ISSN (Print): 2663-9491 ISSN (Online): 2789-6897

Original Article

Reliability of Nodule Size and Fine Needle Aspiration Cytology in Diagnosis of Thyroid Malignancy

DOI: dx.doi.org

Masudul Ahmed[1], Mohammad Mainul Hasan Chowdhury[2], Shahanaz Parvin[3]

Received: 01 OCT 2022
Accepted: 10 OCT 2022
Published: 14 NOV 2022

Published by:
Sheikh Sayera Khatun Medical College, Gopalganj, Bangladesh

ABSTRACT

Introduction: Thyroid nodules are one of the commonest thyroid problems in the world. The importance of size of solitary thyroid nodule lies in the significant risk of malignancy and is known to be an important prognostic factor. Fine-needle aspiration cytology (FNAC) is a highly sensitive and specific test for evaluation of thyroid nodule. Though FNAC is a safe, rapid, cost-effective diagnostic tool for evaluation of thyroid nodules, sometimes it cannot differentiate between benign and malignant disease. This study will find out the role of nodule size as a simple predictor associated with thyroid malignancy and will also provide diagnostic significances of FNAC in diagnosing thyroid nodule. ***Methods:*** This observational study carried out in the department of General surgery and Otolaryngology, Combined Military Hospital, Dhaka and Dhaka Medical College Hospital from Nov 2015 to April 2016. 100 patients who underwent thyroidectomy for nodular goiters were included in this study. Nodule size was measured by USG and fine needle aspiration of nodules performed. Histological data of patients were used to estimate the actual nodule size. Predictive role of nodule size and diagnostic significance of FNAC was evaluated by comparison with histopathology. ***Result:*** Total 100 patients were enrolled (M/F= 24/76) with mean age 42 (±11.3) and 39.3 (±11.4) years among benign and malignant cases respectively. Mean nodule size was larger for malignant than benign nodules (2.8 vs 2.2 cm). Risk of malignancy was found significant among larger nodule (≥2 cm) in comparison to smaller nodule (01– 1.9 cm) (32.5% vs 10%, p= 0.004). Out of 100 nodules, 62 (62%) solid, 11 (11%) cystic and 27 (27%) were mixed in nature. Increase in nodule size was associated with lower proportion of papillary carcinoma and higher proportion of follicular or other carcinoma. FNAC was done in all 100 patients. Among them 68 were benign and 12 were cellular follicular lesion. Malignancy was found among 11 patients and the remaining 09 were suspicious for malignancy. Histopathologically 81 patients were diagnosed as benign. Among them 63 nodular goiter, 10 follicular adenoma, and 08 were thyroiditis. The remaining 19 patients were malignant which comprises 15 papillary carcinoma, 03 follicular carcinoma and 01 anaplastic carcinoma. Altogether 80 benign, 11 malignant

1. *Classified Specialist and Commanding Officer, Department of Surgery, Combined Military Hospital, Cox's bazar, Bangladesh*
2. *Classified Specialist, Department of Medicine, Combined Military Hospital, Cox's bazar, Bangladesh*
3. *Classified Specialist, Department of Gynae and Obstetrics, Combined Military Hospital, Cox's bazar, Bangladesh Bangladesh*

and 09 suspicious cases were confirmed by cytologically. After histopathology 05 of 09 suspicious cases and 03 of 80 benign cases were found malignant. FNAC showed 93% accuracy, 84.21% sensitivity, 95.1% specificity with positive predictive value (PPV) 80% and negative predictive value (NPV) 96.3%. ***Conclusion:*** Risk of thyroid malignancy has been found significant among larger nodule (≥2 cm) in comparison to smaller nodule. FNAC is a highly sensitive, specific, and accurate initial diagnostic test for evaluation of thyroid malignancy.

