# Comparison of Bethesda classification with final HPE diagnosis on thyroid nodules: A prospective observational study

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## Abstract

This study is a Single-centered prospective observational study conducted on 48 patients who underwent thyroid surgery. After evaluating the results of 48 patients, a high degree of correlation. Bethesda classification and Final H.P.E can be inferred.

**Keywords:** ACR-TIRADS, Bethesda, thyroid nodules, thyroid malignancy

## Introduction

With an age-adjusted incidence rate of 12.2 per 100,000 men and women per year between 2006-2010, thyroid cancer is the most frequent endocrine malignancy. The incidence has been increasing by an estimated 6.4% per year between 1997 and 2010 [1], and the incidence rate has been at this level since 2006. Fine needle aspiration (FNA), which comes after a first ultrasound, is the next step in determining the likelihood that a thyroid nodule will develop into cancer [2-5]. The Bethesda system for reporting FNA cytopathology results classifies the results of a biopsy as falling into one of the following six categories: I (non-diagnostic), II (benign), III (atypia of undetermined significance/follicular lesion of undetermined significance), IV (follicular neoplasm), V (suspicious for malignancy), and VI (malignant) [6].

Nodules on the thyroid that are classified by Bethesda as being in categories III or IV have an overall malignancy risk that ranges from 15 to 40 percent. [6, 7]. If it is determined that a Bethesda III or IV nodule is malignant, the follicular variant of papillary thyroid cancer (fvPTC) [4, 8] is the histologic subtype that occurs the most frequently. It has been established that this subtype of papillary thyroid carcinoma has a decreased likelihood of lymph node metastases, extra-thyroidal extension and

recurrence, particularly if the tumour is encapsulated [9-11]. This subtype of papillary thyroid carcinoma is generally less aggressive than traditional PTC.

The identification of markers that can be screened for using FNA to predict the existence of aggressive characteristics in the thyroid has been a primary focus of study over the past few years. Recently, it has been proposed by a few researchers that the Bethesda categorization system itself may be utilised as a prognostic marker for a phenotype that is more aggressive [12]. It was hypothesised by these authors that tumours of the thyroid that were Bethesda category VI on preoperative FNA have more aggressive characteristics than malignancies that were Bethesda category III or IV. However, it is yet unknown if these differences merely indicate an improved capacity to diagnose conventional papillary thyroid tumours as compared to fvPTC. It is not clear whether the presence of this marker invariably indicates the presence of a tumour with a more aggressive profile.

## Materials and Methods

This study was conducted in the Department of Surgery, OBG and Medicine at Srinivas Institute of Medical Sciences, Mangalore.

**Type of Study:** It is a prospective observational study.
**Study Period:** March 2019 to August 2020.
**Study Population:** Patients admitted and planned for thyroid surgery during the study period.

### Inclusion criteria

- Patients who are admitted and planned for thyroid surgery with Bethesda FNAC reports are taken into consideration.

### Exclusion Criteria

- Patients with FNAC or/and TIRADS scan reports from outside hospital/lab.
- Patients with a previous history of thyroid surgery.
- When FNAC Cytology was not reported according to Bethesda Classification.
- Age below 18 years and above 90 years

### Procedure

- Patients admitted and planned for thyroid surgery are recruited in the study as mentioned in inclusion and exclusion criteria after taking proper informed consent.
- Clinical data, imaging data and Cytology reports are collected from the recruited patients as mentioned in the proforma.
- The data so collected is correlated with final Histopathology.

**Statistical analysi**

Statistical analysis was done using AKIBM SPSS Statistics 21.0 (IBM Corp., Armonk, NY, USA).

**Observations and Results**

- A total of 48 patients were included in the final analysis.
- Mean age of the study population is 47 years. Females (87%) forms majority of the study population.

**Bethesda classification**

2 patients had Hurthle cell neoplasm which are included under Bethesda-IV.

