INTERNATIONAL JOURNAL OF MEDICAL AND APPLIED SCIENCES
eISSN:2320-3137
Earthjournals Publisher
www.earthjournals.in

RESEARCH ARTICLE

BETHESDA CLASSIFICATION OF BENIGN THYROID LESIONS IN CORRELATION WITH RADIOLOGY, THYROID FUNCTION TESTS AND ANTI TPO ANTIBODY

ISLAM A[1], MONDAL M[1], KUMAR N[2], CHANGAVI A[3]

1. DEMONSTRATOR, DEPT OF PATHOLOGY, IPGMER & SSKM HOSPITAL, KOLKATA.

2. SENIOR RESIDENT, DEPT OF SURGERY, ESI HOSPITAL, NEW DELHI

3. ASSCOCIATE PROFESSOR, DEPT OF PATHOLOGY, SSMCH, TUMKUR, KARNATAKA

Corresponding author: DR. AYESHA AFREEN ISLAM, 36 A DR. SUDHIR BASU ROAD. KAISER COURT, FLAT NO 12. KOLKATA 700023.

Publication history: Received on 28/09/2016, Published online 15/01/2017

ABSTRACT:

Diseases of the thyroid gland usually result in thyroid enlargement (goitre) which can be due to infections, cystic changes, auto immune diseases and iodine deficiency leading to hyperplasia and neoplasia with or without thyroid dysfunction. Yet, the majority of thyroid nodules are asymptomatic and benign, so the thyroid surgeon must rely on diagnostic studies to determine when surgery is indicated. Nodules are typically found on physical exam or incidentally when other imaging studies are performed. The use of high-resolution ultrasonography (US), sensitive thyrotropin (TSH) assay, and fine-needle aspiration FNA) biopsy is the basis for management of thyroid nodules. Measurement of serum TSH is the best initial laboratory test of thyroid function and should be followed by measurement of free thyroxine and triiodothyronine if the TSH value is decreased, and measurement of anti–thyroid peroxidase antibodies (TPO Ab) if the TSH value is above the reference range. Patients with benign thyroid nodules should undergo clinical and US follow-up. Symptomatic goitres, whether euthyroid or hyperthyroid, may be treated surgically or with radioiodine.

KEY WORDS: Bethesda, thyroid, biochemical status, radioimaging.

INTRODUCTION

Thyroid nodules present a challenge in their diagnosis, evaluation, and management (1). The prevalence of these nodules in a given population depends on a number of factors like age, sex, diet, iodine deficiency, and even therapeutic and environmental radiation exposure. True solitary thyroid nodules (STN) occur in 4 - 7% of the adult population. They are present in 5% of persons at an average of 60 years (1). They are more common in females (6.4%) as compared to males (1.5%) and this predisposition exists throughout all age groups (1). Nodules are typically found on physical examination or incidentally when other imaging studies are performed (2). The use of high-resolution ultrasonography (US), sensitive thyrotropin (TSH) assay, and fine-needle aspiration

(FNA) study is the basis for management of thyroid nodules (2). Ultrasound can determine what nodules should be biopsied. To substantiate the diagnosis of FNA, patient should always be evaluated for the status of thyroid function by performing the thyroid function tests (TSH, T3 and T4) (3). With the availability of highly sensitive TSH assays, it is possible to detect subtle thyroid dysfunction with this test alone (2). If the TSH is abnormal, free thyroid hormones and thyroid antibodies should be the next investigations (4). A thyroid antibody such as thyroid peroxidase (TPO) is found in patients with Grave's disease and Hashimoto's thyroiditis (HT) (3). TSH receptor antibodies are detectable in majority of patients with Grave's disease (3). Most (90%) thyroid nodules are benign and under the Bethesda cytological classification can be classified as colloid nodules, cysts, infectious nodules, lymphocytic or granulomatous nodules, hyper plastic nodules, thyroiditis, congenital abnormalities (1).

OBJECTIVE OF STUDY:

1. To study the correlation of benign thyroid lesions as per Bethesda classification, with biochemical profile.
2. To correlate the cytological diagnosis with radiological findings.
3. To differentiate autoimmune thyroiditis from other thyroiditis based on anti TPO antibody.

