

Original research article

Fine Needle Aspiration of Thyroid Nodules by The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) and its Correlation with Ultrasound Features.

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Abstract

Background: Fine-needle aspiration cytology (FNAC) is the initial screening test for thyroid nodules. The Bethesda system classifies thyroid FNAC into six categories. Each category is linked to a malignancy risk and has a recommended clinical management. The aim of this study was to analyze the thyroid cytology smears by Bethesda system and to correlate the diagnosis of cytopathology with ultrasound features.

Materials and Methods: This study was conducted at a tertiary care teaching hospital in Patna for 6 months from May 2019-October 2019. Institute ethics committee approval was taken. The study included 100 patients attending the pathology department for cytology of thyroid lump after direct or ultrasound guided FNAC.

Results: 8 patients (8%) were in category I. Out of 8, 2 cases contained cyst fluid only, 2 had excessive blood obscuring the smear and 4 cases had scant cellularity. 64 patients (64%) were in category II. Among the 64 cases, 42 were labelled as goitre, 18 as lymphocytic thyroiditis, and 4 cases as granulomatous thyroiditis. 10 patients (10%) were in category III. Out of this, 2 cases had Atypia of undetermined significance and 8 cases had follicular lesion of undetermined significance. 8 cases (8%) were in category IV. Out of this, 6 cases were labelled as Follicular neoplasm and 2 as suspicious for follicular neoplasm. 2 cases (2%) were in category V and were labelled as suspicious for papillary carcinoma. 8 cases (8%) were in category VI (malignant), out of this 4 were labelled as papillary carcinoma and 4 as anaplastic carcinoma of thyroid.

Conclusions: Fine-needle aspiration cytology (FNAC) of thyroid is a good initial screening test for thyroid nodules. The Bethesda System for Reporting Thyroid Cytopathology proved to be an excellent reporting system.

Keywords: Bethesda, fine-needle aspiration cytology, thyroid

Introduction

Thyroid nodules are common in general population. Studies have reported prevalence rates in adult of 4-8% by palpation and up to 67% by ultrasound^[1-3]. The prevalence of nodules increases with age and is greater in female patients. Most thyroid nodules are asymptomatic and benign in general population. However, when patients are further selected on ultrasound criteria, the overall incidence of malignancy in patients who ultimately undergo fine needle aspiration cytology (FNAC) of thyroid nodule is significant- although relatively small at 9.2-13%.^[4-6] Though the risk of malignancy is low, the anxiety produced by the discovery of nodule invariably prompts the patient and the referring physician to proceed with more definitive characterization of the nodule by the findings of cytology and radiology for risk stratification and further management.

Aims & Objectives:

The aim of this study was to analyze the thyroid cytology smears by Bethesda system and to correlate the diagnosis of cytopathology with ultrasound features.

Material and Methods:

This study was conducted at a tertiary care teaching hospital in Patna for 6 months from May 2019-October 2019. Institute ethics committee approval was taken. The study included 100 patients attending the pathology department for cytology of thyroid lump after direct or ultrasound guided FNAC. Patients with previously diagnosed benign or malignant conditions of thyroid on treatment, after surgery, or on follow up for residual disease or recurrence were excluded from the study. Informed consent was taken from all patients. Clinical data was collected using a structured questionnaire. In patients with palpable thyroid nodule, FNA was done directly with 22G needle attached to a 10 ml syringe. In non palpable nodules aspiration was done under ultrasound guidance. Slides were made from the aspirated material. Few slides were air dried and stained by May Grunwald Giemsa stain. On one slide alcohol wet fixation followed by Papanicolaou staining was done. In case of cyst fluid, smears were prepared directly as well as after centrifugation. Stained slides were evaluated under 50, 100 and 400 magnification. The criterion of adequacy for evaluation (and benign) was at least 6 groups of thyroid follicular cells, each group composed of at least 10 cells^[7,8].

Reporting was done according to The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC).

CRITERIA FOR REPORTING:

The Bethesda system for reporting Thyroid Cytopathology: Implied risk of Malignancy and Recommended Clinical Management.

