

*Original Research Article*

**Reporting Fine Needle Aspiration Cytopathology (FNAC) of Thyroid Lesion Per Guidelines of Recent Bethesda System For Reporting Thyroid Cytopathology Markedly Reduces Number of Un Necessary Thyroidectomies**

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**Abstract**

Estimation of accuracy of fine needle aspiration cytopathology (FNAC) of thyroid in diagnosis of different thyroid lesions, and evaluation of the value of reporting FNAC per guidelines of Bethesda system in reducing the number of un necessary thyroidectomies.

This is a case control prospective study conducted on 221 patients with thyroid nodule<sub>[s]</sub>. Patient were recruited to Cytopathology Department, Al-Yarmouk Teaching Hospital in the period from January 2014 to March 2017. Results of FNAC were reported per recent Bethesda System for Reporting of Thyroid Cytopathology (TBSRTC). Final diagnoses were determined by histopathology of surgically removed thyroid tissues.

Females were more than males with a ratio of 5.31/1, median age was 45.67±3.1 years. Twelve of cases (5.43%) categorized as nondiagnostic/ unsatisfactory samples, 128 (57.92%) as benign, and 29 (13.13%) as atypia of undetermined significance/atypical follicular lesion of undetermined significance (AUS/AFLUS), 34 (15.38%) as follicular neoplasm/suspected follicular neoplasm (FN/SFN), 5 (2.26%) as suspicious for malignancy, and 13 cases (5.88%) as malignant. Histopathology found 2 cases from cytopathological benign category, 7 from AUS/AFLUS, 11 from FN/SFN, 3 from SFM, and twelve from malignantcategory to be malignant. FNAC achieved a sensitivity of 85.71%, specificity of 99.21%, positive predictive value of 92.31%, negative predictive value of 98.44%, and total accuracy of 97.87%.

Reporting thyroid cytopathology per Bethesda system increases sensitivity, specificity, accuracy of thyroid cytopathology, increases understanding of reporting system by clinician, improves management plans, and reducing number of un necessary thyroidectomies.

**Key Words:** FNAC thyroid, Bethesda system, TBSRTC system.

**كتابة تقارير الفحوصات الخلوية حسب توجيهات ومبادئ بثيسدا يقلل من عدد عمليات رفع الغدة الدرقية غير الضرورية**

**الخلاصة**

دراسة معدلات الامراض والاورام الخبيثة والغير خبيثة في الغدة الدرقية بواسطة الارتشاف بالابر الدقيقة وكتابة نتائجها حسب نظام بثيسدا. أجريت الدراسة على مائتان واحد وعشرون مريضا ومريضة يشكون من عقد الغدة الدرقية والمراجعين الى مستشفى اليرموك التعليمي في بغداد. تم سحب عينات من الغدة الدرقية بواسطة الرشف بالابر الرفيعة تحت السونار وبعد اكمال الشرائح المجهرية تم الفحص وكتابة التقارير وحسب نظام بثيسدا وتصنيفها الى ستة فئات واحدة حميدة والاخرى خبيثة والبقية هي حالات مشتبه بها تحتاج الى متابعة او اعادة فحص او جراحة وحسب صنفها. نسبة الحالات الحميدة 57,92% والسرطانية 5,88% والبقية مشتبه بها.

أثبتت الدراسة ان استخدام نظام بنيسدا في تدوين التقارير الطبية للفحوصات الخلوية للغدة الدرقية مفيد جدا لانه يساعد الاطباء على فهم الحالات المرضية والتقارير الخلوية ويسهل عليهم علاج مرضاهم ويقلل من عدد عمليات رفع الغدة الدرقية غير الضرورية.

## **Introduction**

**T**hyroid lesions and nodules are common in clinical practice [1, 2]; they have been shown in about 19-67% of adult population by high-resolution ultrasound, and in 50% in autopsy [1-3]. Palpable thyroid nodules have been reported in 4-7% of adult people [1]. International studies reported thyroid nodules more in females than males with a ratio of 5.2/1 [1-4]. Preoperative evaluation of thyroid nodules involves assessing of presence of any risk factors for development of thyroid nodule(s) by taking history of exposure to radiation specially to head and necks areas, low iodine diet, and history of thyroid cancer in the family [4]. Physical examination, and relevant investigations such thyroid function tests, ultrasound and other imaging studies, and finally by cytopathology using fine needle aspiration cytology (FNAC) if indicated [3-6]. The important goal in management of thyroid nodule(s) is the differentiating between benign and malignant thyroid nodules [2-4]. In spite of prevalence of thyroid nodules in clinical practice, malignant thyroid nodules are only fewer than 5% of thyroid nodules in adults, and the remaining majority are non-neoplastic or benign lesions [1, 2, 6, 7]. The ultrasonic findings such as nodes edge, type of calcifications, presence or absence of halo, echogenicity of nodules, the size of nodules, and internal echotexture of thyroid, can't differentiate benign from malignant thyroid nodules although, it may give an idea about malignant suspicious nodules [7, 8]. All over the world, FNAC from thyroid is an important procedure in the management of different thyroid conditions [8-11]. It is cost-effective, minimally invasive, and can performed as an outpatient technique and extremely efficient in identifying benign thyroid nodules and thereby reducing unnecessary surgeries and

