

Cytological study of thyroid lesions by Bethesda System

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Abstract:

Background: Fine needle aspiration (FNA) plays an essential role in the evaluation of the Euthyroid patient with a thyroid nodule, it reduces unnecessary surgery for patients with benign nodules and appropriately triages patients with malignant nodules for timely clinical intervention. The present "The Bethesda System of Reporting" divides the Thyroid Cytological smears under 6 categories. These are helpful to the prognosis.

Materials and methods: A prospective fine needle aspiration study of thyroid lesions by using The Bethesda system of Reporting for Thyroid Cytopathology (TBSRTC) was done in the Department of Pathology, Government Medical College, Ongole, from July'2018 to June'2020.

Results: Present study shows lesions distribution according to TBSRTC, Inadequate and with cystic lesions - 10.0%, benign -70.88%, Atypia of Undetermined Significance /Follicular Lesion of Undetermined Significance- 0.29%, Follicular Neoplasm /Suspicious for a Follicular Neoplasm 15.30%, Suspicious for Malignancy - 0.88%, and malignant 2.65%.

Conclusion: FNA is most useful, safe, accurate, relatively simple, and inexpensive, less time consuming OPD procedures, virtually painless, highly patient compliant and highly accurate dependable tool in the diagnosis of thyroid pathology. Bethesda system of reporting thyroid FNAC has brought uniformity in cytology reporting. It has facilitated better understanding between cytopathologist and clinicians as every category connotes specific risk of malignancy and recommends treatment

Keywords: The Bethesda system of Thyroid Cytopathology, Fine-needle aspiration cytology.

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I. Introduction

Fine needle aspiration cytology of the thyroid gland is first line diagnostic test for evaluation of goiter and single most effective test for the pre-operative diagnosis of solitary thyroid nodule. Fine needle aspiration of the thyroid was first documented in Martin and Ellis paper in 1934¹. Use of technique established & developed in Sweden in the Radium Helmet hospital of Stockholm during 1950. In India, FNAC has been introduced in early 1970s.² First publication on FNAC appeared in 1975 by Gupta et al.³, which was published in the Indian Journal of Cancer. Needle biopsy of the thyroid had been attempted for the first time in 1965 in India,⁴

It is critical that cytopathologists communicate thyroid FNA interpretations to referring physicians in terms that are succinct, unambiguous, and clinically helpful. To address terminology and other issues related to thyroid FNA, the National Cancer Institute (NCI) hosted the "NCI Thyroid FNA State of the Science Conference," which took place on October 22 and 23, 2007, in Bethesda, Maryland.⁵ The conclusions regarding terminology and morphologic criteria from the NCI meeting led to the Bethesda Thyroid Atlas Project and formed the framework for the Bethesda system for reporting thyroid cytopathology (TBSRTC). The NCI Thyroid Conference addressed a wide range of issues other than terminology.^{6,7}

TBSRTC represents a six- category scheme of reporting thyroid cytopathology, with an implied malignancy risk and a brief management plan. These are the objectives of the study to classify the thyroid lesions according to the Bethesda system of reporting, to study the incidence of thyroid lesions with reference to age and sex, to assess the feasibility of adopting TBSRTC in signing out thyroid FNAs, to assess the efficacy of TBSRTC in accurate prediction of thyroid lesions in FNA.

II. Material And Methods

A prospective fine needle aspiration study of thyroid lesions by using The Bethesda system of Reporting for Thyroid Cytopathology (TBSRTC) was done in the Department of Pathology, Government Medical College, Ongole, from July'2018 to June'2020.

A total number of 340 aspirations were performed on patients with thyroid swelling, both male and female who attended medical, surgical and ENT OPs during the above period. Smears prepared and stained with H & E.

Study Design: Prospective, cross sectional and observational study.