MATERIAL AND METHODS:

A cross sectional study was conducted at the Sri Siddhartha Medical College and Research Centre, Tumkur, Karnataka. The study was conducted over a period of 24 months, from January 2012 to December 2014. Study was conducted on 280 patients. Patients presenting with thyroid swelling having undergone Fine Needle Aspiration study and diagnosed as benign lesion on cytology were included in the present study. Each patient was carefully clinically examined and the age, sex and presenting complaints were taken in detail. A thorough examination of the thyroid swelling was done, the USG findings were noted, followed by Fine Needle Aspiration of the thyroid swelling. Thyroid function tests were done in all the cases. Anti TPO profile was studied where ever necessary.

RESULT:

A Cross sectional study was conducted at the Sri Siddhartha Medical College, Tumkur, Karnataka, from January 2012 to December 2014.
280 patients with thyroid swelling reported as benign thyroid lesion on Fine Needle Aspiration were included in the study. Clinical data regarding age, sex and presenting complaints were taken in detail. A thorough examination of the thyroid swelling was done which was correlated with biochemical and radiological findings followed by Fine Needle Aspiration of the thyroid swelling.

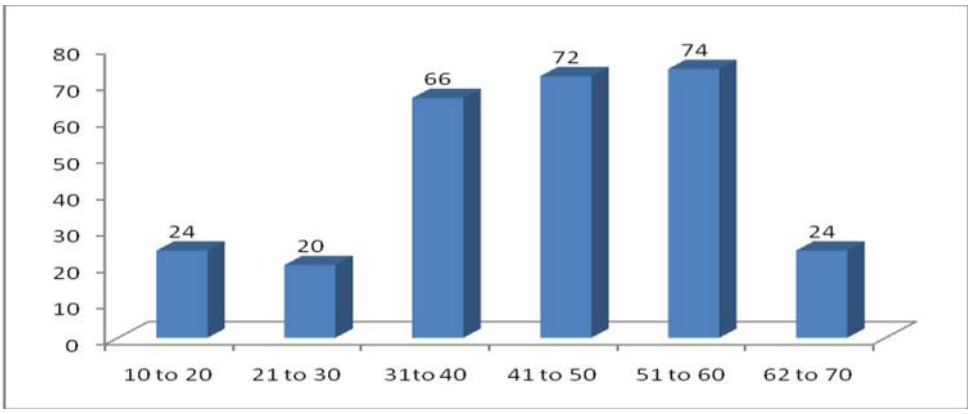
The benign cases were classified as per Bethesda system:

- Colloid Goitre
- Hyperplastic nodule

- Adenomatoid Goitre
- Lymphocytic thyroiditis (Hashimotos')
- Granulomatous thyroiditis.

Among 280 patients, age of the patients ranged from 15 to 70 years. Age distribution for females in ranged from 15- 60 yrs. Age distribution for males ranged from 35-70 yrs.

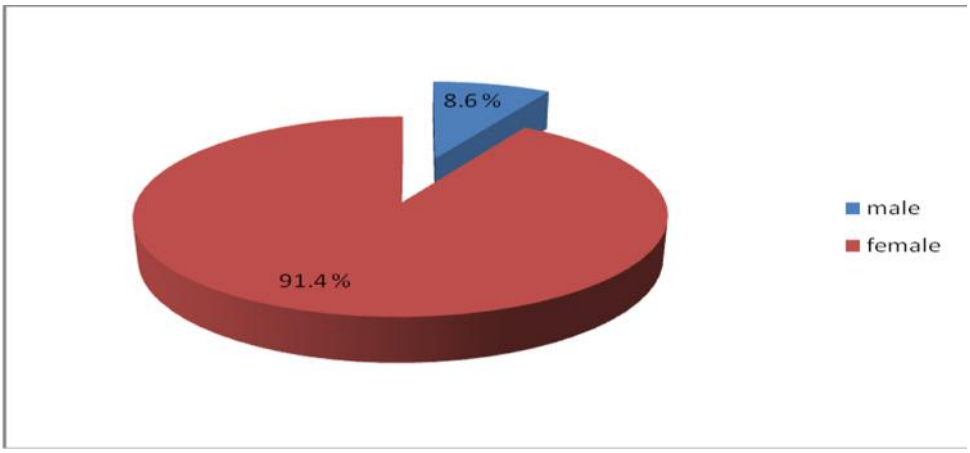
Fig 1: Age distribution of thyroid lesions



In the present study, thyroid lesions were found to be more predominant in the age group of 30 to 60 yrs.

