### **Original Research Article**

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## The Bethesda system for reporting thyroid cytology: a prospective study in a tertiary care institute along with review of literature

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#### ABSTRACT

**Background:** The Bethesda system for reporting thyroid cytology (TSBRTC) was devised by the National Cancer Institute (NCI) to obtain uniformity, reproducibility and a defined management protocol while dealing with thyroid lesions. This study was undertaken with the aim to see the benefits of adopting TBSRTC in the diagnosis of thyroid FNAC, and identify the malignancy risk of each category.

**Methods:** This cross-sectional study was conducted in Indira Gandhi Medical College, Shimla, Himachal Pradesh from June 2016 to July 2017 on 181 thyroid FNACs which were reported according to the Bethesda system for reporting thyroid cytopathology (TBSRTC) under six categories: (I) non-diagnostic/unsatisfactory (II) benign (III) atypia of undetermined significance/follicular lesion of undetermined significance (IV) follicular neoplasm/suspicious for follicular neoplasm (specify if Hurthle cell (oncocytic) type (V) suspicious for malignancy (VI) malignant. Histopathological diagnosis was available for 65 cases where thyroidectomy was performed. Malignancy risk was calculated for each category. Sensitivity, specificity, positive and negative predictive values for TBSRCT were also calculated. All the data was analyzed in SPSS software version 22.0 (IBM, USA).

**Results:** Benign lesions constituted the major bulk. After the use of TBSRTC, there was increased ability to look for follicular neoplasms, improvement in making definitive diagnosis of the cases, an improvement in diagnostic accuracy, and we were in line with the implied risk outlined by TBSRTC in most of the cases.

**Conclusions:** Application of TBSRTC results in uniformity in reporting among pathologists and better interdisciplinary communication and patient management.

Keywords: CYTO-histological correlation, Malignancy risk, TBSRTC

#### **INTRODUCTION**

Thyroid swelling is a common clinical problem faced by clinicians and pathologists. Fine needle aspiration cytology (FNAC) is a rapid and inexpensive method for establishing a diagnosis and deciding the management. The National Cancer Institute (NCI) hosted the NCI Thyroid FNA State of Science Conference in October 2007 at Bethesda, Maryland and formed the Bethesda system for reporting Thyroid Cytology (TSBRTC).<sup>1</sup> It aims at standardization of reports and bridges communication gap between clinicians and pathologists and helps the surgeon to take appropriate therapeutic interventions.

#### **METHODS**

This cross-sectional study was conducted in Indira Gandhi Medical College, Shimla, Himachal Pradesh from June 2016 to July 2017 involving 181 indoor/outdoor patients presenting with palpable thyroid swelling (diffuse/nodular/solitary nodule) referred from the department of Surgery and ENT at IGMC, Shimla after taking their informed written consent. Ethical clearance was taken from the institution's ethical clearance committee before starting the study.

#### Inclusion criteria

Patients of any age having diffuse swelling, palpable thyroid nodule, with multinodular goiter, with suspected malignancy, with enlarged cervical lymph nodes or having compression symptoms were included in the study after taking written informed consent. In case of minors/paediatric cases, consent was taken from their parents/guardians.

#### Exclusion criteria

Patients not giving consent to participate in the study, uncooperative or excessively apprehensive patient, bleeding diathesis, those who could not suppress their cough reflex and were at risk for thyroid laceration by needle were excluded.

#### Methodology

Patients fulfilling the required criteria were subjected to FNAC. Smears were stained with Giemsa stain. Special stains (ZN and Congo red) were done wherever necessary. The reporting of FNA smears was done by Bethesda system under the following six categories-

*Category (I)* Non-diagnostic/Unsatisfactory: comprising of cyst fluid only, virtually acellular specimen, others (obscuring blood, clotting artifact etc.).

*Category (II)* Benign- consistent with benign follicular nodule (includes adenomatoid nodule, colloid nodule etc).

-consistent with lymphocytic (Hashimoto's) thyroiditis in proper clinical context.

-consistent with granulomatous (subacute) thyroiditis and others.

*Category (III)* Atypia of undetermined significance/ follicular lesion of undetermined significance.

