The Bethesda System for reporting thyroid cytopathology: A two year retrospective review in a tertiary care hospital

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Abstract

Background: The Bethesda system for reporting thyroid cytopathology (TBSRTC) has standardized our diagnostic approach to cytomorphological criteria and reporting.

Aims: To study retrospectively the diagnostic utility of TBSRTC at our institution and to correlate the cytopathology and histopathology.

Materials and methods: We retrospectively reviewed thyroid FNA between 2012 and 2014, classified according to the Bethesda system, found out the distribution of cases in each category, analysed the risk of malignancy in each category by the histopathology report and compared with other studies.

Results: The distribution of various categories from 402 FNA of thyroid nodules was as follows: 10.7% non-diagnostic, 81.6%benign, 1.27% atypia of undetermined significance (AUS/FLUS), 1.74% suspicious for follicular neoplasm, 2% suspicious for malignancy and 2.7% malignant. Follow-up histopathologic examination was available for 92 cases. Sensitivity, specificity; positive predictive value and negative predictive value were calculated. Risk of malignancy was 28.6% for suspicious for neoplasm (SFN) category and 71.4% for suspicious for malignancy (SFM) category.

Conclusions: TBSRTC is an excellent reporting system for thyroid FNA. The malignancy risk correlates well with previous studies. It provides clear management guidelines to clinicians to go for follow-up FNA or surgery and the extent of surgery.

Key words: Fine needle aspiration cytology, Bethesda system, histopathology and thyroid nodule

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Introduction

Fine -needle aspiration cytology has been applied routinely as a useful and indispensable method to diagnose thyroid lesions. However, due to lack of a standardized system of reporting, pathologists have been using different terminologies thus creating confusion among clinicians in the interpretation of reports and further management. In 2007, National Cancer Institute, Bethesda, Maryland, United States published guidelines known as Bethesda system of reporting thyroid cytopathology (TBSRTC). It is a six category scheme with individual risks of malignancy that influence management paradigms.[1,2] The present study was undertaken to analyse the risk of malignancy in each category obtained by preoperative fine needle aspiration cytology that were confirmed by histopatho-logical examination and compared with previous studies.

Materials and Methods

A retrospective study of all FNA's of thyroid lesions between 2012-2014 were analysed and classified according to the TBSRTC 6-tier diagnostic categories and tissue sections were obtained subsequently. A concise clinical history, examination, and details of relevant investigations were also obtained. These were helpful in reaching a probable clinical diagnosis as well as in cytohistological evaluation and formulations of the pathological diagnosis. The data included 402 cases of thyroid FNAC and 92 cases of follow-up histopathological specimens. The smears were prepared using conventional methods and stained with Papanicolaou stains. Cell block preparation was made when adequate material was available. Histopathological specimens were processed as per standard methods. We could calculate the risk of malignancy for each category and compare it with other studies. Sensitivity, specificity, positive predictive value and negative predictive value were calculated using histopathology diagnosis as gold standard. These statistical parameters were compared by excluding the suspicious lesions and then including them with benign categories and malignant categories. The statistical analysis was done using SPSS software. Comparative analysis between age groups and diagnosis were performed with chi-square analysis and were not statistically significant. All P-values were

predetermined to be two-sided with the level of significance set as P=0.093.