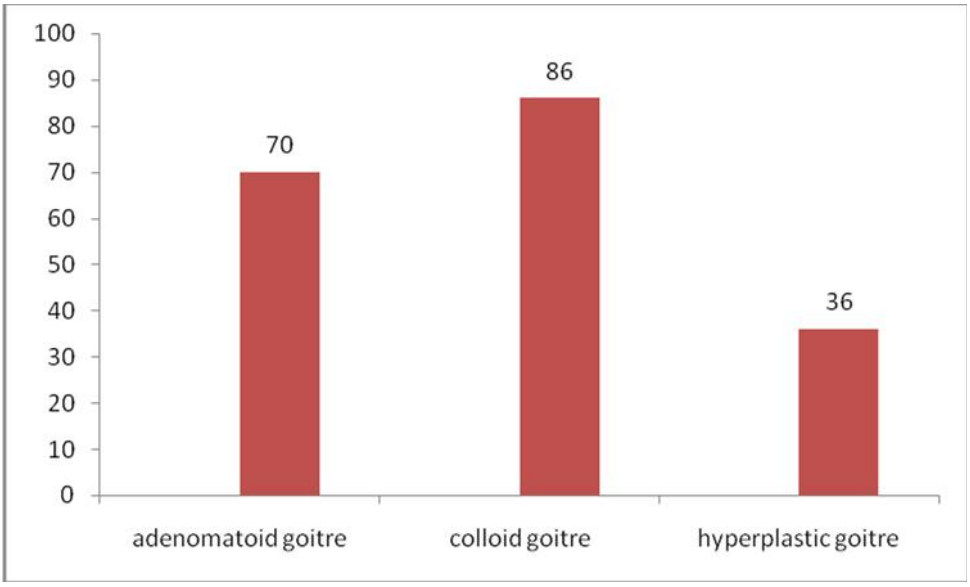
Clinically 168 patients out of the 280 (60%) with diffuse swelling of the thyroid. Among those presenting with nodular swelling mean size of nodule ranged from 3mm to 7mm on radiology.

Fig 2: Sex distribution of benign thyroid lesions (%):



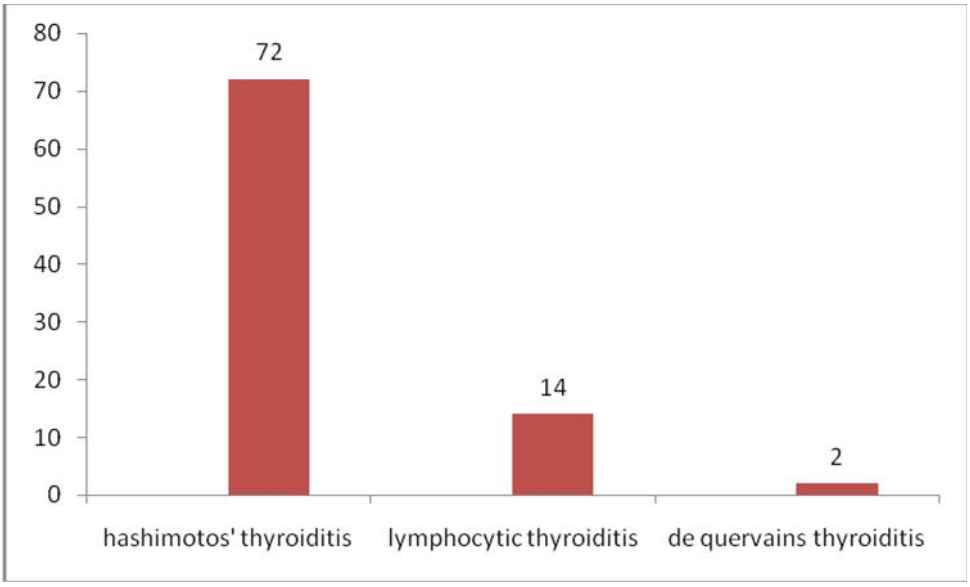
Female preponderance with an incidence of 91.4% was seen in all cases of benign thyroid nodule.