*Category (IV)* Follicular neoplasm/suspicious for follicular neoplasm (specify if Hurthle cell (oncocytic) type.

*Category (V)* Suspicious for malignancy- suspicious for papillary carcinoma, suspicious for medullary carcinoma, suspicious for metastatic carcinoma, suspicious for lymphoma.

*Category (VI)* Malignant- papillary carcinoma thyroid, poorly differentiated carcinoma, medullary thyroid carcinoma, undifferentiated (anaplastic) carcinoma, squamous cell carcinoma, carcinoma with mixed features (specify), metastatic carcinoma, non-Hodgkin lymphoma and others.

Based on FNA report and other investigations, patients were subjected to total/partial thyroidectomy. Specimen was kept in 10% formalin for one day to allow proper fixation. Gross features were noted, representative sections were taken and stained with haematoxylin and eosin stains. Special stains (ZN and Congo red) were used wherever necessary.

*Validation of cytological diagnosis-* was done on the basis of histological diagnosis. The risk of malignancy among various categories under TBSRTC was calculated as number of malignant outcomes in each of the diagnostic categories.

Malignancy risk = Number of malignant cases on histology/ number of cases with cytohistological correlation  $\times$  100.

*Statistical analysis-* The sensitivity, specificity, positive and negative predictive values were calculated. All the data was analyzed in SPSS software version 22.0 (IBM, USA).

#### RESULTS

FNA was performed on 181 cases presenting with thyroid swelling. Histopathological diagnosis was available in 59 cases. 6 patients had undergone FNA twice, and since both the cytological diagnosis were included in TBSRTC, histological follow up represents a total of 65 FNAC.

Most common age group affected was 50 to 59 years constituting 48 out of 181 cases i.e. 26.5%. 32 cases (17.7%) were males and 149 cases (82.3%) were females. Female to male ratio was 4.7:1.

Solitary thyroid nodule was seen in 140 patients (77.3%), diffuse swelling in 32 cases (17.7%) and multinodular swelling in 9 cases (5.0%).

#### **TBSRTC** categories

*Category I (Non-diagnostic/unsatisfactory):* 12 cases (6.6%) were included in this category. Repeat FNAC was performed in 1 case and was categorized as benign. Histologic follow up was available in 2 cases (3.1%). One patient was diagnosed as follicular adenoma and

other as colloid goiter. The malignancy risk of this category was 0%.

*Category II (Benign):* This category comprised of the maximum number of cases i.e. 113 cases (62.4%). Histological follow up was available in 13 cases (20%) which were CG (6 cases), MNG (3 cases), HT (2 cases), papillary carcinoma (1 case) and follicular carcinoma (1 case). Malignancy risk of this category was 15.4%.

*Category III (AUS/ FLUS):* This category comprised of 1 case (0.6%). On repeat FNA it was categorized as category IV (FN/SFN). On histologic follow up, it was diagnosed as follicular carcinoma. Malignancy risk of this category was 100%.

*Category IV (FN/SFN, specify if Hurthle cell type):* 13 cases (7.2%) were reported under this category. Histological follow up was available in 11 cases (16.9%)

which were diagnosed as follicular adenoma (4 cases), Hurthle cell adenoma (3 cases), follicular carcinoma (1 case), Hurthle cell carcinoma (1 case), papillary carcinoma thyroid (1 case) and medullary carcinoma (1 case). Malignancy risk of this category was 36.4%.

*Category V (SFM):* There were 2 cases (1.1%) in this category. On repeat FNAC, 1 case remained in the same category while the other case was included in category VI (M). Both cases were diagnosed as papillary carcinoma on histological follow up. Malignancy risk in this category was 100%.

*Category VI (Malignant):* 40 cases (22.1%) were reported as malignant. Histologic follow up was available in 36 cases (55.4%). The distribution of cases included 31 cases of papillary carcinoma and 5 cases of medullary carcinoma thyroid. Malignancy risk in this category was 100% (Table 1).