Diagnostic Category	Risk of Malignancy (%)	Usual Management
Nondiagnostic or Unsatisfactory	1-4%	Repeat FNA with ultrasound guidance
Benign	0-3%	Clinical follow-up
Atypia of undetermined significance or follicular lesion of undetermined significance	~5-15%	Repeat FNA
Follicular neoplasm or suspicious for follicular neoplasm	15-30%	Surgical lobectomy
Suspicious for malignancy	60-75%	Near –total thyroidectomy or surgical lobectomy
Malignant	97-99%	Near total thyroidectomy

In ultrasound evaluation, we looked for the size, margins, ecogenicity, calcification, composition, vascularity and tall configuration of the nodules (i.e. when the anteroposterior diameter of the nodule is greater than the transverse diameter). Cytological and radiological findings of the nodules were correlated. In inconclusive cases, repeat direct or ultrasound guided FNA was done whenever needed.

Observation:

In the prospective study of 100 patients with thyroid nodule, FNAC was done directly or under image guidance whenever necessary. On the basis of cytology findings, cases were categorized into category I to VI by TBRTCP. 8 patients (8%) were in category I. Out of 8, 2 cases contained cyst fluid only, 2 had excessive blood obscuring the smear and 4 cases had scant cellularity. 64 patients (64%) were in category II. Among the 64 cases, 42 were labelled as goitre, 18 as lymphocytic thyroiditis, and 4 cases as granulomatous thyroiditis. 10 patients (10%) were in category III. Out of this, 2 cases had Atypia of undetermined significance and 8 cases had follicular lesion of undetermined significance. 8 cases (8%) were in category IV. Out of this, 6 cases were labelled as Follicular neoplasm and 2 as suspicious for follicular neoplasm. 2 cases (2%) were in category V and were labelled as suspicious for papillary carcinoma. 8 cases (8%) were in category VI (malignant), out of this 4 were labelled as papillary carcinoma and 4 as anaplastic carcinoma of thyroid.

Table 1: Categorization of patients according to TBSRTC: Implied risk of malignancy and recommended clinical management: (Total number of cases -100)

Diagnostic category	Number of cases	% of cases	Subcategorization of cases	Risk of malignancy	Usual management
I. Non diagnostic or Unsatisfactory	8	8%	Cyst fluid only- 2 case Scant cellularity-4 cases Obscuring blood-2 case	1-4%	Repeat FNA with ultrasound guidance
II. Benign	64	64%	Multinodular goitre-42cases Lymphocytic thyroiditis-18 cases Granulomatous thyroiditis-4 cases	0-3%	Clinical follow-up

III. Atypia of undetermined significance or follicular lesion of undetermined significance	10	10%	Atypia of undetermined significance- 2case Follicular lesion of undetermined significance-8 cases	~5-15%	Repeat FNA
IV. Follicular neoplasm or suspicious for follicular neoplasm	8	8%	Follicular neoplasm-6 cases Suspicious for follicular neoplasm-2 case	15-30%	Surgical lobectomy
V. Suspicious for malignancy	2	2%	Suspicious for papillary carcinoma-2 case	60-75%	Near –total thyroidectomy or surgical lobectomy
VI. Malignant	8	8%	Papillary carcinoma-4 cases Anaplastic carcinoma-4 cases	97-99%	Near total thyroidectomy

Ultrasound findings were collected in all the 100 cases and were correlated with FNAC findings.

Imaging and Cytology concordance was seen in 72 cases (72% of cases) and discordance in 28 cases (28% of cases). Concordance was seen mostly in cases of multinodular goitre (90% of cases) and malignancy (80% of cases). Discordance was seen in 8 cases of follicular lesion of undetermined significance, 4 cases of lymphocytic thyroiditis, 4 cases of granulomatous thyroiditis, 4cases of papillary carcinoma , 2 case of multinodular goitre and 2 case of follicular neoplasm.