Results

Four hundred and two FNAC's were studied and the data included 43cases (10.8%) non-diagnostic / unsatisfactory, 327(81.8%) benign, 5(1.25%) AUS/ FLUS, 7(1.75%) SFN, 8(2%) SM and 10(2.5%) of malignant categories (table1, fig. 1). In our study AUS did not exceed the recommended target of 7%. Out of 402 cases, 92 cases were available for follow-up histopathology. We compared the original FNA diagnosis of these 92 cases with that of HPE and calculated the risk of malignancy for each category (fig. 2).None of the cases categorized as benign, or AUS/FLUS were reported to be malignant on follow-up (fig.3). Thus malignancy risk for these categories is 0%.Out of 7 cases of FN/SFN, two were found to be malignant giving a malignancy risk of 28.6%. Out of 7 cases of SFM, 5 were malignant giving a risk of 71.4% (fig. 2, fig. 4, fig. 5, fig. 6 and fig. 7). The female to male ratio was 8.5:1. Majority of lesions were in 31-40 years of age group (table2). The median age is 37 years. Distribution of lesions in female and male patients in different age group and comparative study with other series is shown in table3. The diagnostic accuracy of FNAC was 97.26% with sensitivity of 80% and specificity of 98.53%. The positive and negative predictive values were 80% and 98.53% respectively.

Table 1: Distribution of subcategories in TBSRTC

S. No	Cytological categories	Subcategories	No. of cases	Total no. of cases
1.	ND/UNS	Cyst fluid	26	43(10.7%)
		Acellular sample	6	
		Obscuring blood	11	
2.	Benign	Adenomatoid nodule, colloid nodule	230	328(81.6%)
		Lymphocytic thyroiditis	97	
		Granulomatous thyroiditis	1	
3.	AUS/FLUS	-	5	5(1.24%)
4.	FN/SFN	-	7	7(1.74%)
5.	SFM	Susp. for papillary carcinoma	7	8(2%)
		Susp.for medullary carcinoma	1	
6.	Malignant	Papillary thyroid carcinoma	11	11(2.7%)
Total				402

*ND/UNS-non-diagnostic/unsatisfactory; AUS/FLUS-Atypia of undetermined significance/Follicular lesion of undetermined significance; SFM-Suspicious for malignancy

Table 2: Comparative analysis of study results of FNAC

Series	No. of cases	Sex		Mean age	Age range	FNA results			
		M (%)	F(%)			Benign	Malignant	Suspicious	Non-diagnostic
Chang et al(2006)	51	13(25)	38(76)	17	2-21	45(74)	6(10)	6(8)	4(7)
Kapila et al(2010)	792	68(9)	724(91)	17	4-21	699(88)	20(2.7)	26(3.5)	47(6)
Vidhya et al(2013)	284	25(9)	259(91)	17	7-21	243(86)	6(2)	12(4)	23(8)
Present study	402	43(10.7)	359(89.3)	37.16	5-75	328(81.6)	11(2.7)	20(4.98)	43(10.7)

Table 3: Comparison of percentages of distribution of fine needle aspiration diagnosis with other studies

Diagnostic category	Present study	Jo et al	Yassa et al	Nayar and Ivanovic	Payal M et al	Shagutta et al
ND/UNS	10.7	18.6	7	5	7.2	11.6
Benign	81.6	59	66	64	80	77.6
AUS/FLUS	1.24	3.4	4	18	4.9	0.8
SFN	1.74	9.7	9	6	2.2	4
SFM	2	2.3	9	2	3.6	2.4
Malignant	2.7	7	5	5	2.2	3.6

*ND/UNS-non-diagnostic/unsatisfactory; AUS/FLUS-Atypia of undetermined significance/Follicular lesion of undetermined significance; SFM-Suspicious for malignancy

Table 4: Comparison of percentages of risk of malignancy of present study with other studies

Diagnostic category	Present study	Jo et al	Yassa et al	Nayar and Ivanovic	Payal M et al	Shagutta et al
ND/UNS	0	8.9	10	9	0	20
Benign	0	11	0.3	2	13	3.1
AUS/FLUS	0	17	24	6	100	50
SFN	28.6	25.4	28	14	25	20
SFM	71.4	70	60	53	50	80
Malignant	80	98.1	97	97	100	100

Chart-1

Cytology categories	Number of cases
ND/UNS	43
Benign	328
AUS/FLUS	5
Suspicious for follicular neoplasm	7
Suspicious for malignancy	8
Malignancy	11