**Table 1:** Describes the distribution of study population according to Bethesda classification

| FNAC (Bethesda classification) | Per cent |
|---|---|
| I-Unsatisfactory | 8.3 |
| II-Benign | 52.1 |
| III-AUS/FLUS | 2.1 |
| IV-Follicular neoplasm/Suspicious of follicular neoplasm | 18.8 |
| V-Suspicious of malignancy | 14.6 |
| VI-Malignant | 4.2 |
| Total | 100.0 |

**Table 2:** Descriptive analysis of Bethesda classification (Benign and Malignant) in the study population (N=48)

| FNAC (Bethesda classification) | Per cent % |
|---|---|
| Benign (2, 3) | 54.2 |
| Malignant (4, 5, 6) | 37.5 |
| Unsatisfactory (1) | 8.3 |
| Total | 100.0 |

**Table 3:** Final H.P.E

| | N | Final H.P.E | |
|---|---|---|---|
| **ACR-TIRADS Score** | | **Benign** | **Malignant** |
| Mostly Benign (TR2,3) | 28 | 25(89.2%) | 3(10.8%) |
| Mostly Malignant (TR4,5) | 20 | 7(35.0%) | 13(65.0%) |
| Total | 40 | 32 | 16 |
| Chi-square value = 15.47; P<0.001:: Kappa Value = 0.56; P<0.001 | | | |

**Comparison of Bethesda classification with final HPE diagnosis (N=48)**

Out of 25 people having Benign, 21 (84.0%) tumours were labelled as benign by HPE diagnosis and 4 (16%) tumours were labelled as malignant by HPE diagnosis.

Out of 9 people whose FNAC came as follicular neoplasm or suspicious for a follicular neoplasm, 5 (55.6%) tumours were labelled as malignant by HPE findings, and 4 (44.4%) tumours were labelled as benign by HPE diagnosis.

Out of 7 people whose FNAC came as suspicious for malignancy, 5 (71.4%) tumours were labelled as malignant by HPE diagnosis and 2(28.6%) tumour was labelled as benign by HPE diagnosis.

All 4 people with Unsatisfactory FNAC report, have got their tumours labelled as benign by HPE diagnosis.

One tumour, which got Atypia of undetermined significance on FNAC, was labelled as benign by HPE diagnosis.

The difference in the proportion of FNAC findings with final HPE diagnosis was statistically significant (p = 0.006).

**Table 4:** Comparison of Bethesda classification of FNAC with Final H.P.E (N=48)

| FNAC (Bethesda classification) | N | Benign | Malignant |
|---|---|---|---|
| 1. Unsatisfactory | 4 | 4(100.0%) | 0(0.0%) |
| 2. Benign | 25 | 21(84.0%) | 4(16.0%) |
| 3. AUS/FLUS | 1 | 1(100.0%) | 0(0.0%) |
| 4. Suspicious of follicular neoplasm | 9 | 4(44.4%) | 5(55.6%) |
| 5. Suspicious of malignancy | 7 | 2(28.6%) | 5(71.4%) |
| 6. Malignant | 2 | 0(0.0%) | 2(100.0%) |
| Total | 48 | 32(66.7%) | 16(33.3%) |
| Chi-square value=16.45; P= 0.006 | | | |

**Comparison of Bethesda classification with final HPE diagnosis (N=48)**

- Bethesda classification II and III are considered as benign and IV, V and VI are considered as malignant for knowing predictive validity of Bethesda classification.
- Bethesda classification I is not included in either of them.
- Out of 26 whose FNAC comes under the Benign group (II and III), 22 tumours (84.6%) were labelled as benign by HPE diagnosis and only 4 tumours (15.4%) were labelled as malignant by HPE diagnosis.
- Out of 14 tumours with FNAC reports under the malignant group (IV, V and VI), 12 tumours (66.7%) were labelled as malignant and 6 tumours (33.3%) were labelled as benign by HPE diagnosis.

**Table 5:** Comparison of Bethesda classification of FNAC (benign and malignant) with Final H.P.E. (N=48)

| | N | Final H.P.E | |
|---|---|---|---|
| FNAC (Bethesda classification) | | Benign | Malignant |
| Benign (II and III) | 26 | 22(84.6%) | 4(15.4%) |
| Malignant (IV, V and VI) | 18 | 6(33.3%) | 12(66.7%) |
| Total | 44 | 28 | 16 |
| Chi-square value = 12.09; P = 0.001: : Kappa Value = 0.52; P = 0.001 | | | |

