

A Study of fine needle aspiration of thyroid lesion by the 2017 Bethesda system for reporting thyroid cytopathology and their correlation with thyroid function test - A prospective study

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Abstract

Introduction: Fine needle aspiration cytology is initial investigation for the diagnosis of thyroid lesions. The revised 2017 Bethesda system for reporting thyroid cytopathology provides a category based reporting system for FNAC of thyroid lesions. Thyroid function test also plays important role to manage patients. The present study was undertaken to categorise all the thyroid lesions according to Bethesda system into 6 categories and correlate with Thyroid function test. **Material and Methods:** The study period was from January 2020 to June 2021. During the study period, a total of 100 cases of thyroid fine needle aspirations were collected and categorized according to "The 2017 Bethesda System for Reporting Thyroid Cytopathology". It was easy to classify the result in 6 categories. Later these cases were followed up with their thyroid profile test. **Result:** A total of 100 cases were studied, out of which 83 patients were females and 17 were males, with Female to Male ratio of 4.8:1. with a mean age of 35.96 years. Among 100 cases, non neoplastic category II lesions were the major proportion constituting 79%, category I unsatisfactory smears were 1%, category III 0%, next highest percentage of cases were in category IV with 14%, category V had 1% cases and category VI had 5% of cases. Patients with hypothyroid were 23%, patients with euthyroid were 68% and 9% patients were in hyperthyroid condition. **Conclusion:** The revised 2017 Bethesda system is an excellent reporting system for thyroid FNA. Both Bethesda categories and TFT are independent variables and there is no correlation between them

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Introduction

It is estimated that about 42 million people in India suffer from thyroid disorders but the frequency of thyroid cancer is only 1 per lakh population for male and 1.8 per lakh population for females[1].

Thyroid carcinoma is the most common endocrine malignancy[2].

Fine needle aspiration cytology is gold standard of all the investigations and the initial investigation for the diagnosis of thyroid lesions. FNA biopsy cytology can be used to diagnose carcinoma, metastatic malignancy, thyroiditis, benign nodular goitres and cyst. The most frequent indication for thyroid FNA is in the evaluation of a solitary thyroid nodule or dominant nodule in the context of a nodular goitre. It is most cost-effective minimally invasive and safe method to diagnose thyroid lesions. There are no contraindications to thyroid FNA. When it is combined with ultrasonography findings and thyroid function test, the accuracy of diagnosis improves greatly[3]. It can effectively categorise patients with neoplastic and non-neoplastic thyroid nodules as whether they require surgery or not. In majority of cases FNAC helps to reduce unwanted surgeries by identifying a substantial proportion of thyroid nodules as benign.

However due to lack of a standardized system of reporting, pathologists were using different types of terminologies and classification. This created confusion among clinicians in the correct interpretation of the report and it makes further management difficult. Thyroid.

FNA smear reported using the Bethesda system helped in achieving more accurate cytological diagnosis.

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The Bethesda system for reporting thyroid cytopathology (TBSRTC) has been widely adopted in the United States and in many countries worldwide and has been endorsed by the American Thyroid Association.

The revised 2017 Bethesda system for reporting thyroid cytopathology provides a standardized category based reporting system for FNAC of thyroid lesions. It is simple and convenient method which classifies cytology smears into 6 categories viz:

- 1). Non diagnostic or unsatisfactory,
- 2). Benign,
- 3). Atypia of undetermined significance or follicular lesion of undetermined significance,
- 4). Follicular neoplasm or suspicious for a follicular neoplasm,
- 5). Suspicious for malignancy,
- 6). Malignant.

Each of these categories have its malignancy risk and management guideline[4,5].

Material and Method

All the patients with thyroid lesion coming to cytology section of department of Pathology G.R. Medical College & J.A. Group of Hospitals, Gwalior for FNAC between January 2020 to June 2021 were included in this study. It is a prospective study. A total of 100 cases were studied. Patients with neck masses which are not originating from thyroid, like Parathyroid cyst, Branchial cyst and Thyroglossal cyst and patient with palpable anterior midline swelling which is subcutaneous and not moving with deglutition, were excluded in this study.

After taking written consent from patient for FNAC, nodule will be examined. Under aseptic conditions with direct supervision using by needle 22-27 gauge which inserted into lesion with several short rapid strokes made in different directions with the needle tip in the nodule.

