

A Comparative Study of the Bethesda System of Reporting of Fine Needle Aspiration Cytology Thyroid with Histopathology

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ABSTRACT

BACKGROUND

The Bethesda system of reporting thyroid cytopathology is an outstanding and systematic approach of reporting thyroid cytology samples, thereby reducing the communication gap between cytopathologist and clinician, leading to a better patient care approach. We aim to study the thyroid fine needle aspiration (FNA) using the Bethesda system and evaluate its accuracy taking histopathology as gold standard.

METHODS

This was a descriptive study including 200 consecutive cases which came to our cytology department between January 2014 and December 2014. All thyroid fine needle aspiration cytology (FNAC) were categorised as per the Bethesda system and followed up with corresponding histopathology.

RESULTS

Out of the 200 cases, adequacy criteria was met in 196 (98 %) cases. 176 (88 %) cases fell in the benign category, 4 (2 %) cases were inadequate samples, 8 (4 %) showed features of follicular neoplasm / suspicious of follicular neoplasm and 12 (6 %) were malignant lesions. Histopathology follow up was available for all cases. Statistical analysis showed a specificity of 100 % (high), sensitivity of 40 % (low). Positive predictive value was 100 %, negative predictive value was 90.4 %. Accuracy rate was 91 %.

CONCLUSIONS

Interpreting the thyroid FNAC results using Bethesda system allowed a superior interlaboratory agreement leading to improved clinical management.

KEYWORDS

Thyroid, Cytology, Bethesda

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BACKGROUND

Fine needle aspiration cytology is a reliable, safe, accurate, less invasive and economical technique and is routinely applied as an indispensable investigation to diagnose thyroid lesions.¹

Over the past 50 years FNAC could dramatically reduce unnecessary thyroid surgeries by 60 - 80 %, thereby increasing the excision rate for malignant nodules by over 50 %.² The usage of standard terminology reduced the rate of non-diagnostic specimens and the so-called "descriptive diagnoses" significantly. This allowed precise communication between clinicians and pathologists thus maintaining inter-hospital consensus.

In 2007, the National Cancer Institute, Bethesda, United States, organised the NCI Thyroid Fine Needle aspiration State-of-the-Science Conference. Various aspects of thyroid aspiration were discussed including pre FNA requirements, the technique, training and post FNA managements. All this culminated in the publishing of an atlas and guidelines for interpretation and standardized nomenclature of thyroid FNACs known as the Bethesda system of reporting thyroid cytopathology.³

The six tiered Bethesda system comprises of an integrated, hierarchical and a clear classification of diagnoses which have individual implicit risk of malignancy that can affect the management.² The present study was conducted to interpret the thyroid FNACs using the Bethesda system and to estimate its efficiency taking into consideration histopathology as gold standard.

METHODS

This was a descriptive study (diagnostic test evaluation) conducted in the Department of Pathology, Government Medical College, Thiruvananthapuram, from January 2014 to December 2014. The study was commenced after obtaining clearance from our institutional research and ethical committee.

Study Population

As per reference 4, sensitivity = 82 %, prevalence = 11 %; applying the formula,

$$Sample\ size = \frac{4 \times Sensitivity \times (1 - Sensitivity)}{\frac{20}{100} \times (Sensitivity)^2 / Prevalence}$$

As per reference (89)⁴

Sensitivity = 82%

Prevalence = 11%

$$Sample\ Size = \frac{4 \times \frac{82}{100} \times (\frac{100}{100} - \frac{82}{100})}{\frac{20}{100} \times (\frac{82}{100})^2 / \frac{11}{100}}$$

$$= \frac{4 \times \frac{0.82 \times 0.18}{(0.2 \times 0.82)^2}}{0.11}$$

$$= \frac{0.5904}{0.026896 / 0.11}$$

$$= 199.55$$

A detailed history was obtained from each patient and it was entered methodically. Fine needle aspiration of thyroid was performed using 23 / 24 gauge needle and 5 ml syringe after cleaning the site of prick using alcohol. Aspirate thus obtained is immediately spread onto a glass slide and fixed in 80 % isopropyl alcohol for a minimum of 15 minutes to avoid drying artefacts. Smears are stained using the Papanicolaou technique. The smears were studied under microscope (4x, 10x & 40x) and a cytological diagnosis is established and then it was categorised according to the Bethesda system.

Thyroidectomy specimens immersed in adequate quantity of 10 % neutral buffered formalin were received in the department which was then kept overnight for fixation. Specimen were cut and appropriate bits were taken the following day. Processing of the samples overnight was ensured. Blocks were prepared and tissue sections of 5 microns were made. Staining of sections with haematoxylin and eosin was done and sections were studied.