Keywords: *Nodule Size, FNAC, Thyroid Malignancy, Diagnosis.*

(The Insight 2022; 5(1): 44-51)

INTRODUCTION

Prevalence of thyroid disease in Bangladesh is 10 –15% which indicates the whole country is endemic. Thyroid nodules are one of the commonest thyroid problem in world and present in 3 – 4% of adult population in the UK and USA[1]. A nodule of 01 cm diameter is detectable by palpation known as discrete thyroid nodule. A discrete nodule in an otherwise impalpable gland is termed as solitary thyroid nodule. About 70% of discrete thyroid nodules are clinically solitary and could be benign or malignant.[1] The importance of solitary thyroid nodule lies in the significant risk of malignancy with an incidence of 10 - 23.7%.[2] The main problem with the asymptomatic nodule is to exclude malignancy. Tumour size is known to be an important prognostic factor in patients with malignant disease as because it directly influences the staging.[3] Nodule size should be used as a separate criterion for recommending surgical therapy or to determine the extent of thyroidectomy. Patient with differentiated thyroid cancer having size more than 4 cm have a higher risk of recurrence and mortality and total thyroidectomy is recommended.[4] Some authors have reported that increased nodule size confers an increased risk of malignancy.[5] Other authors have not found nodule size to be an independent predictor of malignancy.[6] Because of high variability of nodule size, only nodule size does not appear to be a reliable parameter for diagnosing thyroid malignancy. A cost-effective screening test for the evaluation of thyroid nodules, fine-needle aspiration cytology (FNAC) is highly sensitive and specific. In the diagnosis of thyroid cancer, FNAC has an accuracy approaching up to 98%.[7] FNAC has played a significant role in selecting appropriate surgical candidates. Colloid nodules, thyroiditis, papillary carcinoma, medullary carcinoma, anaplastic carcinoma, and lymphoma are all thyroid disorders that may be detected by FNAC. Numerous studies have found FNAC to be an accurate, safe, rapid, cost-effective and minimally invasive diagnostic tool for management of thyroid nodules.[8,9] Evaluation of accuracy of FNAC is important due to its clinical implications. Without other indications, most patients with benign FNAC do not receive surgical resection of thyroid nodules. Complications due to FNAC are extremely rare but may include persistent pain, hematoma, infection, and recurrent laryngeal nerve palsy.[10] However, FNAC is associated with a 0-7% false positive and 1-11% false negative result.[11] FNAC is also unable to distinguish a benign follicular adenoma and follicular carcinoma. As a result, considerable effort has been given to identify clinical parameters that may be associated with an increased risk of thyroid malignancy to improve patient

selection for surgical therapy. This study will find out the role of nodule size as a simple predictor associated with thyroid malignancy. This study will also provide diagnostic significances of FNAC in diagnosing thyroid nodule. This knowledge will help in outline the future plan for early detection, diagnosis and management of thyroid malignancy.

METHODS

This observational study was conducted under the department of surgical division of Combined Military Hospital (CMH), Dhaka and Dhaka Medical College Hospital from November, 2015 to April, 2016. The study protocol was approved by ethical review committee of CMH, Dhaka. Total 100 hospital admitted patients who subsequently underwent operative treatment for nodular thyroid disease during the study period were enrolled purposively. Nodule size was measured by Ultrasonography. Solitary nodules or dominant nodules in multi nodular goiter greater than 1cm were selected for fine needle aspiration cytology (FNAC) and evaluated by Cytopathologist from Armed Forces Institute of Pathology. After thyroidectomy, histopathological data were used to estimate the actual nodule size and diagnosis. Finally, FNAC findings were compared with diagnosis of histopathology to see the diagnostic accuracy. Informed written consent was taken from each patient. Prior to consent they were explained the objectives of the study. Confidentiality was assured and anonymity was maintained. Descriptive statistics were expressed as frequency table and percentages. Data were analyzed by computer based program SPSS (Statistical Package for Social Science) version 16 for windows. The associations between nodule size, histological result, and the other considered factors were analyzed using nonparametric tests such as chi-square.

RESULTS

Total 100 patients were enrolled (M/F= 24/76) with mean age 42 (±11.3) and 39.3 (±11.4) years among benign and malignant cases respectively. Family history of thyroid disorder was present among 07 benign and 02 malignant patients. Most of the patients (n=80) were in euthyroid state. Mean nodule size was larger for malignant than benign nodules (2.8 vs 2.2 cm). Cervical lymphadenopathy was found among 03 malignant patients. Out of 100 nodules, 62 (62%) solid, 11 (11%) cystic and 27 (27%) were mixed in nature (table-1).