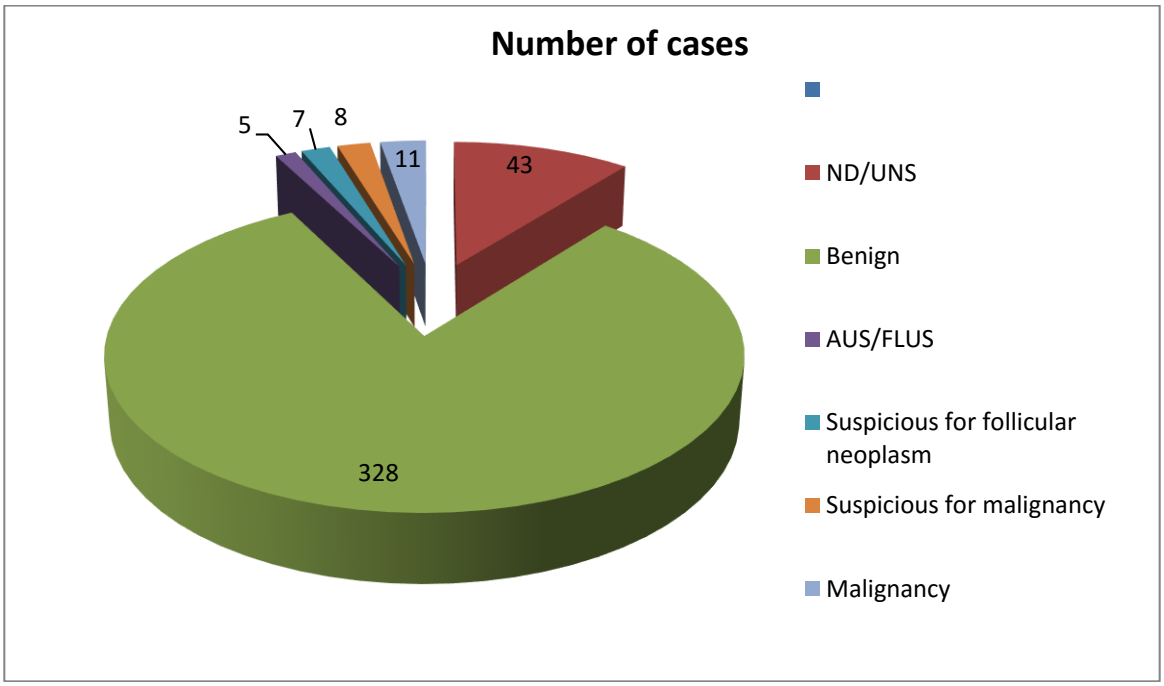

Fig. 1: Chart depicting distribution of categories as per six tier TBSRTC system.

Chart-2

	Benign	Malignant
ND/UNS(n=7)	7	0
Benign(n=61)	60	1
AUS/FLUS(n=5)	5	0
FN/SFN(n=7)	5	2
SFM(n=7)	2	5
Malignant(n=5)	1	4
Total(n=92)	80	12