Inclusion Criteria

Consecutive fine needle aspirations of thyroid done at the Department of Pathology, Government Medical College, Thiruvananthapuram, who further underwent thyroidectomy (total / near total / hemi thyroidectomy) at Government Medical College during the study period were studied.

Exclusion Criteria

- Thyroid fine needle aspirations done without subsequent thyroidectomy.
- Thyroidectomy specimen received in the Department of Pathology without prior fine needle aspirations.

Statistical Analysis

All data were entered in Microsoft Excel and sensitivity, specificity, predictive values were calculated.

RESULTS

During the study period of 12 months from Jan 2014 to Dec 2014, 200 cases of FNAC of the thyroid were collected and categorised based on the Bethesda system, which was subsequently correlated with histopathology.

Out of the 200 patients with thyroid lesions collected during the study period, 182 were females and 8 were males giving a female to male ratio of 10:1. FNAC of thyroid lesion was done in different age groups ranging from 15 years to

65 years and the mean age was 40.33 years of the 200 FNACs, 4 aspirates were cytologically inadequate for opinion and were labelled as unsatisfactory smears; giving an adequacy rate of 98 %. The reason for obtaining such high adequacy rates in our institution is due to our routine practice of repeating cases with an inadequate aspiration and supplementing with an ultrasonographic guidance whenever indicated. Out of the 196 adequate samples, 176 were non neoplastic and 20 were neoplastic.

Bethesda	Count	Percent
Insufficient for opinion	4	2.0
Benign	176	88.0
Follicular neoplasm / suspicious of follicular neoplasm	8	4.0
Malignant	12	6.0

Table 1. Frequency of the Sample Based on Bethesda

In the present study, category II (benign) consisted of 176 cases, which included colloid goitre (100 cases), colloid goitre with degeneration (39 cases), adenomatous goitre (06 cases), Hashimoto's thyroiditis (14 cases) and lymphocytic thyroiditis (17 cases).

Microscopically the cases reported as colloid goitre / colloid goitre with degeneration, showed follicular cells arranged in monolayered sheets and in some cases as three dimensional clusters. Occasional Hurthle cells were present. Colloid stained green to pink in Pap stain and showed pavement like appearance in most cases and dense in a few cases. A good number of cases showed haemosiderin laden macrophages and were reported as colloid goitre with degeneration. In the present study, this group comprised 78.9 % of the category II. Smears cytologically diagnosed as adenomatous nodule showed cellular aspirate with scant colloid, cells had well defined borders with honeycomb pattern and some showing Hurthle cell change.

Out of the 145 cases of colloid goitre (including those with degeneration and adenomatous lesions), 95.17 % cases were positively correlated. Among the remaining cases, all were histologically proven to have a papillary carcinoma or a papillary microcarcinoma. Of the 6 adenomatous nodules which were diagnosed cytologically, 66.6 % remained adenomatous nodule by histology also where as 33.3 % were just colloid nodule on follow up.

All cytologically diagnosed lymphocytic thyroiditis / Hashimoto's thyroiditis were that of female patients. Microscopically smears showed marked cellularity with polymorphous population of lymphocytes in the milieu. Hurthle cells were seen in sheets and occasionally singly. Out of the fourteen cases of Hashimoto's thyroiditis, histological data was available for all, and it was positively correlated for 10 cases. Two cases each of colloid goiter and papillary carcinoma thyroid were identified on follow-up. A bloody aspirate with lymphocytes in background would have resulted in a false diagnosis of Hashimoto's thyroiditis in FNA whereas aspiration of the adjacent thyroid might have missed a papillary carcinoma thyroid. Of the seventeen cases of lymphocytic thyroiditis, only two proved to be purely lymphocytic thyroiditis whereas nine cases were also showing colloid goitre areas on histology and six turned out to be Hashimoto's thyroiditis on follow up.

There were no cases of category III (AUS) and category V (suspicious of malignancy) in the present study. The neoplastic entities of the thyroid gland in the present study included eight cases of follicular neoplasm / Hurthle cell neoplasm or suspicious for follicular neoplasm / Hurthle cell neoplasm (category IV) and twelve cases of papillary carcinoma (category VI). Category IV smears showed moderate to marked cellularity. The follicular cells were predominantly arranged in microfollicular pattern. Cell crowding was noted in areas. Normal sized and relatively uniform follicular cells demonstrating scant cytoplasm with slightly hyperchromatic rounded nuclei and inconspicuous nucleoli were seen. Colloid was scant. Out of the eight cases, histological data showed 2 as follicular adenoma, 4 cases were papillary thyroid carcinoma, 2 were combined lesions which included papillary thyroid areas along with lymphocytic thyroiditis and cellular nodule.

