International Journal of Research

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

Diagnostic Accuracy Of Revised Bethesda System For Reporting Thyroid Lesions With Cyto- Histological Correlation

By

Dr. ROSHAN A MATHEW (Resident, Dept of pathology, Govt medical college Kottayam, Kerala)

Dr. Lillykutty Pothen (Additional professor, Dept of pathology, Govt medical college Kottayam, Kerala)

Dr. Sankar S (Prof. and HOD Dept of pathology Government medical college Kottayam, Kerala)

International Journal of Research

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

STRUCTURED ABSTRACT

STRUCTURED ABSTRACT

Background:

Fine needle aspiration cytology (FNAC), being reliable, minimally invasive, cost effective, having high sensitivity and specificity, has been applied routinely as a useful and indispensable method to diagnose thyroid lesions. FNAC has allowed a dramatic decrease in unnecessary surgeries with thyroid nodular disease, enhancing the percentage of malignant operated nodules over 50%. It is relied upon to distinguish benign from neoplastic/malignant thyroid nodules, thus, influencing therapeutic decisions. However, there is some "gray zone" of thyroid cytology where the diagnostic efficacy of FNA declines sharply, rendering it difficult to exactly categorize the nature of the lesion leading to discrepant cases.

The aim of this study is to determine the sensitivity, specificity, predictive values and diagnostic accuracy of cytology of thyroid lesions which has a surgical follow up with histopathological examination.

Objective:

To evaluate the diagnostic accuracy of the revised Bethesda system for reporting thyroid lesions with cyto-histological comparison.

Methods:

Study design **:**Diagnostic test evaluation

Study population : FNA specimens of the thyroid lesions and its corresponding histopathology specimen received in the Department of pathology, Govt medical college Kottayam during the study period

Study sample : 77

Sampling procedure: continuous sampling

Study procedure: FNAC smears of thyroid lesions are studied and are compared with the gold standard that is histopathology to evaluate the accuracy of diagnosis

Results:

- Sensitivity of reporting thyroid FNAC using the Bethesda system is 67%
- Specificity of reporting thyroid FNAC using the Bethesda system is found to be 100% (as there are no false positive cases)
- PPV of reporting thyroid FNAC using Bethesda system is 100%
- NPV of reporting FNAC thyroid using the Bethesda system is 88.8%
- Hence the accuracy of the test is 90.9%

Conclusion:

We evaluated and reported our FNACs according to Bethesda guidelines and our study validated the accuracy of Bethesda system of reporting thyroid cytopathology in our setup. Therefore we recommend routine use of TBSRTC for reporting thyroid cytopathology for initial workup of patients with thyroid nodule. However, risk of malignancy was found to be significantly high in Bethesda 3 category to warrant further workup including ultrasound/thyroid scan in addition to repeat FNAC. We also recommend adequate sampling from all the possible nodules in thyroid and a better site selection for the needle insertion for a better results.

Keywords : Diagnostic accuracy, The Bethesda system, FNAC, Histopathology.

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

International Journal of Research

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

INTRODUCTION

INTRODUCTION

Fine-needle aspiration (FNA) has an essential role in the evaluation of euthyroid patients with a thyroid nodule. It reduces the rate of unnecessary thyroid surgery for patients with benign nodules and appropriately triages patients with thyroid cancer to appropriate surgery. Before the routine use of thyroid FNA, the percentage of surgically resected thyroid nodules that were malignant was 14%.

A multitude of diagnostic tests like ultrasound, thyroid nuclear scan, and fine needle aspiration cytology (FNAC) is available to the clinician for evaluation of thyroid nodule and other tests like ultrasound and nuclear scan should be used in conjunction with FNAC.

FNAC is simple, cost effective, readily repeated, and quick to perform procedure in the outpatient department with excellent patient compliance. Important factor for the satisfactory test includes representative specimen from the nodule and an experienced cytologist to interpret findings. It is often used as the initial screening test for diagnosis of thyroid nodules [1].

The prevalence of thyroid nodules ranges from 4% to10% in the general adult population and from 0.2% to 1.2% in children [2]. The majority of clinically diagnosed thyroid nodules are non neoplastic; only 5%–30% are malignant and require surgical intervention [3]

In India 42 million people suffer from thyroid diseases[4] . Thyroid cancer is reported to be most prevalent in the coastal areas of Kerala and Karnataka.[5] As per the national cancer registry 3 year report 2009-2011, the relative frequency of thyroid cancer among all the cancer cases was 0.1-0.2% of which Thiruvananthapuram and Kollam had the highest number of registered cases of thyroid cancer.[6]

Patients with differentiated thyroid carcinoma have an excellent 10-year survival ranging between 80 and 95%[7] . This is because the natural course of the disease is relatively mild and treatment of this tumour type, which consists of thyroidectomy followed by high-dose radioiodine and life-long thyroid hormone therapy, is highly successful.[8] Appropriate treatment then rests on the ability of the pathologist to give an accurate diagnosis. Tissue biopsy and routine H&E staining are the gold standard in the diagnosis of thyroid nodules[9] The microscopic distinction between benign and malignant lesions by conventional histology is at times difficult.

Most of the discovered nodules are benign. More than 80 % of the malignancies present in palpable thyroid nodules are papillary thyroid carcinoma followed by follicular carcinoma.[10] Diagnosis of papillary carcinoma thyroid is based on specific nuclear features. However, focal presence of the same features in other follicular epithelial lesions make the distinction of papillary carcinoma thyroid from other lesions difficult.[11]

Diagnostic dilemma also arises when an encapsulated nodule with a follicular pattern of growth exhibits clear nuclei with grooves and hence distinguishing follicular adenoma from encapsulated FVPTC becomes difficult.[12] Multinodular goitre with delicate papillary branching and focal nuclear clearing may often be confused with PTC. Papillae formation can occur focally in follicular adenoma as well.[13]

FNAC is, however, not without limitations; accuracy is lower in suspicious cytology and in follicular neoplasms. The main aim of FNAC is to identify nodules that require surgery and those benign nodules that can be observed clinically and decrease the overall thyroidectomy rate in patients with benign diseases. The present study was undertaken to correlate the FNAC findings with histopathology so that rate of unnecessary thyoidectomies in benign pathologies can be avoided.