#### Table 1: Category wise distribution of TBSRTC and its comparison with other studies.

	Cat I (ND)	Cat II (B)	Cat III (AUS/FLUS)	Cat IV (FN/SFN)	Cat V (SFM)	Cat VI (M)	Total (n)
Theohars et	357	2368	95	176	43	168	3207
al <sup>7</sup> (2009)	(11.1%)	(73.8%)	(3.0%)	(5.5%)	(1.4%)	(5.2%)	(100%)
Wu et al <sup>8</sup>	278	539	376	116	36	37	1382
(2012)	(20.1%)	(39.0%)	(27.2%)	(8.4%)	(2.6%)	(2.7%)	(100%)
Bongiovanni	3271	15104	2441	2571	680	1378	25,445
et al <sup>9</sup> (2012)	(12.9%)	(59.3%)	(9.6%)	(10.1%)	(2.7%)	(5.4%)	(100%)
Tepeoglu et	122	697	100	41	36	25	1021
$al^{10}$ (2014)	(11.9%)	(68.3%)	(9.8%)	(4.0%)	(3.5%)	(2.4%)	(100%)
Deniwar et al <sup>11</sup>	31	192	65	42	17	28	375
(2015)	(8.0%)	(51.0%)	(17.0%)	(11.0%)	(5.0%)	(8.0%)	(100%)
Pantola et al <sup>6</sup>	12	151	23	18	05	09	218
(2016)	(5.5%)	(69.3%)	(10.5%)	(8.2%)	(2.3%)	(4.1%)	(100%)
Present study	12	113	01	13	02	40	181
(2017)	(6.6%)	(62.4%)	(0.6%)	(7.2%)	(1.1%)	(22.1%)	(100%)

#### Table 2: Category-wise distribution of cases as per TBSRTC with histologic follow-up.

Diagnostic category	No. of cases	Percentage (%)
Non-diagnostic/ Unsatisfactory (ND/UNS)	2	3.1
Benign (B)	13	20.0
AUS/FLUS	1	1.5
FN/SFN (specify if Hurthle cell neoplasm)	11	16.9
SFM	2	3.1
Malignant (M)	36	55.4
Total (n)	65	100

Among the 65 cases in which histologic follow up, maximum number of cases were under category VI (M)

i.e., 36 cases (55.4%) followed by category II (B) comprising of 13 cases (20%) and category IV (FN/SFN) 11 cases (16.9%). 2 cases (3.1%) each were seen in category I (ND/UNS) and category V. Only 1 case (1, 5%) was included in category III (AUS/FLUS) (Table 2).

In 6 cases with repeat FNA due to suspicious clinicradiological profile, both the cytological diagnosis were considered since both the FNAs were independent event and it helped to include the malignant cases with previous benign/indeterminate diagnosis on cytology. Out of these 6 cases, 3 cases were of category II (B). One case remained in same category while in remaining two cases one turned into category IV (FN/SFN) and other in category V (M). The rest of 3 cases, one from category I (ND/UNS) was found to be category II (B), category V (SFM) was changed to category VI (M) and category III (AUS/FLUS) was changed to category IV (FN/SFN) respectively (Table 3).

# Table 3: Outcomes of repeat FNAC with their histological outcomes.

No. of cases	Diagnosis on initial FNAC	Diagnosis on repeat FNAC	Histological outcomes
1	Category III (AUS/FLUS)	FN/SFN	FC
1	Category V (SFM)	Malignant	РСТ
1	Category II (B)	Malignant	PCT
1	Category II (B)	FN/SFN	FC
1	Category II (B)	Benign	MNG
1	Category I (ND/UNS)	Benign	CG

Histologically, maximum number of cases were of papillary carcinoma i.e. 35 cases with 1 case showing Hashimoto's thyroiditis along with papillary carcinoma. Medullary carcinoma and colloid goiter comprised of 6 cases and 7 cases respectively. There were 3 cases of HCA in our study followed by 3 cases of MNG and 2 case of Hashimoto's thyroiditis. We had 5 cases of FA and 1 case each of HCC and 3 cases of FC respectively. Cytohistological correlation was maximally seen in AUS/FLUS category and SFM category i.e., 1 out of 1 and 2 out of 2 respectively. In category FN/SFN and malignant category (M), it was seen in 11 out of 13 and 36 out of 40 respectively (Table 4).

