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Leading Article

Beyond the horizon of current thyroid cytology reporting in Sri Lanka....

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Thyroid enlargement is a commonly encountered clinical problem among Sri Lankan patients, be it diffuse enlargement of the gland, a single nodule or multiple nodules involving both lobes. Affected patients are often referred for fine needle aspiration biopsy (FNAB), causing a heavy thyroid cytology workload in comparison to breast cytology in our setting. The cost effective, simple FNAB test is valuable in identifying malignancy in euthyroid patients with single nodules, facilitating early surgical intervention.

Thyroid FNABs have been performed and reported by Sri Lankan pathologists over the past two decades. Kumarasinghe analysed 1797 thyroid aspirates in 1997, documenting a malignancy rate of 2% in multi nodular goitres, 5% in solitary nodules and 3% in diffuse nodular swellings. No malignancies were recorded in diffuse smooth swellings. The prevalence of malignancy ranged from 4-4.5% in the study population. The author had arrived at these figures after considering actual malignancies diagnosed on cytology and projected figures of malignancy on follicular proliferations and atypical lesions based on the accuracy tested in the local setting(1).

Thyroid cytology reporting was not uniform among the pathologists initially, with most using the classification system recommended by the Papanicolau society(1). This included five broad diagnostic categories including inadequate, benign, atypical, follicular lesions/proliferations and malignant (2). A consensus document for thyroid cytology reporting was compiled in 2007 in Sri Lanka, under the auspices of the Ministry of Healthcare and Nutrition, funded by the World Bank through the Health Sector Development Project.Pathologists reporting on thyroid cytology contributed to the development of the current guide lines through a subcommittee appointed by the College of Pathologists (3)(Table 1).The guidelines were developed in keeping with those of the British Thyroid Association of the Royal College of Pathologists(4).The clinical and radiological contribution for development of the guidelines was minimal. Thus no definite management guidelines were incorporated in to the document, though some recommendations were made for management of certain categories.Eg. Urgent histological assessment was recommended for Thy 3 and Thy 4 categories.

This consensus document is credited for achieving a degree of uniformity in thyroid cytology reporting in our setting. The 'Thy' categories were expected to convey the diagnosis to the clinicians in less ambiguous terms, though it has not been formally evaluated for its clinical utility to date.

Thus, though the guidelines made thyroid cytology reporting relatively more uniform, we are yet unsure of its clinical impact. It is apparent that the perceptions of diagnostic terminology for thyroid FNABs show some discordance among pathologists and clinicians. This is based on the queries we receive from our clinical colleagues regarding the management of patients falling into inadequate, follicular proliferation and suspicious for malignancy categories.

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- *Should all inadequate smears be repeated? If so, should it be done under radiological guidance?*
- *What do you favour in this follicular proliferation? A neoplasm or an adenomatoid nodule?*
- *Could you be confident this is papillary carcinoma or not, so we could do a total/near total thyroidectomy straight away?*

The Bethesda System for Reporting Thyroid Cytology (TBSRTC)

The TBSRTC (Table 2) was developed in October 2007, by a multidisciplinary team of Pathologists, Endocrinologists, Radiologists and Surgeons, in keeping with the multidisciplinary approach to management of thyroid diseases(5).

Categories	Description of category	Expected clinical management (not mentioned in the guidelines)
Thy 1	Inadequate	Repeat FNA with or without ultrasound guidance based on the clinical setting.
Thy 2	Benign (Colloid storing nodule, thyroiditis, toxic goitres)	Clinical follow up
Thy 3	Follicular proliferation (hyperplastic nodule, Hurthle cell neoplasm, follicular neoplasm, Medullary carcinoma)	Lobectomy
Thy 4	Suspicious for malignancy	Lobectomy or near total thyroidectomy
Thy 5	Malignant (Papillary, Medullary, Anaplastic carcinoma)	Total thyroidectomy