In case of unsatisfactory smears FNAC is repeated. The smear is immediately spread onto glass slides, air dried smears stained with Giemsa and smears are fixed in 95% ethanol, stained with Papanicolaou stain (Rapid PAP method). The smear will be observed under microscope and categorized according to The 2017 Bethesda system for reporting thyroid cytopathology. Thyroid function test will also be performed in same patients by chemiluminescence method using machine Snibe Maglumi 800. Association with neoplastic and non- neoplastic lesion will be analyzed and compared with cytopathology result of patient.

Reference values for Thyroid Function Test T3- 0.69-2.15 ng/ml, T4- 52-127ng/ml, TSH- 0.3-4.5miu/ml.

Results

In this study there were 100 cases of thyroid fine needle aspirations were collected and categorized according to “The 2017 Bethesda system for reporting thyroid cytopathology”, and it was correlated with their Thyroid function test.

Patients with thyroid lesions in this study ranged from 18 years to 70 years. With the mean Age (Years) was 35.96 ± 12.41.

Distribution of patients according to age (N=100)

47 (47.0%) of the participants were of Age: 18-30 Years. 19 (19.0%) of the participants were of Age: 31-40 Years. 22 (22.0%) of the participants were of Age: 41-50 Years. 10 (10.0%) of the participants were of Age: 51-60 Years. 2 (2.0%) of the participants are of Age: 61-70 Years.

The mean (SD) of Age (Years) was 35.96 (12.41). The median (IQR) of Age (Years) was 35.00 (25-45). The Age (Years) range from 18 - 70.

Distribution of the Participants in Terms of Gender (n = 100)

Out of the 100 patients with thyroid lesions 83 were females and 17 were males. Female to male ratio is 4.8:1. The youngest patient was 18 years old female and the eldest was 70 year old male.

Comment

17.0% of the participants are Male. 83.0% of the participants are Female.

Distribution of patients according to Adequacy rates in cytology (N=100)

Out of 100 FNACs, only one aspirate was inadequate for cytological evaluation, hence that was labelled as unsatisfactory smears. That was categorized into category I of The Bethesda system.

The unsatisfactory smears had less than six clusters of follicular cells containing less than ten cells per cluster in a single smear.

The adequacy rate in our institution was 99%, the reason behind this high adequacy rate as we performed multiple passes to obtain sufficient material, repeat FNAs in inadequate aspirates and if necessary FNAs are performed with ultrasound guidance.

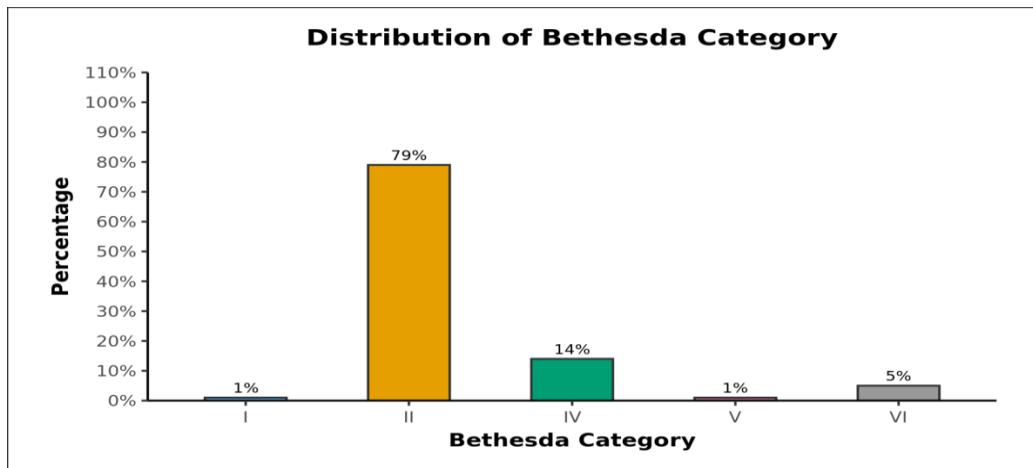
Distribution of lesions

The Fine needle aspiration smears which were adequate for evaluation were categorized into non neoplastic and neoplastic lesions.

The non neoplastic lesions which included colloid goitre, colloid goitre with cystic degeneration, and thyroiditis. They come under category II of The Bethesda system. The non neoplastic lesions constituted the major proportion 79%.

The neoplastic lesions comprise of, “Follicular neoplasm or suspicious for follicular neoplasm and follicular carcinoma, “suspicious of papillary carcinoma”, and “malignancy.