Fig 3: Incidence of Goitre on FNA (no. Of cases):



Goitre was found to be 68.57% of all benign thyroid lesions.

Fig 4: Incidence of Thyroiditis on FNA (no. Of cases):



Incidence of thyroiditis was 31.43%.

TABLE 1: Correlation of the benign thyroid lesions with thyroid function tests:

Lesion	Euthyroid	Hypothyroid	Subclinical Hypothyroid	Hyperthyroid	Subclinical Hyperthyroid
Colloid Goitre (86)	66(76.74%)	11(12.80%)	05(5.8%)	__	___
Hyperplastic goitre (36)	__	__	__	33(91.67%)	03(08.33%)
Adenomatoid goitre (70)	45(64.29%)	10(14.29%)	13(18.57%)	__	02(2.86%)
Lymphocytic thyroiditis(14)	09 (64.29%)	__	__	03 (21.43%)	02 (14.29%)
Hashimotos' thyroiditis (72)	30(41.67%)	33(45.83%)	05(6.94%)	__	__
De quervains' thyroiditis (2)	___	___	___	02(100%)	___

TABLE 2: Correlation of thyroiditis with antibodies (anti TPO)

Lesion	Anti TPO status	%(percentage)
Hashimotos' thyroiditis(72)	Positive (72)	100%
Lymphocytic thyroiditis(14)	Positive (3)	21.43%
de quervains' thyroiditis (2)	negative	zero

Cases reported as Hashimotos' thyroiditis, all patients had raised Anti TPO antibodies proving its autoimmune origin. Three out of the 14 cases of lymphocytic thyroiditis were positive for anti TPO. These cases were retrospectively diagnosed as Hashimotos thyroiditis and treated for the same. Cases of de quervains thyroiditis and lymphocytic thyroiditis were negative for anti TPO which proved its non autoimmune origin.

TABLE 3: Correlation of clinical and cytology with radiological findings for Goitre.

No. Of cases	Clinical findings	USG Diagnosis	Cytology findings (on USG guided/ superficial FNA)	USG Correlation with clinical finding.	USG correlation with cytology
25	No Palpable swelling	Nodular goitre	colloid goitre	zero	100%
80	Diffuse swelling	Colloid goitre	Colloid goitre	100%	100%
40	Single nodular swelling	nodular colloid goitre	colloid goitre	90% (4 cases showed increased no. Of nodules on USG)	100%
47	Multiple nodular swellings	Multi nodular goitre	Nodular colloid goitre	76.6% (11 cases on USG showed increased no. Of nodules)	100%

Clinically 39 cases out of the 88 cases of thyroiditis were given a diagnosis of Goitre. Two cases of de quervains thyroiditis were diagnosed as Hyperplastic nodule. Out of the 88 cases of thyroiditis, the radiological diagnosis of 75 cases was of thyroiditis showing a correlation of 85.23%. Specifically type of thyroiditis was not possible on radiology. The other cases were reported as Goitre.

TABLE 4: Laterality of thyroid nodule.

Diagnosis	Right lobe	Left lobe	Isthmus
Colloid nodule	44	35	07
Hyperplastic nodule	15	10	11
Adenomatoid nodule	53	15	02

In the present study we found preponderance of benign thyroid nodule in the right lobe of the thyroid.

DISCUSSION:

Clinical examination, ultrasound finding and thyroid hormone status, followed by Fine needle aspiration study together are essential to treat a patient with thyroid enlargement. FNA has allowed a dramatic decrease in surgical treatment of patients with thyroid nodular disease, enhancing the percentage of malignant operated nodules over 50% (5).In the present study we have made an attempt to find the correlation between FNA findings of benign thyroid lesions, radiological findings and thyroid function tests with special reference to anti thyroid antibodies in autoimmune thyroiditis.

TABLE 4: Comparison of sex distribution in other studies with present study.