International Journal of Research

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

OBJECTIVE

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

OBJECTIVE

To evaluate the diagnostic accuracy of revised Bethesda system for reporting thyroid lesions by cyto-histological comparison.

International Journal of Research

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

RELEVANCE

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

RELEVANCE

A uniform reporting system for thyroid FNA will facilitate effective communication among cytopathologists, endocrinologists, surgeons, radiologists, and other health care providers; facilitate cytologic-histologic correlation for thyroid diseases; facilitate research into the epidemiology, molecular biology, pathology, and diagnosis of thyroid diseases, particularly neoplasia; and allow easy and reliable sharing of data from different laboratories for national and international collaborative studies. Hence credibility of such a system should be checked regularly and maintained[74]. This study emphasis on an institution based evaluation of the diagnostic accuracy of the Bethesda system for reporting thyroid lesions with respect to histopathology in an institution based set up and hence the pitfalls in those areas can be located and corrected in the long run set up of the institution.

International Journal of Research

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

METHODOLOGY

METHODOLOGY

RESEARCH QUESTION:

What is the diagnostic accuracy of revised Bethesda system for reporting thyroid cytology compared to histo pathologic diagnosis

TYPE OF STUDY: Diagnostic test evaluation

PERIOD OF STUDY: 18 months

STUDY SETTING: Department of Pathology, Govt.. Medical College, Kottayam.

STUDY POPULATION:

FNA specimens of the thyroid lesions and its corresponding histopathology specimen received in the department of pathology, Govt. medical college Kottayam during the study period

SAMPLE SIZE[14] :

$$\text{Sample size } N = \frac{Z\alpha^2 \text{x sensitivity (1-sensitivity)}}{d^2}$$

$Z\alpha = 1.96$ at $\alpha = 0.05$,d= absolute precision = 10

Sensitivity in previous study=72.7%

$$\text{Sample size, } N = \frac{Z\alpha^2 \text{ sensitivity(1-sensitivity)}}{d^2}$$

$$= \frac{(1.96)^2 \times 72.7 \text{x} 27.3}{100}$$

$$= 76.21$$

Taking sample size as 77

RESEARCH HYPOTHESIS:

Reporting of FNA cytology of thyroid lesions by using the revised Bethesda system has high accuracy and concordance rates with histo pathological diagnosis

SAMPLING METHOD:

Continuous sampling.

INCLUSION CRITERIA:

Patients of all age groups and both sex, with palpable thyroid swelling, who comes for FNAC.

EXCLUSION CRITERIA:

Inadequate biopsy samples, history of previous thyroidectomy, cases where hisopathology is not available

STUDY TOOLS:

1. Instruments for tissue processing.
2. Reagents for tissue processing.
3. Glass slides and cover slips for mounting.
4. Microscope
5. Reagents for Haematoxyline & eosin staining
6. Reagents for PAP and giemsa staining for cytology
7. Proforma to record serial number, Cytology number, Biopsy number, Name, age, sex, histopathology and cytology features as per the revised Bethesda system , radiological diagnosis.

STUDY PROCEDURE:

In all the patients with thyroid lesions, history, physical findings and probable diagnosis will be noted. FNAC is performed by conventional method. Direct smears are prepared and are giemsa and pap stained. Thyroid specimens of these patients received are fixed in 10% formalin for 12 to 24hrs after recording the gross morphological features. The specimens are routinely processed, embedded in paraffin wax and sections were cut at 3 to 6μm thickness. Sections were stained routinely with H and E stain. The cytology smears were reported based on the revised Bethesda system for reporting thyroid lesions. The histopathological classification of the thyroid lesions were made based on the WHO classification. The cytological and histopathological diagnosis were compared after grouping the lesions as benign and

malignant. Taking histopathology diagnosis as gold standard, the accuracy, sensitivity, specificity, positive and negative predictive values of cytological diagnosis by the revised Bethesda system was determined.

DATA MANAGEMENT AND ANALYSIS:

The data was entered in Microsoft excel and further statistical analysis was

done using SPSS software (version 22).

PERSONNEL RESPONSIBLE FOR DATA COLLECTION: Dr. Roshan A Mathew

PERSONNEL RESPONSIBLE FOR DATA ANALYSIS: Dr. Roshan A Mathew

FUNDING AGENCY: Self

CONSENT: This study was conducted on specimens and FNAC samples received in the Department of Pathology, Govt. medical college Kottayam. Hence implied consent was present.

International Journal of Research

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

RESULTS

RESULTS

This study was conducted on 77 FNAC samples of thyroid lesions and its corresponding histopathology specimens which were submitted to the department of pathology, Govt. Medical college, Kottayam during the period of study time (18 months). The histopathological diagnosis, which is taken as the gold standard , is kept as the reference to compare the accuracy of reporting the FNAC specimen of the corresponding thyroid lesions based on the revised Bethesda system for reporting thyroid lesions, and hence a birds eye view of the areas of mistakes are decoded.

Clinically, the most frequent symptom was painless swelling in the anterior neck region. The most frequent age group was between 40-60 years of age.

