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### RESEARCH ARTICLE

#### THYROID DISORDERS IN NORTH INDIA AND THEIR REPORTING BY BETHESDA SYSTEM – “1 YEAR RETROSPECTIVE STUDY”

Dr. Rekha Rani<sup>1</sup>, Ishani Gupta<sup>1</sup>, Dr. Jyotsna Gupta<sup>2</sup> and Anil Kumar<sup>3</sup>

1. Senior Resident Department of Pathology GMC Jammu.
2. Professor Postgraduate Department of Pathology GMC Jammu.
3. Senior Resident Department of Surgery GMC Jammu.

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#### Abstract

**Background:** Thyroid nodules are very common clinical problem and thyroid cancer is becoming more prevalent. Fine needle aspiration cytology (FNAC) has become a well established modality in the diagnosis, staging and follow up of thyroid nodules. FNAC results are routinely classified using the Bethesda system for reporting thyroid cytopathology. The Bethesda system for reporting thyroid cytopathology is a significant step to standardize the thyroid FNA reporting. It has high reproducibility, predictive value and improved clinical significance.

**Aims And Objectives:** To determine the spectrum of thyroid disorders in north India and to determine the accuracy and reliability of FNAC in our center.

**Material And Method:** A retrospective study of FNAC thyroid nodules was carried out on 133 patients referred to our Department from July 2021 to August 2020. Slides were retrieved from the cytopathology section of the Department of Pathology, GMCH, reviewed and then classified as per the Bethesda system for reporting thyroid cytopathology. Patients of all ages and gender were included in the study.

**Results:** Total 133 FNAC procedures were performed during the study period. 86 cases were females and 47 were males with male to female ratio of 1:1.83. The nodules of 9 patients were classified as Bethesda category-I, 74 patients as Bethesda category-II, 11 patients as Bethesda category-III, 8 patients as Bethesda category-IV, 9 patients as Bethesda category-V and 22 patients as Bethesda category VI. Out of 133 patients, only 36 patients underwent for surgery; among these 36 cases, 4 were classified as Bethesda category-IV, 9 as Bethesda category-V and 22 as Bethesda category-VI on cytology which were further confirmed as cases of thyroid malignancy on histopathology reports.

**Conclusion:** Our study substantiates greater reproducibility among Pathologists using TBSRTC to arrive at a precise diagnosis with an added advantage of predicting the risk of malignancy which enables the clinician to plan for surgery, extent of surgery or follow-up of the patients by repeating the FNA of thyroid nodules at specific intervals.

**Corresponding Author:- Dr. Anil Kumar**

Address:- Senior Resident Department Of Surgery Gmc Jammu.

### Introduction:-

Thyroid is one of the largest endocrine organ and both non-neoplastic and neoplastic abnormalities are frequent source of specimens for surgical pathology laboratories. Thyroid nodules are very common clinical problem and thyroid cancer is becoming more prevalent. Every patient with a palpable thyroid nodule is a candidate for FNAC. Fine needle aspiration cytology (FNAC) is now a well-established modality in the diagnosis, staging and follow up of thyroid nodules. Majority of thyroid nodules prove to be localized, non neoplastic. Benign neoplasms outnumber the thyroid carcinomas by a ratio of 10:1<sup>1</sup>. Less than 5% of all nodular swellings of thyroid are documented as malignant<sup>2</sup>. The fifth most common cancer in women is thyroid cancer. The number of new cases in women in their twenties is 5 times higher than for men in their twenties. Thyroid FNAC is very useful in identifying a substantial proportion of thyroid nodules as benign and reducing unnecessary surgery for patients with benign diseases. FNAC results of thyroid cytopathology are routinely classified using the Bethesda system. The Bethesda system for reporting thyroid cytopathology has attempted to standardize the reporting and cytological criteria in aspiration smears<sup>3</sup>. Proper communication among clinicians, radiologists, surgeons and pathologists along with cytohistological correlation is essential for reporting of thyroid FNA. Hence, a diagnostic terminology which is consistent is vital. TBSRTC is a six category scheme of thyroid cytopathology reporting. The categories and their risk of malignancy for I-Non diagnostic, II- Benign, III- AUS/FLUS, IV- FN/SFN, V- Suspicious for malignancy (SM), VI- Malignant were 1-4%, 0-3%, 5-15%, 15-30%, 60-75% and 97-99% respectively<sup>4</sup>. The Bethesda system for reporting thyroid cytopathology is a significant step to standardize the reporting of thyroid FNA. It has high reproducibility, predictive value and improved clinical significance. Although FNAC is widely used in clinical diagnosis, cytologically indeterminate thyroid nodules still present a diagnostic challenge for pathologists. This makes reaching a definitive histologic diagnosis difficult in a large number (10-30%) of patients undergoing thyroidectomy<sup>5</sup>. The difficulty in defining the exact diagnosis of thyroid nodules is underlined by the fact that the probability of malignancy in AUS/FLUS or FNAC specimens remains unclear<sup>6, 7, 8</sup>. Some malignancy criteria such as thyroidal or tumoral capsular and / or lymphovascular invasion are determinative, when establishing a cancer diagnosis, which represents a significant limitation of the FNAC method.

