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Morphologic assessment of thyroid disease by cytology and pattern of thyroid enlargement in Sri Lanka

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Introduction

Thyroid diseases are common in Sri Lanka and the high prevalence is indicated by the large number of patients attending medical and surgical clinics daily with diseases related to the thyroid. One study done in a surgical unit at the General Hospital Kandy estimates it to be 5% of total clinic attendance[1]. Another study done in a surgical unit in Colombo, records a total of 1153 thyroidectomies being performed over period of 4 years[2]. At present no less than 5% of the world's population are known to have goitres and associated disorders[3]. Seventy five percent of this live in less developed countries where iodine deficiency is prevalent[3]. Endemic goitre appears to be related to the incidence rates of papillary, follicular and anaplastic carcinomas and to hyperthyroidism and autoimmunity indirectly, as a result of effects of ingestion and administration of Iodine.

It is mentioned in the literature that lack of knowledge of other causative factors of goitres has prevented complete eradication of goitre in spite of prolonged and adequate Iodine supplementation[3].

Endemic goitre in Sri Lanka has been estimated to occur between 6.5%-30.2% and 66% of the Sri Lankan population live in the endemic areas including the Western, Central, Sabaragamuwa, Southern and the Uva provinces[4,5]. However the pattern of thyroid enlargement in Sri Lanka has been studied only by a few in the past. There have been a few reports documenting the pattern of thyroid diseases in Sri Lanka on the basis of histologic findings in thyroidectomies[1,6,7] and on functional status[8].

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Thyroid function tests, serology, radiology and isotope studies are the non invasive modalities available in the assessment of thyroid disease. Morphologic assessment is the final confirmation of the true nature of thyroid enlargement. Tru cut or excision biopsy, nodulectomy, lobectomy or total or subtotal thyroidectomy are the surgical options for morphologic assessment of thyroid enlargement/ disease. They are neither feasible nor desirable to assess all thyroid enlargements[9]. At present the next best option available is fine needle aspiration biopsy examination of thyroid to arrive at a morphologic diagnosis. Cytologic assessment by fine needle aspiration biopsy of thyroid is a first line diagnostic procedure accepted in the diagnostic work-up of patients both locally and abroad[9,10].

The accuracy rates for fine needle aspiration biopsy for the assessment of thyroid disease in Sri Lanka has been documented in previous publications on the basis of analysis of 3577 thyroid aspirates[11]. Cytologic assessment is superior to clinical examination and is comparable to other studies although an integrated approach gives the best results[10,12,13].

Considering the comparable and acceptable accuracy rates obtained in previous studies cytologic assessment was considered to be a satisfactory method to evaluate the thyroid disease pattern.

Objectives

1. To assess the pattern of thyroid diseases on a morphologic basis by cytology.
2. To present the advances made in the cytologic assessment of thyroid diseases in Sri Lanka.

Method

All cytologic samples of the thyroid gland examined by the author over 2 years from 1995

January to December 1996 were included in a prospective study. The samples were either obtained by me or by a pathology trainee under my guidance or submitted for analysis by other clinicians. The technique used by us was the non aspiration needle jab technique except in exceptional circumstances. The cysts were emptied by aspiration.

The smears obtained were fixed in 95% alcohol.

Some smears which were received from outstation hospitals were air dried without wet fixation. The smears were either stained with haematoxylin and eosin (H & E) or with Romanawsky stains depending on whether they were wet fixed or air dried.

The age and the sex were recorded for majority of the patients. Place of residence for the preceding 10 years and the nature of the thyroid enlargement were recorded as apart of the study.

The criteria used for cytologic assessment of thyroid aspirates including broad categorisation and further subtyping were based on those described by Orell[12], Kini[13] and others and recommended by the Papanicolau Society later[14]. The broad categorisation include inadequate, benign, atypical, follicular lesions/proliferations and malignant. These broad categories were further assessed and sub-typed as in histology where ever possible.

False positive and negative rates established in previous studies were considered in the estimation of actual numbers. Cytologic appearance of rarer lesions or those in which the criteria are not well laid down were studied in detail retrospectively with histologic comparison and were documented.

Two separate studies one prospective and another prospective and retrospective were designed to study the following specific aspects during the same period.

