Scholars Journal of Applied Medical Sciences
Abbreviated Key Title: Sch J App Med Sci
ISSN 2347-954X (Print) | ISSN 2320-6691 (Online)
Journal homepage: https://saspublishers.com

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Cytological Diagnosis of Thyroid Follicular Lesion and Its Correlation with Histological Findings

Dr. Md Hasibur Rahman[1*], Dr. Md. Saiful Islam[2], Dr. Mahmud Asif Rifat[3], Dr. Md. Abdullah Al Mamun[4], Dr. Muhammad Ariful Islam[5]

[1]Registrar, Department of Ear, Nose, and Throat, National Institute of ENT, Dhaka, Bangladesh
[2]Registrar, Department of Ear, Nose, and Throat, Sher-E-Bangla Medical College Hospital, Barisal, Bangladesh
[3]Indoor Medical Officer, Department of Ear, Nose, Throat and Head Neck Surgery, Dhaka Medical College Hospital, Dhaka, Bangladesh
[4]Junior Consultant, Department of Ear, Nose, and Throat, Sreenagar Upazila Health Complex, Munshiganj, Bangladesh
[5]Consultant, Department of Ear, Nose, and Throat, Bangladesh National Parliament Secretariat Medical Center, Dhaka, Bangladesh

DOI: 10.36347/sjams.2023.v11i04.004 | **Received:** 05.02.2023 | **Accepted:** 14.03.2023 | **Published:** 05.04.2023

***Corresponding author:** Dr. Md Hasibur Rahman
Registrar, Department of Ear, Nose, and Throat, National Institute of ENT, Dhaka, Bangladesh

Abstract **Original Research Article**

***Introduction*:** Follicular neoplasms represent a wide clinical spectrum of diseases, with tremendous overlap in clinicopathologic diagnosis, management, and prognosis. Suspicious sonographic features in conjunction with FNAC of thyroid nodules provide the most accurate preoperative diagnosis to guide therapy. Keeping the perception in mind, we summarize our experience with thyroid nodules that were defined as cellular follicular lesions by comparing the clinical, sonographic, and cytological features that were examined histologically to define the most reliable criteria of malignancy. ***Aim of the Study*:** The aim of the study was to find out the cytological diagnosis of thyroid follicular lesions and their correlation with histological findings. ***Methods*:** This cross-sectional observational study was conducted at the department of Otolaryngology, National institute of ENT, Tejgaon, Dhaka following approval of the protocol for the duration of 6 months. A total of 30 patients were included and they were subjected to details history taking, physical examination, and necessary investigations. We analyzed the data using SPSS version 23, and Chi-square test was used to analyze the significance level of P (<0.05). ***Results*:** A total of 30 consecutive patients with a follicular lesion on FNAC (5 men and 25 women) were included in this study. Their mean (SD) age was 46.7 (±13.0) years. Thyroid cancer was diagnosed on histopathology in 8 patients (27%). Papillary cancer was the most common cytologic finding in 6 patients [75%]) and 2 patients (25%) had a diagnosis of follicular cancer. Of the 6 patients with papillary cancer, 2 (33%) had a follicular variant of papillary cancer. The benign histologic diagnoses were follicular adenoma in 6 cases (27%), thyroiditis in 3 cases (13%), and nodular goiter in 13 (60%). The presence of a solitary nodule was not predictive of malignancy (p=0.57). Solid echo structure (p<0.02), presence of microcalcification (p<0.01), and hypoechoic nodules (p<0.01) on ultrasonography were predictive of malignancy. Older age, male sex, solitary nodule, and larger size of the nodule were not predictive of malignant neoplasms (P>0.5). ***Conclusion*:** The study found that a significant number of follicular lesions (27%) were malignant and that the size of the nodule is predictive of malignancy. However, no correlation was found between patient age or gender and the tendency toward malignancy. Additionally, specific cytologic features appear to play an important role in distinguishing malignant from benign nodules.

Keywords: Thyroid, Follicular, Carcinoma, Adenoma, Cytology.