to give a plan for ideal surgical approach [8, 9]. Standard terminology is not widely implemented in reporting cytopathology of thyroid fine-needle aspiration (FNAC) [12, 13]. Various institution give varying diagnostic terminology in reporting thyroid cytopathology [14, 15]. Standardizing the nomenclature for reporting thyroid cytopathology will enhance communication and understanding between clinicians and pathologists [15, 16]. Various methods have been used all over the world for reporting thyroid FNAC, ranging from two to six or more categories.

Two category systems include benign and malignant categories only. Other category systems are more complicated such as; inconclusive, equivocal, atypical, indeterminate, uncertain, suspicious of malignancy, possible malignant, and probable malignant [15]. Clinicians find a great difficulty in the interpretation of these reports and making plans for management [16-19]. The purpose of the present study is to standardize reporting of thyroid cytopathology in Iraqi patients per Bethesda system for reporting thyroid cytopathology (TBSRTC). This system is composed of six categories including: The non-diagnostic, the benign, the atypia of undetermined significance/atypical follicular lesion of undetermined significance (AUS/ AFLUS), the follicular/ Hürthle cell neoplasm/ suspicious of follicular neoplasm (FN/SFN), the suspicious of malignancy (SFM), and the malignant [20-22]. The second objective is to determine the accuracy of cytopathological reports by correlating them with histopathological diagnoses (gold standard method) of resected specimens.

## **Materials and Methods**

### **Patients**

The current study was a prospective study on 221 patients with thyroid swelling

referred to the Department of Pathology, Al-Yarmouk Teaching Hospital in the period from January 2014 to March 2017.

The study was approved by Ethical Committee at Almustansiriyah University, College of Medicine, and a signed consent has been taken from all participant before starting of the study. Medical history, relevant clinical examination, and laboratory investigations were performed in accordance with recommendations issued by Bethesda System for Reporting of Thyroid Cytopathology (TBSRTC) system and National Cancer Institute (NCI) [15, 16]. Cases included in the present study were those with preoperative FNAC and postoperative histopathological diagnosis. All cases without subsequent histopathological diagnosis were excluded from the study.

#### **Technical details of ultrasound guided FNAC from thyroid**

Before aspiration from any patient a signed informed consent taken and the wright was given to patient to withdraw from study at any time. Patient should be asked about history of bleeding disorders or use of antithrombotic drugs such as warfarin to avoid formation of local hematoma at the site of aspiration. The aspiration needles were disposable gauge-23 attached to 10ml disposable syringe. Aspiration must be performed and smeared by the cytopathologist and under ultrasound guideness. The site of aspiration should be cleaned with antiseptic. Aspiration usually performed without local anesthesia, but it might be needed for some patients whom can't tolerate pain, and those in those with deep seated thyroid nodules. Infiltration by 1 – 2 milliliters of lidocaine 1 – 2% over the nodule was enough for local anesthesia. Aspiration was performed using 4-5 passes at different sites of nodule under ultrasound guideness. After aspiration, the patient should stay in the clinic for ½ to 1 hour before leaving. The aspirated materials immediately expelled on labelled slides and smeared using conventional methods. Most of

smears immediately fixed in 95% methanol for atleast ½ hour and stained with Papanicolaou stain. One to 2 slides left to dry in air and stained by Giemsa stain to identify inflammatory cells especially lymphocytes and plasma cells in cases of thyroiditis.

#### **Interpretation of smears**

The diagnostic cytomorphologic criteria issued by Bethesda system for reporting thyroid cytopathology (TBSRTC) were followed rigorously for identifying the six categories of the TBSRTC [15, 16]. Each case must be examined by three pathologists separately and reached to the same conclusion. Unsatisfactory or non-diagnostic category (ND/UNS) was applied for all smears with insufficient or absent follicular epithelium, composed predominately of blood, thick smear cases, and cases with extensive air-drying artifact. Benign category was introduced for cases of thyroiditis, adenomatoid and colloid nodules. Follicular lesion of undetermined significance or atypia of undetermined significance category (FLUS/AUS) was applied for cases in which the cytopathological features were not typical for benign category, and insufficient to be suspicious of follicular neoplasm or follicular/Hürthle cell neoplasm category. Cases with micro-follicles, scant to absent colloid, and with moderate to high cellularity were categorized as follicular neoplasm/suspicious of follicular neoplasm category (FN/SFN). Cases from this category with cells having oncocyctic cytoplasm were identified as Hürthle cell neoplasm. Suspicious of malignancy category (SFM) includes all cases with low cellularity or degeneration of aspirated cells but with some features suggestive of anaplastic carcinoma, papillary carcinoma or lymphoma. Malignant category includes cases with adequate and well prepared smears allowing definitive cytopathologic diagnosis of carcinoma [15]. Occult micropapillary thyroid carcinoma detected