1. Efficacy of methanol as an alternative to ethanol as a cytologic fixative.

Method:

One hundred and three cases of thyroid aspirates were included. One set was fixed in 95% ethanol, the routine fixative and another set of the same aspirate in commercially available methanol. Nuclear and cytoplasmic preservation of cells and preservation of colloid were scored and statistically analysed.

1. Pitfalls of the cytological diagnosis of autoimmune thyroiditis (AT).

Method:

One hundred aspirates which were either diagnostic or highly suspicious of AT were included in the study. Follow-up was done with available results of histology, serology and biochemical tests. Pitfalls were analysed in detail.

Results

The total number studied was 1797
In 1774 sex distribution was known and this number form the basis of the study.

Place of residence was documented according to the district in 736 patients. Figure 1 depicts the draining districts of the patients with numbers. Forty eight percent (48%) were form the Colombo district, 15% form Gampaha and 9% from the Puttalam District. Eighty six percent of the present study population drained from the endemic zone of Sri Lanka, around half coming from the Colombo district, therefore the results of this survey are a fair indication of the thyroid disease pattern in Sri Lanka. Comparative percentage population in the above districts is 11%, 9% and 3%[15].

Three hundred and ninety eight (398) samples were those obtained by the clinicians and the others were sampled by the author or by the author and a pathology registrar.

The aspirates were categorised under 5 broad categories; benign, malignant, follicular proliferations, atypical and inadequate.

Table 1 shows the broad catergorisation of the overall disease pattern in males and females separately.

Table 2 shows the nature of thyroid enlargement in 1112 cases with the number which were cytologically malignant under each category.

Female to male ratio of thyroid disease was 8:1. The median age was 40 with a range of 12-72 years. The overall benign to malignant ratio was 34:1. Malignacies were commoner in males than in females. Malignancy rate was 2% in multi nodular goitres and 5% in solitary nodules. In diffuse smooth swellings no malignancies were recorded while in diffuse nodular swellings a malignant rate of 3% was recorded.

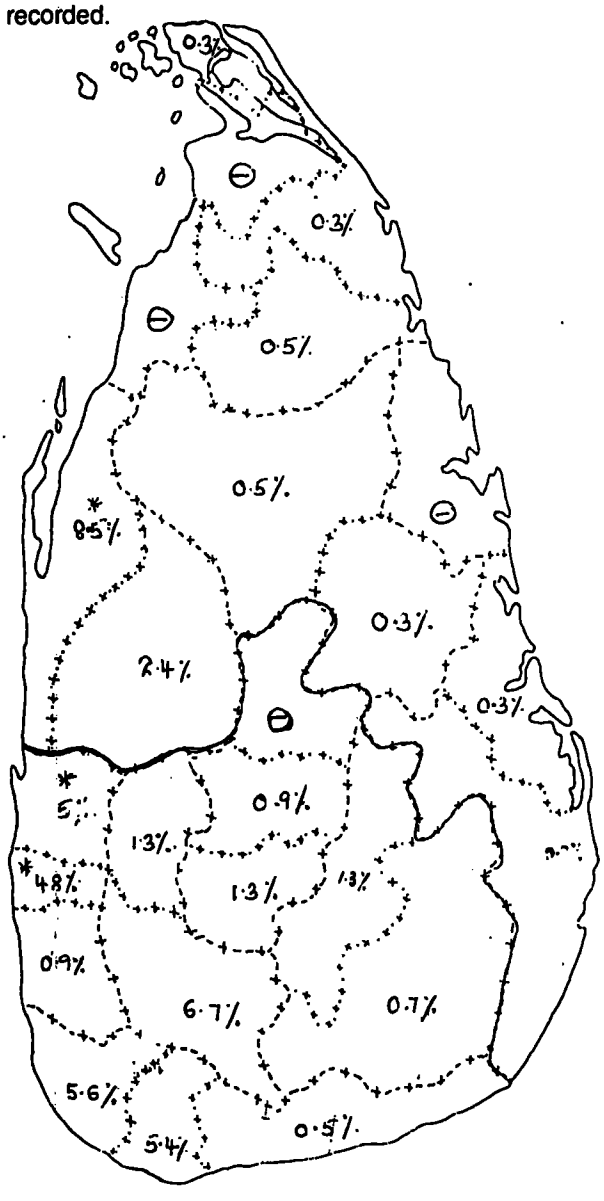

Figure 1. The distribution of the study population according to districts in Sri Lanka (the endemic area is highlighted).