Study period: 2 years from July 2018 to June 2020

III. Results

Among 340 cases aspirated material obtained was sufficient for diagnosis in 306 cases. In remaining 34 cases 14 cases showed only blood cellular elements and with occasional thyroid acinar cells and 20 cases showed cystic fluid and these kept under Bethesda Category –I.

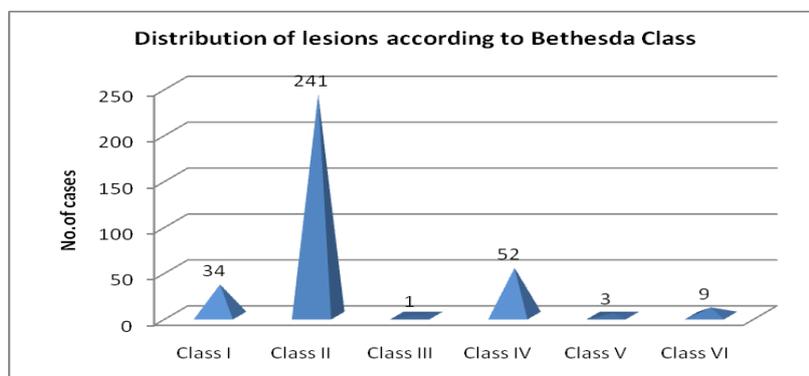
Table –1 Showing details of adequacy of samples.

Item	Number	Percentage
Adequate for reporting	306	90.0%
Inadequate for reporting	34	10.0%
Total aspirations done	340	100%

Out of 340 smears taken from thyroid lesions, as per criteria of adequacy 306 smears were adequate.34 smears were inadequate and hence categorized according to TBSRTC as Category I

Table -2 Bethesda category distributions of lesions

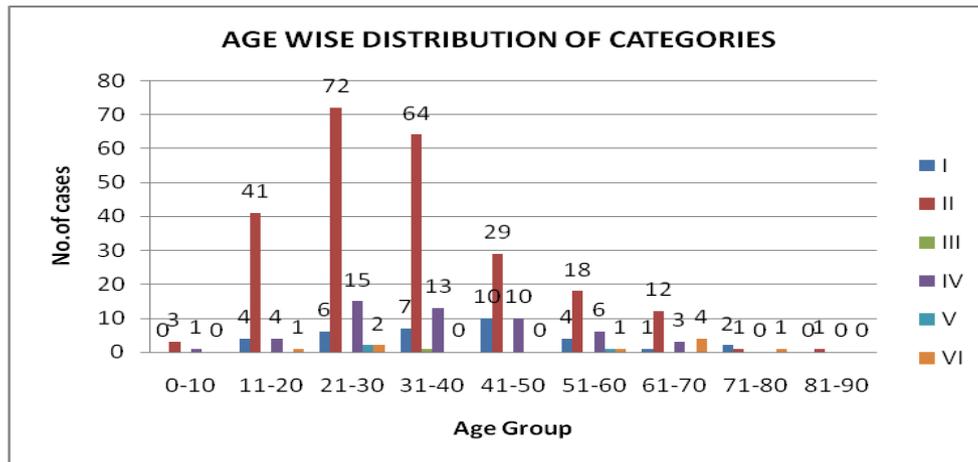
Bethesda Category	No. of cases	Percentage
Class I-ND/US	34	10.0%
Class II- benign	241	70.88%
Class III-AUS/FLUS	1	0.29%
Class IV-FN/SFN	52	15.30%
Class V-SM	3	0.88%
Class VI-Malignant	9	2.65%
Total	340	100.00%



Most common lesions were seen in benign category with 71.48%. Most common lesion was benign follicular nodule

Table -3 Age wise distribution of categories

Age Group	I	II	III	IV	V	VI
0-10	0	3	0	1	0	0
11-20	4	41	0	4	0	1
21-30	6	72	0	15	2	2
31-40	7	64	1	13	0	0
41-50	10	29	0	10	0	0
51-60	4	18	0	6	1	1
61-70	1	12	0	3	0	4
71-80	2	1	0	0	0	1
81-90	0	1	0	0	0	0
Total	34	241	1	52	3	9