by histopathology of multinodular goiters was not included in this category [16]. Details of reporting thyroid cytopathology and

categories, expected risk malignancy, and the suggested management per TBSRTC [16], are seen in table -1.

**Table 1:** Reporting thyroid cytopathology according TBSRTC system.

Diagnostic Category	Risk Of Malignancy	Usual Management
<b>1. Non-diagnostic or unsatisfactory (ND/UNS);</b> a. Fluid only (cyst). b. Acellular specimen c. Others (clotting artifact, obscuring blood, etc.)		Repeat FNA under ultrasound guidance
<b>2. Benign;</b> a. Adenomatoid nodule. b. Colloid nodule etc.) c. Lymphocytic (Hashimoto) thyroiditis. d. Granulomatous (subacute) thyroiditis. e. Others	0 – 3%	Follow-up clinically
<b>3. Follicular lesion of undetermined significance or Atypia of undetermined significance or (AUS/FLUS).</b>	5 – 15%	Repeat FNAC
<b>4. Suspicious of follicular Neoplasm or follicular neoplasm (FN/SFN).</b> Specify if Hurtle cell (oncocytic) type.	15- 30%	Surgical lobectomy
<b>5. Suspicious for malignancy (SFM) including;</b> a. Papillary carcinoma b. Medullary carcinoma c. Metastatic carcinoma d. Lymphoma e. Others	60 – 75%	Surgical lobectomy or Near-total thyroidectomy
<b>6. Malignant, including;</b> a. Papillary thyroid carcinoma. b. Medullary thyroid carcinoma. a. Poorly differentiated carcinoma b. Undifferentiated (anaplastic) carcinoma c. Carcinoma with mixed features (specify). d. Squamous cell carcinoma. e. Non-Hodgkin lymphoma. f. Metastatic carcinoma. g. Others.	97 – 99%	Near total thyroidectomy

### Statistics

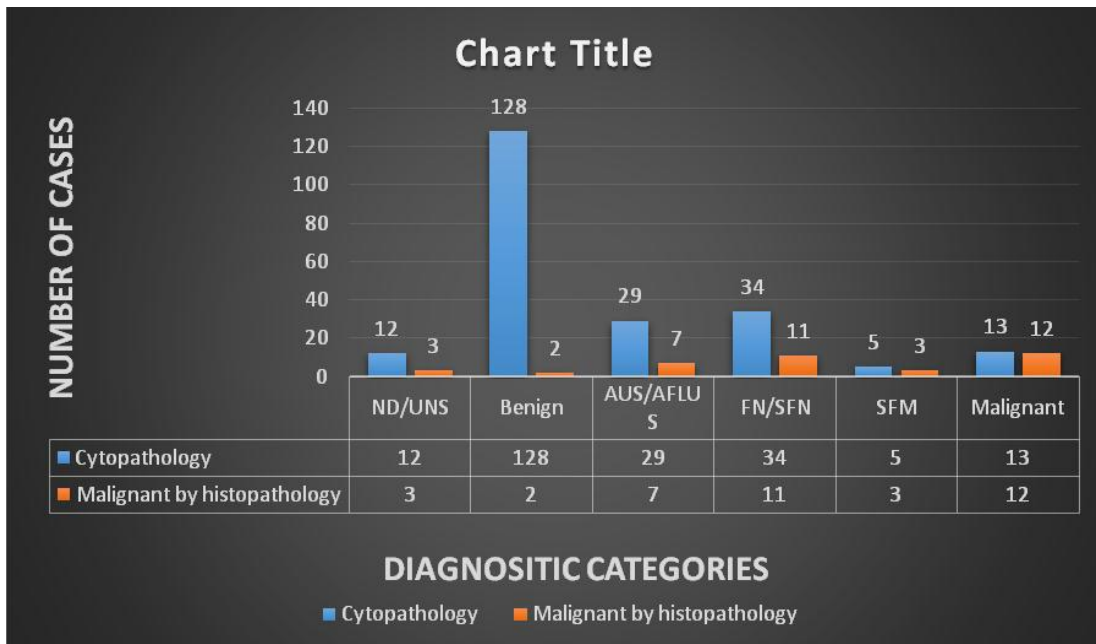
The results were analyzed using IBM SPSS statistical software 24 and Microsoft Excel 2010. Numerical data was tabulated as mean and standard error. The *t*-test was used in comparison between two groups when data were normally distributed. Mann-Whitney U

test was carried out on non-parametric data that were not normally distributed. All data were considered statistically significant when the (*p-values*) were below 0.05.