Benign thyroid disease

Table 3 shows further categorisation of benign diseases. Colloid goitres, thyroiditis and hyperactivity occurred in equal proportions in males and females in the population studied. This is contrary to the world literature which states higher prevalence of thyroiditis and hyperactivity among femlaes. There were 2 cases of acute suppurative thyroiditis: one was a 60 year old female who had an abscess in the thyroid and the other was a 14 year old boy who gave a history of immediately preceding respiratory tract infection. There were no cases of other specific infectious thyroiditis which could be detected cytologically. Of the 129 who had thyroiditis 99 were typed as lymphocytic, 25 as Hashimotos and 5 as sub acute. Therefore prevalence of autoimmune thyroiditis among the enlarged thyroids was 6.98%. Hyperactivity was found to be around 2%.

Follicular proliferations

There were 40 follicular proliferations in this series of 1774. Follicular proliferations include follicular adenomas, carcinomas and some adenomatous nodules. It is well known that there are no definite criteria to differentiate various kinds of follicular proliferation by cytology alone.

In the analysis of 5194 fine needle aspiration biopsies the overall accuracy rate for predicting a lesion as benign or malignant was 94%[14]. False positive rate for thyroid malignancies in a local series was 5.3%[14]. Approximately 20-21% of follicular proliferations are estimated to become malignant according to previous data both locally and abroad. Therefore about 8 of the 40 follicular proliferations can be estimated to be malignant in this series. Therefore this number needs to be added to the number which was diagnosed by cytology in the calculation of actual malignancies in this population.

Atypical lesions

There were 49 atypical lesions. Considering the previous data[14], 40% of atypical lesions are expected to be malignant, in which case 20 of this 49 are expected be malignant. The exact figure may be lower than this as the cytologic criteria for the category of atypia have been made clearer at present than earlier.

Malignant thyroid disease

Table 4 shows the subtypes of thyroid malignancies diagnosed with certainty by cytology.

Table 1

Overall disease pattern in males and females

	Number	Benign	Malignant	Follicular proliferations	Atypical lesions	Inadequate
Males	200	158	15 (7.5%)	5	12	7
Females	1574	1449	33 (2.1%)	35	37	23
Total	1774	1607 (90%)	48 (2.7%)	40 (2.3%)	49 (2.8%)	30 (1.7%)

Table 2

Frequency of malignancies according to the nature of thyroid enlargement

	Multi nodular	Solitary nodule	Diffuse smooth	Diffuse nodular
Malignant	14 (2%)	11 (5%)	- (0%)	2 (3%)
Total no: 1112	720	234	98	60

Table 3

Further categorisation of benign thyroid disease

	Benign un-specified	Colloid goitre	Thyroiditis	Hyperactivity	Total
Females	448 (28%)	854 (54%)	113 (7%)	34 (2%)	1449
Males	37 (18%)	101 (51%)	16 (8%)	4 (2%)	158
Total	483 (27.2%)	957 (54%)	129 (7.2%)	38 (2%)	1607

Table 4

Subtypes of malignancy diagnosed by cytology (excluding the projected figures for follicular proliferations and atypical lesions)

	Papillary carcinoma	Medullary carcinoma	Anaplastic carcinoma	Hurthle cell carcinoma	Total
Females	27	1	4	1	33
Males	12	0	3	0	15
Total	39	1	7	1	48

The prevalence of malignancy in males (7.5%) was higher than in females (2%) and the difference was statistically significant. Papillary carcinoma was commoner than anaplastic carcinoma. Two papillary carcinomata also showed anaplastic areas cytologically.

Two other cases of papillary carcinoma occurred in 2 children aged 12 and 13, a girl and a boy respectively. These 2 were confirmed to be an uncommon variant of papillary carcinoma known as diffuse sclerosing variant of papillary carcinoma (DSCP). The 48 malignancies included 39 papillary carcinomas, 7 anaplastic, one medullary and one Hurthle cell carcinoma.

Follicular carcinomas were not diagnosed by cytology with certainty due to lack of definite criteria for cytologic differentiation of follicular proliferations at the moment. However with the estimated figure of 8 malignancies in the follicular proliferations and 20 in the atypical lesions the total malignancies are estimated to be 76. The figure corrected for accuracy of 94% will therefore range form 71-81 (4.0%-4.5%). The prevalence of malignancy in thyroid enlargement as detected by cytology therefore range from 4.0%-4.5% in this population.