### Material And Methods:-

A retrospective study of FNAC thyroid nodules was carried out on 133 patients attending a tertiary care centre in Jammu, J&K from July 2021 to August 2020 after taking clearance from the institutional ethical committee. Both May Grunwald Giemsa (MGG) and Pap-stained slides were retrieved from the cytopathology section of the Department of Pathology, GMCH, reviewed and then classified as per the Bethesda system for reporting thyroid cytopathology into six categories. All the necessary clinical details, laboratory values of T3, T4, TSH and ultrasonographic details were noted from the cytology forms. Patients of all ages and gender were included in the study.

### Results:-

Total of 133 FNAC procedures were performed on clinically significant thyroid nodules over a period of 1 year. Out of 133 patients 86 were females and 47 were males with male to female ratio of 1:1.83. The youngest patient was a female of 17 years with papillary carcinoma thyroid and oldest of 82 years with anaplastic carcinoma thyroid. The nodules of 9 patients were classified as Bethesda category-1, 81 patients as Bethesda category-2, 11 patients as Bethesda category-3, 8 patients as Bethesda category-4, 9 patients as Bethesda category-5 and 15 patients as Bethesda category-6 respectively (TABLE-1). Further distribution of benign and malignant lesions is tabulated in TABLE-2 and 3. Out of these, total 133 patients only 36 patients underwent for thyroid surgery. Out of these 36 cases, 4 were classified as Bethesda category-4, 9 patients as Bethesda category-5 and 22 patients as Bethesda category-6 which were further confirmed as cases of thyroid malignancy on histopathology reports.

**Table 1:-** Distribution of cases as per Bethesda category system.

Bethesda category	Number of cases (n)	Percentage (%age)
I. Non-diagnostic	9	6.77
II. Benign	81	60.90
III. AUS/FLUS	11	8.27
IV. SFN	8	6.01
V. Suspicious for	9	6.77

malignancy		
VI. Malignant	15	11.28

**Table 2:-** Distribution of benign category cases.

Benign cases	Number of cases (n)	Percentage (%age)
Colloid goiter	47	58.02
Colloid cyst	7	8.64
Adenomatoid goiter with features of hyperactivity	8	9.88
Lymphocytic thyroiditis	16	19.76
De Quervains thyroiditis	3	3.70
TOTAL	81	100

**Table 3:-** Spectrum of malignant lesions.

Malignant cases	Number of cases (n)	Percentage (%age)
PTC	8	53.34
Medullary carcinoma	5	33.33
Anaplastic carcinoma	2	13.33
TOTAL	15	100

**Discussion:-**

FNAC is a safe, rapid and relatively inexpensive procedure. Early diagnosis of thyroid nodules is important due to their low malignant potential and slow progressive nature. Thyroid FNAC plays an important role in the diagnosis of thyroid nodules.

This study shows the one year experience in reporting thyroid aspirations by TBSRTC in Government Medical College Jammu. This system of reporting thyroid FNA improves the clarity of communication between cytopathologists and treating clinicians, predicts the risk of cancer and reduces the unnecessary surgery of the patients with benign thyroid lesions and appropriately triages patients with malignant lesions for timely surgical interventions. TBSRTC does not recommend surgery for ND, Benign and AUS/FLUS category.

**TBSRTC Category-I - Non diagnostic or unsatisfactory (ND/UNS)-**

Non-diagnostic (ND) thyroid FNA results have major limitation in arriving at a definitive diagnosis and is a most common cause of false negative reports<sup>9</sup>. Some of the studies stated that the operator experience and the number of passes made during FNA correlate with the non diagnostic result<sup>10,11</sup>. As per WHO Criteria, a thyroid FNA sample is considered adequate for evaluation if it contains a minimum of 6 groups of follicular cells, with at least ten cells per group on a single slide<sup>12</sup>. The use of this WHO criteria for adequacy of thyroid FNA is helpful because they improve the diagnostic efficiency of thyroid FNA and avoid unnecessary surgery for benign non neoplastic thyroid lesions<sup>13</sup>. In our study we have categorized 9 patients (6.76%) in category-I. This correlates with the studies conducted by Bhat et al. and Mehra et al.<sup>14,3</sup>. When these patients came back to us for repeat FNAC after a month then all these cases revealed features of benign thyroid lesions. Study carried out by Renshaw<sup>15</sup> shows that the TBSRTC category –I had significantly lower risk of malignancy (0%) which is comparable to our study.