**Results**

The patients participated in the current study were 221, females were 186 (84.16%), and males 35 (15.84%). Females were more than males in a ratio of 5.31/1. The mean age of patient was 45.67±3.1 years, ranging from 15 – 88 years. Cases reported as non-diagnostic/unsatisfactory (ND/UNS) category by cytopathology were 12/221 (5.43%), 3 of them (3/12) 25% were found to be malignant by subsequent histopathological examination of resected lesions. Number of cases in benign category was 128/221 (57.92%) by cytopathology, 2 of them (2/128) 1.56% were found to be malignant on subsequent histopathology.

Cases categorized by cytopathology as AUS/AFLUS were 29/221 (13.13%), 7 of them (7/29) 24.13% were proved to be malignant by histopathology. The number of cases in the category of follicular neoplasm/suspicious of follicular neoplasm (FN/SFN) were 34/221(15.38%), 11 of them (11/34) 32.35% were found to be malignant on histopathology. Cases categorized as suspicious for malignant were 5/221 (2.26%), 3 of them (3/5) 60% proved to be malignant by histopathology. Finally, cases labelled as malignant by cytopathology were 13/221 (5.88%), 12 of them (12/13) 92.3% proved to be malignant on histopathology figure 1.



**Figure 1:** No. of cases in each diagnostic cytopathological category, and number of malignant cases by histopathology.

(ND/UNS= nondiagnostic/unsatisfactory, AUS/AFLUS=atypia of undetermined significance/ follicular lesion of undetermined significance, FN/SFN=follicular neoplasm/suspected follicular neoplasm, and SFM=suspicious for malignancy).

**Discussion**

The aim for FNAC of thyroid is to separate benign from malignant conditions. Fine needle aspiration cytopathology from thyroid have markedly reduces the number of un necessary surgeries in most of the studies [3-5]. Most of these systems used in interpretation of thyroid cytopathology were

not comprehensive, they are not including strict criteria of diagnosis of each category, and they are not including any suggestion for further management or risk of malignancy in each category. This resulted in increased of un necessary thyroidectomies and in inappropriate management. Bethesda system for reporting thyroid cytopathology

(TBSRTC) implementing diagnostic criteria for cytopathological diagnosis of each and guidelines for management of each category. In the present study, the number of benign cases reported by TBSRTC system were 128 (57.92%), while malignant cases were 13 (5.88%), and remaining other categories were 36.2% collectively, and all results were statistically significant with *p-values were* <0.001. On comparing results of benign and malignant categories in this study with other international studies there were no great differences in rate of benign and malignant conditions in most of these studies. The great differences were in cases intermediate between benign and malignant condition and in their reporting by cytopathologist and management by clinicians. Studies by Heydar Ali Esmailiet al [8], and Jogai et al [9], showed benign thyroid lesions constituting 64.3%, and 33.1% of studied cases, while malignant cases 7.8% and 19.5% respectively. The results of studies by Mehrali Rahimi et al [13], Santosh Kumar Mondal et al [14] were high for benign conditions 90.3%, and 80%, low for malignant 9%, and 6% respectively. In the studies by Richa Sharma et al [1], and Sinna et al [18] the rate of benign thyroid nodules was 51.58%, and 13.5%, while malignant conditions were 46.32%, and 7.1% respectively. The high results of malignant conditions in Sharma et al [1] study were due to use of different method of reporting thyroid cytopathology there by increasing the number of false positive cases on the expense of inconclusive cases. The difference in the methods of reporting system of thyroid cytopathology is confusing to pathologists as well as to clinicians, and making the clinical management as a personal decision thereby increasing the number of unnecessary thyroidectomies.

### **Conclusion**

Fine needle aspiration cytopathology from thyroid nodule(s) is a safe, quick outpatient, cost effective and easy procedure if done by expert hands, but it needs a unified system of

interpretation, reporting language and guidelines for proper categorization and management. Bethesda System for Reporting Thyroid Cytopathology is a comprehensive system for cytopathological diagnosis of thyroid nodule(s) and with strict diagnostic criteria for each category, predicting risk of malignancy and guidelines for planning of further management. The results of present study recommended the use of TBSRTC system in Iraq for reporting thyroid cytopathology in the future.

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