Table 1. Current Sri Lankan guidelines for thyroid cytology reporting

The multidisciplinary nature of the team is credited with the TBSRTC, which incorporates management guidelines ensuring effective linkage between thyroid cytology reporting and clinical management plans. Six well defined and morphologically distinct diagnostic categories have been developed based on the probability of finding malignancy (Risk of malignancy-ROM) in each diagnostic category. Diagnostic criteria have been developed and documented for each category,together with explanatory notes and relevant images in the TBSRTC monograph,published in January 2010(6).TBSRTC is thus expected to ensure better cytohistologic correlation, inter observer reproducibility and clinical utility.

Comparison of TBSRTC with the thyroid cytology reporting system in Sri Lanka

Table 3 compares the six diagnostic categories of TBSRTC with the 'Thy' categories of the current thyroid cytology reporting system in Sri Lanka. The cellularity criteria for adequacy in the two classification systems are different. The Sri Lankan system defines adequate cellularity as more than 6 clusters of 20 cells each as opposed to more than 6 clusters of 10 cells each in the TBSRTC.The adequacy criterion is less stringent in the TBSRTC. However as these definitions are only rough guides they cannot be considered a major difference between the two systems.

Non diagnostic/unsatisfactory *Limited cellularity, acellular, technically unacceptable samples and cyst fluid only*	1-4	Repeat FNA with ultrasound guidance
Benign *Adenomatoid or colloid nodule, chronic lymphocytic thyroiditis, other*	0-3	Clinical follow up
Atypia of undetermined significance (AUS)/Follicular lesion of undetermined significance (FLUS)	20-25 (for repeat AUS)	Repeat FNA
Suspicious for a follicular neoplasm/Follicular neoplasm	**15-30**	Surgical lobectomy
Suspicious for malignancy *Papillary carcinoma, Medullary carcinoma, lymphoma, Metastatic neoplasm, other*	**60-77**	Surgical lobectomy or near total thyroidectomy
Malignant	**97-99**	Near total thyroidectomy (Radiation/chemotherapy for some)

Table 2. Bethesda system for reporting thyroid cytology (TBSRTC)

A technically unacceptable slide (which is not assigned a category in our system) is included in this category in TBSRTC making the 'non diagnostic/unsatisfactory' terminology used justifiable, in comparison to the term 'inadequate' in the Sri Lankan system. TBSRTC requests all laboratories to maintain the non-diagnostic/unsatisfactory category at <10%, promoting improvement of quality in obtaining smears in each setting. TBSRTC management guidelines request a repeat FNAB under ultrasound guidance after a suitable interval (3 months) for this category.

This is to prevent false positive interpretation of reactive/reparative changes resulting from the initial FNAB (6).

TBSRTC	Categories used for thyroid cytology reporting in SL
Non diagnostic /unsatisfactory	**Thy 1 - Inadequate**
Limited cellularity, acellular, technically unacceptable samples and cyst fluid only	
Atypia of undetermined significance (AUS)/Follicular lesion of undetermined significance (FLUS)	**Thy 3 - Follicular proliferation**
Suspicious for a follicular neoplasm/ Follicular neoplasm	**Thy 3 - Follicular proliferation**
Specify if Hürthle cell (oncocytic) type	(hyperplastic nodule, hurthle cell neoplasm, follicular neoplasm, Medullary carcinoma)
Suspicious for malignancy	**Thy 4 - Suspicious for malignancy**
Papillary carcinoma, Medullary carcinoma, lymphoma, Metastatic neoplasm, other	
Malignant	**Thy 5 - Malignant**
Papillary carcinoma, Medullary carcinoma, lymphoma, Metastatic neoplasm, other	(Papillary, Medullary, Anaplastic carcinoma)

Table 3. Comparison of categories used for thyroid cytology reporting in Sri Lanka with TBSRTC

The significance of 'cyst fluid only' is highlighted in TBSRTC as a special subset of nondiagnostic/unsatisfactory cases, emphasising that it could be considered adequate and benign, in the appropriate clinical setting of an entirely cystic lesion (unilocular cyst < 3cm) with no suspicious ultrasound scan/clinical findings or a family history of thyroid malignancy. A 4% ROM for cystic papillary carcinoma is found in this subset of 'cyst fluid only' category. Thus TBSRTC says it still requires an inadequate diagnosis enabling a repeat aspirate to exclude this possibility, in the clinical context of suspicious clinical/radiological findings and a positive family history (5).