INTRODUCTION

Follicular lesions of the thyroid encompass a wide range of diseases, including benign follicular adenoma, follicular carcinoma, and the follicular variant of papillary carcinoma. These tumors of follicular cell differentiation consist of a micro follicular architecture with follicles lined by cuboidal epithelial cells. Follicular adenomas are the most common benign neoplasm of the thyroid gland, with a ratio of follicular adenoma to follicular carcinoma in surgical specimens of approximately 5 to 1 [1]. Follicular carcinoma, however, has microscopic features that are similar to a follicular adenoma. It can be distinguished from a follicular adenoma by its more cellular appearance,

thick irregular capsule, and frequent areas of necrosis and mitosis. It is also distinguished by capsular invasion, vascular invasion, extrathyroidal tumor extension, lymph node metastases, or systemic metastases [2]. Vascular invasion is considered the most reliable sign of malignancy. Follicular carcinoma is further divided into minimally invasive and invasive variants based on morphologic criteria. Minimally invasive follicular carcinoma is an encapsulated tumor with microscopic penetration of the tumor capsule without vascular invasion [3]. It is considered a less aggressive tumor with a disease- free survival that has been reported to be similar to that of a benign follicular adenoma [4]. Patients with minimally invasive follicular carcinoma tend to be younger than those with invasive follicular carcinoma, and it has been suggested that it may be a precursor to its invasive counterpart [5]. In contrast, invasive follicular carcinoma has been associated with a 10-year disease-specific mortality of 15%–28% as reported by Van Heerden and colleagues [6]. Most patients with a follicular adenoma or carcinoma present with a solitary thyroid nodule, which is either palpable or incidentally discovered on imaging in an otherwise asymptomatic patient. However, large tumors may present with compressive symptoms such as dyspnea, coughing, choking sensation, dysphagia, inability to lie flat, or hoarseness. Follicular carcinoma accounts for 10% of all cases of thyroid malignancy in iodine-sufficient areas and 25%–40% of thyroid malignancies in areas of iodine deficiency [7]. It occurs more often in women and older patients with a female-to-male ratio of 3:1 and a mean age of 60 years at the time of diagnosis [8]. The diagnostic evaluation of a patient who presents with a thyroid nodule consists of an ultrasound examination of the thyroid gland with neck, fine needle aspiration cytology (FNAC), and a screening serum TSH level. FNAC remains the most important diagnostic modality for evaluating patients with a thyroid nodule; however, a major limitation of FNAC is the inability to distinguish a follicular adenoma from a follicular carcinoma. According to the Bethesda system, cytological features of follicular adenoma and carcinoma are characterized by abundant follicular epithelial cells in sheets with crowding and overlapping of cells, micro follicle formation, and scanty or no colloid [9]. The Bethesda system classifies a certain cytologic appearance as a follicular neoplasm or as suspicious for it. The study aims to find out the cytological diagnosis of thyroid follicular lesions and their correlation with histological findings.

METHODS

This cross-sectional observational study was conducted at the department of Otolaryngology, National institute of ENT, Tejgaon, Dhaka following approval of the protocol for the duration of 6 months. All patients who underwent Fine-needle aspiration cytology for thyroid swelling and were diagnosed with a cellular follicular lesion that warranted surgery were approached for inclusion in the study. Ethical issues were ensured properly throughout the study period. Ethical approval was obtained from the Institutional Review Board and written consent was obtained from all participants. A total of 30 patients were included and they were subjected to details history taking, physical examination, and necessary investigations. The researcher conducted all of the interviews and data collection. All data were recorded into a case record form for each patient. We analyzed the data using SPSS version 23, and Chi-square test was used to analyze the significance level of P (<0.05).

Inclusion Criteria

- All patients underwent Fine-needle aspiration cytology for thyroid swelling and were diagnosed with a cellular follicular lesion that warranted surgery.