Authors	Total cases	Male	Female	M:F
Korah et al (6)(2005)	100	20	80	1:4
Handa et al (7)(2008)	434	151	273	1:6.4
Taddesse et al (8)(2011)	104	14	90	1:6.4
Rahman et al (5)(2011)	50	8	42	1:5.3
Present study	280	13	137	1:10.6

Female preponderance was seen in our study which was comparable to the studies by Rahman et al and others.

TABLE 5: Comparison of the distribution of Non Neoplastic lesions.

Lesion	Korah et al (6) (Total cases:100)	Handa et al(7) (Total cases: 434)	Rahman et al (5) (Total cases: 100)	Present study (Total cases: 280)
Goitre	60	250	45	192
Hashimoto's thyroiditis	8	109	05	72
Other thyroiditis	1	10	0	16

Colloid goitre was the commonest lesion (including hyper plastic goitre and goitre with secondary changes). Cytology showed benign follicular epithelial cells in singles and clusters with a background of colloid and in some cases even cyst macrophages.

Oxyphilic cells with abundant pale basophilic cytoplasm were seen in cases of goitre with hurthle cell change. The cytological features were comparable with the studies done by Handa et al and others in their respective studies. The diagnostic evaluation of patients with MNG should involve the exclusion of malignancy by assessment of thyroid function, the estimation of goitre size and evaluation of local symptoms (5). FNAC should be included in the initial diagnostic procedures for evaluation of clinically suspected MNG (11).

TABLE 6: Comparison of TPO antibodies in Hashimotos thyroiditis.

Study	**Total cases of Thyroiditis (on cytology)**	**Total cases of Hashimotos thyroiditis (on cytology)**	**Significant findings of Anti TPO antibody titre.**
Shinto et al (12) (2010)	100	89	Positive in 89 patients.
Kandi et al (13) (2012)	110	88	80% (88 cases) were positive
Staii et al (14) (2012)	102	91	89.2% (91 cases) were positive.
Present study	88	72	Positive in 75 cases.

Anti TPO antibodies were raised in cases of Hashimoto's thyroiditis which was comparable to all the other studies done by Shinto et al and others. Cytology showed follicular epithelial cells and Hurthle cells in a background of abundant lymphocytes, some of them clinging to the follicular cells and occasional giant cells. The FNA features were similar to the findings of Maia et al and others. Cytology of other thyroiditis predominantly lacked features of follicular destruction. Lymphocytic Thyroiditis, granulomatous thyroiditis and other thyroiditis were negative for TPO antibodies confirming its non immune origin. In the present study 3 out of the 14 cases of lymphocytic thyroiditis (diagnosed on FNA) were positive for anti TPO. These cases were retrospectively diagnosed as Hashimotos thyroiditis and treated for the same.

Thyroid ultrasound is used to evaluate index of nodule size, location, characteristics, number and presence of additional thyroid nodules and to detect suspicious appearance of lymph nodes. Patients with multiple thyroid nodules have the same risk of malignancy as those with solitary nodules. It is recommended that all patients with nodular thyroid glands should be submitted to US evaluation (10).

The position, shape, size, margins, content, echogenic pattern and vascular features of the nodules can be described. A pure cystic nodule or a nodule with spongiform appearance, defined as an aggregation of multiple micro cystic components in more than 50% of the nodule volume, is specific for identification of benign thyroid nodule (15).

The reported specificities for predicting malignancy are marked hypo echogenicity compared to normal thyroid parenchyma, micro calcifications, irregular or micro lobulated margins, and increased intra nodular vascularity. On Gray scale radiology, thyroidits shows features such diffuse enlargement , marked hypervascularity and heterogenous appearance. Presence of discrete hypoechoic micronodules is stongly suggestive of chronic thyroiditis. Hashimotos thyroidits, De quervains thyroidits, Graves disease have similar sonographic features with different biochemical profile and clinical presentation (15).

Lay field et al and Pacini et al, in their respective studies have advocated ultrasound guided Fine needle aspiration for thyroid nodules. Retrospective studies have reported lower rates of non diagnostic and false –negative cytology specimens from FNA performed by US guidance compared to palpation (3).