Age group	Frequency	Percentage
0-20	3	3.8
21-40	28	36.4
41-60	37	48.05
61-80	9	11.7
80+	0	0

Table 1 : Age wise distribution of patients

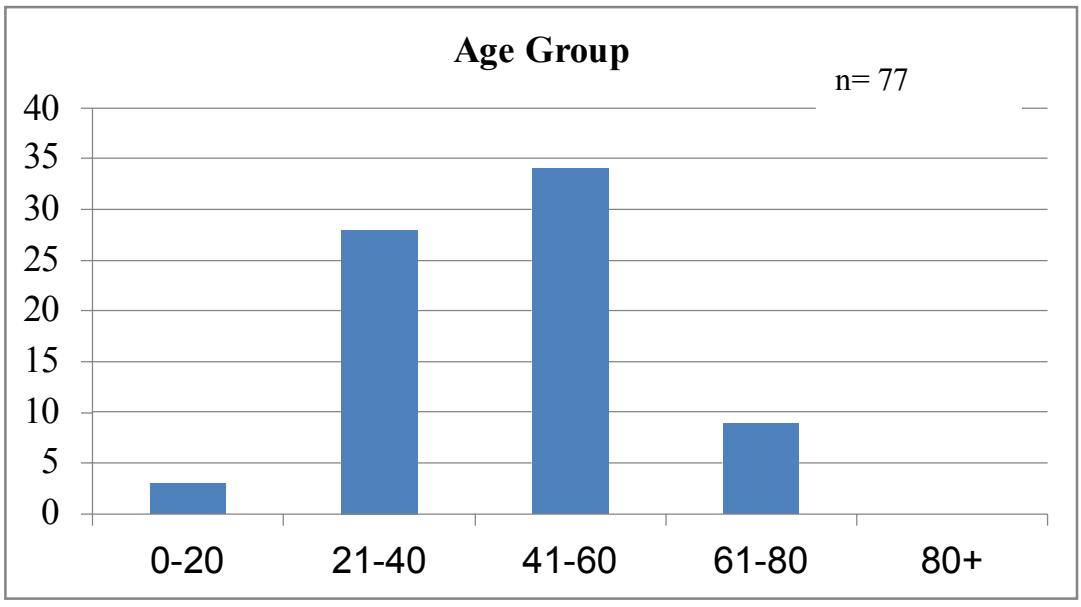

Fig 1 : Age wise distribution of patients

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

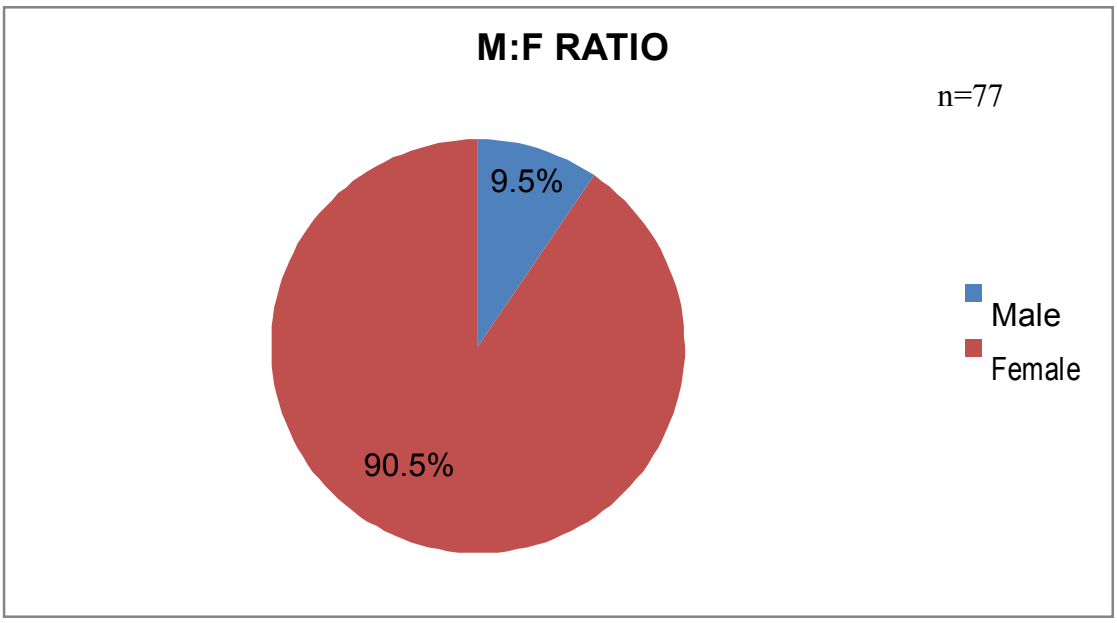