Table 2: FNAC Imaging concordance cases

Result	Number of cases	Percent of cases
Imaging FNAC concordance	72	72%
Imaging FNAC discordance	28	28%

Ultrasound findings were collected in all the 100 cases and were correlated with FNAC findings. Imaging and Cytology concordance was seen in 72 cases (72% of cases) and discordance in 28 cases (28% of cases). Concordance was seen mostly in cases of multinodular goitre (90% of cases) and malignancy (80% of cases). Discordance was seen in 8 cases of follicular lesion of undetermined significance, 6 cases of lymphocytic thyroiditis, 4 cases of granulomatous thyroiditis, 4cases of papillary carcinoma , 4 cases of multinodular goitre and 2 cases of follicular neoplasm.

Table 3: FNAC Imaging discordance cases

Total number of cases(n=28)	Diagnosis on imaging	Diagnosis on FNAC
4	Colloid nodule	Papillary carcinoma
2	Thyroiditis	Goitre
4	Multinodular goitre	Granulomatous thyroiditis
2	Malignancy	Goitre with cystic degeneration
4	Multinodular goitre	Lymphocytic thyroiditis
8	Multinodular goitre	Follicular lesion of undetermined significance
2	Goitre	Follicular neoplasm
2	Malignancy	Lymphocytic thyroiditis

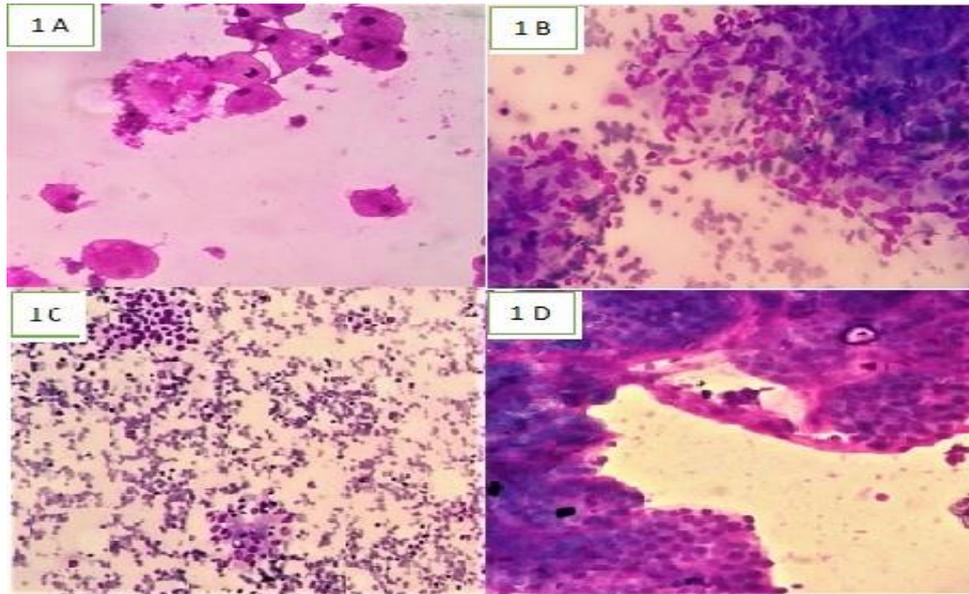


Figure 1A: Cyst fluid only. Photomicrograph showing few cyst macrophages against an amorphous eosinophilic background (Smear, Giemsa, 400x magnification),

1B Granulomatous thyroiditis Photomicrograph showing many lymphocytes and aggregates of histiocytes (Smear, Giemsa, 400x magnification)

1C Lymphocytic thyroiditis. Photomicrograph showing many lymphocytes impinging on aggregates of thyroid follicular cells (Smear, Giemsa, 400x magnification)

1D Nodular goitre Photomicrograph showing monolayered sheets of evenly spaced follicular cells against a background of colloid (Smear, Giemsa, 400x magnification)