Exclusion Criteria

- Patients who were diagnosed with papillary carcinoma by cytology.
- Recurrence case of thyroid swelling.
- Patients in whom histological data were missing.
- Patients who will refuse to take part in this stud

RESULTS

Table 1: Age distribution of the patients (n=30)

Years	No of patient	Histopathologic Findings		P value
		Benign nodule	Malignant nodule	
20-25	1 (3.33%)	0	1	
25-30	1 (3.33%)	1	0	
30-35	2 (6.66%)	2	0	
35-40	5 (16.66%)	4	1	
40-45	3 (10%)	2	1	0.13
45-50	10 (33.33%)	7	3	
50-55	5 (16.66%)	3	2	
55-60	3 (10%)	2	1	
Total	**30**	**21**	**9**	
Mean±SD	46.7±13.0yrs			

Among the participants mean age was 46.7 ± 13.0 years. The patient's ages ranged from 20 years to 60 years. The majority of the patients (33.33%) were aged between 45 to 50 years. The current study shows, in patients below 45 years (n=12) 9 were benign and 3 were diagnosed as malignant histologically. Above 45 years (n=18) there were 12 benign and 6 malignant nodules diagnosed histologically. So, in patients older than 45 years, the risk of malignancy increased (p-value is 0.13).

Table 2: Sex distribution of the patients (n=30)

Sex	No of patient	Histopathologic Findings		P value
		Benign nodule	Malignant nodule	
Male	5 (16.66%)	4 (80.0%)	1 (20.0%)	0.15
Female	25 (83.33%)	18 (72.0%)	7 (28.0%)	
Total	**30**	**22**	**8**	

The study shows, females were the common sex group (83.33%) in the cytological diagnosis of the follicular lesion, among them (n=25) benign nodules were more common (72.00%). Also, in male patients (n=5) predominant histological finding was benign (80.00%) where the p-value is 0.15.

Table 3: Symptoms in the study population (n=30)

Symptoms	No. of patient	Percentage
Swelling in front of the neck	30	100%
Discomfort in throat	11	36.67%
Occasional pain	4	13.33%
Dysphagia	2	6.67%
Hoarseness of voice	1	3.33%
Total no. of patient	**30**	

Among all patients (100%) came with the complaint of swelling in front of the neck with occasional pain in the swelling (13.33%). A few patients also presented with complaints of discomfort in the throat (36.66%), dysphagia (6.66%), and hoarseness of voice (3.33%).

Table 4: Duration of symptoms (n=30)

Duration	No. of patient	Percentage
<6 months	4	13.33%
6-12 months	11	36.67%
>12 months	15	50.00%
Total	**30**	**100%**

In this table majority of patients, 15 (50.00%) came with a history of more than 6 months duration. Only 23.33% of patients presented with symptoms less than 6 months whereas no patients with a short duration of history less than 2 months.

Table 5: Clinical signs in the study population (n=30)

Signs	Features	No. of patient	Percentage
	Single	7	23.33%
	Multiple	23	76.67%
Consistency	Firm	10	33.33%
	Hard	16	53.33%
	Cystic	4	13.33%
Mobility	Mobile	27	90.00%
	Fixed	3	10.00%
Palpable lymph node		3	10.00%
Vocal cord palsy		1	3.33%

Among the percipients, 23 (76.67%) came with multiple nodules in the thyroid gland which were diagnosed cytologically as a cellular follicular lesion. On clinical examination, the majority of nodules were hard in consistency (53.33%) and mobile (90%). There were 3 patients (10%) who presented with palpable neck nodes. Vocal cord palsy was found in a single patient (3.33%) preoperatively.

Table 6: Socio-economic status of the study population (n=30)

Socio-economic status	No. of patient	Percentage
Lower class	8	26.67%
Lower middle class	12	40.00%
Middle class	7	23.33%
Upper middle class	3	10.00%
Upper class	0	0
Total	**30**	**100%**

According to this table, the majority of the respondent came from a lower middle-class socio-economic condition which was 12 (40.00%).