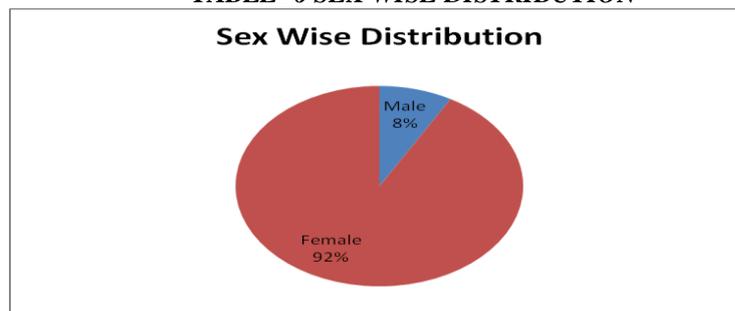
Most of the lesions were in the 21-30 years age & in the benign group

Table-4 Age wise distribution of lesions

Age Group in years	No.of cases	Percentage
0-10	4	1.18%
11-20	50	14.70%
21-30	97	28.53%
31-40	86	25.30%
41-50	49	14.42%
51-60	30	8.82%
61-70	19	5.58%
71-80	4	1.18%
81-90	1	0.29%
Total	340	100%

Most common age group involved was 21-30years, with 97 cases(28.53%).

TABLE -6 SEX WISE DISTRIBUTION



Out of 340 cases the Males were 25 and Females were 315. Thyroid lesions most common in females with Male:Female ratio 1:12.6. The thyroid lesions were nodular in 201(59.12%) cases and diffuse in 139(40.88%) cases. Most common was nodular presentation with 59.12% of cases. Male: female ratio – 1:12.6, In Males lesions mostly seen in benign category. In all cases the history of present lesion was recorded. Most of the lesions revealing a history of months to years. Least duration was 2 days and highest duration was 40 years.

Among the lesion studies, Most of the lesions were small in size. Most common size was 1-3 cm. In this most of the patients showed thyroid swelling with 3cm size. All patients attended with thyroid swelling& most common associated symptom was pain (38cases).Thyroid profile available in 43 cases. Most of them were euthyroid. Hypothyroidism in 13 cases & hyperthyroidism in 5 cases. Most common benign lesion seen in this study is benign follicular nodule with nodular goiter. Only 9 cases seen in malignant category,mostly papillary carcinoma seen.

IV. Discussion

This is a prospective study conducted on 340 patients presenting with thyroid enlargement, who underwent fine needle aspiration biopsy. The aspiration cytology findings were then classified under TBSRTC. An FNA sample of a thyroid nodule should be representative of the underlying lesion, in order to provide useful diagnostic information. FNA reduces the rate of unnecessary thyroid surgery in patients with benign nodules and detects those with thyroid cancers who have to be surgically treated. For clarity of communication and uniformity of terminology NCI hosted “The NCI thyroid FNA state science conference”. The conclusions from this meeting led to the Bethesda Thyroid Atlas project and formed the frame work for TBSRTC. In present study, the age of patient ranged from 9 years to 85 years. The age group of 21-30 yrs showed the maximum number of cases (96) which account for 28.24%, followed by 31-40 years. In less than 10 years age group four cases were seen and more than 80 years one case was seen. Eighty five years female patient with benign follicular nodule was seen.

Laishram, et al⁸ showed major age group involved 21-30 years with preponderance of benign lesions. In this study ages of patients ranged from 7-83 years. The present study showed malignant lesions in 61-70 years age group. **Sirish chandanvale et al⁹** showed malignant lesions ranged from 50-70 years with mean age of 41 years.