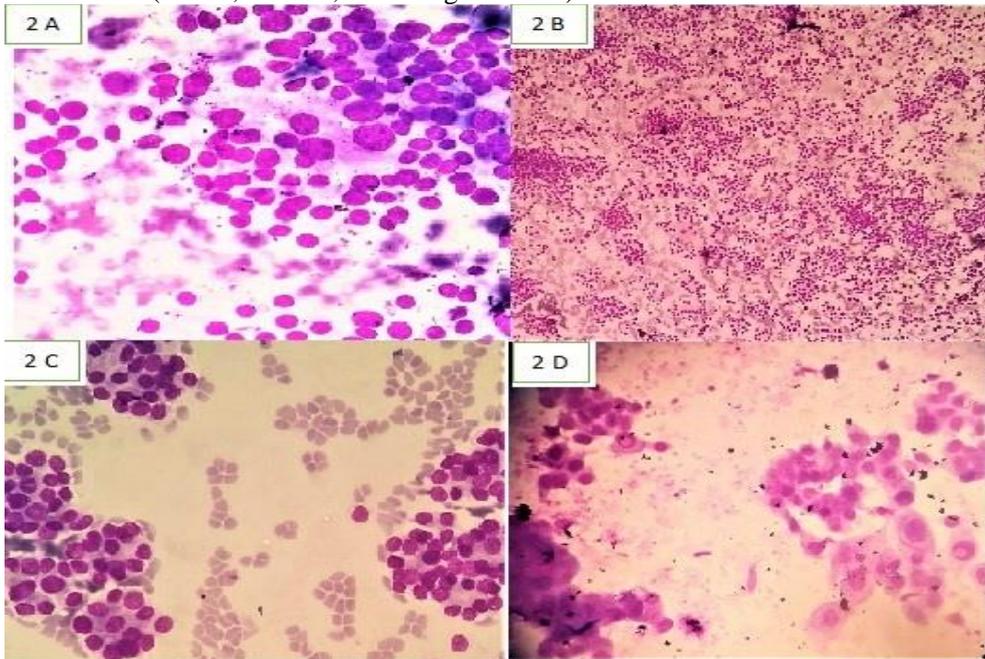


Figure 2A: Atypia of Undetermined significance Aspirate shows thyroid follicular cells with mild nuclear atypia (Smear, Giemsa, 400x magnification)

2B: Follicular lesion of Undetermined significance Aspirate shows microfollicular aggregates and scattered follicular cells (Smear, Giemsa, 400x magnification)

2C: Follicular Neoplasm: Aspirate shows microfollicular aggregates .of uniform follicular cells(Smear, Giemsa, 400x magnification)

2D: Suspicious for papillary carcinoma Aspirate shows thyroid follicular cells with basophilic cytoplasm and occasional intranuclear inclusions (Smear, Giemsa, 400x magnification)

Discussion:

Every thyroid FNA must be evaluated for adequacy. Inadequate samples are reported as “nondiagnostic” (ND) or “unsatisfactory” (UNS). This category applies to specimens that are unsatisfactory owing to obscuring blood, overly thick smears, air drying of alcohol-fixed smears, or an inadequate number of follicular cells. For a thyroid FNA specimen to be satisfactory for evaluation (and benign), at least 6 groups of benign follicular cells are required, each group composed of at least 10 cells^[7,8]. The minimum size requirement for the groups allows one to determine (by the evenness of the nuclear spacing) whether they represent fragments of macrofollicles. There are several exceptions to the numeric requirement of benign follicular cells. Any specimen that contains abundant colloid is considered adequate (and benign), even if 6 groups of follicular cells are not identified: A sparsely cellular specimen with abundant colloid is, by implication, a predominantly macro follicular nodule and, therefore, almost certainly benign. Whenever a specific diagnosis (eg, lymphocytic thyroiditis) can be rendered and whenever there is any atypia, the specimen is, by definition, adequate for evaluation. ND/UNS results occur in 2% to 20% of cases but ideally should be limited to no more than 10% of thyroid FNAs, excluding samples composed exclusively of macrophages^[9-11]. In our study the cases in Category I is 8% of total cases, which is within the range given by TBRTCP. Other recent studies had 1.2% to 16.4% cases in this group^[12-19]. All of them were advised to be reaspirated after a minimum period of 3 month to prevent false positive interpretations due to reactive or reparative changes. A benign result is obtained in 60%-70% of thyroid FNAC, according to TBRTCP. The false negative rate of a benign interpretation is low (0%-3%).^[20,21] Number of cases in category II in our study is 64%. The “benign” category had a range of 34% to 87.5% in recent studies^[12-19]. Some cases can not be easily classified into the benign, suspicious or malignant categories. These cases are reported as atypia of undetermined significance (AUS) or follicular lesion of undetermined significance. This category constitutes 3%-6% of thyroid FNAC.^[11,20] In our study, the number of cases in this category is 10%. This could possibly be due to overuse of this category. An AUS result has been reported in 3.2–29% of thyroid cases in recent studies^[12-19]. The recommended management is clinical correlation and repeat FNAC at an appropriate interval.^{20,22} In most cases, repeat FNAC results in a more definitive diagnosis: only about 20% of nodules are repeatedly AUS.^[20] The number of cases falling in category IV (Follicular Neoplasm or Suspicious for a Follicular Neoplasm FN/SFN) constitute 8% of cases in our study. Recent studies have shown 2.2–16.1% cases in this group^[12-19]. The purpose of this category is to identify a nodule that might be a follicular carcinoma and triage it for surgical lobectomy. About 15% to 30% of cases in this category turned out to be malignant.^{11,20,23,24} The majority of FN/SFN cases turned out to be follicular adenomas, or adenomatoid nodules of multinodular goitre, both of which are more common than follicular carcinoma. Among the malignant cases, many are follicular carcinomas, but a significant number of cases are follicular variants of papillary carcinoma^{9,20,23,25}. Category V (Suspicious for malignancy) constitutes 2% in our study and was constituted by 2 case (2%). It varies from 1.3 to 10% in recent studies^[12-19]. Our case was suspicious for papillary carcinoma. The cases in this category are resected by lobectomy or thyroidectomy. Most (60%-75%) prove to be papillary carcinomas and the rest are usually follicular adenomas^{11,20,21,26}. Category VI included 8 cases (8%), which included 4 cases of papillary carcinoma and anaplastic carcinoma. The category malignant had a range of 2.9% to 11% in recent studies^[12-19].

The imaging evaluation of a thyroid nodule includes numerous ultrasound features like size, echogenicity, composition (cystic, solid, mixed), presence or absence of calcifications, borders (irregular vs smooth), and presence and quality of internal color Doppler flow. Although some characteristics of thyroid nodules are not predictive of malignancy (e.g., size), other

characteristics (e.g., solid composition, hypo echogenicity, calcifications, disorganized internal vascularity, irregular borders, absence of halo) have been associated with an increased risk of malignancy. However, these ultrasound characteristics have low sensitivity and low positive predictive value for malignancy; moreover, the sensitivity, specificity, and predictive values of these ultrasound characteristics are highly variable in the literature^[27]. Of all the ultrasound characteristics, a predominantly solid composition is the feature with the highest sensitivity at 69–75%, but its positive predictive value is low: Approximately 25% of solid or predominantly solid nodules will prove to be malignant ^[27]. On the other hand, the presence of micro calcifications holds a positive predictive value of 41.8–94.2% but suffers from a low sensitivity because micro-calcifications are found in fewer than 60% of patients with thyroid cancer^{27]}. Simultaneous consideration of several ultrasound characteristics has proven to increase the positive predictive value so that a predominantly solid nodule with micro calcifications has a 31.6% chance of being malignant, whereas a predominantly cystic nodule without calcification has a 1% chance of being malignant ^[6, 27, 28].

Conclusions:

Fine-needle aspiration cytology (FNAC) of thyroid is a good initial screening test for thyroid nodules. The Bethesda System for Reporting Thyroid Cytopathology proved to be an excellent reporting system.

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