The results of the 2 studies conducted revealed the following.

1. **Methanol as an alternative to ethanol as a cytologic fixative**[16]

Commercially available Methanol commonly known as methylated spirit was as efficacious as ethanol as a cytologic fixative. When Ethanol which is expensive (4 times that of methanol) and subject to pilferage is not freely available methanol can be substituted as a cytologic fixative with equally good results. The use of methanol as a cytologic fixative has not been documented in world literature before, although its value as a tissue dehydrant has been reported.

These findings were published in the *Malaysian Journal of Pathology* in 1997: 19(2) (Kumarasinghe, Constantine and Hemamli)

2. **Pitfalls in cytodiagnosis of autoimmune thyroiditis**[17]

Of the 100 cases studied, 78 had diagnostic features while 22% had suggestive features of autoimmune thyroiditis. In the latter category in 83%, a definite diagnosis could be arrived at following an integrated approach of correlating clinical and laboratory findings with the cytologic features. Pitfalls in cytodiagnosis include neoplasms such as Hurthle cell neoplasms and papillary carcinomas occurring in a setting of thyroiditis and non specific lymphoid infiltrates occurring in other thyroid pathologies. Lymphocytic preponderance with lymphocytic invasion of the follicular epithelial cells were found to be a finding favouring autoimmunity against a non specific lymphocytic infiltrate.

These findings were presented at the Annual Scientific Sessions of the Royal College of Pathologists of Australasia in 1997 and are accepted for publication in *Journal of Pathology* (Kumarasinghe and De Silva)

Advances made

Technique:

A study was conducted to compare the classical aspiration and the non-aspiration needle jab technique in 3 sites, including the thyroid. This study jointly done by the Departments of Surgery and Pathology was funded by the University of Colombo. The conclusions were that the non aspiration needle jab technique was excellent for sampling of thyroid as it is easier to perform, yields a less blood stained, adequately cellular sample with less distortion of cells and causes less patient discomfort. Separate syringes were not required for the non aspiration technique recording a financial saving on syringes, as the technique does not require the negative pressure created by the syringe[18].

These findings were published in the *Journal of Pathology* 1995; **27**: 330-332. (Kumarasinghe and Sheriffdeen)

This study was not included in the present series as it was done as prospective study in 1994/93 and included in the previous series reported by the author.

Method of fixation:

1. The popular fixative used is 95% alcohol. Many clinicians in the peripheral hospitals found it difficult to find 95% alcohol. Therefore air drying with

Romonawsky staining was advocated with satisfactory results to many smears received from peripheries as far as Chilaw, Puttalam and Matara.

2. Methanol was found to be as efficacious as ethanol as a cytologic fixative in our study and is used as an excellent cytologic fixative in many laboratories in Sri Lanka today.

Discussion

In Sri Lanka thyroid disease is one major health problem as evident by the heavy load at both medical, surgical and endocrinology clinics. This is also manifested by the large number of thyroid cytologies handled by pathologists in Sri Lanka. In contrast, in most developed countries breast aspirations are the commonest samples received at a cytology laboratory. In Sri Lanka the thyroid load is about 3 times that of the breast and this has been pointed out in author's previous publications.

Thyroid enlargement or goitre is a common manifestation of thyroid disease although it is well known that certain thyroid diseases may present without thyroid enlargement. In developed countries where iodine deficiency is not a major health problem autoimmune thyroiditis, hypothyroidism, hyperthyroidism and thyroid carcinoma are responsible for so called "iodine sufficient goitres"[3]. Iodine deficiency has been incriminated as a major cause of thyroid enlargement in Sri Lanka where goitre is endemic. However various studies done recently have shown that there may be other significant pathologic processes which may contribute to thyroid enlargement[19,22]. The lack of knowledge of such causative factors are known to be responsible for persistence of goitres in spite of successful iodine supplementation.

Therefore this study is timely as the Government of Sri Lanka has introduced legislation to supplement all edible salts with Iodine since 1993. As 86% of the study population represents the giotre zone of Sri Lanka the present situation is a fair indication of the pattern of thyroid enlargement in Sri Lanka.

