

Histopathological and Cytological Correlation of Thyroid Nodules with Emphasis on Bethesda System for Reporting Thyroid Cytology- A 7 Year Study

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ABSTRACT

Introduction: Fine needle aspiration cytology (FNAC) has become the dominant method in the evaluation of thyroid nodules, being fast, reliable, safe, minimally invasive, cost effective and reaching high sensitivity and specificity. The study was undertaken with the main aim of evaluating the utility and efficacy of fine needle aspiration cytology and to study the histopathological pattern of various diseases of thyroid gland and evaluation of Grey-zone lesions of thyroid on FNAC and their pattern on histopathology

Material and methods: The study was a hospital based study and was done in the department of pathology, Sher-i-Kashmir institute of medical sciences (SKIMS), Srinagar, Kashmir, to analyse patients with thyroid swellings and underwent both FNAC and histopathological examination of the swellings were included. This was a seven year study extending from May 2006 to April 2013 including a two year prospective study extending from May 2011 to April 2013, five year retrospective study from May 2006 to April 2011.

Results: On FNAC according to Bethesda system most patients belong to Group II (benign). Grey-zone (B3 and B4) comprised of 46 cases (11.5%) out of which 15 (32.2%) were malignant and 31 (67.3%) were benign on histopathology. Colloid goitre is the most common benign lesion of thyroid and papillary carcinoma is the most common malignancy observed. On excluding grey-zone cases the sensitivity, specificity and accuracy of FNAC is 92.2%, 72.5% and 83.5% respectively.

Conclusion: A six tier reporting system for thyroid FNA is effective in categorizing the lesions and determining which patients need surgery versus follow-up and also guide the clinician on the extent of surgery. So, the Bethesda system of reporting thyroid cytology should be meticulously followed to minimise these errors

Keywords: FNAC, Bethesda System

INTRODUCTION

Fine needle aspiration cytology (FNAC) has become the dominant method in the evaluation of thyroid nodules, being fast, reliable, safe, minimally invasive, cost effective and reaching high sensitivity and specificity¹. FNAC has allowed a dramatic decrease in the surgical treatment of the patients with thyroid nodular diseases² enhancing the percentage of malignant operated nodules over 50%³. To assess terminology, description and interpretation of cytological appearances and transmit them to the clinicians in a clear and reproducible way, several classifications for thyroid

cytology report have been proposed^{4,8}.

The study was undertaken with the main aim of evaluating the utility and efficacy of fine needle aspiration cytology and to study the histopathological pattern of various diseases of thyroid gland and evaluation of Grey-zone lesions of thyroid on FNAC and their pattern on histopathology

MATERIAL AND METHODS

This study was conducted in the department of pathology Sher-i- Kashmir institute of medical sciences Soura, five year retrospective from May 2006 to April 2011 and two year prospective from May 2011 to April 2013. There were a total of 400 cases of thyroid lesions where both FNAC and Histopathology was available.

Inclusion/exclusion

All patients with thyroid swellings, irrespective of the age who have undergone Fine needle aspiration cytology of the swelling, followed by its subsequent Histopathological examination were included in the study. Patients in whom either of one (HPE/FNAC) was not available were excluded.

Method in prospective study

The patients with thyroid swellings were evaluated in following order.

- i. History
- ii. Physical examination.
- iii. Informed / written consent was taken for FNAC.
- iv. Histopathological evaluation of resected specimen was done
- v. Finally statistical evaluation and correlation of the two methods, viz., FNAC and Histopathological evaluation was done.

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Statistical values of present studies

The statistical analysis method used was chi-square test.
 P value = <0.0001
 Sensitivity = 92.2%
 Specificity = 72.05%
 Positive predictive value (PPV) = 79.82%
 Negative predictive value (NPV) = 88.5%
 Accuracy = 83.5%

RESULTS

There were a total of 74 male patients and 326 female patients. The male to female ratio being 1:4.4 of thyroid lesions. Females comprised 81.5% and males comprised 18.5% of the total cases. Most of the patients belonged to 4th decade 116 (29%), of life followed by 3rd decade. 92 (23%) and least number of patients were seen in 8th decade of life 2 (0.5%). Females out numbered males in all the age groups.