The risk of malignancy among various categories under TBSRTC is an important parameter and is calculated as number of malignant outcomes in each of the diagnostic categories (Table 5).

#### Table 4: Cytologic and histologic correlation (TSBRTC) (n=65).

Cytologic category	Histologic diagnosis									
	CG	MNG	AT (HT/LT)	FA	HCA	FC	HCC	РСТ	MC	Total (n)
ND/UNS	1	0	0	1	0	0	0	0	0	2
В	6	3	2	0	0	1	0	1	0	13
AUS/FLUS	0	0	0	0	0	1	0	0	0	1
FN/SFN	0	0	0	4	3	1	1	1	1	11
SFM	0	0	0	0	0	0	0	2	0	2
Μ	0	0	0	0	0	0	0	31	5	36
Total (n)	7	3	2	5	3	3	1	35	6	65

#### Table 5: Comparison of malignancy risk.

	Cat I (ND)	Cat II (B)	Cat III (AUS/FLUS)	Cat IV (FN/SFN)	Cat V (SFM)	Cat VI (M)
Theoharis et al <sup>7</sup> (2009)	Not calculated	9.8%	48.0%	34.0%	87.0%	100%
Jo et al <sup>24</sup> (2010)	8.9%	1.1%	17.0%	25.4%	70.0%	98.1%
Wu et al <sup>8</sup> (2012)	14.0%	9.5%	22.0%	27.0%	67.0%	100%
Bongiovanni <sup>9</sup> meta-analysis (2012)	16.8%	3.7%	15.9%	26.1%	75.2%	98.6%
Park et al <sup>25</sup> (2014)	35.3%	5.6%	69.0%	50.0%	98.7%	98.9%
Prathima et al <sup>26</sup> (2016)	33.3%	2.1%	50.0%	1.0%	67.0%	100%
Limlunjakorn et al <sup>27</sup> (2017)	19.2%	14.0%	37.9%	20.9%	81.5%	93.6%
Present study (2017)	0.0%	15.4%	100%	36.4%	100%	100%

#### Table 6: Comparison of statistical analysis of TBSRTC with other studies.

	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Bongiovanni et al <sup>9</sup> (2012)	97.0%	50.7%	55.9%	96.3%
Muratli et al <sup>28</sup> (2014)	87.1%	64.6%	76.1%	79.5%
Garg et al <sup>29</sup> (2015)	88.9%	84.3%	50.0%	97.7%
Arul et al <sup>30</sup> (2015)	94.4%	97.6%	98.1%	93.2%
Mehrotra et al <sup>31</sup> (2016)	69.2%	89.5%	81.8%	81.0%
Kujur et al <sup>32</sup> (2017)	80.0%	91.9%	92.9%	97.5%
Present study (2017)	90.4%	100%	100%	72.2%

Sensitivity and negative predictive value of TBSRTC was 90.38% and 72.22% respectively. Specificity and positive predictive value was 100% (Table 6).

#### DISCUSSION

Palpable thyroid swellings are a common clinical problem affecting 4-7% of middle aged population.<sup>2</sup> The annual incidence of thyroid carcinoma is 1-2 per 100,000 which accounts for 90% of malignancies of the entire endocrine system. In India, there are 21600 new cases of thyroid malignancy every year.<sup>3</sup>

In our study, 181 cases were evaluated. 113 cases were benign (62.4%). Thus, there were more number of non-neoplastic lesions as compared to neoplastic lesions which was consistent with the studies conducted by Hariprasad et al and Bhatia et al i.e., 109 (68.6%) and 21 (84%) cases.<sup>4,5</sup>

*Category I:* We had 12 cases (6.6%) in this category which was comparable to Pantola et al i.e., 12 cases (5.5%).<sup>6</sup> The studies conducted by Theoharis et al, Her-Juing Wu et al, Bongiovanni et al, Tepeoglu et al and Deniwar et al showed a higher percentage of cases in this category i.e., 357 cases (11.1%), 278 cases (20.1%), 3271 cases (12.9%), 122 cases (11.9%) and 31 cases (8%) respectively.<sup>7-11</sup> The may be related to operator factor and/or the inherent nodule characteristics like cystic change or fibrosis. Thyroid being a very vascular organ has higher chances of yielding non-diagnostic yield consisting of blood only.<sup>12</sup> Multiple passes, on-site adequacy testing and USG guided FNAC can improve the diagnostic yield.<sup>13</sup>