The present study shows female (92.65%) were most commonly effected than males (7.35%) with male: female ratio 1:12.6. **Mittal, et al¹⁰** study also showed females were more commonly affected than males with male: female ratio 1:4.6. In present study also most of the patients presented with a painless swelling in the thyroid region. Pain present in 38 cases. In the present study out of 340 patients 201 patients (59.12%) presented with nodular enlargement. **Sirish chandanvale et al⁹** show 66.6% had thyroid nodular enlargement.

In the present study duration of symptoms ranging from 2days to 40 years. **Sirish Chandanwale et al⁹** shows the duration of symptoms gave no clue regarding the nature of thyroid swelling.

In present study commonest symptom was painless enlargement of thyroid. Associated symptoms were pain (11.17%) followed by dysphagia/dyspnoea (9.11%) **Handa et al¹¹** study shows major presenting symptom is in all the patients was diffuse swelling and or nodular swelling of the thyroid, other associated symptoms are pain, dysphagia, hoarseness of voice and cough.

In present study the thyroid cytology was categorized under TBSRTC. In TBSRTC first category was **Unsatisfactory/Non diagnostic(UN/ND)** this was based upon adequacy of the cytology.

In present study out of 340 cases 34 cases (9.8%) were under this category. This category also includes cystic fluid cases. (Figure-1,2)These were 20 cases out of 34 cases. In these 34 cases, 27 female patients and 5 of them are male in patients with m:f ratio1:5.4. In this category age distribution seen between 12-80years. Most common age group affected was 41-50 years. The rate of non-diagnostic specimens may be influenced by the nature of the thyroid nodules, the experience of the aspirates. According to TBSRTC the management is repeat FNAC with ultrasound.

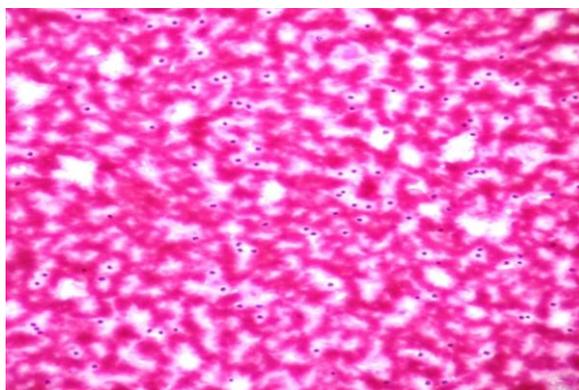


Figure 1: Bethesda Category -1, Unsatisfactory/ Non Diagnostic, H&E, 40x.
Smear showing only blood cellular elements.

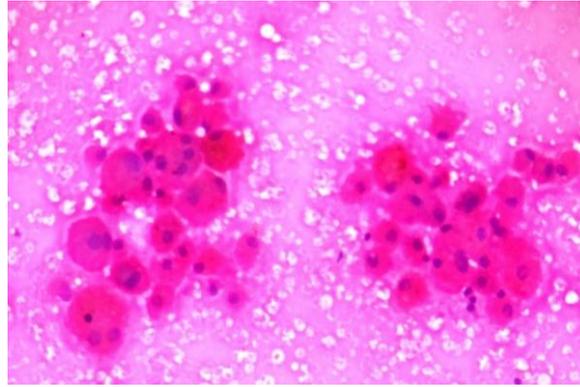


Figure 2: Bethesda Category-I Cystic Fluid only, H&E, 40x.
Showing cystic fluid with hemosiderin laden macrophages.

The study done by **Theoharis et al**¹² showed 230 cases (9.3%) in unsatisfactory cases. In his study 25 cases had follow up and underwent surgical resection. Out of 25 cases 9 were MNG, 8 were follicular adenoma, 7 were PTC, 1 was follicular carcinoma. **Jo et al**¹³ study showed 18.6% of cases in unsatisfactory category.