Among 100 cases, non neoplastic category II lesions were the major proportion constituting 79%, category I unsatisfactory smears were 1%, category III 0%, next highest percentage of cases were in category IV with 14%, category V had 1% cases and category VI had 5% of cases.



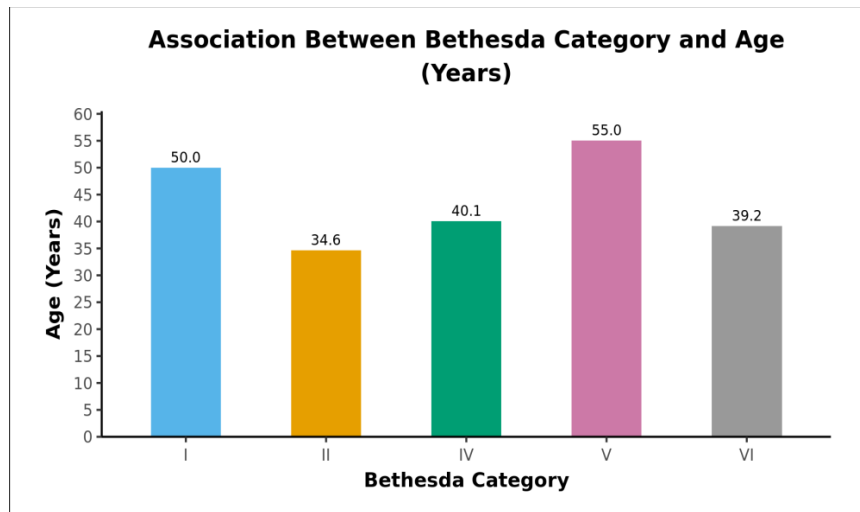
Distribution of the patients according Bethesda category

Association between Bethesda Category and different age groups

Age groups	Bethesda Category					P-value
	I n (1)	II n (79)	IV n (14)	V n (1)	VI n (5)	
18-30 years	0 (0.0%)	40 (50.6%)	4 (28.6%)	0 (0.0%)	3 (60.0%)	0.132
31-40 years	0 (0.0%)	14 (17.7%)	5 (35.7%)	0 (0.0%)	0 (0.0%)	
41-50 years	1 (100.0%)	18 (22.8%)	2 (14.3%)	0 (0.0%)	1 (20.0%)	
51-60 years	0 (0.0%)	6 (7.6%)	2 (14.3%)	1 (100.0%)	1 (20.0%)	
61-70 years	0 (0.0%)	1 (1.3%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	

Comment

Not significantly associated (P-value >0.005).



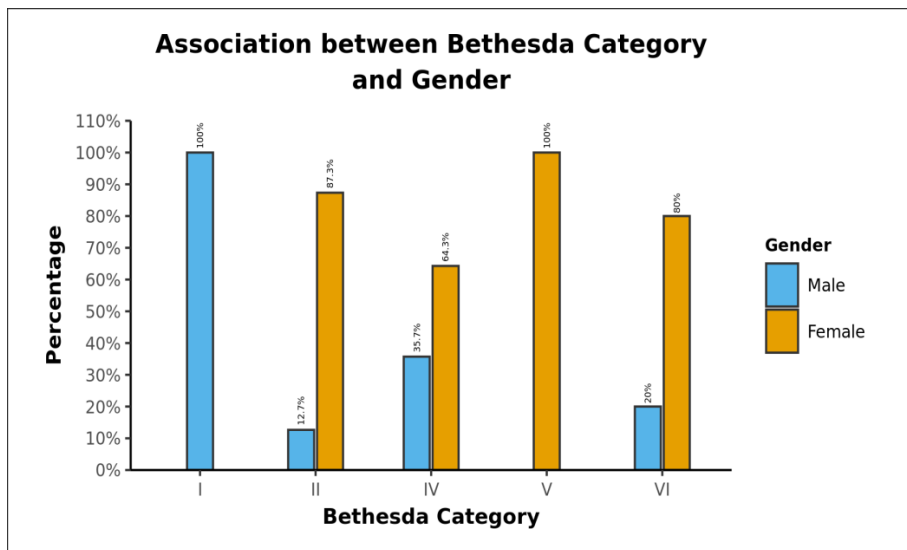
Association between Bethesda Category and different age groups

Association between Bethesda Category and Gender

Sex	Bethesda Category					Total	P-value
	I	II	IV	V	VI		
Male	1 (100.0%)	10 (12.7%)	5 (35.7%)	0 (0.0%)	1 (20.0%)	17 (17.0%)	0.044
Female	0 (0.0%)	69 (87.3%)	9 (64.3%)	1 (100.0%)	4 (80.0%)	83 (83.0%)	
Total	1 (100.0%)	79 (100.0%)	14 (100.0%)	1 (100.0%)	5 (100.0%)	100 (100.0%)	

Comment

Gender is significantly associated (p<0.05) with the variable Bethesda Categories.