Serologic tests to screen for autoimmunity, thyroid function tests, radiologic examination are among the various non invasive investigations which could be done to assess thyroid disease pattern. These are neither routinely available nor cheap and not done as a first line investigation for thyroid enlargement. From recent times FNAB has been used as a first line investigation to assess the nature of thyroid enlargement in Sri Lanka and the numbers are increasing daily. Therefore it was felt that morphologic assessment by cytology is a reasonable way of assessing the pattern of thyroid enlargement.

Female thyroid disease is much commoner than in males and this is in keeping with the findings by others. Herath, Gunesekera and others have documented the pattern of thyroid disease on the basis of Iodine uptake studies done on a population who attended their clinic with thyroid disease reported that euthyroid goitres were the commonest both in females and males. In their study population female to male ratio was 8:1, which is very similar to the present finding. Male to female ratio for thyroid disease is comparable to that found in other local and some overseas series.

Prof. Cooray in 1970 reported the findings at 328 thyroidectomies as 127 colloid goitres (39%), 41 exophthalmic goitres, 8 Hashimotos and Riedel's thyroiditis (2.46%), 77 adenomas, and 38 carcinomas (11.6%). In 157 thyroidectomies performed and reported by Wickramasinghe and others the histologic assessment revealed 98 cases of colloid goitres (62%), 44 (28%) cases of adenomas, 7 (5%) carcinomas, 7 (5%) cysts and 1 (0.6%) case of Hashimotos disease. The prevalence of in the present series is 7% which is higher than the Cooray series and much higher than in the series done by Wickramasinghe et al.

Colloid goitres, thyroiditis and hyperactivity occurred in equal proportions in males and females in this section of Sri Lankans. This on the contrary to the world literature which states higher prevalence of thyroiditis and hyperactivity among females. The high prevalence of autoimmunity and hyperactivity in our population needs our attention.

At this point I like to point out the prevalence of autoimmune thyroiditis (AT) in other countries (23-26). In iodine sufficient countries a fair number of goitres are associated with autoimmune thyroiditis where as the majority of goitres in iodine deficient countries (mainly less developed) are believed to be colloid goitres due to iodine deficiency. Table 5

compares the available data from various countries. The first three sets of data, 2 from Sri Lanka including the present study and one Singapore are based on author experience. The present series records the prevalence of autoimmune thyroiditis to be 7.0%. In my general analysis of 5194 fine needle aspirates of all sites, 193 of 3577 (5.3%) thyroid lesions were categorised as AT. The two previous studies document the frequency of thyroiditis as 1.2% and 0.6% on thyroidectomy specimens. A recent study documents the frequency of focal AT in thyroidectomies to be as high as 49%. Another analysis done by the author at the Singapore General Hospital records a frequency of 5.5%.

Table 5

A comparison of the frequency of thyroid malignancies and autoimmune thyroiditis

Location	Malignant	Thyroiditis	Period
Sri Lanka *	4.0-4.5%	7.0%	1995-1997
Sri Lanka *	7.0%	5.3%	1990-1995
Sri Lanka	11.5%	1.2%	1936-1945
Sri Lanka	4.4%	0.6%	1976-1981
Sri Lanka	15.7%	-	1985-1986
Singapore *	2.8%	5.5%	1997-1998
India	5.0%	2.8%	
Ethiopia	-	1.2%	
Spain	4.0%	4.3%	
Japan †	-	*13.1% (F)*	
		6.2% (M)	
USA (North Carolina)	2%	4.2%	
Australia	-	50% **	

* - Series done by the author

† - Frequency assessed by antibody testing

** - A series of 50 patients with bilateral non toxic goitre

The occurrence of thyroiditis in more than expected proportions in a region where goitre is believed to be endemic has been highlighted only after cytologic assessment of thyroid lesions became popular in Sri Lanka[19,22]. This was further highlighted after serologic tests for AT were made available in Sri Lanka. The recent study done on histologic samples of thyroids reiterated that there is a higher occurrence of AT by their observation of occurrence of focal autoimmune thyroiditis in 49% of euthyroid giotres affecting males and females equally[27].

In our population autoimmunity was recorded in equal proportions in males and females. This is another significant and noteworthy observation which has not been stressed previously. Therefore more attention should be given to this situation of higher occurrence of autoimmunity in our population. On the recommendation of the World Health Organisation the government of Sri Lanka passed legislation in 1993 to implement idodisation of all edible salts[28]. If the content of iodine is not monitored properly there can be adverse effect as shown by some studies. An increase of hyperthyroidism and autoimmunity has been reported with excessive iodinisation as indicated by human and animal studies[3,29].

