Paper

Comparison of Fine Needle Aspiration Cytology (FNAC) and thyroid ultrasonography in the diagnosis of thyroid nodules

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Abstract

Introduction: Occurrence of thyroid nodules is a common clinical problem in Sri Lanka. Clinical assessment, biochemical investigations, ultrasonography, fine needle aspiration cytology (FNAC) and histology are used in the diagnosis.

Objectives: To determine the value of FNAC and ultrasonography (USS) to distinguish neoplastic nodules from non-neoplastic nodules of the thyroid.

Method: A retrospective cross sectional study involving 73 patients from Base Hospital Embilipitiya, during the period 2009 January to 2013 December was carried out.

Results: Study population was female predominant 70(95.9%) with the age ranging from 17-70 (mean 42.7). Sensitivity, specificity, positive predictive value, negative predictive values and accuracy for FNAC were 94.1%, 87.2%, 86.5%, 94.4%, and 90.4% respectively. The corresponding values for ultrasonography were 64.7%, 69.2%, 64.7%, 69.2% and 67.1% respectively.

Conclusion: The findings of this study are in keeping with the other studies in Sri Lanka and the region. In addition, FNAC has a higher validity than USS in detection of thyroid neoplasms.

Key words: Thyroid neoplasm, FNAC, Thyroid ultrasound scan

Introduction

A nodular thyroid gland is a common occurrence, especially among females although chances of these lesions being malignant are rare.(1) In Sri Lanka, thyroid cancer is one of the five leading cancers in females and has a life time risk of 0.357% in both males and females.(2) The gold standard for diagnosis of thyroid nodules is histopathology. However, it is important to arrive at a correct diagnosis

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initially to plan management. The available pre operative investigations for diagnosis include biochemical, cytological and radiological investigations. Of these, FNAC is one of the most accurate and cost-effective methods of evaluating thyroid nodules, which can be further improved by incorporation of genetic and immunohistochemical tests.[3,4] In recent studies sensitivity, specificity and accuracy of FNAC have shown a wide range of values ranging from 65-98% ,72-100 % and 95% respectively.[3,5]

Thyroid FNAC has some limitations in cases of suspicious, inadequate, and indeterminate cytology and it is reported that, even in adequate cellular specimens, an "undetermined" result can occur in 4-15% of all cases.[6] Therefore, a definitive distinction between neoplasms and non-neoplastic lesions can be difficult. In addition, there are false-positives and false-negatives. Therefore, another investigation is used in combination to compensate for these limitations. Ultrasonography (USS) of the thyroid gland is considered as the most sensitive method for the diagnosis of intrathyroid lesions in some research.[7]

The reported features of malignancy in USS include marked hypoechogenecity, presence of micro calcifications, irregular margins, a nodule which is taller than wide and intra-nodular hypervascularity in colour Doppler.[8] The presence of more than one of the above features, and combination of some features, increase the probability that a thyroid nodule represents a malignancy.[8] In addition, it is non invasive, relatively inexpensive and widely available in Sri Lanka. Therefore it is necessary to assess the validity of FNAC and USS in the diagnosis of thyroid diseases in the local setting.

Objectives

To determine the value of FNAC and USS in the diagnosis of thyroid nodules

Methods

This is a retrospective cross sectional study involving patients with thyroid nodules who received treatment from Base Hospital Embilipitiya from January 2009 to December 2013. The data was extracted from the FNAC, USS and histopathology reports of the patients who had undergone surgery during the study period.

Definition of terms

Cytological diagnosis was categorized into 4 groups.

1. A non-neoplastic category - Included colloid nodules, chronic autoimmune thyroiditis (CAT) and adenomatoid nodules.
2. An indeterminate (follicular proliferation) category-Included hyperplastic nodules and follicular neoplasms (follicular adenoma or follicular carcinoma) which could be either neoplastic or non-neoplastic.

3. Neoplastic category -These belonged to the suspicious for malignancy group
4. Suspicious for malignancy category - These were smears in which criteria for malignancy were not fulfilled; when the varying cytological abnormalities associated with papillary carcinoma such as nuclear membrane irregularity, nucleolar abnormality, abnormal nucleus-to-cytoplasmic ratio were present, but did not fulfill all the criteria for a diagnosis of papillary carcinoma.
5. Malignant category - This category included papillary carcinoma including variants (eg: follicular variant), follicular carcinoma, medullary carcinoma and anaplastic carcinoma or any other malignancy.

Histological classification was as follows.

- Neoplastic- Follicular adenoma, follicular carcinoma, papillary carcinoma and variants and Hurthle cell adenoma
- Non neoplastic- Colloid nodule, chronic autoimmune thyroiditis, hyperplastic nodule and adenomatoid nodule.