Association between Bethesda Category and Gender

Distribution of the Participants in Terms of Diagnosis of Thyroid Profile Test (n = 100)

Patients with hypothyroid were 23%, patients with euthyroid were 68% and 9% patients were in hyperthyroid condition.

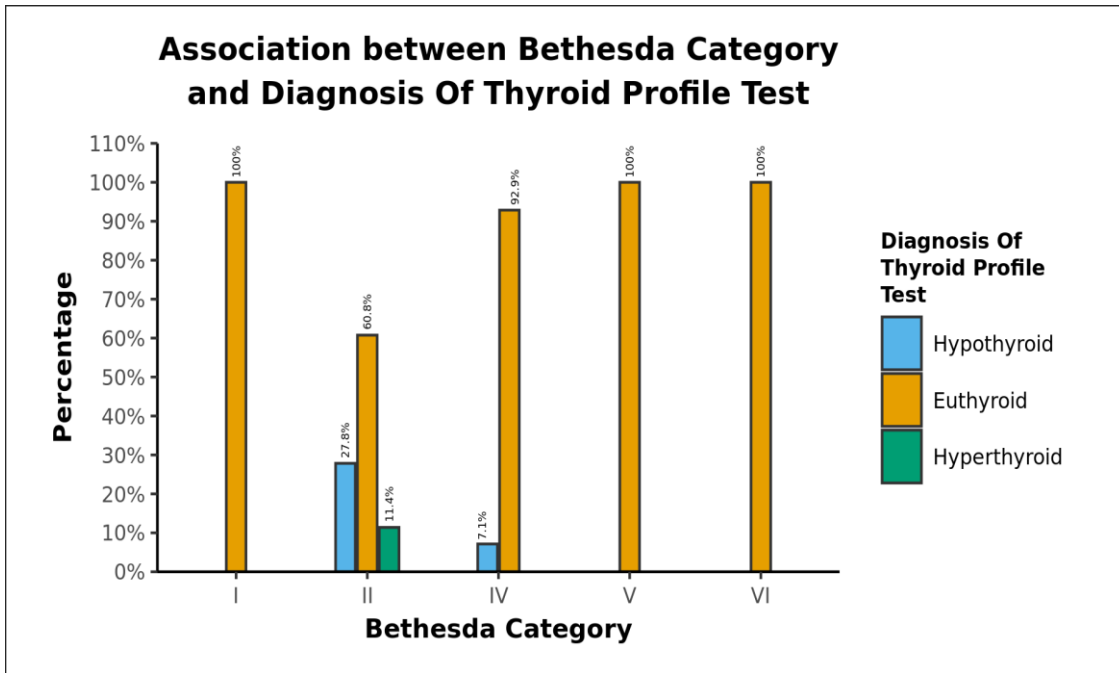
Association Between Bethesda Category and Diagnosis of Thyroid Profile Test (n = 100)

Diagnosis Of Thyroid Profile Test	Bethesda Category					Total	P Value
	I	II	IV	V	VI		
Hypothyroid	0 (0.0%)	22 (27.8%)	1 (7.1%)	0 (0.0%)	0 (0.0%)	23 (23.0%)	0.325
Euthyroid	1 (100.0%)	48 (60.8%)	13 (92.9%)	1 (100.0%)	5 (100.0%)	68 (68.0%)	