In present study **Benign category** most common with 241 cases (70.88%). In this benign category most common was benign follicular nodule with nodular goiter (Figure-3) with 102 cases (42.39%) followed by colloid nodule (Figure-4) in 76 cases (31.28%), lymphocytic / Hashimoto's thyroiditis (Figure-5) in 55 cases (22.63%) Graves' disease seen in 7 cases (3.29%) and showed one case of granulomatous thyroiditis. In both females and males, benign follicular nodule with nodular goiter is most common finding with M:F ratio 1:17.53. Most common affected age group was 21-30 years.

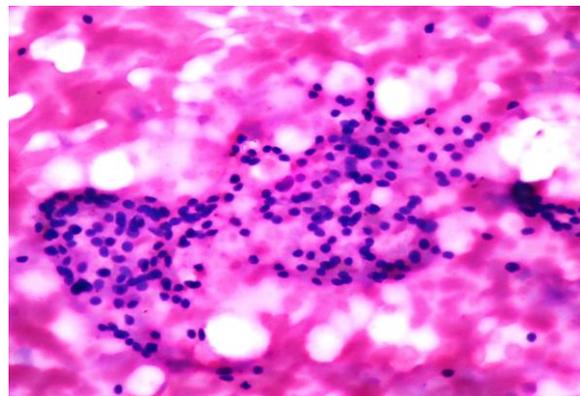


Figure 3: Bethesda category II - Benign Follicular nodule, H&E, 40x.
Smear showing benign thyroid follicular cells and colloid.

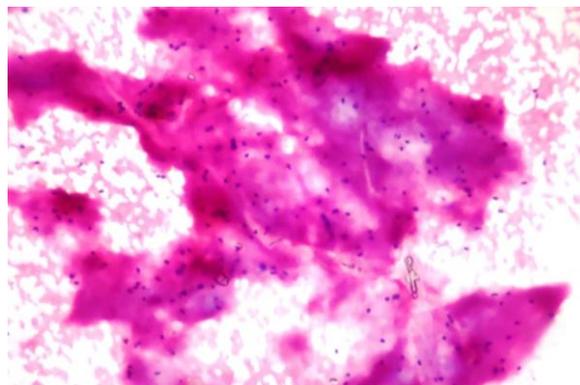


Figure 4: Bethesda Category II - Colloid Nodule, H&E, 40x
Smear showing Benign follicular epithelial cells and colloid

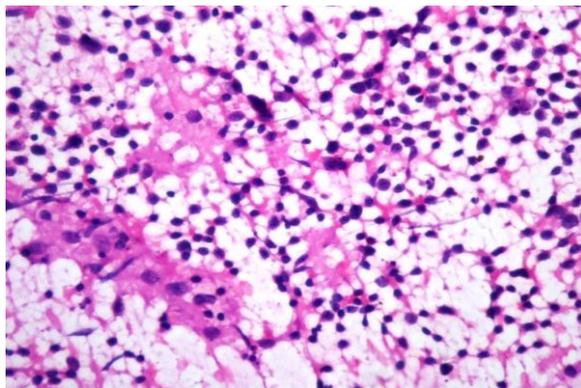


Figure 5: Bethesda Category II- Hashimotos Thyroiditis, H&E, 40x.
Smear showing thyroid follicular cells and some with Oncocytic change

In this category ages of patients ranged from 9-85 years, one case with 85 years presents nodular goiter. In this category 168 patients presents with diffuse enlargement and 73 cases with nodular enlargement. 30 cases thyroid profile available, 17 euthyroid, 9 hypothyroidism and 4 with hyper thyroidism showed cytological features of Hashimotos and colloid nodule. In this duration of symptoms from 10 days -23 years, most common age group involved in both male and female were 21-30 years. In this category size of lesion ranged from 1-12cms In the TBSRTC it is 0.3% with usual management is clinical follow-up.

In **Theoharis et al**¹², **Mittal, et al**¹⁰ studies showed benign category 72.91%, 78.9% cases. In this majority of them were nodular goiter, followed by lymphocytic thyroiditis and colloid nodules.