Follicular tumours of unknown malignant potential (FTUMP) were considered as neoplastic since they have a 5-10% malignant risk.[9]

A true positive (TP) for cytology indicated a neoplastic lesion on cytology which was confirmed by histology; a true positive (TP) for ultrasonography indicated a neoplastic lesion on ultrasonography which was confirmed by histology.

A true negative (TN) for cytology indicated a non-neoplastic lesion on cytology which was confirmed by histology; a true negative (TN) for ultrasonography indicated a non-neoplastic lesion on ultrasonography which was confirmed by histology.

A false positive (FP) has a neoplastic cytology/ ultrasonography with a non-neoplastic histology.

A false negative (FN) has a neoplastic histology with a non neoplastic cytology/ ultrasonography.

Few of the specimens contained papillary microcarcinoma (a focus less than 10 mm in greatest diameter). For the purpose of the current study, micro carcinomas were categorized as a non neoplastic histology if a macroscopic cancer was not present, because the sub centimeter foci could not be targeted by FNAC.

Data Analysis: All data was analysed using a statistical package for the social sciences (SPSS) (version 20.0) using descriptive statistics. Histological diagnosis was taken as the gold standard and the FNAC and USS diagnoses were compared with it.

Results

In the sample of 73, mean age was 42.7 (range 17-70) and the majority 22(30.1%) were in the 31–40 year age group. The majority 70(95.9%) were females with a ratio of 1: 0.04

Histologically, non neoplastic conditions included colloid nodules 17(23.3%), chronic autoimmune thyroiditis 5(6.8%), hyperplastic nodules 15(20.5%), FTUMP 1(1.4%),

The benign neoplasms were follicular adenoma 10 (13.7%) and Hurthle cell adenomas1 (1.4%). The commonest malignancy was papillary carcinoma 12(16.4%) which included the follicular variant 5 (6.8%) and papillary microcarcinoma 3 (4.1%).

The percentage of follicular carcinoma was 4 (5.5%). The majority of the cases were categorized as follicular proliferations 31(42.5%). Seventeen (23.2%) were suspicious for a neoplasm. Non neoplastic category included colloid nodules 22(30.1%) and CAT 3(4.1%). All 3 investigations showed a concordance in the diagnosis in 46 (63%) of cases.

There were 3 cases of papillary microcarcinoma which were not considered in the accuracy calculation.

Table 1. Comparison of FNAC and USS findings with the histological diagnosis.

	HISTOLOGY		
	Positive Neoplastic No (%)	**Negative Non-neoplastic No (%)**	**Total No (%)**
Positive	32 (43.9)	5 (6.8)	37(50.7)
Neoplastic	TP	FP	
FNAC			
Negative	2 (2.7)	34 (46.6)	
Non-neoplastic	FN	TN	36 (49.3)
Total	34	39	73 (100.0)
USS			
Positive	22 (30.1)	12 (16.4)	34(46.5)
Neoplastic	TP	FP	
Negative	12 (16.5)	27 (37)	39(53.5)
Non-neoplastic	FN	TN	
Total	34	39	73 (100.0)

(TP – True positive, TN- True negative, FP –False positive, FN- False negative)

Table 2. Histological diagnosis of false positive and false negative.

	False positives	False negatives
FNAC	Colloid nodule with chronic autoimmune Thyroiditis (1) Colloid nodules (2) Hyperplastic nodules (1) CAT and hyperplastic nodule(1)	Follicular adenoma (2)
USS	Hyperplastic nodules(4) Colloid nodules (5) CAT(1) CAT with hyperplastic nodule (2).	Follicular adenomas(5) Follicular carcinomas(2) Papillary carcinoma(1) Follicular variant of papillary carcinoma(3) Hurthle cell adenoma(1).

(CAT – Chronic autoimmune thyroiditis)

Table 3. Validity of FNAC and USS in diagnosing neoplastic lesions of the thyroid gland

	FNAC (For neoplasm)	USS (For neoplasm)
Sensitivity	94.1%	64.7%
Specificity	87.2%	69.2%
PPV	86.5%	64.7%
NPV	94.4%	69.2%
Accuracy	90.4%	67.1%

(PPV- Positive predictive value, NPV- Negative predictive value)

Comparison of FNAC and USS findings with the histological diagnosis, histological diagnosis of false positive and false negative results and validity of FNAC and USS in diagnosing neoplastic lesions of the thyroid gland are shown in tables 1-3.