*Category II:* comprised of the maximum number of cases i.e.113 cases (62.4%). These results are consistent with the studies conducted by Bongiovanni et al i.e., 15104 cases (59.3%), Theoharis et al i.e., 2368 cases (73.8%), Tepeoglu et al i.e. 697 cases (68.3%) and Pantola et al 151 (69.3%) respectively.<sup>6,7,9,10</sup> However, studies conducted by Deniwar et al and Her-Juing Wu et al had lesser number of cases in this category comprising of 192 cases (51%) and 539 cases (39%) respectively.<sup>8,11</sup>

Amongst the 65 FNACs with histological follow up, 13 were benign In 3 cases, repeat FNAC was done in view of suspicious clinico-radiological profile. One of the patients remained benign while 2 patients were reported under FN/SFN (category IV) and malignant (category VI) respectively. Thus, it highlights the inherent pitfalls in sampling in thyroid FNAC and reinforces the usefulness of multidisciplinary approach for evaluation and management of patients with thyroid lesions. Patients with suspicious radiological findings being reported either into category I or II may benefit from USG guided repeat FNA which will help to minimize financial burden as well as reduce the cytological false negatives.

Category III: Certain cases show some degree of atypia which is more than that can be confidently ascribed to reactive changes but are not sufficient enough to diagnose malignancy. Such cases are categorized in this category. The use of this category has been from 3% by Theoharis et al, 27.2% by Her-Juing Wu et al, 9.6% by Bongiovanni et al, 9.8% by Tepeoglu et al, 10.5% by Deniwar et al and 17% by Pantola et al.<sup>6-11</sup> In our study it was used in 1 case (0.6%) which is significantly lower from the other studies. On repeating the FNAC, diagnosis of FN/SFN (category IV) was made and was follicular carcinoma on histopathology.<sup>14,15</sup> There is considerable overlap in the cytological features of adenomatoid goiter, hyperplastic nodule in MNG and follicular neoplasm. However, cases with cellular smears which show focal changes probably reflects the 'gray area' in thyroid cytology rather than sampling error. Thus, we feel that patients with AUS diagnosis despite cellular smears may not benefit from repeat FNAC. This 'gray area' in cytology may simply reflect the overlapping features and diagnostic challenges which are faced even on histology, which is regarded as gold standard. This is because features like nuclear enlargement, prominent nucleoli, crowding and even some degree of microfollicular formation may be seen in both adenomatoid goiter and follicular neoplasm. The interpretation of atypia is somewhat subjective and hence there are differences in the usage of this category despite certain guidelines. This difference may reflect lack of confidence with the new diagnostic criteria. However, despite being subjective, the category is useful since studies have found significantly lower malignancy rate than that of category IV. In a novel study, Shi et al have showed that eliminating the AUS/FLUS category caused decreased sensitivity as 53% of neoplastic lesions were downgraded to benign.<sup>16</sup> Moreover, once categorized as benign (category II), the patients might not be reevaluated for months or may even be lost for follow up. Thus this category must be viewed more as for screening purpose rather than for diagnostic one.

Renshaw sub classified AUS/FLUS category smears morphologically into different subclasses. He concluded that sub classifying the AUS/FLUS smears into atypia for PCT and atypia for follicular lesion may help as these have different malignancy percentage outcome.<sup>17</sup> Nayar et al found that repeat FNAC yielded diagnostic yield in 60% cases while the malignancy rate was 5%.<sup>18</sup> Vanderlaan et al have found that though repeat FNAC proved diagnostic in 68% cases, there was no significant difference in the malignancy rate among patients who had surgery after single AUS/FLUS diagnosis as compared to those who had a repeat FNAC.<sup>19</sup> We thus recommend that in patients with AUS/FLUS diagnosis, the decision of whether to follow up with repeat FNAC or whether to proceed with surgery should be based on clinicoradiological features.

