and Poropatch *et al.* [20-22] also reported similar findings. Furthermore, the antibody titre changes during the course of the disease but cytomorphological features tend to persist. This further supports the fact that Hashimotos thyroiditis should not be diagnosed on the basis of serology alone and cytomorphological features should be taken into consideration.

Our study showed a predominance of non-neoplastic lesions. Our results were in agreement with other similar studies conducted (Table 4) i.e. more number of non-neoplastic as compared to neoplastic lesions.

Table-4: Comparison with other similar studies

Study names	Non-neoplastic	Neoplastic
Uma H *et al.* (2008)	381	31
Sengupta *et al.* (2011)	148	30
Sathiyamurthy et al (2014)	100	10
Gogoi G *et al.* (2016)	97	12
Chakrabarti P (2016)	161	23
Our study	1371	40

Malignant thyroid lesions were seen in only 1.96 % of the cases (n=34). This is much lower in comparison to studies conducted at other tertiary care hospitals, 4.31%, 3.361%, 2.15%, and 16.1% by Gogoi G *et al*, Bhatiya R *et al*, Chakrabarti PR *et al*, Kartha P *et al*. respectively [23-26]. Jo *et al.* [27] has explained that studies which are usually carried out at tertiary care centres for thyroid lesions do not actually reflect the general population as they are dealing with referred patients. Thus it is likely that the figures for malignant thyroid lesions are an over representation of the malignant cases in the population. In our study, though we are tertiary care hospital, we get both referred patients as well as those who come directly. Therefore we observed a high number of benign lesions. The low cost of investigations & cost free services for below poverty line patients gives us access to a large population of patients at our centre. This allows us to observe a spectrum of cytomorphological features of thyroid lesion.

CONCLUSION

FNAC is a cost effective, simple investigation for diagnosing thyroid lesions, especially in Hashimoto's thyroiditis which may present as non-palpable lesion. In the palpable swellings, an accurate cytological diagnosis can avoid unnecessary biopsy.

Iodine may not be the sole factor in the pathophysiology of goitre. Other goitrogenous food may have a part to play in it. Iodine supplementation as a prophylactic measure for goitre has its own demerits. The substantial number of cases of thyroiditis that emerged in our study clearly indicates that a thorough research regarding any anticipated detrimental side effects must be carried out prior to the implementation for such programs to achieve maximum benefits for the targeted population.

LIMITATIONS OF THE STUDY

The diagnosis of autoimmune/Hashimoto's thyroiditis was made on cytomorphological features only. Hashimoto's per se is not an indication for lobectomy or thyroidectomy therefore a histological correlation was not possible in majority of the cases. The antibody titres are not routinely available in our practice, limiting the serologic correlation as well.

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