Fig 2 : Male to female ratio of patients

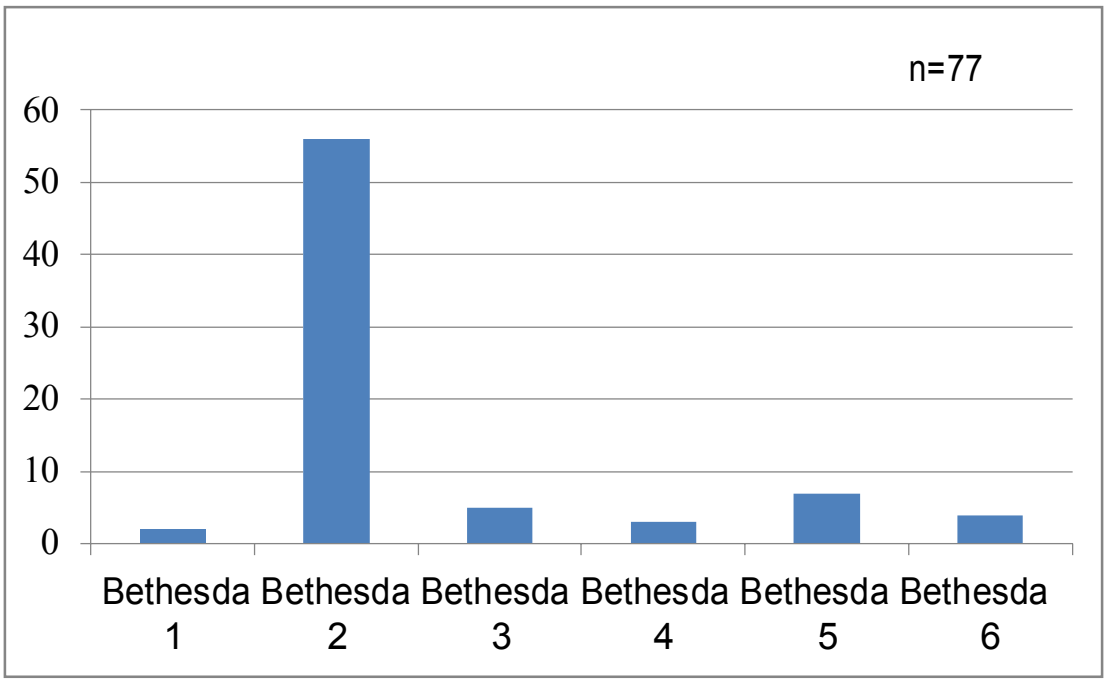

Fig 3 : Case distribution according to Bethesda category

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

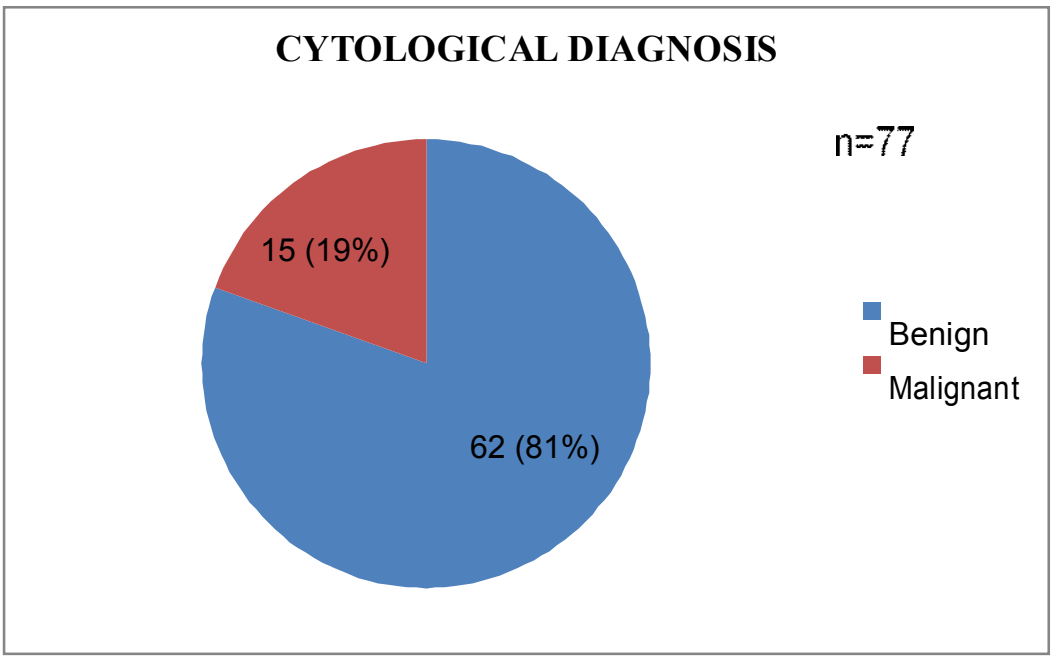

Fig 4 : Benign vs malignant in cytology(according to TBSRTC)