*Category IV:* In our study this group constituted 13 cases (7.2%) which was comparable to studies conducted by Wu et al and Pantola et al that comprised of 116 cases

(8.4%) and 18 cases (8.2%).<sup>6,8</sup> There were more number of cases in this category by studies conducted by Bongiovanni et al and Deniwar et al comprising of 2571 cases (10.1%) and 42 cases (11%) while the studies conducted by Theoharis et al and Tepeoglu et al showed less number of patients i.e., 176 cases (5.5%) and 41 (4%) respectively.7,9,10,11 Histopathological cases correlation was available in 11 cases. Of them, 4 cases were of follicular adenoma, 3 of Hurthle cell adenoma and 1 case each of follicular carcinoma, Hurthle cell carcinoma. papillary carcinoma and medullarv carcinoma.

Though it is desirable to differentiate between follicular carcinoma and adenoma, none of the cytologic criteria or markers have been found to be reproducible and of diagnostic value. Moreover, follicular variant of PCT is an important differential diagnosis on because of characteristic nuclear features.<sup>20</sup> Thus, in our opinion, the role of cytology is to select cases with a greater likelihood of having carcinoma. Since every adenoma on cytology may turn out to be carcinoma, it may be said that every follicular adenoma missed on cytology is like missing a potential follicular carcinoma.

There have been numerous attempts to define the features that may help to differentiate follicular adenoma from carcinoma. Montironi et al have suggested that a combination of nuclear diameter, percentage of nucleolated cells and number of nucleoli may help to improve distinction between adenoma and carcinoma.<sup>21</sup> Harach et al noted that presence of necrotic debris is associated with carcinoma.<sup>22</sup> Suen et al emphasizes that various features like cellularity, follicular arrangement, colloid content, nuclear size, nucleoli and others must be considered together in making a diagnosis keeping in mind that cytological features often overlap.<sup>23</sup> Baloch et al tried to predict the risk of malignancy by considering the clinical features like age and sex of the patient and size of the nodule.<sup>20</sup>

Category V: 2 cases (1.1%) were reported in this category in our study which was comparable to study conducted by Theoharis et al who had 43 cases (1.4%).<sup>7</sup> There were more number of cases in this category in the studies done by Wu et al, Bongiovanni et al and Pantola et al constituting 36 cases (2.6%), 680 cases (2.7%) and 5 cases (2.3%) respectively.<sup>6,8,9</sup> Studies conducted by Tepeoglu et al and Deniwar et al showed significantly higher number of patients comprising of 36 cases (3.5%) and 17 cases (5%) respectively.<sup>10,11</sup> In both the cases, cytological suspicion correlated with the histopathological diagnosis, thus yielding a malignancy risk of 100%. The aim of segregating 'suspicious' category apart from 'malignant' category is to preserve the very high positive predictive value of the malignant category without compromising the overall sensitivity of the procedure.

Category VI: There were 40 cases (22.1%) in this category in our study. However, studies conducted by Theoharis et al, Wu et al, Bongiovanni et al, Tepeoglu et al, Deniwar et al and Pantola et al showed less number of cases i.e., 168 cases (5.2%), 37 cases (2.7%), 1378 cases (5.4%), 25 cases (2.4%), 28 cases (8%) and 9 cases (4.1%) respectively in this category.<sup>6-11</sup> Histopathological correlation was available in 36 cases. 30 cases were of PCT, 1 case of PCT along with Hashimoto's thyroiditis and 5 cases of medullary carcinoma. 1 case that was diagnosed as PCT on FNAC came out to be medullary carcinoma on histopathology. There were no false positive cases in this category suggesting that as per TBSRTC only the cases with definitive evidence of malignancy were categorized in this category. Thus, frank malignant cases do not pose diagnostic difficulties and majority of the cases are reported without difficulty.

