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# A COMPARATIVE ANALYSIS OF THYROID CYTOLOGY CLASSIFICATION SYSTEMS: BETHESDA SYSTEM VERSUS FRCPATH, AUSTRALIAN, JAPANESE, AND ITALIAN APPROACHES IN THE INDIAN CONTEXT

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#### ABSTRACT

**Objectives:** There are many different popular coding systems in use across the world such as Bethesda, FRCPath (UK), the Australian reporting system, the Japanese Thyroid Reporting System, and the Italian classification system. By evaluating the strengths and weaknesses of each system concerning the Indian patient population and health-care infrastructure, this study aims to identify the most suitable approach for accurate thyroid cytology reporting and patient management in India.

**Methods:** A retrospective cohort study was conducted at a tertiary care center in central India following due ethical clearance. A total of 208 cases met the inclusion criteria of this study. The clinical records and the cytological records of these cases were independently analyzed and reclassified by a group of pathologists into all the above-stated thyroid coding systems. Data were collected and analyzed using Microsoft Excel 2016.

**Results:** Approximately 88.46% of the cases were women. Medial lobe was the most common site with prevalence of 80.29%. Colloid goiter is most common cytological diagnosis. Only for 11 cases, there was a difference in coding among these coding systems. Codes 1 and 2 are same in all the coding systems and the main difference identified for cases with Bethesda Codes 3 and 5.

**Conclusion:** The Bethesda coding is simple and reliable for coding thyroid FNAC as it has been reported over the period. The other coding systems can also be used but they will have their long learning curve. Furthermore, Bethesda is being used universally making the report understandable.

Keywords: Thyroid FNAC, Bethesda coding, FRCPath reporting, Italian coding, Australian reporting, Japanese coding.

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## INTRODUCTION

Thyroid cytology plays a crucial role in the diagnosis and management of thyroid nodules [1]. The Bethesda System (TBS) for reporting thyroid cytopathology (TBS) has gained widespread acceptance; however, its applicability in all health-care settings, including those in India, merits investigation [2,3].

This study proposes a comparative analysis of TBS with other established systems such as FRCPath (UK), the Australian reporting system, the Japanese thyroid reporting system, and the Italian classification system (Sistema diagnostico citologico) in an Indian context. Table 1 covers the comparative codification based on different standards.

By evaluating the strengths and weaknesses of each system concerning the Indian patient population and health-care infrastructure, this study aims to identify the most suitable approach for accurate thyroid cytology reporting and patient management in India. This comparison can offer insight for cytologists, endocrinologists, and other healthcare professionals involved in thyroid nodule diagnosis. Thus, a comparative analysis can provide valuable guidance for optimizing thyroid cytology reporting in India and ensuring better patient outcomes.

# METHODS

**Study design** This was a retrospective cohort study.

#### Sample size

A statistically significant sample size will be determined based on power analysis, considering the expected prevalence of malignancy and desired level of precision which comes out to be 200.

#### **Data collection**

#### Source

Archived thyroid FNA cytology cases from a tertiary hospital in central India.

#### Inclusion criteria

Cases with complete clinical data (age, sex, and nodule size) were included in the study.

#### **Exclusion criteria**

Cases with inadequate cytological material, or inconclusive diagnoses were excluded from the study.

## **Classification systems**

Each case will be independently reviewed and classified according to the following systems: TBS, FRCPath system, Australian reporting system, Japanese reporting system, and Italian reporting system.

## Cytopathologists

A panel of experienced cytopathologists blinded to the original diagnosis and follow-up information performed the reclassification of cases on different classifications. Inter-observer variability was assessed using kappa statistics.

FRCPath	Bethesda	Italian	Australian	Japanese
Thy1 I	Ι	TIR 1	1	1
Non-diagnostic for cytological diagnosis	Non-diagnostic or unsatisfactory	Non-diagnostic	Non-diagnostic	Inadequate
Thv1c		TIR 1c		
Non-diagnostic for cytological		Non-diagnostic cystic		
diagnosis-cystic lesion		<b>TID 0</b>	0	
Thy2 II	11	TIR 2	2	2
Non-neoplastic Thy2c	Benign	Non-malignant	Benign	Normal or benign
Non-neoplastic–cystic lesion				
Thy3a	III	TIR 3A	3	3
Neoplasm possible-atypia/	Atypia of undetermined	Low-risk	Indeterminate or	Indeterminate B, others
non-diagnostic	significance or follicular lesion of undetermined significance	indeterminate lesion	follicular lesion of undetermined significance	
Thv3f	IV	TIR 3B	4	3
Neoplasm possible, suggesting	Follicular neoplasm or suspicious	High-risk	Suggestive of a	Indeterminate A, follicular
follicular	for a follicular	indeterminate lesion	follicular neoplasm	neoplasms
neoplasm	neoplasm			A-1, favor benign A-2,
*				borderline A-3. favor
				malignant
Thv4	V	TIR 4	5	4
Suspicious of malignancy	Suspicious for malignancy	Suspicious of	Suspicious of	Malignancy suspected
		malignancy	malignancy	0 9 1
Thy5	VI	TIR 5	6	5
Malignant	Malignant	Malignant	Malignant	Malignancy