At this point it may be appropriate to state that the finding of high rates of thyroiditis in Sri Lanka in cytologic samples is looked at with suspicion by many clinicians. There have been a few studies done in this regard documenting satisfactory correlation of cytologic findings with other parameters of assessment of thyroiditis[21]. This also prompted me to conduct the study correlating the cytologic, serologic, biochemical and clinical presentation in a group of patients in whom the aspirates were either diagnostic or suspicious of thyroiditis, and to appreciate the pitfalls in the cytologic diagnosis. According to this study it can be concluded that adherence to strict criteria and to an integrated approach in difficult situations will minimize pitfalls with good accuracy rates[17].

Given all these considerations it can be concluded that the occurrence of thyroiditis is higher in the Sri Lankan population with males and females affected in equal proportions.

The prevalence of malignancy in the previous studies range from 4.4%-15.6%. Present finding is that it ranges form 4.0-4.5%. As described under results this figure was arrived at taking into account the actual malignancies diagnosed on cytolgoy, projected figures of malignancy on follicular proliferations and atypical lesions on the accuracy tested in the local setting in previous study[14]. The occurrence of malignancy in a sample of thyroidectomy samples is not a true prevalence of malignancy of enlarged thyroids as thyroidectomies are done on selected patients for a specific indication such as obstruction, cosmetic consideration or

suspicion of malignancy. Therefore the frequency in the previous studies may not be close to the true prevalence. The previous data from my own series indicate a higher rate of malignancy than that of the present series. Several years back FNAB of thyroid was probably performed when the clinical suspicion of malignancy is high. As I have stressed earlier at present the tendency to use FNAB as an initial investigation to assess all types of thyroid enlargement is more, therefore the present selection is considered less biased.

One main objective of this study is to have a better impression of the true situation of the disease pattern for both benign and malignant diseases of the thyroid. The closest one can go to get a morphologic assessment without surgery is no doubt FNAB. An assessment done on FNABs would be less biased although may not be totally representative of the actual prevalence. For a very accurate assessment a population based study by FNABs will be ideal. **Such a study will be launched in near future.** The total cost for material (chemicals and slides) for a FNAB test varies form Rs. 60-180 and depends partly on the number of aspirates, the method of fixation and stains used among others. I have already shown various methods of cost cutting by modification of the technique and method of fixation.

Papillary, anaplastic and follicular carcinoma (8 of the 40 follicular prolifeartions) were commoner than Medullary and Hurthle cell carcinoma in this study. These 3 histologic subtypes are the more frequent malignancies found in endemic goitres.

When the nature of the enlargement was considered, as was believed earlier solitary nodules harbour malignancies more than multi nodular goitres. Males are more likely to have thyroid malignancies than females and this is in keeping with the finding in this study and others done locally and abroad.

There were a few uncommon thyroid malignancies diagnosed within the study population. One was a Hurthle cell carcinoma. This is a lesion which can be mistaken for a severe Hashimotos thyroiditis was in the study conducted to assess the pitfalls of cytologic diagnosis of thyroiditis.

Two cases of diffuse sclerosing variant of a papillary carcinoma occurring in children were diagnosed as papillary carcinoma. The exact subtyping of one case was done on subsequent histopathologic examination. The second case of a papillary carcinoma was suspected to be DSPC on cytology based on the previous observations and confirmed at histology. This variant known to have widespread involvement and possible aggressive behaviour has not been reported in Sri Lanka previously. Also a literature search revealed only a single case report describing the cytological appearance of the entity in an adult. Therefore the cytomorphology of diffuse sclerosing variant of papillary carcinoma in 2 children was described for the first time in the world literature and published in the Journal of the International Academy of Cytology, *Acta Cytologica*[31].

There are no satisfactory cytologic criteria to differentiate follicular carcinoma from an adenoma from a cellular adenomatous nodule. There are many on going studies both locally and overseas to make the distinction on cyto morphology, proliferative markers and DNA ploidy studies. Therefore there is hope for the future. According to Mayo Clinic statistics approximately 50% of follicular proliferation they label as suspicious straight away turn out to be true adenomas or carcinomas[30]. In some centres including at Mayo Clinic the terminology includes categories; benign, suspicious, ad inadequate. There is no atypical category in their terminology. This no doubt will be welcome by our clinicians too. However as a result of this terminology the suspicious category includes a fair number of follicular adenomas and adenomatous nodules which will be reported as suspicoius and not as atypical or follicular lesions as occurs in our set-up. As a result, the number of surgeries are higher in those institutions.