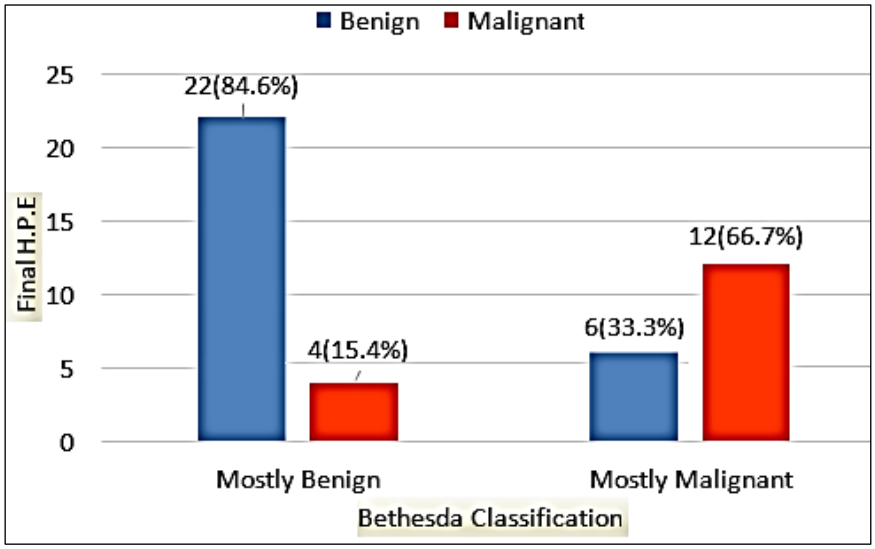


**Chart 1:** Clustered bar chart comparison of Bethesda classification of FNAC with Final H.P.E (N=48)

**Comparison of Bethesda classification with final HPE diagnosis (N=48)**

The Bethesda classification of FNAC also shows high Sensitivity of 75% and a specificity of 78.57% in predicting final HPE malignancy. Overall diagnostic accuracy of Bethesda classification is 77.27%.

**Table 6:** Predictive validity of Bethesda classification in predicting Final HPE diagnosis (N=48)

| Statistic | Value | 95% CI |
|---|---|---|
| Sensitivity | 75.00% | 47.62% to 92.73% |
| Specificity | 78.57% | 59.05% to 91.70% |
| Positive Predictive Value | 66.67% | 48.24% to 81.10% |
| Negative Predictive Value | 84.62% | 69.73% to 92.92% |
| Diagnostic Accuracy | 77.27% | 62.16% to 88.53% |

## Discussion

### Methodology

Our study is a prospective observational study in a surgical cohort of 48 participants. Studies that are being compared here either prospective or retrospective.

### Methodology

**Table 7:** Comparing methodology of different studies

| Study | Type of Study | Sample size | |
|---|---|---|---|
| Nam *et al*., (2017) [13] | Prospective | 630 | TIRADS VS HPE/FNAC<br>FNAC VS HPE |
| Zhang *et al*., (2015) [14] | Prospective | 220 | TIRADS VS HPE/FNAC |

| | | | |
|---|---|---|---|
| | | | FNAC VS HPE |
| Chakravarthy *et al*., (2018) [15] | Prospective | 290 | TIRADS VS HPE/FNAC<br>FNAC VS HPE |
| Chandramohan *et al*., (2016) [16] | Prospective | 238 | TIRADS VS HPE/FNAC |
| Current study | Prospective | 48 | ACR TIRADS VS H.P.E, ACR TIRADS VS FNAC, FNAC VS H.P.E. |

**Correlation of FNAC with HPE**

- Our study shows good sensitivity, specificity and negative predictive value comparable to other studies mentioned below.
- Positive predictive value is lower in our study (66.67%) compared to study by Nam *et al*., (85.2%) and study by Zhang *et al*., (98.1%).

**Table 7:** Comparing predictive validity of FNAC among different studies

| **Parameter** | **Current study** | **Zhang *et al*., (2015)[14] (TIRADS)** | **Nam *et al*., (2017)[13]** |
|---|---|---|---|
| Sensitivity | 75% | 77.6% | 83.9% |
| Specificity | 78.57% | 97.7% | 76.3% |
| PPV | 66.67% | 98.1% | 85.2% |
| NPV | 84.62% | 73.7% | 74.4% |
| Diagnostic accuracy | 77.27% | | 81% |

**Conclusion**

- ACR-TIRADS was found to be a highly specific and accurate classification system for categorizing the thyroid nodules based on ultrasound features, for assessing the risk of malignancy.
- Initial screening of a thyroid lesion with USG with ACR-TIRADS score will help to rule out benign lesions.
- Lesions suspicious of malignancy to be investigated with FNAC.
- This helps in decreasing the risk and cost of subjecting patients with benign nodules or indolent cancers with unnecessary biopsy and treatment.

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