**TBSRTC Category-II – Benign**

Present study shows highest incidence of category-II lesions. In our study, 81 patients (60.90%) were reported as TBSRTC category-II with colloid goiter being the predominant group followed by lymphocytic thyroiditis, adenomatoid goitre with features of hyperactivity and De Quervains thyroiditis respectively which is comparable with the studies conducted by Mondal et al<sup>16</sup>, Gupta et al<sup>17</sup> and Nandedkar et al<sup>18</sup>. The risk of malignancy for category-II is 0% to 3% with the recommended management being clinical follow-up of patients<sup>19</sup>. Although surgery is not recommended for category-II lesions still 6 out of 81 patients in category-II were underwent for thyroid surgery for cosmetic purpose and pressure symptoms. 2 cases were diagnosed as a cases of follicular adenoma, 3 were reported as colloid goiter and one as PTC on histopathology. Case of PTC was incidental finding in thyroid specimen and was mural nodule in a cystic lesion.

**TBSRTC Category – III- atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS)**

Cases categorized as category – III are those for which cytological findings are not convincingly benign, but the degree of architectural and cellular atypia is also not sufficient for a diagnosis of follicular neoplasm or suspicious for malignancy. In our series, 11 patients (8.27%) were reported as category – III. Studies conducted by Jo et al<sup>20</sup> and Yassa et al<sup>21</sup> have reported 3.4% and 4% lesions as AUS/FLUS, respectively. Out of these 11 patients, 5 were underwent for thyroid surgery and 2 were reported as follicular adenoma, 1 was reported as PTC and 2 were reported as granulomatous thyroiditis on histopathology.

**TBSRTC category – IV – Follicular neoplasm or suspicious for follicular neoplasm (FN/SFN)**

Based on cytology it is difficult to distinguish follicular carcinoma from follicular adenoma. Thyroid FNA with cytomorphologic features of moderate to high cellularity, scant or absent colloid or microfollicular arrangement of follicular cells in repetitive pattern were grouped under the category-IV. In our study, 8 patients (6.01%) were categorized as category-IV. Out of 8 cases, 4 underwent for thyroid surgery. 3 were reported as follicular carcinoma and 1 was reported as follicular adenoma on histopathology.

**TBSRTC category – V- Suspicious for malignancy.**

Most of the thyroid malignancies can be diagnosed with certainty by FNA. But the nuclear and architectural changes of some PTCs are subtle and focal. This is especially true for the follicular variant of PTC which can be difficult to distinguish from a benign follicular nodule. In the present study, 9 cases (6.76%) diagnosed as Suspicious for malignancy on FNAC which showed only one or two characteristic features of PTC focally and the sample is sparsely cellular. There was difficulty in giving them as truly malignant so we kept them in SFM category and advised follow-up. Recent studies show that application of molecular techniques such as RET/PTC gene and analysis of BRAF mutation are helpful and improve the differentiation of malignant from their benign counterparts among the patients with category-V<sup>22, 23</sup>. On follow up, we have found that only 6 cases underwent for thyroid surgery and 4 were diagnosed as PTC and 2 were diagnosed as follicular carcinoma on histopathology.

**TBSRTC Category-VI- Malignant**

This category is applied whenever the cytomorphologic features are conclusive for malignancy. In the present study we reported 15 cases (%age) as category-VI, 8 cases were reported as papillary thyroid carcinomas, 5 cases were reported as medullary carcinoma and 2 cases were reported as anaplastic carcinoma. Papillary carcinoma is the most common malignancy of thyroid in our study which is similar to the findings of Laishram et al<sup>24</sup>. All of these cases were confirmed and correlated with histopathological diagnosis. Anaplastic carcinoma is a highly aggressive malignancy of thyroid and accounts for less than 2% of thyroid malignancy, and characteristically occurs in older adults.

The correlation of cytology and histopathology diagnosis is an important quality assurance method as it allows cytopathologists to calculate their false positive and false negative results. In present study, only few cases were available for HPE after their cytological diagnosis and there was not much discrepancy in cytological and histopathological diagnosis.

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