CONCLUSION:

Clinical examination, ultrasonography, hormonal status and fine needle aspiration cytology, together helps in the accurate diagnosis of thyroid lesions. Females are most commonly affected. The most common age group is 4th, 5th and 6th decade. Among the benign lesions (as per Bethesda) Colloid goitre was the most common lesion followed by Hashimotos' thyroiditis and Adenomatoid goitre. On cytology goitre showed thick colloid as homogeneous material with cracking artefacts. Goitre with secondary changes like cystic degeneration showed abundant foamy macrophages and clusters of Hurthle cells without any inflammatory infiltrate. Hyper plastic goitre showed increased cellularity with large clusters of hyper plastic follicular cells showing prominent anisonucleosis and abundant cytoplasm.

Colloid goitre and Adenomatoid goitre predominantly presented with euthyroid status and Hypothyroidism was seen in majority of cases with Hashimotos' thyroiditis. Hyperthyroid and subclinical hyperthyroid status was seen in cases of Hyperplastic goitre which presented with symptoms like proptosis, palpitations and tremors. Among other thyroiditis cases lymphocytic thyroiditis was predominantly euthyroid in contrast with hypothyroid status of HT. Anti TPO antibodies were distinctly positive for Hashimotos' thyroiditis and negative in others, indicating its autoimmune origin. Cytology of HT showed features of follicular destruction.

REFERENCES:

1. Neki NS, Kazal HL. Solitary thyroid nodule: An insight. Journal, Indian academy of clinical medicine 2006;7(4): 328-33.
2. Gharib H, Papini E et al. American association of endocrinologist, associazione medici endocrinology and European thyroid association medical guidelines for clinical practise for the diagnosis and management of thyroid nodules. Endocrine practice 2010;16(1): 63-102.
3. Joshi S R. Laboratory Evaluation of Thyroid Function. Journal of the Association of Physicians of India 2011; 59:14-20.
4. Hughes K. Goitre: causes, investigation and management. Australian family physician 2012;41(8): 572-76.
5. Rahman MM. Biochemical status and cytopathology of patients with multinodular goitre. Journal of Medicine 2011; 12:26-29

6. Korah T, Habashi A E.Clinical Utility of Fine Needle Aspiration Cytology for Thyroid Lesions with Emphasis on Hashimotos' Thyroiditis. Journal of Medical Research Institute 2005; 26(4):356-362.
7. Handa U, Garg S, Mohan H, Nagarkar N. Role of fine needle aspiration cytology in diagnosis and management of thyroid lesions: A study of 434 patients. J Cytol 2008; 25:13-17.
8. Taddesse A, Yaqub A. Clinical, sonographic and cytological evaluation of small versus large thyroid nodules. JPMA 2011; 61:466.
9. Thoresen A, Schofield K M et al. The Bethesda Thyroid Fine-Needle Aspiration classification System: Year 1 at an Academic Institution. Thyroid 2009; 19(11).
10. Pacini F et al. European Consensus for the management of patients with differentiated thyroid carcinoma of follicular epithelium. European journal of Endocrinology 2006; 154:787-803.
11. Tamhane S, Gharib H. Thyroid nodules update in diagnosis and Management. Clinical Diabetes and Endocrinology 2015;1:11.
12. Shinto A et al. Prevalence of Antithyroid Antibodies in Histologically Proven Autoimmune Thyroid Diseases and Correlation with Thyroid Dysfunction in South India. Thyroid Science 2010; 5(9):1-5.
13. Staii A et al. Hashimoto thyroiditis is more frequent than expected when diagnosed by cytology which uncovers a pre-clinical state. Thyroid Research 2010, 3:11.
14. Kandi S, Rao P. Anti-thyroid peroxidise antibodies its effect on thyroid and breast tissue. Ann Trop Med Pub Health 2012; 5:1-2.
15. Choudhury V, Bano S. Thyroid Ultrasound. Indian journal of endocrinology 2013;17(2):219-227.
16. Bomeli SR et al . Evaluation of thyroid nodule. Otolaryngol Clin North Am. 2010 April ; 43(2): 229–238.

Paper cited as: ISLAM A, MONDAL M, KUMAR N, CHANGAVI A.BETHESDA CLASSIFICATION OF BENIGN THYROID LESIONS IN CORRELATION WITH RADIOLOGY, THYROID FUNCTION TESTS AND ANTI TPO ANTIBODY. International Journal of Medical and Applied Sciences, 5(4), 2016, pp.53-62.