On following Bethesda classification maximum number of patients belonged to group B2 (51.8%) followed by B6, B5, B4, B1 and B3 (20%, 12.8%, 8.5%, 4% and 3%) respectively.

Bethesda classification	Histopathology		Total
	Benign	Malignant	
B1	15	1	16
B2	163	44	207
B3	7	5	12
B4	24	10	34
B5	11	40	51
B6	4	76	80
Total	224	176	400

Table-1: Comparison of FNAC and Histopathology of thyroid lesions

Histopathology	B3 (AUS=12 cases)		B4 (FL= 34 cases) A	
	No.	%age	No.	%age
BENIGN				
Cavernous hemangioma	0	0%	1	2.9%
Colloid goitre	4	33.4%	1	2.9%
Follicular adenoma	2	16.6%	14	41.3%
Hashimotos thyroiditis	0	0%	2	5.9%
Hurthle cell adenoma	1	8.3%	6	17.6%
MALIGNANT				
Follicular carcinoma	1	8.3%	4	11.8%
Hurthle cell carcinoma	0	0%	4	11.8%
Medullary carcinoma	0	0%	1	2.9%
Papillary carcinoma	4	33.4%	1	2.9%

Table-2: Histopathology of Grey- zone cases

FNAC of thyroid lesions showed maximum number of benign and malignant (63 and 25 respectively) cases belonging to 4th decade. Benign lesions were more common in the age group of 31-40 years were malignant lesions were more common in the age group of 21-30 years. In both benign and malignant groups, females outnumbered males with male to female ratio of 1: 5.4 in benign and 1: 3.5 in malignant lesion.

Histopathological diagnosis of various thyroid lesions, most cases were of papillary carcinoma 140 (35%) followed by Colloid goitre 125 (31.2%).

While as single case of each Cavernous hemangioma and Simple epithelial cyst

Were same. In the malignant group most of the cases were of PTC 140 (78.4%)

followed by follicular carcinoma 19 (10.8%).

FNAC and Histopathological correlation of thyroid lesions, out of 207 cases which were benign on FNAC, 44 turned out to malignant on histopathology and out of 80 malignant cases on FNAC, 4 cases turned out to be benign on histopathology. Out of 31 benign patients 7 fall in Bethesda group 3 and 24 in Bethesda group 4. (Table-1)

$P1 = 7/31 = 0.22$

$P2 = 24/31 = 0.77$

With the help of two sample proportion test;

Test stats (z) = -4.318

P value = < 0.0001

Hence, we conclude that most cases of B4 grade come out to be benign on histopathology with 99% confidence with 1% level of significance. Out of 15 malignant cases 5 fall in Bethesda group 3 and 10 fall in Bethesda group 4.