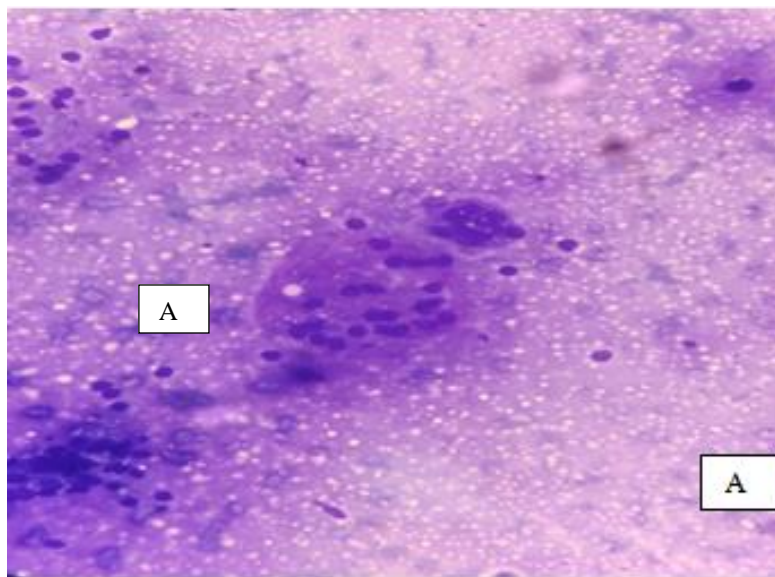
Diagnosis Of Thyroid Profile Test	Bethesda Category						P Value
	I	II	IV	V	VI	Total	
Hyperthyroid	0 (0.0%)	9 (11.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	9 (9.0%)	
Total	1 (100.0%)	79 (100.0%)	14 (100.0%)	1 (100.0%)	5 (100.0%)	100 (100.0%)	

Comment

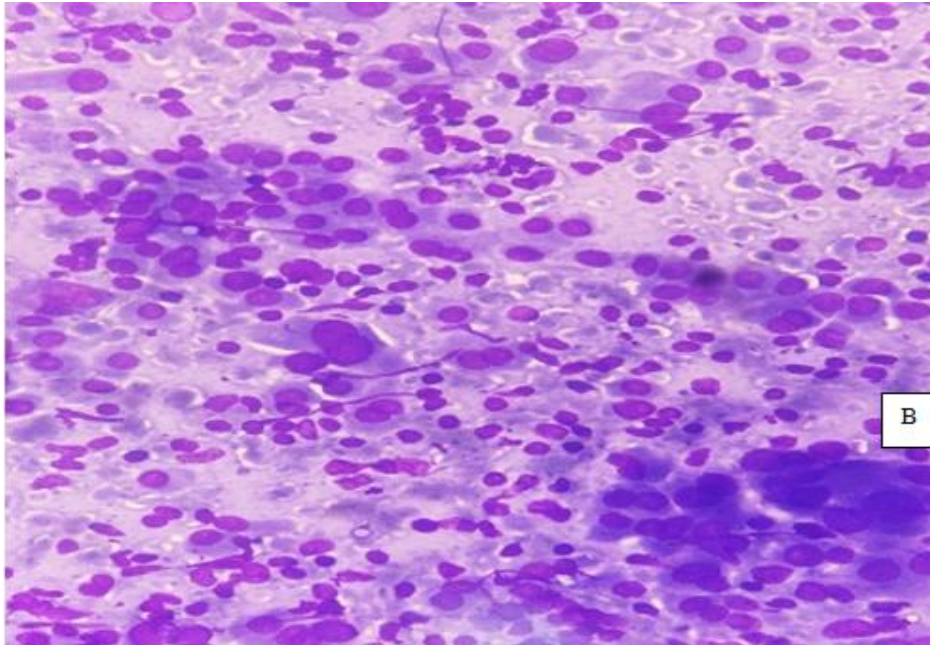
Not significantly associated (P-value >0.005).



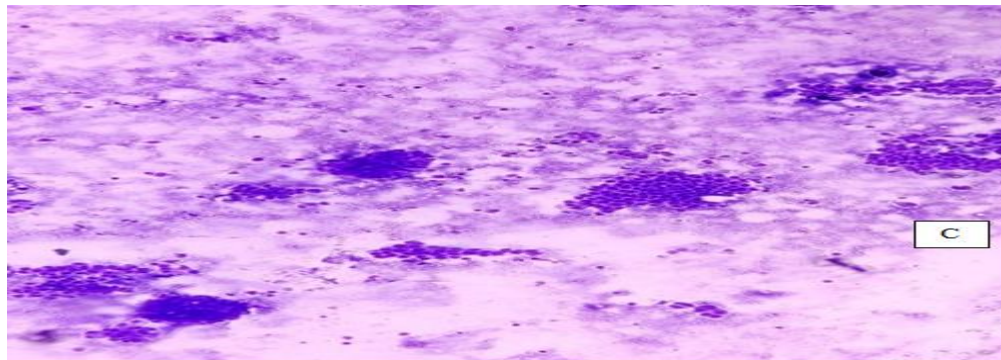
Association Between Bethesda Category and Diagnosis of Thyroid Profile Test



A. Follicle in Colloid goitre (40X) MGG stain.
B.



B. Mixed population of Hurthel cells (oncocytes) with prominent anisonucleosis and polymorphic lymphocytes in Hashimoto thyroiditis.