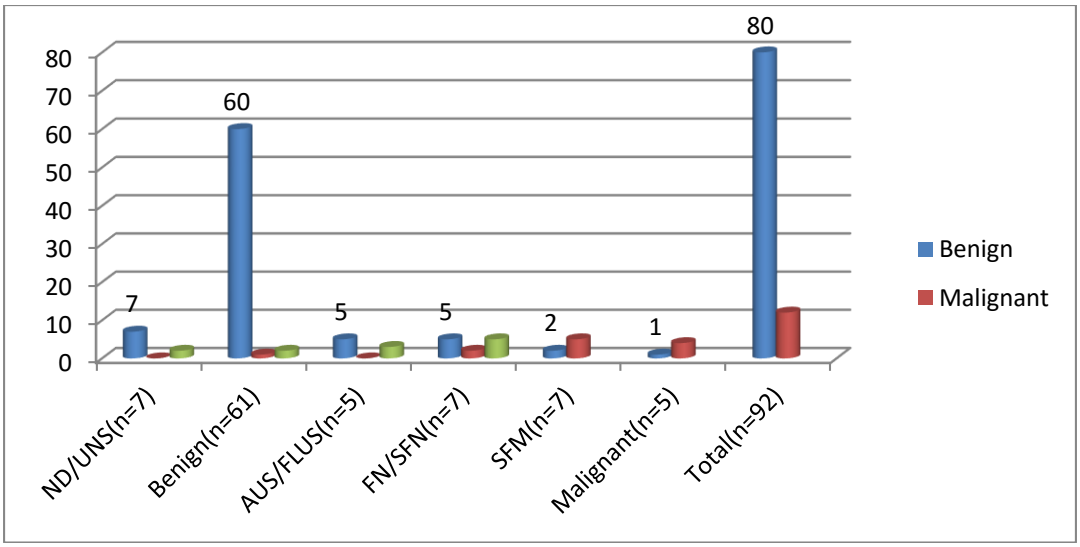

Fig. 2: Chart depicting correlation of cytological and histopathological diagnosis

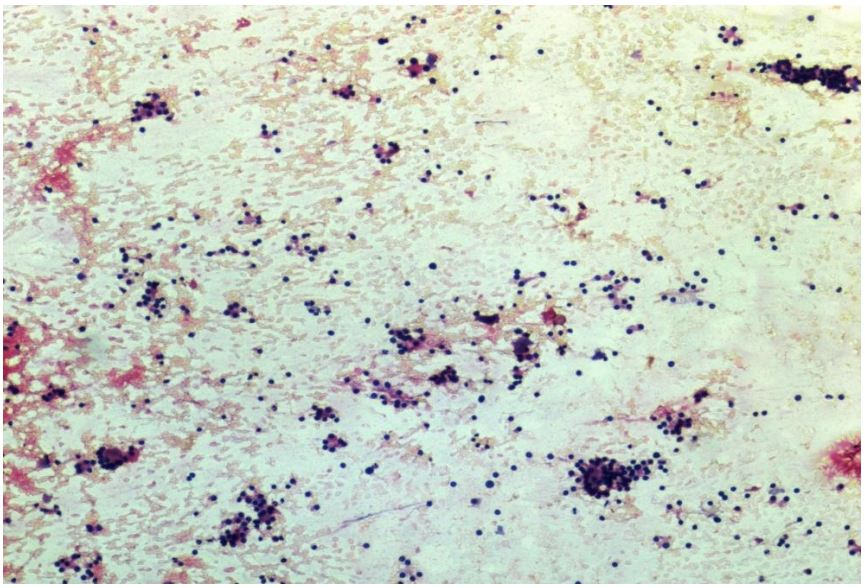

Fig. 3: Microphotograph of follicular neoplasm (Pap x100)

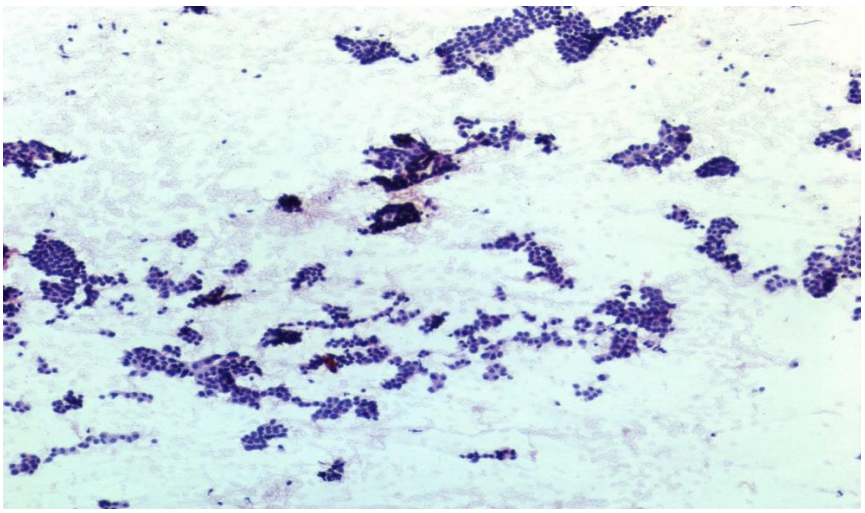

Fig. 4: Microphotograph of papillary carcinoma (Pap x100)