At this point I have failed in my duty if I have do not give an overview of the evolution of this technique with recent advances and modifications made regarding thyroid cytology in Sri Lanka. The technique of FNAB has tremendously helped in the management of thyroid diseases as being highlighted in many recent publications and presentations. The procedure is performed both by pathologists and clinicians in many centres. Many

clinicians in centres outside main teaching Hospitals advocate this technique in their routine practice now. They record cost and time saving with better patient management.

Air drying of smears is popular with clinicians practicing in outstations and methanol is used as routine fixative in many cytology laboratories.

In the past needle aspiration has been performed on a limited scale in a few centres, mostly by clinicians. The technique used was the classical aspiration technique. The method of sampling in the present study was modified as the non aspiration technique except under exceptional circumstances following a comparative study comparing the most popular aspiration technique with the modified non aspiration technique. I am happy to say that all pathologists trained by me in cytology use this technique for thyroid sampling now.

The advantages as shown in the study done by us were that the technique is easier to perform with a better grip, excellent for vascular lesions such as those of the thyroid, and the aspirates were less blood stained with a satisfactory and comparable cellularity. The patient discomfort was also less. Separate syringes are not necessary for sampling as the technique does not involve aspiration at all, and this records a saving on sterile syringes.

Conclusions

1. Thyroid samples comprise a large proportion of specimens received in laboratories indicating the heavy burden of thyroid diseases in Sri Lanka.

2. Cytologic assessment provides a quick, cost effective way of diagnosing the nature of thyroid enlargement.

3. Thyroid enlargement is commoner among the older age group (> 40 years).

4. Benign thyroid diseases are commoner than malignant lesions and colloid goitre is the commonest cause of thyroid enlargement.

5. Females are affected more than males with thyroid disease, but malignancies are commoner in males.

6. Prevalence of thyroid malignancies in enlarged thyroids ranges from 4.0-4.5%.

7. A higher prevalence of autoimmunity affecting both males and females equally is recorded. Efforts should be made to establish the exact aetiology. Iodine supplementation of edible salts should be closely monitored.

8. Regular audits should be conducted in centres where cytologies are performed on a routine basis to maintain a high degree of accuracy levels. The knowledge obtained from such audits may be used for community based studies and evaluation.

9. Fine needle aspiration biopsy procedure can be modified appropriately to suit the local setting to reduce the costs and to overcome difficulties in fixation, transportation and actual performance of the technique.

10. Our population records a heavy thyroid disease load. Efforts to study various aspects of thyroid diseases comprehensively to contribute new knowledge to aetiology, pathogenesis and diagnosis of thyroid disease including tumours should be encouraged.