We do not distinguish 'cyst fluid only' subset in our classification system. These would always be categorised as inadequate and most patients would under go reaspiration.

Commonly encountered, abundant colloid coating the smears without the required cellularity is considered inadequate in the Sri Lankan system.This would be considered satisfactory and categorised as benign in TBSRTC in the appropriate benign clinical/radiological context even when the adequacy criteria are not met (6).

Diagnostic criteria for the benign category are provided in the TBSRTC monograph, suggesting subsequent clinical follow up for these patients. There is no major difference in the benign category between the two systems other than carefully laid down diagnostic criteria and the management guideline in the TBSRTC. The major difference between the two systems is seen in the 'Thy 3 - follicular proliferation' category.

This is split in to two categories having different clinical management options in TBSRTC. The two categories in TBSRTC are 'Atypia of undetermined significance (AUS) /Follicular lesion of undetermined significance (FLUS)' and 'Suspicious for follicular neoplasm/Follicular neoplasm'.

AUS/FLUS category ('Thy 3'- 1st subset) will be managed by repeating the FNAB and Suspicious for follicular neoplasm/Follicular neoplasm category ('Thy 3'- 2nd subset) will be

directed towards a lobectomy. Management guidelines laid down for the two categories explicitly would ensure better clinical management of patients. AUS/FLUS are mostly due to compromised specimens and reaspiration yields a definitive diagnosis in most instances. All Thy 3's in the Sri Lankan system are expected to undergo histological assessment leading to unnecessary surgical intervention in at least a minority of patients. We are also faced with a dilemma when we encounter smears with architectural and/or nuclear atypia, yet, not sufficient enough to diagnose a follicular proliferation. We do not have a separate category for this type of smear. However they would be categorised as AUS/FLUS in TBSRTC.

Diagnostic criteria for these two categories are also documented in TBSRTC. TBSRTC, while acknowledging that it is not possible to document all scenarios leading to an AUS/FLUS diagnosis, highlights eight situations in which this diagnosis is appropriate. TBSRTC also mentions that this diagnosis should not exceed 7% in any individual laboratory to prevent it from becoming a wastepaper basket (5).

However the reproducibility of this category among different pathologists may vary undermining usefulness of this percentage cut off. The 2nd Thy 3 category of cellular smears with a predominant micro follicular pattern is categorised as suspicious for follicular neoplasm/ follicular neoplasm in TBSRTC recognising that cytological distinction between follicular adenoma and carcinoma is arbitrary on a cytological basis.Thus this diagnostic category is managed by a lobectomy (5).A significant number yet turn out to be adenomatoid nodules on histological follow up (6).The suspicious for malignancy category in TBSRTC includes cases with sufficient cellular atypia, lacking the quantitative and/or qualitative features for a definite diagnosis of malignancy, or sparsely cellular smears where a malignant diagnosis cannot be made with certainty.The malignant category includes cases with cytomorphologic features diagnostic of cancer.These two categories are the same in our classification (Thy 4 and Thy 5). In the TBSRTC monograph diagnostic criteria are mentioned for the two categories with explanatory notes and management guidelines.