Twelve cases of papillary carcinoma were observed in this study, out of whom four were males. The smears were moderately to markedly cellular showing follicular cells in papillary pattern with anatomical bordering and in monolayered sheets. The follicular cells exhibited enlarged nuclei, nuclear moulding, longitudinal nuclear grooves (Fig. 1), intra nuclear cytoplasmic pseudo-inclusions & powdery chromatin. Thick chewing gum like colloid was present (Fig. 2).

Histopathology distribution of the cases were as follows; nodular colloid goitre / colloid goitre with degeneration collectively accounted for 108 cases. Hashimoto's thyroiditis constituted 20 cases, 6 cases each of cellular nodule and lymphocytic thyroiditis, 2 were follicular adenoma and 22 were papillary carcinoma. Rest 36 cases had a combination of various neoplastic and non-neoplastic lesions. Out of the 8 cases cytologically diagnosed as follicular neoplasm / suspicious of follicular neoplasm histological data showed 2 as follicular adenoma, 4 cases were papillary thyroid carcinoma, 2 were combined lesions which included papillary thyroid areas along with lymphocytic thyroiditis and cellular nodule. Among the 12 cases of papillary carcinoma diagnosed cytologically, ten cases were papillary carcinoma histopathologically as well and the rest two turned out to be follicular carcinoma.

FNA-Bethesda Category	CG / MNG / DEG	Cellular Nodule	Hashimoto's Thyroiditis	Lymphocytic Thyroiditis	Follicular Adenoma	Follicular Carcinoma	Papillary Carcinoma	Combined Lesions	Total
I	00	00	00	00	00	00	00	04	04
II	108	06	20	06	00	00	08	28	176
III	00	00	00	00	00	00	00	00	00
IV	00	00	00	00	02	00	04	02	08
V	00	00	00	00	00	00	00	00	00
VI	00	00	00	00	00	02	10	00	12

Table 2. Histopathologic Correlation

The malignancy risk for each category of Bethesda system was calculated using the available histopathological

data. The malignancy risk was 8.1 % for category II and 100 % for category VI according to the present study. True positive, true negative, false positive and false negative were obtained. The sensitivity and specificity of FNAC for neoplastic lesions were calculated using true positive (TP), true negative (TN), false positive (FP) & false negative (FN). In the present study, statistical analysis of thyroid lesions by Bethesda has high specificity (100 %), low sensitivity (40 %), positive predictive value of 100 %, negative predictive value of 90.4 % and a high accuracy rate of 91 %.

DISCUSSION

The present study attempted to report thyroid fine needle aspirations according to the recently proposed six-tier diagnostic classification system. This was a prospective study which was held during the period of January 2014 through December 2014. During this study period, a total of 200 cases of FNAC of the thyroid were collected and categorized based on the Bethesda system. This was followed by a histopathologic correlation. M: F ratio in our study was 1:10 which was comparable to that of a study by Gupta M et al⁵ (11.5:1), Tabaqchali et al⁶ (8.2:1) and Melo Uribe et al⁷ (7.9:1).

The mean age of presentation of thyroid lesions in the present study was 40.33 yr. Gupta M et al⁵ found out a mean age of incidence of thyroid lesions to be 38.7 yrs which was comparable with our study. Mean age in the studies by Melo Uribe et al⁷ and Tabaqchali et al⁶ were 50.02 years and 48 years respectively which was higher than our study. Adequacy rates of the present study was 98 % which was comparable with that of study conducted by Melo Uribe et al⁷ (95.6), Naz et al⁸ (94), and Handa U et al⁹ (94.9) The non-neoplastic lesions in the study included were colloid goitre, colloid goitre with degeneration, cellular nodule, lymphocytic thyroiditis and Hashimoto's thyroiditis. The neoplastic lesions included follicular adenoma, follicular carcinoma and papillary carcinoma. There were 176 (88 %) non neoplastic lesions and 20 (10 %) neoplastic lesions.

The ratio of non-neoplastic to neoplastic lesions in our study was 8.8:1 which was akin with that of Handa U et al⁹ (12.3:1) whereas the values obtained in studies by Tabaqchali et al⁶ (1.54:1) and Melo Uribe et al⁷ (0.75:1) were much lesser than our study and reason for this might be that the above studies were conducted in oncology institutes. Out of the 176 benign lesions diagnosed by aspiration cytology, 100 cases were colloid goitre, 39 cases were colloid goitre with degeneration, 06 cases were adenomatous goitre (together accounting for 82.3 %), 14 cases were Hashimoto's thyroiditis and 17 cases were lymphocytic thyroiditis (together accounting for 17.61 %).