Table 7: Results of ultrasound findings among the study population (n=30)

Characteristic Features	No. of patient	Histopathologic Findings			*P value*
		Benign nodule	Malignant nodule		
No of nodule	Solitary	7	5	2	<0.57
	Multinodular	23	17	6	
Nodule size	< 4cm	20	19	1	<0.01
	≥ 4cm	10	3	7	
Echo structure	Solid	16	10	6	<0.02
	Cystic	4	4	0	
	Mixed	10	8	2	
Micro-Calcification	Present	6	1	5	<001
	Absent	24	21	3	
Echogenicity	Hypoechoic	12	7	5	<001
	Hyperechoic	5	4	1	
	Isoechoic	9	8	1	
	Mixed	4	3	1	

Out of 30 patients with cellular follicular lesions in cytology, 20 (66.67%) came with nodule size <4 cm in ultrasound and were predominantly diagnosed as benign neoplasm (95%) in histopathology. Among the study population, 23 (76.66%) patients were sonographic ally diagnosed as multinodular whereas the majority (17, 73.91%) were benign. The majority of the nodules were solid in echotexture (53.33%) where 10 were benign predominantly and were hypoechoic in nature (40%) where 7 were benign predominantly. Only 6 (20%) patients had microcalcification in nodules and the rest (80%) had none in sonography. So, the presence of a solitary nodule was not predictive of malignancy (p-value 0.57). Nodular size more than 4cm (p-value <0.01), solid echo structure (p-value <0.02), presence of microcalcifications (p-value <0.001), and hypoechoic nodules (p-value <0.001) on ultrasonography were predictive for malignancy.

Table 8: Histological diagnosis of the study population (n=30)

FNAC	Histopathology	No. of patient	Percentage
Cellular Follicular Neoplasms (N=30)	**Benign**		
	Nodular goiter	13	43.33%
	Follicular adenoma	6	20.00%
	Thyroiditis	3	10.00%
	Malignant		
	Papillary carcinoma	6	20.00%
	Follicular carcinoma	2	6.67%
Total		**30**	**100%**

This table shows that a total of 30 patients with thyroid follicular lesions in cytology were included in this study. The final histopathological report revealed that among the study population, thyroid cancer was diagnosed in 8 patients (26.67%). Papillary cancer was the most common cytologic finding (6 patients, 75%) and 2 patients (25%) had a diagnosis of follicular cancer. Of the 6 patients with papillary cancer, 2 (33%) had a follicular variant of papillary cancer. The benign (n=22) histologic diagnoses were follicular adenoma in 6 cases (27%), thyroiditis in 3 cases (13%), and nodular goiter in 13 (59%).

Table 9: Histological outcome of the study population (n=30)

FNAC finding with its prediction		Histopathologic Findings	
		Malignant (+)	Benign (-)
Cellular follicular lesion	Suspicious for malignancy (+) [n=6]	3 (a)	3 (b)
	No features of malignancy (-) [n=24]	5 (c)	19 (d)

A total of 30 patients of thyroid follicular lesions (in cytopathology) were included in this study. The final histopathological report depicted those 24 cases had no features of malignancy among them 19 appeared as non- neoplastic (true negative) and 5 cases appear as neoplastic (false negative). Among 6 suspicious lesions, 3 were neoplastic lesion and 3 were non-neoplastic. So true positive value was 3 and the true negative value was 19.