The malignancy risk in our study for category I was 0%. However, in other studies conducted by Jo et al, Wu et al, Bongiovanni et al, Park et al, Prathima et al and Limlunjakorn et al it was significantly higher i.e. 8.9%, 14%, 16.8%, 35%, 33.3% and 19.2% respectively.<sup>8,9,24-27</sup>

In category II, it came out to be 15.4% which was comparable to study conducted by Limlunjakorn et al i.e., 14%.<sup>27</sup> Malignancy risk in other studies conducted by Theoharis et al, Wu et al, Park et al and Bongiovanni et al was 9.8%, 9.5%, 5.6% and 3.7% respectively.<sup>7,8,9,25</sup> The malignancy risk was significantly lower in studies conducted by Prathima et al and Jo et al i.e., 2.1% and 1.1% respectively.<sup>24,26</sup>

The category III of our study yielded malignancy risk of 100%. In studies conducted by Theoharis et al, Jo et al, Wu et al, Bongiovanni et al, Park et al, Prathima et al and Limlunjakorn et al it was lower, comprising of 48%, 17%, 22%, 15.9%, 69%, 50% and 37.9% respectively.<sup>7-</sup> 9,24-27

Category IV showed malignancy risk of 36.4% which was comparable to study conducted by Theoharis et al with malignancy risk of 34%.<sup>7</sup> It was higher in study conducted by Park et al i.e., 50% while it was lower in studies conducted by Jo et al, Wu et al, Bongiovanni et al and Limlunjakorn et al constituting 25.4%, 27%, 26.1% and 20.9% respectively.<sup>9,24,25,27</sup> The malignancy risk was significantly low in study conducted by Prathima et al i.e., 1%.<sup>26</sup>

In category V of our study malignancy risk was 100% which was comparable to study conducted by Park et al i.e., 98.7%.<sup>25</sup> However, in other studies conducted by Theoharis et al, Jo et al, Wu et al, Bongiovanni et al, Prathima et al and Limlunjakorn et al it was 87%, 70%, 6%, 75.2%, 67% and 81.5% respectively.<sup>7-9,24,26,27</sup>

In category VI, the malignancy risk was 100% which was comparable to studies conducted by Prathima et al, Theoharis et al and Wu et al i.e., 100% each respectively. It was less in studies conducted by Jo et al, Bongiovanni et al, Park et al and Limlunjakorn et al i.e., 98.1%, 98%, 98.9 % and 93.6% respectively (Table 5).<sup>7-9,24,26,27</sup>

The sensitivity of TBSRTC in our study was 90.4% which was comparable to the study conducted by Muratli et al and Garg et al i.e., 87.1% and 88.9% respectively.<sup>28,29</sup> It was higher in studies conducted by Bongiovanni et al and Arul et al i.e. 97% and 94.4% while it was lower in studies conducted by Mehrotra et al and Kujur et al constituting 69.2% and 80% respectively.<sup>9,30-32</sup>

Specificity in our study was 100%, comparable to Arul et al i.e., 97.6%.<sup>30</sup> It was lower in studies conducted by Bongiovanni et al, Muratli et al, Garg et al, Mehrotra et al i.e. 50.7%, 64.6%, 84.3% and 89.5% respectively.<sup>9,28,29,31</sup> It was slightly lower in study conducted by Kujur et al i.e., 91.9%.<sup>32</sup>

Positive predictive value in our study was 100%, comparable with Arul et al i.e. 98.1%.<sup>30</sup> It was slightly less in study conducted by Kujur et al i.e. 92.9% while it was significantly lower in studies conducted by Bongiovanni et al, Muratli et al, Garg et al and Mehrotra et al comprising of 55.9%, 76.1%, 50% and 81.8% respectively.<sup>9,28,29,31,32</sup>

Negative predictive value in our study was 72.2% which was comparable with the study conducted by Muratli et al i.e., 79.5%.<sup>28</sup> In study conducted by Mehrotra et al it was slightly higher i.e., 81% while it was significantly higher in the studies conducted by Bongiovanni et al, Arul et al, Garg et al and Kujur et al constituting 96.3%, 93.2%, 97.7% and 97.5% each respectively (Table 6).<sup>9,28-31</sup>

#### CONCLUSION

The advantage of Bethesda system is that it states the risk of malignancy for each category and thus helps in deciding the further management protocol for the patient. Category with a lower malignancy risk is managed conservatively with follow up or repeat FNAC whiles the ones with higher risk for malignancy are operated.

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Ethical approval: The study was approved by the Institutional Ethics Committee of Indira Gandhi Medical College, Shimla

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