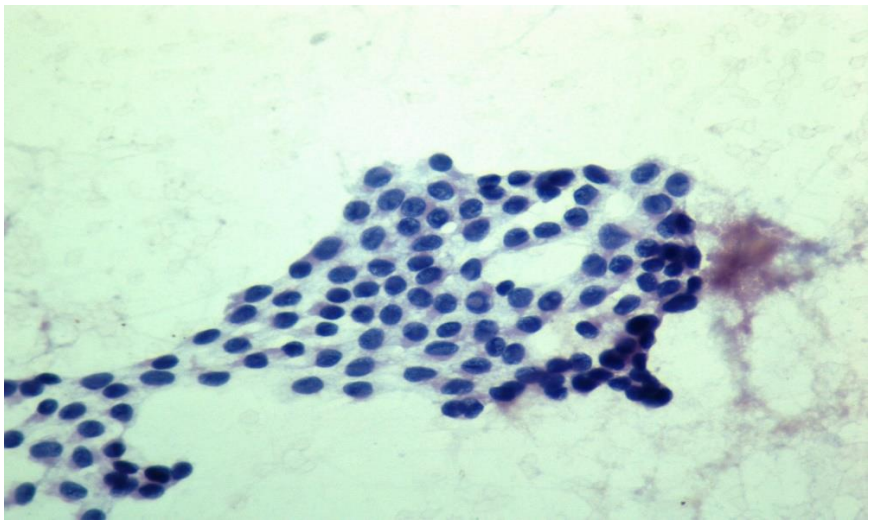

Fig. 5: Microphotograph of papillary carcinoma (Pap x400)

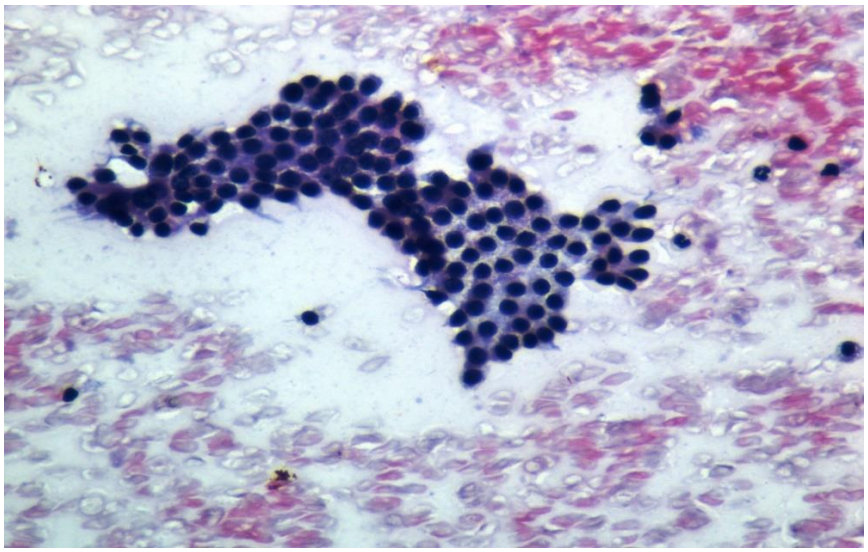

Fig. 6: Microphotograph of suspicious for papillary carcinoma (Papx400)