C. Highly cellular smear in Papillary thyroid carcinoma showing numerous monolayered sheets (10X) MGG stain.

Discussion

FNAC of thyroid gland has an extremely important role in the evaluation of thyroid nodules or swellings as it is the most effective and safe method. In this study thyroid fine needle aspirations findings were categorized according to The 2017 Bethesda system of reporting thyroid cytopathology a six tier category system.

The study period was from January 2020 to June 2021. During the study period, a total of 100 cases of thyroid fine needle aspirations were collected and categorized according to "The 2017 Bethesda System for Reporting Thyroid Cytopathology". It was easy to classify the result in 6 categories. Later these cases were followed up with their thyroid profile test.

The age of patient with thyroid lesion ranged from 18-70 year. The mean age of presentation of patients in present study is 35.96 ± 12.4 . Similar results were noted in the study performed by Poudel et al[6] with mean age 37.91 and 20-49 years being the most common age group that presented with thyroid lesion which was similar to present study. Studied done by Gupta et al[7] with mean age 38.7, Naz et al[8] with mean age 39.7 and Mehrotra et al[9] with mean age 36.2 were in concordance with present study.

The present study showed that out of the 100 patients with thyroid lesions 83 were females and 17 were males. Female to male ratio was 4.8:1. Thyroid lesions were more common in female. This figure is comparable with studies Ji Hye park et al[10] with 3.8:1, Naz et al[8] with 3.6:1, Thakor et al[11] with F:M ratio 5.1:1. Present study

showed similar findings stated by Singh et al[12] with F:M ratio 4.7:1 and Muratli et al[13] with 4.8:1. Adequacy rate of present study is 99% which is comparable with similar studies Melo Uribe et al[14] with adequacy rate 95.6%, Mondal et al[15] with 98.8%, Kim et al[16] with 98.2%, Joshi et al[17] with 100%, Mehrotra et al[9] with 95.92% of adequacy rate.

The present study showed distribution of thyroid lesion as Neoplastic 20.2% and as Non neoplastic 79.8%. Majority of the patients presented with Non neoplastic lesion. The ratio of Non neoplastic and Neoplastic lesion was 4:1. This finding is similar with following studies Tabaqchali et al[18], Melo uribe et al[14], Yang et al[19] which also showed that non neoplastic thyroid lesion far more common. Distribution of categories according to the 2017 Bethesda system of reporting thyroid cytopathology in present study showed that category I (unsatisfactory) contributed to 1%, category II (benign)- 79%, category III (Atypia of undetermined significance or follicular lesion of undetermined significance)- 0%, category IV (Follicular neoplasm or suspicious for a follicular neoplasm)-14%, category V (Suspicious for malignancy)- 1%, category VI (Malignant)-5%. Majority of patients were reported as category II contributing 79% followed by category IV which correlates well with the studies conducted by Mondal et al[6] which categorized the various lesions as (Cat-I-1.2%, Cat-II-87.5%, Cat-III- 1%, Cat-IV- 4.2, Cat-V- 1.4, Cat-VI-4.7%).

A study done by Mehra et al[20] done in 2015 presented the various lesions as (Cat-I-7.2%, Cat-II-80%, Cat-III- 4.9%, Cat-IV- 2.2, Cat-V- 3.6%, Cat-VI-2.2%) by Thakor et al[21] in 2020 as (Cat-I-6.4%, Cat-II-80%, Cat-III- 2.4%, Cat-IV- 4.4, Cat-V- 4.0%, Cat-VI-3.2%) and by Anand et al¹⁰⁰ in 2020 as (Cat-I-13.8%, Cat-II-75.9%, Cat-III-2.6%, Cat-IV- 3.7, Cat-V- 2.6%, Cat-VI-2.8%).