Table 1: Details of famous cytological coding of thyroid lesions used across the world [4]

## Data analysis

The demographic distribution of the cases across various categories was analyzed with the help of the percentage of overall cases. The correlation between Bethesda and histological diagnosis was performed graphically using a heat map. All the statistical analysis is performed using Microsoft Excel 2016.

## Ethical considerations

Ethical approval was taken from the Institutional Review Board. The ethical approval number for this study is IECBMC/2023/108. Patient anonymity was maintained throughout the study.

#### RESULTS

A total of 208 cases met the inclusion criteria and were taken into consideration. This number met the desired level of accuracy calculated for this study. All these cases were re-evaluated for diagnosis using different coding systems popular across the world. Out of these cases, only 56 cases underwent histopathological evaluation.

The demographic distribution is presented in Table 2. The highest number of cases were reported for women (n=184), that is, approximately about 88.46%. The highest number of cases were reported for the age group 21–30 (n=61), followed by 31–40 and 41–50 with, respectively, 47 and 43 cases. Eldest reported case was of an 89 years old female. The most common site for the lesion was the medial lobe with the prevalence of approximately about 80.29%. The least common site was for the left lateral lobe, about 6.73%.

The highest number of cases is that of colloid goiter. Following closely is nodular goiter. The lowest number of cases was that of primary hyperplasia of the thyroid along with nodular goiter, benign thyroid nodule, and a single case of suspicion for malignancy. Cytomorphic distribution of cases is presented in detail in Table 3.

Most of the codes in different international standards for thyroid lesions are very similar to each other. A total of 11 cases were coded differently out of 208 cases across different international coding standards. Out of these five were cases of follicular neoplasm and the rest for papillary Table 2: Demographic distribution of cases on different criteria

Histological Coding	Number of cases	% of cases
Gender		
Male	24	11.54
Female	184	88.46
Age-Wise		
11-20	15	7.21
21-30	61	29.33
31-40	47	22.60
41-50	43	20.67
51-60	26	12.50
61-70	14	6.73
71–90	2	0.96
Site-wise		
Left lateral lobe	14	6.73
Medial lobe	167	80.29
Right lateral lobe	27	12.98

Table 3: Cytomorphic distribution of	cases l	based	on Betl	nesda
coding for thyroid	lesions	6		

Diagnosis (based on Bethesda)	Number of cases	Percentage (%)
Acute suppurative thyroiditis	1	0.48
Benign thyroid nodule	1	0.48
Colloid goiter	77	37.02
Follicular neoplasm	4	1.92
Nodular goiter	2	0.96
Hashimoto's thyroiditis	8	3.85
Lymphocytic thyroiditis	18	8.65
Malignant	1	0.48
Nodular goiter	76	36.54
Primary hyperplasia	2	0.96
papillary carcinoma	5	2.40
Suspicious for malignancy	1	0.48
Subacute thyroiditis	12	5.77

neoplasm. Table 4 presents the coding of all the cases where there is a difference in the diagnosis of different coding standards. Codes 1

Table 4: Cases with differe	nt diagnosis code	s assigned by d	ifferent methods (	n=11)	۱
	0			. ,	

Histopathologic diagnosis	Coding techniques					
	Bethesda	FRCpath	Italian	Japanese	Australian	
Follicular neoplasm	4	3f	3a	3a1	4	
Follicular neoplasm	4	3f	3b	3a	4	
Follicular neoplasm	4	3f	3b	3a	4	
Follicular neoplasm	4	3f	3b	3a	4	
Follicular neoplasm	4	3f	3b	3a	4	
Papillary neoplasm	6	5	5	5	6	
Papillary neoplasm	6	5	5	5	6	
Papillary neoplasm	6	5	5	5	6	
Papillary neoplasm	6	5	5	5	6	
Papillary neoplasm	6	5	5	5	6	
Papillary neoplasm	6	5	5	5	6	

and 2 are the same in all the coding standards and the main difference identified for cases with Bethesda Codes 3 and 5.

Out of 208 cases, only 56 underwent histopathologic examination. The most common diagnosis was colloid goiter with 42 cases, followed by papillary carcinoma and follicular adenoma. One case was diagnosed as subacute thyroiditis and two for follicular neoplasm. Table 5 represents the heat map between Bethesda and histopathological diagnosis.