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References

1. Wickramasinghe SYDC, Welgama SP, Buthpitiya AG, Edirisinghe GS. Simple goitre in Sri Lanka. *Sir Lanka Journal of Surgery* 1985; 27-33.
2. Wickramasinghe SYDC. The solitary thyroid nodule. *Sri Lanka Journal of Surgery* 1986; 19-23.
3. Gaitan E, Nelson NC, Poole GV. Endemic goitre and endemic thyroid disorders. *World Journal of Surgery* 1991; **15**(2): 205-15.
4. Mahadevan K, Seneviratne DA, Jayatilake DB. Further studies on the problem of goitre in Ceylon. *British Journal of Nutrition* 1968; 527-34.
5. Katugampola SL. The prevalence of goitre in pregnancy. *Ceylon Medical Journal* 1989; **32**: 85-9.
6. Cooray GH. Some aspects of the pathology of the thyroid. *Ceylon Journal of Surgery* 1970; **1**(1): 33-36.
7. Sinnatamby CS, Atygalle D, Fernando HKT. The solitary thyroid nodule. *Ceylon Medical Journal* 1977; 41-44.
8. Herath KB, Gunasekera RD, Hemawardena DM, Reginald GJ, Weerasekera DA. A study of thyroid disease pattern in Sri Lanka. Proceedings of Kandy Society of Medicine Academic Sessions 1984.
9. Ratnatunga C. Endemic multinodular goitre. *Ceylon Medical Journal* 1995; **40**(1): 3-4.
10. Bibbo M. Comprehensive Cytopathology. 1st ed. Philadelphia, WB Saunders Company 1991.
11. Kumarasinghe MP. An analysis of 5149 fine needle aspiration biopsy samples. *Ceylon Medical Journal* 1996; **41**: 57-60.
12. Orell SR, Sterrett GF, Whitaker DW, Walters MNI. Manual and Atlas of Aspiration Cytology. 2nd ed. New York: Churchill Livingstone 1986.
13. Kini SR. Guides to Clinical Aspiration Biopsy. 2nd ed. New York: Igaku-shoin 1996.
14. Guidelines of the Papanicolaou Society of Cytopathology Task force on Standards of Practice. Diagnostic Cytopathology 1997; **17**(4): 239-47.
15. Annual Health Bulletin of Sri Lanka, Ministry of Health 1994.
16. Kumarasinghe MP, Constantine SR, Hemamali R. Methanol as an alternative to ethanol as a cytologic fixative. *Malaysian Journal of Pathology* 1997; **19**(2).
17. Kumarasinghe MP, De Silva S. Pitfalls in cytologic diagnosis of autoimmune thyroiditis. *Pathology* (In press).
18. Kumarasinghe MP, Sheriffdeen AH. Fine needle sampling without aspiration. *Pathology* 1995; **27**: 330-332.
19. Kumarasinghe MP, Perera ASND. Cytodiagnosis of thyroiditis. Proceedings of the Annual Scientific Sessions of Sri Lanka Medical Association 1994.
20. Rajaratnam HN, Kumarasinghe MP. Autoimmune goitres in Sri Lanka: a study based on fine needle aspiration biopsy of thyroid. Proceedings of Annual Scientific Sessions of Ceylon College of Physicians 1994.
21. Rajaratnam HN, Kumarasinghe MP. Autoimmune goitres in Sri Lanka - a correlation study of thyroid antibody in serum and FNAB. Proceedings of the Annual Scientific Sessions of Sri Lanka Medical Association 1994.
22. Dissanayake A, Fernando MS, Hewage UCL, Siribaddana SH, Kumarasinghe MP, De Silva MVC, Fernando DJS. The frequency of chronic autoimmune thyroiditis among hypothyroid patients. Proceedings of the 111th Anniversary Sessions of SLMA 1998.
23. Konno N, Yuri K, Taguchi H, Muira K. Screening for thyroid disease in an iodine sufficient area with sensitive thyrotrophin asseys, and serum thyroid autoantibody and urine iodide determinations. *Clinical Endocrinology* 1993; **38**(30): 273-81.
24. Mandreker SRS, Nadkarni NS, Pinto RGW, Menezes S. Role of fine needle aspiration cytology as an initial modality in the investigation of thyroid lesions. *Acta Cytologic* 1995; **39**(5): 898-904.
25. Hawkins F, Dieogo B, Bernal K, Fine needle aspiration biopsy in the diagnosis of thyroid cancer and thyroid disease. *Cancer* 1987; **57**: 1206-1209.
26. Silvermann J, West L, Larkin E, Park K, Finley J, Swamson M, Fore W. The role of fine needle aspiration biopsy in the rapid diagnosis and management of thyroid neoplasm. *Cancer* 1986; **57**: 1164-1170.
27. Fernando MS, de Silva MVC, Fernando DJS. Prevalence of focal autoimmune thyroiditis in euthyroid goitres. Proceedings of the 111th Anniversary Sessions of SLMA 1998.
28. Gazette of the Democratic Socialist Republic of Sri Lanka 1993 October; 18-21.
29. Boullin R. Thyroid and antithyroid drugs. In dukes MNG ed. Meylers side effects of drugs 11th ed. New York: Elsvier 1988; 876-888.
30. Goellner J, Johnson D, Proceedings of Workshop on thyroid cytology conducted by the Mayo Clinic, American Society of Cytopathology, Boston, USA, November 1997.
31. Kumarasinghe MP. Cyto-morphologic features of diffuse sclerosing variant of papillary carcinoma of thyroid - a report of 2 cases in children. *Acta Cytologica* 1998; **42**.