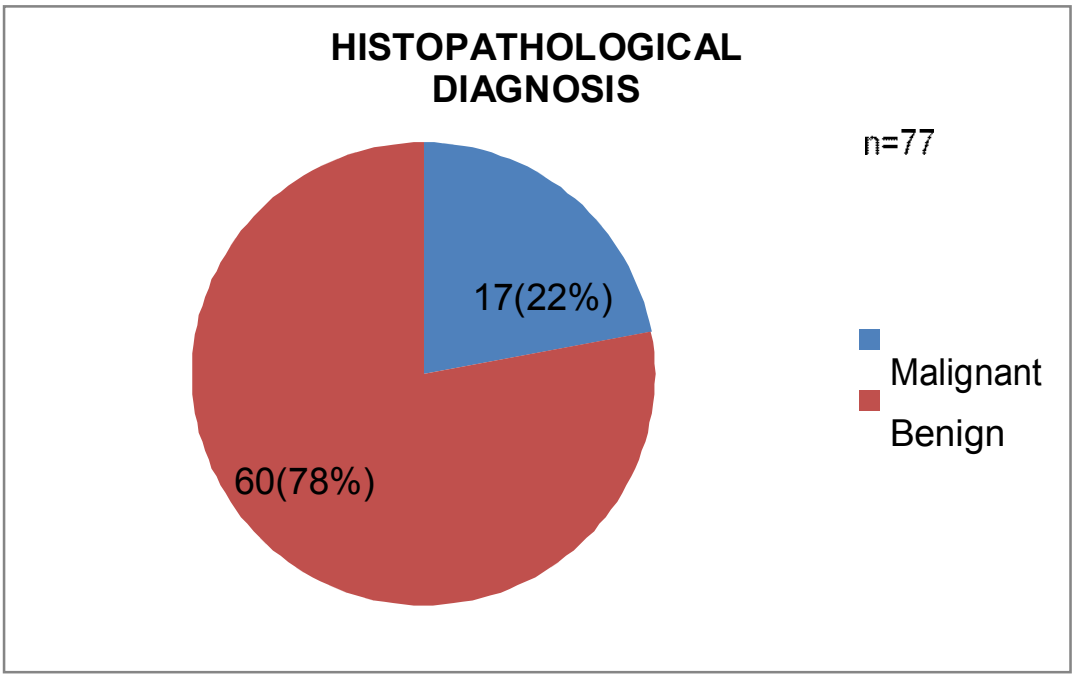

Fig 5: Benign vs malignant according to histopathology diagnosis

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

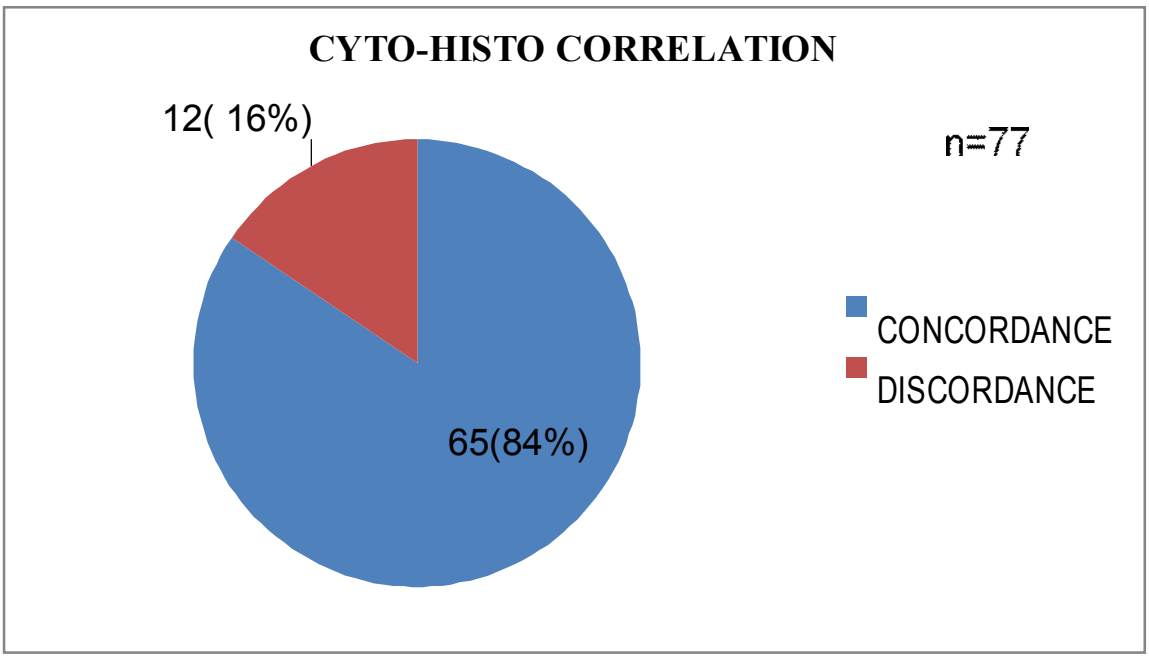

Fig 6 : Cytohisto correlation

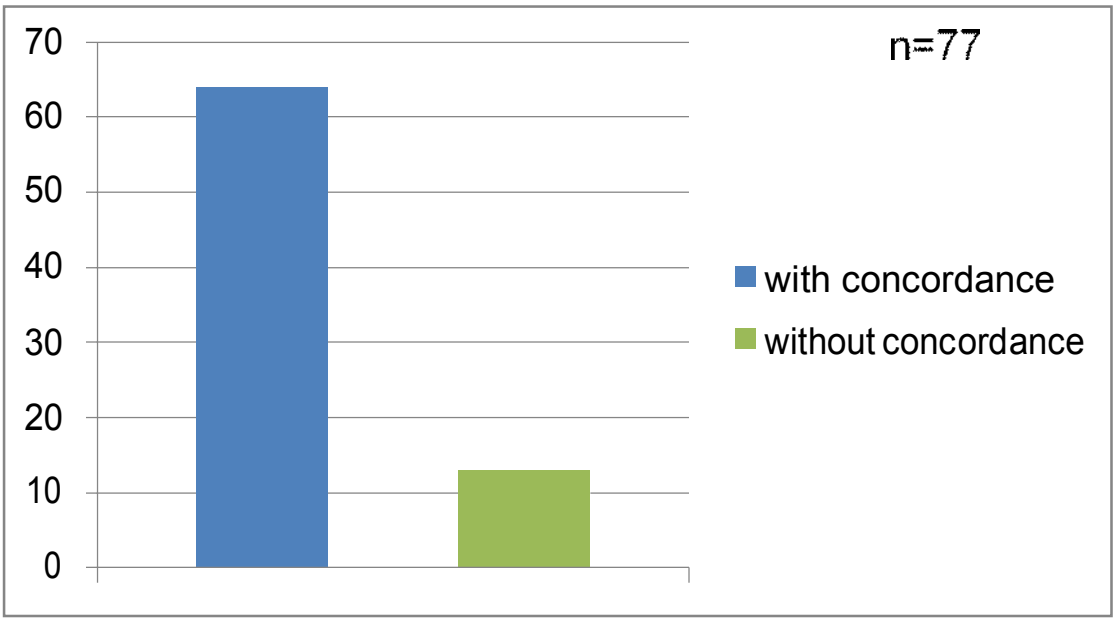

Fig 7 : Clinico radio correlation

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

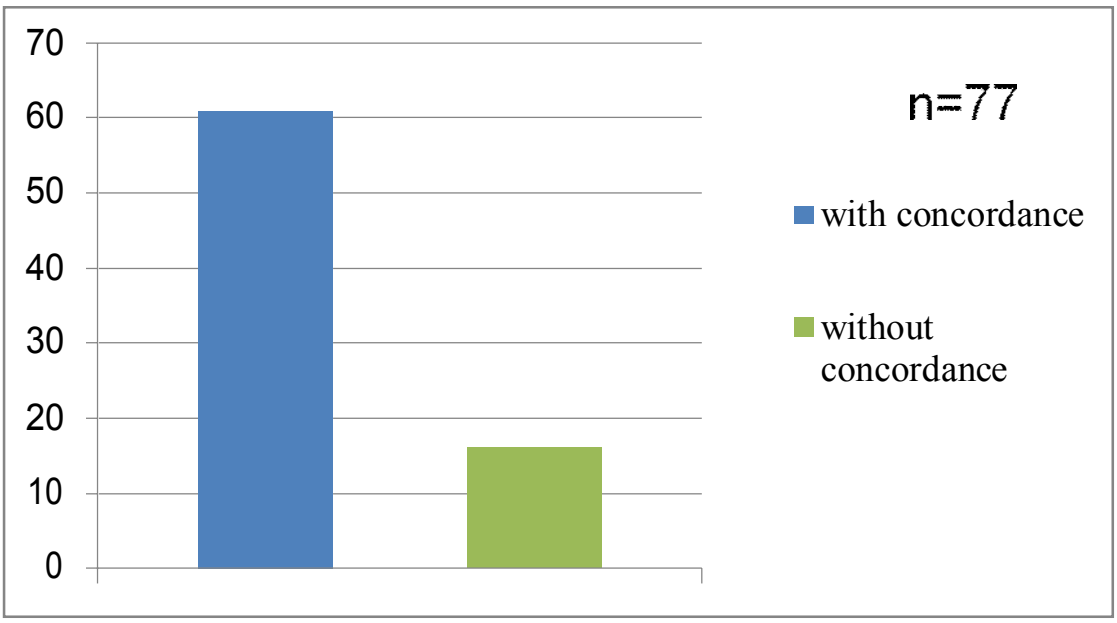

Fig 8 : Clinico pathological correlation

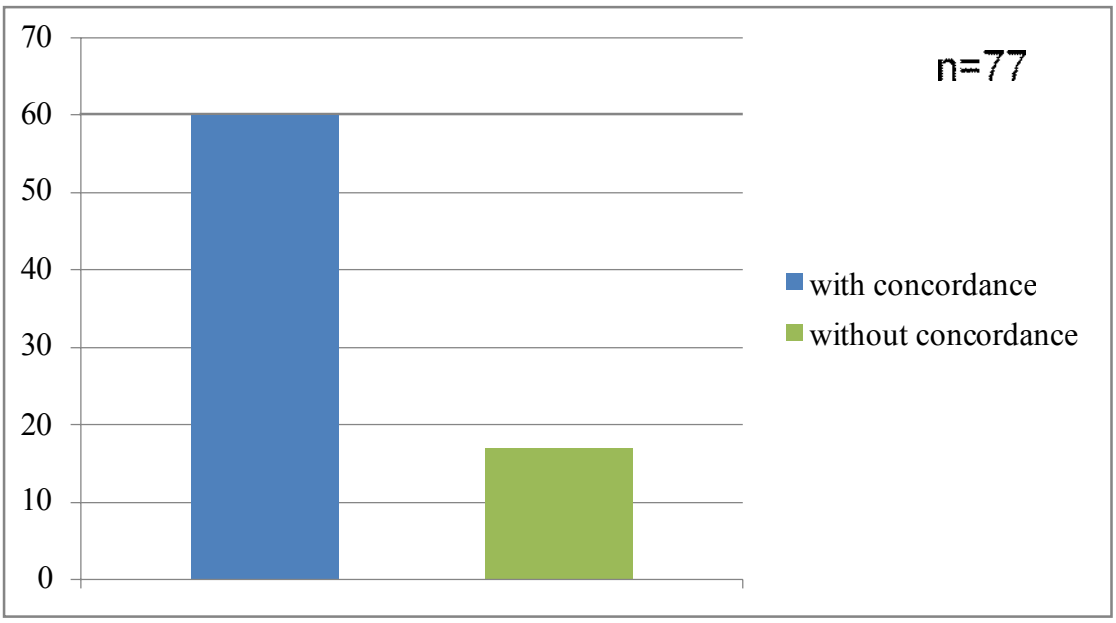

Fig 9 : Pathological radiological correlation

CYTOLOGICAL DIAGNOSIS	BETHESDA CATEGORY	HISTOPATOLOGY DIAGNOSIS
Suspicious Of hurthle cell neoplasm	4	Hyalinised trabecular adenoma
Blood with scant colloid	1	Nodular colloid goitre
BFN with degeneration with occasional follicular cells showing nuclear grooving and inclusions	3	Multifocal PTC
Acellular specimen	1	PTC
Follicular epithelial cell clusters with some showing microfollicular pattern	3	MNG with foci of fibrosis
Suggestive of lymphocytic thyroiditis	2	MNG with thyroiditis
AUS	3	MNG
AUS	3	MNG with calcification
AUS	3	PTC
Suspicious. Of follicular neoplasm	4	Upper pole- PTC Lower pole- follicular neoplasm
BFN with occasional papillary clusters showing nuclear grooving	2	Multi focal PTC
Blood with occasional follicular cells with nucleomegaly	2	PTC

Table 2 : Cyto histological discordant cases(12 cases)

	MALIGNANT(Histo)	BENIGN(Histo)
MALIGNANT(cyto)	14 (True positive)	0 (False positive)
BENIGN(Cyto)	7 (False negative)	56(True negative)

Total= 77

Table 3: 2x2 table for calculation of diagnostic accuracy of FNAC compared to histopathology

Validity of the reporting of the FNAC thyroid by TBSRTC :