In the present study one case (0.29%) with **AUS/FLUS** (figure-6) category. This was FLUS case in 40 years female patient with nodular presentation, and showed 3cms nodule with one month duration. This case was not had follow up. In TBSRTC the given malignancy rate was 5-15% and management is repeat FNA.

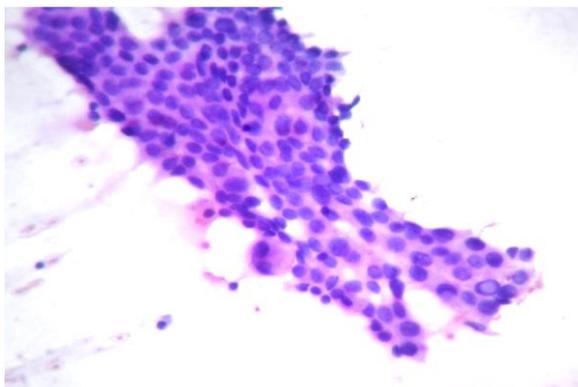


Figure 6: Bethesda Category III- AUS/FLUS, H&E, 40x.
Smear showing thyroid follicular cells with atypia

The diagnostic category **FN** (Figure-7) was applied to cellular aspirates that demonstrated predominant micro follicular pattern with little or no colloid. In this present study FN/SFN showed 52 cases (15.30%), in this 5 males and 47 female patients with M:F ratio 1:9.4. Age distribution seen between 10-68years, most common group affected was 21-30 years. In this 9 diffuse, 43 cases with nodular enlargement. Thyroid profile available in 7 cases, 5 euthyroid, 1 hypothyroid and 1 was hyperthyroid. Duration of the symptoms ranged from 15days to 15 years. Size of the lesions varied from 1-8cms. Pain was seen in 5 cases, change of voice present in 2 cases, dysphagia seen in 3 cases. 3 cases had menstrual irregularities, 1 case on thyroxin treatment and one case had thyroid surgery 14years back and showed recurrence. In TBSRTC the given malignant risk is 15-30% and management is surgical lobectomy.

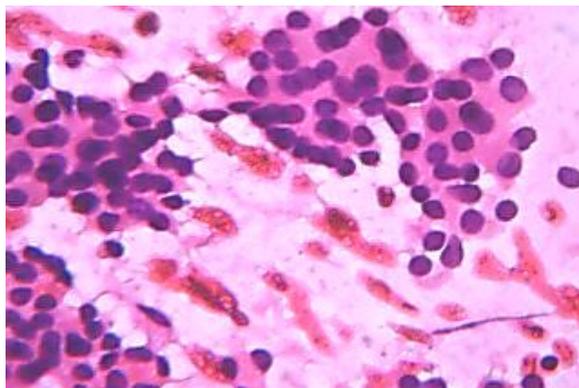


Figure 7: Bethesda Category IV- Follicular Neoplasm, H&E, 10x. Smear showing repetitive thyroid follicles.

In present study **SM** showed 3 cases (0.88%) with one male and 2 female patients. No case had follow up. Most effected age group was 21-30 years. All three cases reported as suspicious of papillary carcinoma. Duration of symptoms ranged from 3 months-2years, size of the lesions varied from 2-10 cms. In TBSRTC the malignant risk is 60-75% and with management is near total thyroidectomy or surgical lobectomy.

In the present study 9 cases were categorized as **malignancy**. In this 7 cases were papillary carcinoma and 2 cases were anaplastic carcinoma and showed 2 male patients one with papillary carcinoma and another one with anaplastic carcinoma and 7 female patients, 6 with papillary carcinoma and one with anaplastic carcinoma. The age for papillary carcinoma 12-75 years, most of them in 61-70 age group. Anaplastic carcinoma patients presented one with 60, and another with 70 years.

In papillary carcinoma(Figure-8) 5 patients presented with diffuse enlargement, 1 with nodular enlargement. Duration of the symptoms ranged from 10days-30 years. The size of the lesion varied from 2-5cms. One papillary carcinoma had post operative history and showed recurrence. In this no case had surgery follow-up.