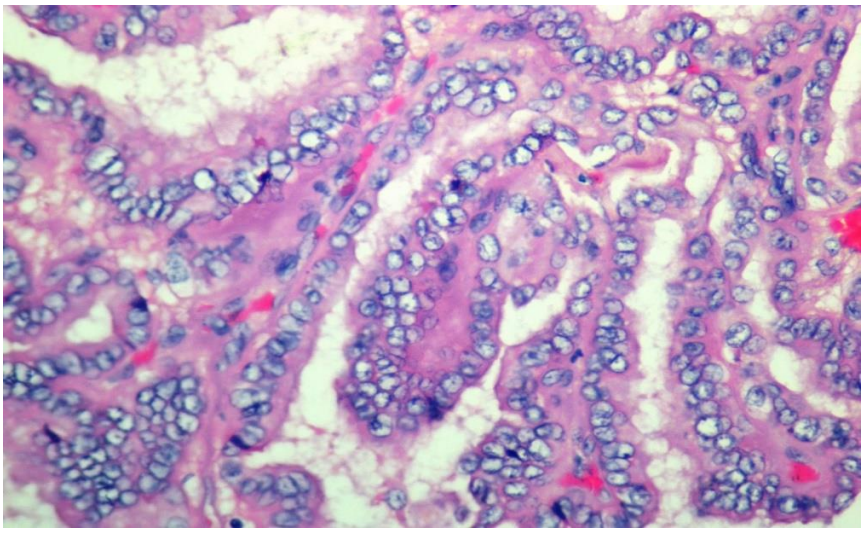

Fig. 7: Microphotograph of papillary carcinoma in thyroidectomy specimen (H&Ex400)

Discussion

FNAC is the most accurate, rapid, safe, reliable and cost- effective method for the evaluation of thyroid nodule. Ultrasound guided FNAC is recommended for non-palpable nodules, on-diagnostic aspirate and technically difficult location. The TBSRTC system is a simple, systematic universal reporting system with good clarity; thus creating understanding between pathologists and clinicians and helping in predicting prognosis and management of thyroid nodules.[3,4] Managing pediatric patients with thyroid nodules can be challenging. Accurate pre-operative diagnosis is necessary to avoid thyroidectomy for benign nodule.[5]

We compared the results in our study with Jo et al.,[6] Chang et al.,[7] kapila et al.,[8] Yassa et al.,[9] Payal M et al[10] and Nayar and Ivanovic[11]. The distribution of cases as per six-tier Bethesda system is different from other studies, with the percentage of cases in benign category being higher and that of non-diagnostic and AUS/FLUS category is lower (table 3).

As per the guidelines of the Bethesda system, only aspirates with features of atypia, microfollicles and focal occurrence of hurthle cell that could not be categorized as benign, SFN, SFM and malignancy were described as AUS/FLUS. In our study the distribution of AUS is 1.24% that did not exceed the target 7%. [10, 12]The median age of AUS is 42 years with female predominance.

The risk of malignancy for different categories in our study correlated well with the risks mentioned in the Bethesda system and with studies of Jo et al, Yassa et al and Nayar and Ivanovic and differences with the studies of Payal M et al and Shagutta et al.[13] In our study number of cases under non-diagnostic and AUS category are less when compared to studies of Nayar and Ivanovic and hence the malignancy risk cannot be accurately compared (table 4). The recommended management for AUS/FLUS is clinical correlation and repeat FNAC at an appropriate interval thus reducing the incidence of surgery.

In our study the sensitivity was 80%, Specificity 98.53% and accuracy 97.26%.Similar results were observed by Kessler et al. [14] in the false positive case, the presence of nuclear grooves and papillary fragments misled to the diagnosis of papillary carcinoma. The nuclear grooves are also seen in cases of Hashimoto's thyroiditis, nodular hyperplasia and follicular adenoma. In the false negative case papillary carcinoma was misdiagnosed as hyperplastic nodule on cytology since tiny focus was not aspirated during FNAC. If suspicious lesions are considered positive, the sensitivity increases while the specificity decreases. If suspicious lesions are excluded, then the sensitivity decreases and the false negative rates increase [10, 15]

Limitations

The Bethesda system has to be validated by more prospective studies on a larger number of cases with histopathological correlation. Other diagnostic options like molecular assays (BRAF) can identify the low-risk patients who may or may not require surgery.[16]

Conclusions

FNAC is a screening test for thyroid nodules, in children and adults because of its high sensitivity. Detection of suspicious lesions or malignant cells is a definite indication of surgery. However; a negative FNAC from a nodule must be viewed with caution and should have a close follow-up.