SENSITIVITY	=	**TRUE POSITIVE/ (TRUE POSITIVE+FALSE NEGATIVE)**	=	**67%**
SPECIFICITY	=	**TRUE NEGATIVE/ (TRUE NEGATIVE + FALSE POSITIVE)**	=	**100%**
POSITIVE PREDICTIVE VALUE	=	**TRUE POSITIVE /(TRUE POSITIVE+ FALSE POSITIVE)**	=	**100%**
NEGATIVE PREDICTIVE VALUE	=	**TRUE NEGATIVE/(TRUE NEGATIVE+ FALSE NEGATIVE)**	=	**88.8%**
ACCURACY	=	**TP +TN/ (TP+ FP+ TN+ FN)**	=	**90.9%**

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

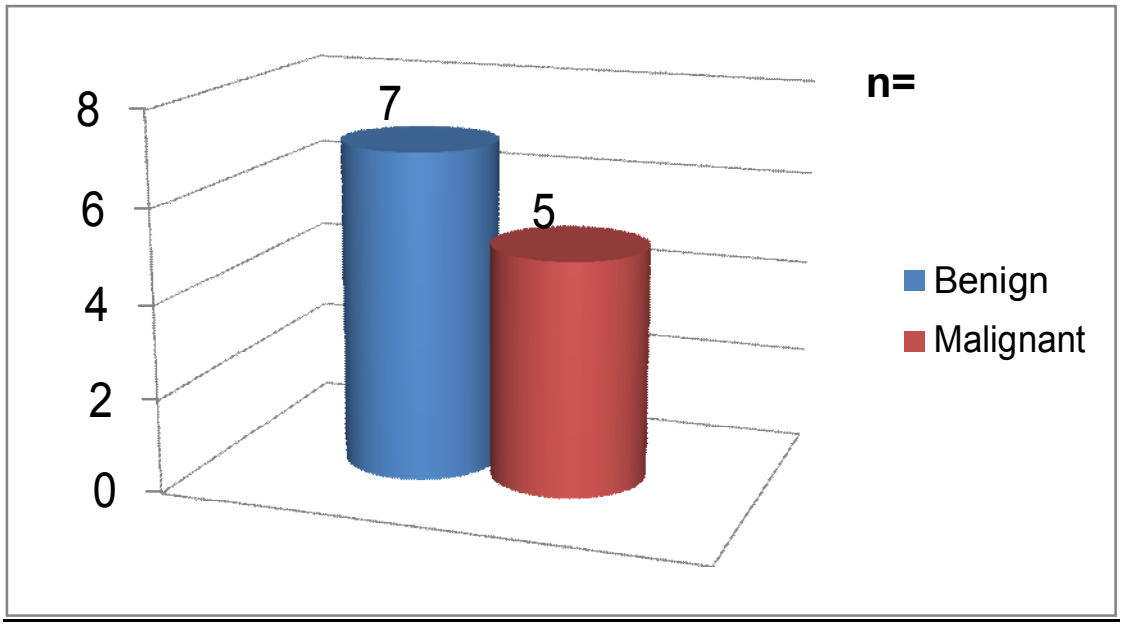

Fig 10 : Case wise distribution in discordant cases

Among the 12 cases showing cyto- histo discordance between the results, 7 cases diagnosed as benign in cytology, changes to malignancy in histopathology. 5/12 cases diagnosed as benign in cytology, remains as benign in histopathology but with discordance with the cytological diagnosis.

International Journal of Research
p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

DISCUSSION

DISCUSSION

Early detection and management of thyroid diseases has been accomplished by the introduction of FNAC in thyroid lesions and its reporting via the Bethesda system. Thyroid abnormalities varies from country to country and also from region to region of a country. According to different studies conducted in different parts of the world, variable accuracy results have been obtained. There may be many factors which results in these variations including sample size, Selection criteria, Difference in population, Experience of the health professional collecting and reporting the smears and H and E sections. The accuracy of FNAC reporting of thyroid lesions by revised Bethesda system in different places of world and different regions of India is compared in Table 4 and 5.

No	Author	Year	Place	No of Patients	Accuracy (%)	Validity (%)			
						Se	Sp	PPV	NPV
1	Knezevic et al	2004	Serbia	398	97	98	100	100	95
2	Himakham et al	2014	Istambul	174	-	100	100	90	93
3	Mammon et al	2016	Islamabad	81	89.7	65.3	96	89.8	93.8
4	Musaini et al	2000	Lahore	95	87.6	73.4	93	91	95

Table 4: Comparison accuracy of FNAC reporting of thyroid lesions by revised Bethesda system in different places of world.

No	Author	Year	Place	No of Patients	Accuracy (%)	Validity (%)			
						Se	Sp	PPV	NPV
1	Dorairajan	2007	Tamil Nadu	100	93.4	72.1	96.5	82	93.7
2	Purushotham reddy	2015	Hubli	75	90.7	71	95.3	80	93.1
3	AgarwalS et al	2010	Ahmedabad	84	90	64	100	100	85
4	Present study	2018	Kerala	77	90.9	67	100	100	88.8

Table 5: Comparison of accuracy of FNAC reporting of thyroid lesions by revised Bethesda system in different regions of India

All the Indian based studies show more or less uniform pattern in expression of accuracy and the predictive values. In international comparison the values varies and shows more better results in developed nations like Russia but shows a less accurate values in south Asian countries.

Most of the studies conducted to date revealed a good accuracy of FNAC concordant with the results of our study, due to which it became a prime investigation of choice for initial evaluation of patients with thyroid nodule. However, literature review revealed that almost all the studies categorized their FNAC findings into three groups, benign, suspicious for malignancy and malignant with most of the patients falling in the first group. Unfortunately most patients undergoing surgeries with an initial diagnosis of suspicious for malignancy turned out be a benign lesion like adenomatous hyperplasia. Newly proposed Bethesda reporting guidelines categorized FNAC results of thyroid into 6 categorizes which eases the clinical intervention criteria and further reduces the chances of inadvertent surgeries.