$P1 = 5/15 = 0.333$

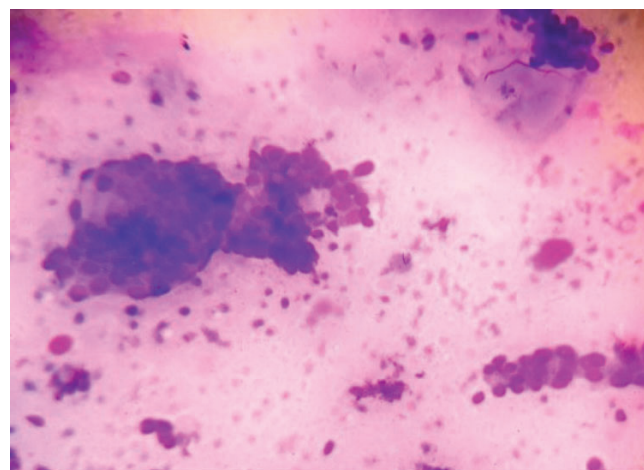


Figure-1: Atypia of undetermined Significance

Author (year)	Place	No. of cases	Sensitivity % age	Specificity % age	PPV %age	NPV %age	Accuracy %age
Gharib and Goellner (1987) ¹¹⁹	USA	10000	83	92	-	-	90
Leonard and Melcher (1997) ¹²⁰	UK	184	88	78	46	97	80
Settakorn et al. (2001) ¹¹⁷	Thailand	230	85	92	83	93	90
Mazeh et al. (2006) ¹¹²	Israel	242	87	89	89	87	75
Manoj Gupta et al. (2010) ¹⁰³	India	75	80	86	80	86	80
Present Study (2013)	India	400	92.2	72	79.8	88.5	83.5

Table-3: Comparative statistical values on cyto-histological correlation:

$P2 = 10/15 = 0.666$

With the help of above test;

Test stats (z) = -1.825

P value = 0.067

Therefore, we conclude that most of the cases of B3 grade come out to be malignant on histopathology with 90% confidence and 10% level of significance.

Hence on histological evaluation on the basis of data obtained, indicates that AUS (B3) (Fig-1) is associated with higher malignancy rates compared to FN. (B4) (Table-2).

DISCUSSION

A total of 400 cases of thyroid swelling aspirations followed by histopathological diagnosis were included in the study. The results of cytological findings and histopathological findings were compared and scrutinized for accuracy and other statistical values. Out of 400 cases 74 (18.5%) were males and 326 (81.5%) were females, with a male female ratio of 1:4.4. The age range was between 11-75 years with youngest patient being a case of papillary carcinoma thyroid and the oldest patient a female of colloid goitre. The highest number of cases were seen in the age group of 31-40 years (29%) followed by the age group of 21-30 years (23%).

Mandekar et al. (1995)⁹ reported a male female ratio of 1:6.1 in their study of 238 cases of various thyroid lesions. Male female ratio in the study conducted by Sirpal Y (1996)¹⁰ on 1123 cases was 1:1.4 with the highest number of cases seen in the 4th decade of life. Al Rikabi et al. (1998)¹¹ observed a male female ratio of 1:5.2 in their study on 125 cases of various thyroid lesions.

Cytology

We applied Bethesda system of reporting thyroid cytopathology on our 400 thyroid aspirates, which included Non-diagnostic (B1) 16 cases (4%), Benign (B2) 207 cases (51.8%), AUS (B3) 12 cases (3%) (Fig-1), FN (B4) 34 cases (8.5%), SM (B5) 51 cases (12.8%) and Malignant (B6) 80 cases (20%). This observation did not correspond with the study conducted by Her-Junig Wu H et al. (2011)¹² where they reported ND (20.1%), B (39%), AUS (27.2%), FN (8.4%), SM (2.6%) and M (2.7%) on 1328 thyroid aspirates. This discrepancy can be explained because of huge difference in the sample size.

Benign and Malignant lesions

The total number of benign lesions were 224 (56%) and malignant were 176 (44%). The ratio of malignant to benign lesions being 1:1.27.

Altavilla et al. (1990)¹³ observed malignant to benign ratio of 1: 59.1. Mandrekar et al (1995)⁹ observed malignant to benign ratio of 1:51.9. Al Rikabi et al. (1998)¹¹ observed malignant to benign ratio of 1:14.8. In our study the ratio was lower than observed in the above studies due to the inclusion of only those cases where FNAC was followed by surgical resection. Most of the benign cases on FNAC do not undergo subsequent surgical resection.

In this study out of 224 benign lesions of thyroid, colloid goitre was the most common lesion (55.8%) followed by

follicular adenoma (26.8%). Among the malignant lesions papillary carcinoma was the most common (78.4%) followed by follicular carcinoma (10.8%).