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References:

1. Cibas ES.Fine -needle aspiration in the work-up of thyroid nodules.Otolaryngol Clin North Am.2010; 43:257-71.
2. OzlukY, Pehlivan E, Gulluoglu MG, Poyanli A,Salmaslioglu A,Colak N,et al.The use of the Bethesda terminology in thyroid fine-needle aspiration results in a lower rate of surgery for non-malignant nodules: A report from a reference centre in Turkey.Int J Surg Pathol.2011;19:761-71.
3. Wang HH.Reporting thyroid fine-needle aspiration: Literature review and a proposal. Diagnostic Cytopathology.2006; 34:67-76.
4. Cibas ES and Sanchez MA.The National cancer institute thyroid fine-needle aspiration state of the science conference: inspiration for a uniform terminology linked to management guidelines. Cancer cytopathology.2008; 114:71-73.
5. Vidhya V,Hemalatha AL,Rakhi B,Gitanjali S.Efficacy and pitfalls of FNAC of thyroid lesions in children and adolescents. Journal of clinical and diagnostic research.2014;8:35-38.
6. Jo VY,Stelow EB,Dustin SM,hanley KZ.Malignancy risk for fine-needle aspiration of thyroid lesions according to the Bethesda system for reporting thyroid cytopathology.Am J Clin Pathol.2010;134:450-6.
7. Chang SH,Joe M,Kim H.Fine needle aspiration biopsy of thyroid nodule in children and adolescents.J Korean Med Sci.2006;21:469-73.
8. Kapila K, Pathan SK, Hali BE, Das DK.Fine- needle aspiration cytology of the thyroid in children and adolescents. Experience with 792 aspirates.Acta Cytologica.2010; 54:569-74.
9. Yassa L,Cibas ES, Benson CB,Frates MC,Doubilet PM,Gawande AA, et al. Long-term assessment of a multidisciplinary approach to thyroid nodule diagnostic evaluation.Cancer.2007;111:508-16.
10. Mehra P, Verma AK.Thyroid cytopathology reporting by the Bethesda system: A two-year prospective study in an academic institution. Pathology Research International.2015:1-11.
11. Nayar R,Ivanovic M.The indeterminate thyroid fine-needle aspiration: Experience from an academic centre using terminology similar to that proposed in the 2007 national cancer institute thyroid fine-needle aspiration state of the science conference.Cancer.2009;117:195-202.
12. Bhasin TS, Mannan R, Manjari M, Mehra M, Gill AK, Chandey M et al. Reproducibility of the Bethesda system

for reporting thyroid cytopathology: A multicentre study with review of the literature. Journal of clinical and diagnostic research.2013; 7:1051-54.
13. Mufti ST, Molah R.The Bethesda system of reporting thyroid cytopathology: A five year retrospective review of one centre experience. International journal of Health Sciences, Qassim University.2012; 6:131-143.
14. Kessler A, Gavriel S, Zahav et al.Accuracy and consistency of fine-needle aspiration biopsy in the diagnosis and management of solitary thyroid nodules. Israel Medical Association Journal.2005; 7:371-373.
15. Mondal SK,Sinha S,Basak B,Roy DN,Sinha SK.The Bethesda system for reporting thyroid fine needle aspirates: A cytologic study with histologic follow-up.J Cytol.2013;30:94-99.
16. Ali SZ. Thyroid cytopathology. Bethesda and beyond. Acta cytologica.2011; 55:4-12.