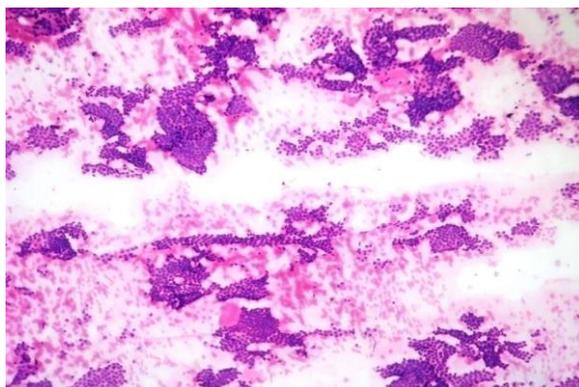


Figure 8: Bethesda Category VI Malignancy-Papillary Carcinoma, H&E, 10x. Smear showing papillary arrangement of thyroid follicular cells

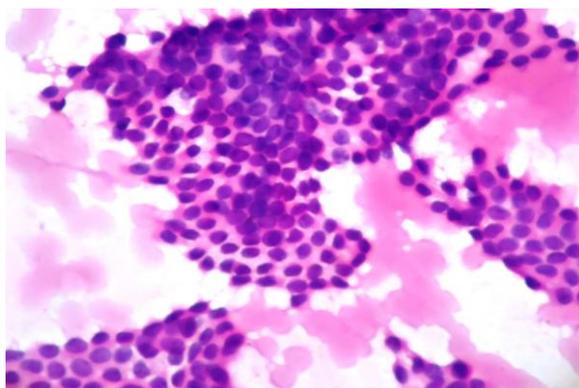


Figure 9: Bethesda Category VI Malignancy- Papillary Carcinoma, H&E, 40x. Smear showing papillary carcinoma cells with nuclear features.

In anaplastic carcinoma (Figure-10) 2 cases presented with diffuse enlargement of thyroid, duration of symptoms one with 10 days and another with 40 years. The size of the lesions 1 with 3cms and another with 7cms, and 1 case presented with associated symptoms pain, change of voice, dyspnoea. In TBSRTC, to this category 97-99 malignant risk given and with usual management was near total thyroidectomy.

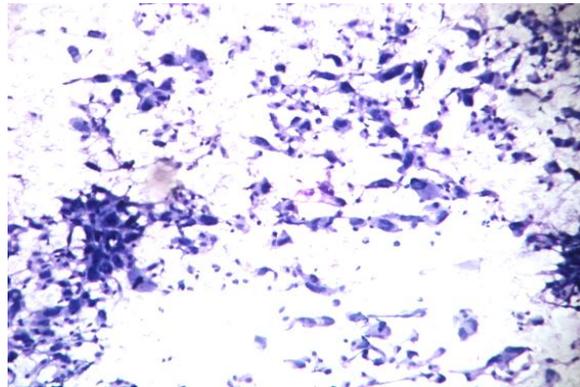


Figure 10: Bethesda Category VI, Malignancy-Anaplastic Carcinoma, H&E, 40x. Smear showing cells with marked pleomorphism and bizarre cells.

V. Conclusion

- FNA is most useful, safe, accurate, relatively simple, and inexpensive, less time consuming OPD procedures, virtually painless, highly patient compliant and highly accurate dependable tool in the diagnosis of thyroid pathology.
- FNA helps in reducing the cost of care and avoidance of unnecessary surgery in patients with benign lesions.
- TBSTRC reduces inter-observer variability in reporting thyroid FNAs and provides good communication between the surgeon and pathologist. It also implicates guidelines for cancer risk and clinical management to the surgeons, thus avoiding unnecessary surgery.
- It is essential that the cytopathologist communicates thyroid FNA interpretations to referring surgeons in terms that are succinct, unambiguous and helpful in clinical management.

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