DISCUSSION

Fine-needle aspiration cytology, although very sensitive for the discrimination of malignant and benign nodules, has limited accuracy with follicular lesions. The cytological diagnosis of follicular neoplasm has continued to be a frustrating entity for pathologists, surgeons, and patients. The recommended treatment for follicular neoplasm is surgery, and up to 70% of these patients undergo surgery for benign disease. In this case, besides the increased costs, the patients are prone to increased risk of surgical morbidity. Moreover, in the case of a malignant lesion, the need for a completed thyroidectomy increases the risk of complications and doubles the cost. A total of 30 patients with thyroid follicular lesions were included in this study. The mean age of the subjects was 46.7 ± 13.0 years. The patient's ages ranged from 20 years to 60 years. The majority of the patients (33.33%) were aged between 45 to 50 years. The current study shows, in patients below 45 years (n=12) 9 were benign and 3 were diagnosed as malignant histologically. Above 45 years (n=18) there were 12 benign and 6 malignant nodules diagnosed histologically. So, in patients older than 45 years, the risk of malignancy increased (p-value is 0.13). In the present study, patient age was not associated with a malignant outcome of cytologically follicular lesions. The data in the literature are controversial. Schlinkert *et al.*, [10] noted that younger patients with a suspected follicular neoplasm on FNA cytology had an increased risk of malignancy, with a 0.7-fold decrease in risk for every 10 years of age. By contrast, in a study of specimens identified as follicular or Hurtle cell neoplasm by FNAC, Tyler *et al.*, [11] developed an algorithm based on the finding that patients 50 years or older had an increased incidence of malignancy. The current study shows, that female was the common sex group (83.33%) in the cytological diagnosis of the follicular lesion, among them (n=25) benign nodules were more common (72.00%). Also, in male patients (n=5) predominant histological finding was benign (80.00%) where the p-value is 0.15. The male: female ratio is 1:5. The result is supported by a few studies [12, 13]. Regarding presenting complaints, we found that all patients (100%) came with the complaint of swelling in front of the neck with occasional pain in the swelling (13.33%). A few patients also presented with complaints of discomfort in the throat (36.66%), dysphagia (6.66%), and hoarseness of voice (3.33%). The majority of the patients (50.00%) came with a history of more than 6 months duration. Only 23.33% of patients presented with symptoms less than 6 months whereas no patients with a short duration of history less than 2 months. The facts are well supported by other studies [14, 15]. During clinical assessment out of 30 patients, 23 (76.67%) came with multiple nodules in the thyroid gland that were diagnosed cytologically as cellular follicular lesions. Among them, there were 3 patients (10%) who presented with palpable neck nodes. Vocal cord palsy was found in a single patient (3.33%) preoperatively. The majority of the respondent came from a lower middle-class socio-economic condition which was 12 (40.00%). Another important clinical finding was the consistency of thyroid nodules. Hard nodules were the commonest form of a thyroid nodule. In this series of thyroid nodules constituted 16 (53.33%) hard, 10 (33.33%) firm, and 4 (13.33%) cystic. On final histopathology out of 16 hard nodules 6 were malignant and the rest were benign; out of 10 firm nodules 2 were malignant and 8 were benign; among 4 cystic lesions, none were malignant. So, among malignant lesions 75% were hard and 25% were firm. Islam and colleagues found up to 70% of malignant thyroid nodules were hard [16]. An ultrasound study was conducted in every case. According to the report majority (66.67%) came with nodule size 0.05). In the current study, my findings extend previous reports those noted that older age, male sex, solitary nodule, and larger size of the nodule has no predictive value for malignant neoplasms [17, 18] where certain clinical, ultrasonographic and cytologic criteria can predict malignancy in follicular lesions [19, 20].

Limitation of the Study

A small sample size may not be representative of the larger population and may not allow for the generalization of the findings.

CONCLUSION

The study found that a significant number of follicular lesions (27%) were malignant and that the size of the nodule is predictive of malignancy. However, no correlation was found between patient age or gender and the tendency toward malignancy. Additionally, specific cytologic features appear to play an important role in distinguishing malignant from benign nodules.

RECOMMENDATION

When it comes to thyroid nodules with a diagnosis of follicular lesion on FNAC, it is important to consider multiple factors to assess the risk. Factors such as clinical features and ultrasonographic findings should be taken into account. For low-risk patients, observation may be an option, especially for those who are reluctant to undergo surgery or have significant underlying medical conditions. However, these patients need to understand the small risk of cancer and the need for careful follow-up, including repeated biopsies. With the modalities available today, the main question regarding treatment protocol is whether to choose surgery or observation. We recommend that every follicular lesion should be excised through a hemithyroidectomy to obtain a definitive histological diagnosis. This will ensure that the patient receives the most accurate and appropriate treatment.

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