Discussion

Our study revealed that in the patients with thyroid nodules, a significant majority were females. This is further substantiated by many authours in their studies.[9, 10] However the increased concern on cosmesis and the

higher health seeking behaviour of females may be additional factors contributing to this. The highest number of patients was in the 30-40 year age group in our study population. Comparison of results for sensitivity and specificity from different studies are shown in tables 4-5.[11,12]

Table 4. Comparison of the current study with other studies.

Study	Our study	Stephenson et al.(5)	Beneragama et al.(13)	Priyani et al.(14)	Basharat et al.(12)
Sensitivity	94.1%	65-98	84.05	77.78	80
Specificity	87.2%	76-100	86.74	83.00	97.7
PPV	86.5%	-	84.05	93.33	80
NPV	94.4%	-	86.74	88.41	97.7
Accuracy	90.4%	69-97	-	90	96

(PPV- Positive predictive value, NPV- Negative predictive value)

There is a wide variation in the global statistics relating to the validity of FNAC as a tool for diagnosing thyroid pathology. The Royal College of Pathologists Australasia (RCPA- Australasia) has allowed a wide range for sensitivity and specificity for FNAC with regard to thyroid neoplasms.[5] In the current study, the sensitivity and specificity for FNAC correlated with local and regional studies.

Table 5. Comparison of our USS statistics with the other studies.

	Current study	Yunus et al.(15)	Ozel et al. (16) nodule>1cm	Ozel et al. (16) nodule=or<1cm	Kim et al. (17)
Sensitivity	64.7%	93.8%	62.5%	83.3%	93.8%
Specificity	69.2%	66%	91.5%	94.9%	66%
PPV	64.7%	56.1%	30.3%	62.5%	56.1%
NPV	69.2%	95.9%	97.7%	98.2%	95.9%
Accuracy	67.1%	74.8%	89.9%	93.8	74.8%

(PPV- Positive predictive value, NPV- Negative predictive value)

Our USS sensitivity is lower than in other studies. However, Ozel et al. has excluded non diagnostic FNAC and patients with non diagnostic histology, while Yunus et al. has included only solid nodules and excluded the nodules with cystic components and toxic nodules[15,16] thus explaining their higher sensitivity. Even though less in number, false positives and negatives are a major concern. Regarding false positive and false negative FNAC the commonest reason is the inability to distinguish follicular proliferations in CAT from neoplastic microfollicular proliferations. In addition, some features of papillary carcinoma can be seen in CAT even in the absence of a neoplasm.[18] To overcome this, RET /PTC mutation detection can be done to detect the papillary carcinomas.[18]

Mentioned below are some other reasons which account for FP and FN in thyroid FNAC.

Hypercellular specimens from follicular or Hürthle cell lesions may have features suggestive of, but not diagnostic for malignancy. Thus, these are diagnosed as "suspicious for malignancy" and histology is necessary for a definitive diagnosis.

Small nodules less than 10 mm and larger nodules more than 40 mm may not have been accurately sampled in unguided FNAC. Inadequate slide preparation, technical issues and interpretation errors can also cause both false positives and negatives.

In Sri Lanka, general pathologists interpret both histology and cytology unlike in other countries where FNAC diagnosis is done by cytopathologists.

The false positives and negatives in USS findings could be due to a considerable overlap of characteristics in benign and malignant lesions on ultrasound.[17] For example, hypoechogenecity is suggestive of malignancy but benign nodules can also be hypoechoic. Neoplastic malignant nodules have irregular margins but in many studies 55% of solid nodules have been shown to have irregular margins.[17, 19]

Mistaking diffusely infiltrative thyroid carcinomas and multifocal carcinomas in a multinodular thyroid for benign disease and failing to recognize microcalcifications in papillary thyroid cancer can result in errors. Potential diagnostic pitfalls on ultrasonagraphy include routinely dismissing small nodules, assuming that multiple nodules are most likely benign, mistaking carcinomas for cystic hyperplastic nodules and Graves' disease, misdiagnosing cystic or calcified nodal metastases for nodules and misinterpreting adjacent nodal metastases for benign thyroid nodules.[17]

Conclusion and recommendations

The findings reveal that the results of our study were in keeping with the other studies of this country and the region. In addition, FNAC has a higher sensitivity and a specificity than the USS in detection of thyroid neoplasms.

Therefore, we recommend the following for further improvement.

1. USS guided FNACs at all times especially for all small (<10mm) and single suspicious lesions in a multinodular goiter.
2. To improve sampling, aspirates should be obtained from multiple sites of the nodule rather than repeatedly from a single site, especially in a large nodule.
3. Clinical assessment, FNAC diagnosis and USS diagnosis should always be considered in combination to improve the quality of the management of thyroid nodules.

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