Advantages and disadvantages of TBSRTC and its utility in our setting

The greatest advantage of TBSRTC appears to be the recommendations made for clinical management of all categories.The clinical utility of TBSRTC is significant as the cytological diagnosis of each category is linked with definite management guidelines.Our current thyroid cytology reporting system lags behind in this respect. TBSRTC monograph with the documented diagnostic criteria, appropriate supporting images and explanatory notes for each diagnostic category serves as a guide facilitating uniformity in thyroid cytology diagnosis.The risk of malignancy mentioned in TBSRTC for each diagnostic category gives an idea of same to both the pathologist and the clinician. At the same time it implies the limitations of cytological diagnosis of thyroid smears in all categories.TBSRTC also provides answers to some of the clinical queries we receive.

Should all inadequate smears be repeated? If so should it be done under radiological guidance?

TBSRTC highlights the inadequate smears that need not be repeated and mentions that those

that are repeated should preferably be done under ultrasound guidance.

What would you favour in this follicular proliferation? A neoplasm or an adenomatoid nodule?

The Thy3 category which is split into AUS/FLUS and Suspicious for follicular neoplasm/Follicular neoplasm in TBSRTC is helpful in refining the diagnosis of smears that are likely to be truly follicular neoplasms, whilst acknowledging that there is still a chance for them to be adenomatous/ malignant nodule based on the ROM.

Can you be confident whether this is papillary carcinoma or not, so we could do a total/near total thyroidectomy straight away?

Both systems retain the suspicious for malignancy category. However the well documented diagnostic criteria with the explanatory notes and supporting images in the TBSRTC monograph will help to refine the diagnosis of this suspicious for malignancy category further.

On a less positive note, the increased number of diagnostic categories in TBSRTC though expected to refine the diagnosis, could be considered more complicated. Recommendations that are made regarding the cut off percentages of certain categories (inadequate and AUS/FLUS), to prevent over diagnosis could also be arbitrary in different settings. Though there are these concerns regarding TBSRTC its adoption would enable easy exchange of data in the international arena facilitating research, ultimately resulting in better patient care.

The recent document on 'Guidance on the reporting of thyroid cytology specimens' compiled by the Royal College of Pathologists in November 2009 (7) has again amended 'Thy' diagnostic categories to be on par with the TBSRTC (Table 4). It also mentions that the most important role of any reporting system is to provide clarity for patient management. It further states that it is also important to be able to audit outcomes to refine and improve the reporting process, to give a relative risk of thyroid cancer for each cytological diagnosis and to bring the process to a level of national standardisation to compare with other international systems.

RCPath	TBSRTC
Non-diagnostic for cytological diagnosis (Thy 1) **Non-diagnostic for cytological diagnosis - Cystic lesion (Thy 1 c)**	**Non-diagnostic or unsatisfactory** *Limited cellularity, acellular, technically unacceptable samples and cyst fluid only*
Non-neoplastic (Thy 2) **Non-neoplastic, cystic lesion (Thy 2 c)**	**Benign** **Adenomatoid or colloid nodule, chronic lymphocytic thyroiditis, other**
Neoplasm **Possible atypia/non diagnostic (Thy 3 a)**	**Atypia of undetermined significance (AUS) or follicular lesion of undetermined significance (FLUS)**
Neoplasm possible, suggesting follicular neoplasm (Thy 3 f)	**Follicular neoplasm or suspicious for a follicular neoplasm** *Specify if Hürthle cell (oncocytic) type*
Suspicious of malignancy (Thy 4)	**Suspicious for malignancy** **Papillary carcinoma, Medullary carcinoma, lymphoma, Metastatic neoplasm, other**
Malignant (Thy 5)	**Malignant** **Papillary carcinoma, Medullary carcinoma, lymphoma, Metastatic neoplasm, other**

Table 4.Comparison of current RCPath thyroid cytology reporting system with the TBSRTC

Any system used must also be easy to understand and apply in clinical practice and should show good intra and inter observer reproducibility between the various categories (7). Therefore is the time now appropriate, for us to look beyond the horizon of current thyroid cytology reporting in Sri Lanka?

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