These studies including present study showed wide variation in distribution of lesion in category I. This is probably due to the nature of lesion for example some nodules are very vascular and with repeated passes yield only blood or due to FNA technique, proper training may improve cellularity by using a smaller gauge needle, avoiding negative pressure and with proper staining technique.

According to Bongiovanni M and Spitale A et al[23] the malignancy rate is 9-32% in surgically excised nodules which were initially reported as unsatisfactory so it should be re-aspirated for better results, even after two successive unsatisfactory specimens there should be close clinical and radiological follow up.

In our set up when smears were looked for adequacy if they were found inadequate, re-aspiration was performed on those patients and were diagnosed accordingly.

Maximum percentage of distribution of lesions were in category II (Benign) which is similar in the other studies. Ability to identify benign thyroid nodules is of great clinical value because a simple procedure like FNA can save unwanted surgeries. In our study abundant colloid was seen in colloid goitre, multinodular goitre, colloid nodule, benign cystic lesions & thyroid adenoma. Mild to moderate amount of colloid was seen in thyroiditis. Hurthle cell changes were also noted in goitre as it is not specific of only Hashimoto thyroiditis. According to Gharib H et al[24] and Yassa L et al[25] a benign lesion is the most common FNA interpretation in approximately 60-70% of all cases.

Category III- Atypia of undetermined significance or follicular lesion of undetermined significance also showed variation in different studies that is probably because it is somewhat heterogeneous and subjective. The incidence also varies with experience and training of cytopathologists. Cibas and Ali suggest that the upper limit of category III should not be more than 10%.

AUS is an interpretation of last resort and should be used judiciously. After benign category the next most common category in the present study was category IV with 14% which is similar to study done in 2015 by Mehrotra et al[9] (Cat-I-4.57%, Cat-II-68.5%, Cat-III-5.72%, Cat-IV- 17.14, Cat-V- 1.14%, Cat-VI-2.85%). Here FNA can be considered as a screening test, to detect a great probability of malignancy in thyroid nodules for performing surgical resection. Final diagnosis done by histopathological examination which show vascular invasion in follicular carcinoma.

In malignant category, category VI all cases were described as Papillary carcinoma thyroid, because all cases presented nuclear features which are diagnostic in papillary carcinoma of thyroid this includes intranuclear inclusion and grooves. this result is in concordance with study conducted by Kukar et al[26].

Thyroid function tests (TFT) were performed in all cases and were distributed euthyroid, hypothyroidism and hyperthyroidism according to TSH level as TSH level is more sensitive TFT. Patients with hypothyroid were 23%, patients with euthyroid were 68% and 9% patients were in hyperthyroid condition.

Similar results showed in studies done by Thakor et al[11]and by Mehrotra et al[9] in both studies patients with hypothyroidism were 34-35% which is little higher from present study. It is probably because of level of TFT is highly associated with geographical distribution of thyroid disorders in population.

All results of TFT were distributed according to thyroid categories to see the correlation.

Maximum number of cases with altered TFT were found in category II. There was only one case in category IV out of total 14 case which was hypothyroid. All cases in category V and VI were euthyroid. Present study showed there is no any significant correlation between Bethesda categories and TFT. Which is in concordance with the study done by Yasmeen Khatib et al[27].

Conclusion

Fine needle aspiration cytology is most cost-effective minimally invasive and safe method to diagnose thyroid lesion. When coupled with thyroid function test the diagnostic accuracy of the procedure improves greatly.

The classification of thyroid FNA smear according to the Bethesda system into six categories is a simple, convenient method which gives precise cytological diagnosis and also provides the clinician a better management plan.

Thyroid function test also plays important role to manage patient, it should be done simultaneously for proper management of patient with thyroid lesion. Alteration in TFT is seen in benign conditions mostly in thyroiditis, hyperthyroid state in graves diseases and hypothyroid state in Hashimoto thyroiditis and sometimes hyperthyroid state in nodular colloid goitre. The TFT generally is of no use in cases of neoplastic aetiology.

Both Bethesda categories and TFT are independent variables and there is no correlation between them.

Most of our cases were lost to follow up after cytological diagnosis were offered. This eventually can be averted by keeping the patient in strict follow up and offer surgical treatment wherever necessary.

Though this study involved only 100 cases it is mandatory the large group be studied (Viz. 1000 cases) with histological, molecular and TFT correlation. This will enable us to almost conclude about the incidence of various lesions, a detailed study of molecular changes and also a detailed study of correlation of various lesion with thyroid function test.

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