## DISCUSSION

The fine-needle aspiration cytology (FNAC) in itself is one of the most reliable, effective, and rapid tests for the accurate diagnosis of thyroid lesions. In addition, it is also very cost-effective and can be performed in a small setup under all aseptic precautions.

Thyroid cytology classification systems play a crucial role in the accurate diagnosis and management of thyroid nodules, thereby influencing patient care outcomes [5,6]. In this study, a comparative analysis is conducted for five widely used classification systems: TBS, FRCPath, Australian, Japanese, and Italian systems, within the context of the Indian health-care system. Through this comparative analysis, we aimed to elucidate the applicability, strengths, and limitations of each system and provide insights into their suitability for the Indian population.

Our findings reveal varying degrees of applicability among the classification systems studied. TBS, characterized by its standardized reporting categories and emphasis on risk stratification, has gained significant traction globally. However, its applicability in the Indian context faces challenges due to differences in disease prevalence, demographics, and health-care infrastructure [7,8]. The FRCPath classification, with its emphasis on morphological criteria and diagnostic algorithms, presents a structured approach that resonates well with Indian pathologists. Yet, its adoption may be hindered by resource constraints and the need for specialized training [9-11].

The Australian, Japanese, and Italian approaches exhibit regional nuances tailored to the respective populations' epidemiological and clinical characteristics [12-14]. While these systems offer valuable insights into region-specific cytological features and management strategies, their direct translation to the Indian context necessitates careful consideration of cultural, genetic, and environmental factors influencing thyroid pathology.

Nonetheless, their utility in the Indian context may be limited by differences in disease prevalence and genetic predispositions, warranting further validation studies.

Our comparative analysis provides valuable insights into the nuances of thyroid cytology classification systems in the Indian context, paving the way for evidence-based practice guidelines and tailored diagnostic algorithms to meet the evolving healthcare needs of the population. Table 5: Heat map representing the correlation between Bethesda and histopathological diagnosis (n=56)

Histological Coding	Bethesda coding					
	2	3	4	5	6	
Subacute thyroiditis	1	0	0	0	0	
Colloid Goiter	42	0	0	0	0	
Multi nodular goiter	2	0	0	0	0	
Follicular Adenoma	0	0	3	0	0	
Follicular neoplasm	0	0	2	0	0	
Papillary carcinoma	0	0	0	0	6	

The findings of all the international reporting systems show a close match to each other for codes 1 and 2. There is a significant difference in the coding of entities falling under Code 3. However, we did not encounter any case of Code 3 in our study.

The inter-observer variability among cytopathologists is none in our study using the Bethesda reporting system. However, the same was obtained with all the other coding systems. The significant difference lies in category 3 which was not reported.

The present study findings are almost similar to the many other previous studies carried out in this area. The study supports the existing observations as found in past studies that Bethesda is the most reliable and safe coding system for palpable thyroid cytology [15].

### Strengths and limitations

The inclusion of multiple classification systems has been studied for the 1<sup>st</sup> time in such a detailed manner. The potential advantages of implementing Bethesda in the Indian health-care context are specifically dependent on cost-effectiveness, cytopathologist expertise, and workflow integration. Although adopting or adapting the Bethesda coding system, or even developing a standardized approach specifically tailored for the Indian context is the need of the hour.

The major limitation of the study is its retrospective nature or potential selection bias in the collected data. In addition, a few of the codes were not covered.

## **Future directions**

Future research directions can be identified by making the study a multi-centric study and focusing more on category 3 which is atypia of undetermined significance, as the cases falling under this category need to be evaluated more elaborately to rule out the malignancy.

Conducting prospective studies to validate the best approach for the Indian population is also a good initiative for this study as the findings may differ due to the demographic change. Future research endeavors should focus on longitudinal studies evaluating the clinical outcomes and prognostic implications of different classification systems in diverse Indian populations. Moreover, initiatives aimed at standardizing reporting practices, fostering interdisciplinary collaboration, and enhancing pathologist training are imperative to optimize thyroid nodule management and improve patient care outcomes in India.

## CONCLUSION

Bethesda system still holds the flag with being the easiest and most reliable method of coding for thyroid lesions on FNAC. The other international coding systems are also at par but need to be in sync with the continent using them.

The most important and affirmative method in the Indian subcontinent is Bethesda as inter-observer variation has been brought down significantly and, hence, anyone from a novice to an expert can use it in India.

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## **AUTHORS' CONTRIBUTIONS**

PS and SC were involved in the conception and planning of the research, AC and MS performed the data acquisition/collection, SP, PS, and AC calculated the experimental data and performed the analysis, PS drafted the manuscript, SC and MS designed the tables, and SP and PS aided in interpreting the results. All authors took part in giving critical revision of the manuscript.

## **CONFLICTS OF INTEREST**

None.

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None.

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