Naggada H.A et al. (2006)¹⁴ observed that the most common benign lesion in thyroid was nodular goitre followed by follicular adenoma. Fernandes H et al. (2009)¹⁵ observed that the commonest lesion encountered in thyroid gland was nodular goitre and among the malignant neoplasms papillary carcinoma was the most common lesion noted

Cyto-histological correlation of thyroid lesions

In the study 213 cases were cytologically diagnosed as benign, 80 cases as malignant and 51 cases as suspicious for malignancy.

Out of 213 benign cases 45 (21.1%) were diagnosed to be malignant on histopathology. Out of 80 malignant cases on cytology 4 cases proved to be benign on subsequent histopathology. And out of 51 suspicious for malignancy, 40 (78.2%) were malignant on histopathology. In the study most of the false negative cases were of papillary carcinoma thyroid with cystic change that were misdiagnosed as cystic degeneration in colloid goitre.

Bakhos et al. (2000)¹⁶ had described 22 cases of false negative cases out of 543 cases of histological confirmation. They also quoted cystic degeneration in papillary carcinoma as the commonest cause of false negative results.

Settakorn et al. (2001)¹⁷ had adenomatous goitre cases misdiagnosed as follicular adenoma and vice versa.

In this study also 1 case of adenomatous goitre was misdiagnosed as follicular neoplasm on histopathology.

Lagan Y et al. (2004)¹⁸ described 11 cases of false negatives in their study out of 255 cases on histological confirmation (from 1253 cases on cytology). The most common cause of false negative result was the presence of micropapillary carcinoma in the setting of adenomatous goitre. In the study 11 false negative cases were identified, the most common cause of these false negative results was the presence of micropapillary carcinoma in the setting of adenomatous goitre.

And also 4 cases of papillary carcinoma were misdiagnosed as follicular neoplasm on cytology.

Cyto- histological correlation of Grey- zone lesions (Table-3)

Baloch NM et al. (2008)¹⁹ described 40 patients of indeterminate follicular lesions on FNAC. Of these 25 (62%) had carcinoma on histopathology, 13 had follicular variant of papillary, 8 had papillary and 4 had follicular carcinoma on final histopathology report.

Goldstein RE et al. (2002)²⁰ described 9 patients of follicular neoplasm with atypia out of which 4 (44.4%) were malignant on histopathology, and 15 lesions of atypia, 3 (20%) were malignant. out of 25 highly suspicious for malignancy (84%) proved to be malignant on histopathology.

Ohori NP et al. (2010)²¹ described 117 cases of follicular lesions of undetermined significance/ atypia of undetermined significance 29.9% had neoplastic outcome and 17.1% were carcinomas on histopathology In study, among 46 undetermined FNACs [12 AUS and 34 FL] on histological

follow-up 41.7% were carcinomas, 24.9% were adenomas and 33.4% were non-neoplastic lesions in AUS and 20.8%, 58.9% and 11.7% were carcinomas, adenomas and non-neoplastic lesions respectively in FL.

In this study out of 51 suspicious for malignancy 43 (84%) were malignant on histopathology. we also found that AUS (B3) is associated with higher malignancy rates than FL (B4).

CONCLUSION

Although FNAC is used with success in diagnosis of Papillary, Medullary and Anaplastic thyroid carcinomas, it is difficult to assess its value in follicular lesions/Atypia of undetermined significance. The main problem is the distinction between benign lesions, such as follicular adenoma or adenomatous goitre and follicular carcinoma or follicular variant of papillary carcinoma.

A six tier reporting system for thyroid FNA is effective in categorizing the lesions and determining which patients need surgery versus follow-up and also guide the clinician on the extent of surgery.

The classification and follow-up recommendations of the Bethesda system of reporting thyroid cytopathology are appropriate for each category. So, the Bethesda system of reporting thyroid cytology should be meticulously followed to minimise these errors.

ABBREVIATIONS

AUS: Atypia of undetermined significance, ND: Non diagnostic, FN: Follicular Neoplasm, SM: Suspicious of Malignancy, M: Malignancy, TBSRTC: The Bethesda System for reporting thyroid cytology

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