Sl. No	Cytological diagnosis	Histological diagnosis	Probable reason for discordance
1	Suspicious of hurthle cell neoplasm	Hyalinised trabecular adenoma	The cells of both the lesions look similar and it is difficult to distinguish between benign and malignant cells
2	Blood with scant colloid	Nodular colloid goitre	Fibrosis/ Calcification/Poor aspiration technique
3	BFN with degeneration with occasional follicular cells showing nuclear grooving and inclusions	Multifocal PTC	Size of individual lesion is small/ FNAC didn't yield adequate material
4	Acellular specimen	PTC	Thick capsule/Wrong site
5	Follicular epithelial cell clusters with some showing micro follicular pattern	MNG with foci of fibrosis	MNG showing cellular area/ Long standing MNG may show minimal atypia
6	Suggestive of lymphocytic thyroiditis	MNG with thyroiditis	Finding of thyroidits overshadowed nodular goitre
7	AUS	MNG	Long standing MNG may show features of minimal atypia
8	AUS	PTC	Only minimal atypia might be seen in well differentiated PTC
9	Suspicious of follicular neoplasm	Upper pole-PTC Lower pole- Follicular neoplasm	FNAC was not done from other site
10	BFN with occasional papillary clusters showing nuclear grooving	Multifocal PTC	Poor yield
11	Blood with occasional follicular cells with nucleomegaly	PTC	Poor yield/ Cystic degenerative changes

Table 6: Cyto histological discordant cases and the probable cause for discordance

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

Likewise, in the concordant cases, most of the concordance was noted in Bethesda category 2 followed by Bethesda category 6. The most probable reason for this might be, in both the scenario its easy to diagnose the cases, because its easy to recognise the features of these lesions in a fine needle aspiration cytology smear.

LIMITATIONS OF THE STUDY:

The sample size of the study is small.

Pauci cellularity of a few smears

International Journal of Research

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

CONCLUSION

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

CONCLUSION

In the present study FNACs of thyroid was classified according to the revised Bethesda guidelines and this was compared to the histopathology of the corresponding cases. On analysis, the accuracy of the revised Bethesda system for reporting of thyroid cytology is 90.9 %.The sensitivity, specificity, positive predictive value and negative predictive value are also equally good. (67% ,100% ,100% ,88.8% respectively). The study thus validates the use of this system for reporting thyroid FNA.

Based on our study and according to the various studies conducted around the globe ,we recommend routine use of TBSRTC for reporting thyroid cytopathology for initial workup of patients with thyroid nodule. However, risk of malignancy was found to be significantly high in Bethesda 3 category to warrant further workup including ultrasound/thyroid scan in addition to repeat FNAC. We also recommend adequate sampling from all the possible nodules in thyroid and a better site selection for the needle insertion for a better result.

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

REFERENCES

REFERENCES

1. Castro MR,Gharib H. Thyroid fine-needle aspiration biopsy: progress, practice, and pitfalls. Endocr Pract. 2003;9:128-36.
2. Gharib H. Fine-needle aspiration biopsy of thyroid nodules: advantages, limitations, and effect. Mayo Clin Proc. 1994;69: 44-9.
3. Pacini F, Schlumberger M, Dralle H, Elisei R, Smit JW, Wiersinga W. European consensus for the management of patients with differentiated thyroid carcinoma of the follicular epithelium. Eur J Endocrinol. 2006 ;154:787-803.
4. Unnikrishnan AG, Menon UV. Thyroid disorders in India: An epidemiological perspective. Indian J EndocrinolMetab. 2011;15:78-81.
5. Marimuthu P. Projection of cancer incidence in five cities and cancer mortality in India. Indian J Cancer. 2008;45:4-7.
6. Nandakumar A, Gupta PC, Gangadharan P, Visweswara RN, Parkin DM. Geographic pathology revisited: development of an atlas of cancer in India. Int J Cancer. 2005;116:740-54.
7. Klein Hesselink EN, Klein Hesselink MS, de Bock GH, Gansevoort RT, Bakker SJ, Vredeveld EJ et al. Long-term cardiovascular mortality in patients with differentiated thyroid carcinoma: an observational study. J Clin Oncol. 2013;31:4046-53.
8. Links TP, Van Tol KM, Jager PL, Plukker JT, Piers DA, Boezen HM et al. Life expectancy in differentiated thyroid cancer: a novel approach to survival analysis. EndocrRelat Cancer. 2005;12:273-80.
9. Shahebrahimi K, Madani SH, Fazaeli AR, Khazaei S, Kanani M, Keshavarz A. Diagnostic value of CD56 and nm23 markers in papillary thyroid carcinoma. Indian J PatholMicrobiol. 2013;56:2-5.
10. Alshenawy HA. Utility of immunohistochemical markers in diagnosis of follicular cell derived thyroid lesions. PatholOncol Res. 2014 ;20:819-28.
11. Abouhashem NS, Talaat SM. Diagnostic utility of CK19 and CD56 in the differentiation of thyroid papillary carcinoma from its mimics. Pathol Res Pract. 2017;213:509-17.

p-ISSN: 2348-6848
e-ISSN: 2348-795X
Volume 08 Issue 03
March 2021

12. Bose D, Das RN, Chatterjee U, Banerjee U. Cytokeratin 19 immunoreactivity in the diagnosis of papillary thyroid carcinoma. Indian J Med PaediatrOncol. 2012;33:107-11.

13. Baloch ZW, LiVolsi VA. Our approach to follicular-patterned lesions of the thyroid. J ClinPathol. 2007;60:244-50.

14. MithatGonen. A review of ─ Statistical methods in Diagnostic medicine. In: X.H Zhou,N A Obuchowski, and D. K McClish. Editors. Journal of Biopharmaceutical Statistics, Second edition. 2012, 612-614.