The proportion of colloid goitre and Hashimoto's thyroiditis in the present study (4.48:1) was similar to the studies by Handa U et al⁹ (2.18:1) but differed from the study by Tabaqchali et al⁶ (19.5:1). The incidence of follicular neoplasm in this study (4 %) was close to that of studies conducted by Handa U et al⁹ (3.22) and Theoharis et al¹⁰ (5.5) but was much lesser than what was obtained in the study by Gupta M et al⁵ (24 %). There were 12 cases of

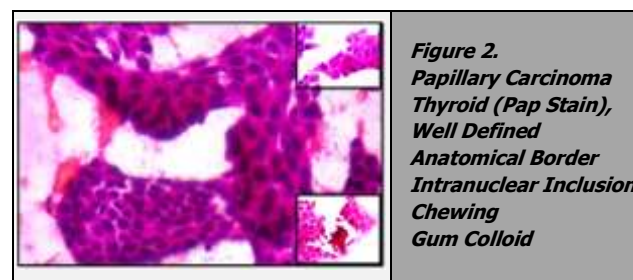
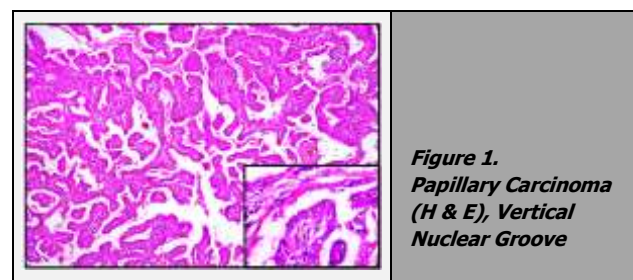
papillary carcinoma in the current study with an incidence of 6 % and agreed with that obtained by Theoharis et al¹⁰ (4 %) but was lesser than incidence in Gupta M et al.⁵ The higher incidence of papillary thyroid carcinoma in study by Gupta M et al⁵ may be due to the smaller sample size.

Study	Bethesda I	Bethesda II	Bethesda III	Bethesda IV	Bethesda V	Bethesda VI
Theoharis ¹⁰	11.1 %	73.8 %	3 %	5.5 %	1.3 %	5.2 %
Naz et al ⁸	0	73.77 %	9.84 %	6.56 %	6.56 %	3.28 %
Melo Uribe ⁷	4.08 %	23.47 %	2.04 %	16.84 %	37.24 %	16.33 %
Present	2 %	88 %	0	4 %	0	6 %

Table 3. Comparison of Incidence of Bethesda Categories

The current study is akin with that by Theoharis et al¹⁰ in all aspects except the category I. The low incidence of category I in our study is probably due to the repeated aspirations we perform in our institution for thyroid lesions.

When it comes to the study by Naz et al,⁸ our study is comparable regarding the category II. In our study we did not get any case in category III and category V. Again this could be attributed to the repeated aspirations which we do routinely in our institution which have resulted in a considerable reduction in ambiguity of results. All the 200 cases were followed up with the histopathological diagnosis. From the histological and cytological data, the true positives (12), true negatives (170), false positives (0) and false negatives (18) were identified. Sensitivity (40 %), specificity (100 %), positive predictive value (100 %) and negative predictive value (90.4 %) and accuracy (91 %) were calculated. The present study was observed to have a specificity, positive predictive value, negative predictive value and an accuracy which was comparable to other similar studies conducted by Gupta M et al,⁵ Handa U et al⁹ and Tabaqchali et al.⁶



Perhaps the positive predictive value and specificity were reaching 100 % which indicates the accuracy with which we are obtaining fine needle aspiration samples in our institution partly due to the repeated aspirations we are

routinely doing in order to provide the best possible pre-operative diagnosis for our patients. We lagged behind in our sensitivity for fine needle aspiration with other similar studies. An important thing to be noted at this point is that 36 cases (18 %) of histopathology report showed a combined lesion, six of them showed a papillary carcinoma and two showed follicular carcinoma. Larger size of the gland, smaller size of the malignant lesion, and wrong site of entry of the needle might have resulted in the false low sensitivity in the present study. The malignancy rate of category II and VI in the present investigation was commensurable with other similar studies including Theoharis et al¹⁰, Naz et al⁸ and Melo Uribe et al.⁷ We observed a higher degree of malignancy result for category IV. All category I cases were nodular colloid goitre on follow up and hence category I had a malignancy rate of 0 %.

CONCLUSIONS

The present study made an attempt to classify the thyroid aspirations based on the Bethesda system for reporting thyroid lesions. The cytology results were compared with the corresponding histopathology reports and it was found to have a high specificity and positive predictive value. It indirectly indicates its significance in the management. A large proportion of thyroid surgeries can be avoided if the pre surgical evaluation yields a better understanding of the underlying pathology.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

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