Table- 1. Demographic characteristics and clinical features of patients (n=100)

Features		**Benign (n=81)**	**Malignant (n=19)**
Age, Mean (SD)		42 (±11.13)	39.3 (±11.37)
Sex – M : F (24 : 76)		18 : 63	6 : 13
Family history of thyroid disease		7 (8.6%)	2 (10.5%)
Thyroid function status	**Euthyroid (n=80)**	66 (81.5%)	14 (73.7%)
	Hyperthyroid (n=09)	7(8.5%)	2(10.5%)
	Hypothyroid (n=04)	3(3.7%)	1(5.3%)
Cervical LN		0 (0%)	3 (15.8%)
Mean nodule size (cm)		2.24(±.83)	2.84(±.99)
Nodule character	**Solid**	51(63%)	11(58%)
	Cystic	9(11%)	2(10.5%)

	Mixed	21(26%)	6(31.5%)

Risk of malignancy was found significant among larger nodule (≥2 cm) in comparison to smaller nodule (01– 1.9 cm) (32.5% vs 10%, p= 0.004) (table-2).

Table- 2. Thyroid node size and risk of cancer (n=100)

Nodule size	**Total nodule**	**Benign**	**Malignant**	**P- value**
1.0-1.9 cm	60	54(90.0%)	6(10.0%)	0.004*
≥ 2 cm	40	27(67.5%)	13(32.5%)	
a) 2.0-2.9 cm	23	17(73.9%)	6(26.1%)	
b) 3.0-3.9 cm	11	6(54.5%)	5(45.5%)	
c) ≥ 4 cm	6	4(66.7%	2(33.3%)	

*P value estimated by Chi-square test, *significant*

Increase in nodule size was associated with lower proportion of papillary carcinoma and higher proportion of follicular or other carcinoma (table-3).

Table- 3. Nodule size and the histological subtype of malignancy (n-19)

Nodule size	**Total**	**Type of thyroid carcinoma**		
		Papillary	**Follicular**	**Other/anaplastic**
1.0-1.9 cm	6	6(100.0%)	0	0
2.0-2.9 cm	6	6(100.0%)	0	0
3.0-3.9 cm	5	3(60.0%)	1(20.0%)	1(20.0%)
>4 cm	2	0	2(100%)	0
Total	19	15(78.9%)	3(15.8%)	1(5.3%)

Fine Needle Aspiration Cytology (FNAC) was done in all 100 patients. Among them 68 were benign and 12 were cellular follicular lesion. Malignancy was found among 11 patients and the remaining 09 were suspicious for malignancy (table- 4).

Table- 4. FNAC findings of thyroid nodules (n=100)

Cytology	**Thyroid nodule size (cm)**				**Total N (%)**
	1.0-1.9	**2.0-2.9**	**3.0-3.9**	**≥ 4.0**	
Non malignant	52	10	03	03	68(68%)
Cellular follicular lesion	02	05	03	02	12(12%)
Suspicious for malignancy	02	03	03	01	09(9%)

Malignant	04	05	02	00	11(11%)
Total	60	23	11	06	100

Histopathologically 81 patients were diagnosed as benign. Among them 63 nodular goiter, 10 follicular adenoma, and 08 were thyroiditis. The remaining 19 patients were malignant which comprises 15 papillary carcinoma, 03 follicular carcinoma and 01 anaplastic carcinoma (table- 5).

Table- 5. Histopathological findings of thyroid nodules (n=100)

Histopathological diagnosis		**Thyroid nodule size (cm)**				**Total N (%)**
		1.0-1.9	**2.0-2.9**	**3.0-3.9**	**≥ 4.0**	
Benign N=81	**Nodular goiter**	49	09	02	03	63(77.8%)
	Thyroiditis	03	03	01	01	08(9.9%)
	Follicular adenoma	02	05	03	0	10(12.3%)
Malignant N=19	**Papillary**	06	06	03	00	15(78.9%)
	Follicular	00	00	01	02	03(15.8%)
	Anaplastic	00	00	01	00	01(5.3%)
	Total	60	23	11	06	100

Altogether 80 benign, 11 malignant and 09 suspicious cases were confirmed by cytologically. After histopathology 05 of 09 suspicious cases and 03 of 80 benign cases were found malignant (table-6).

Table- 6. Comparison of FNAC and histopathological findings of thyroid nodules (n=100)

FNAC findings	**Histopathological diagnosis**
Malignant - 11	Malignant- 11
Benign- 80	Malignant- 03
	Benign- 77
Suspicious- 09	Malignant- 05
	Benign- 04

For statistical evaluation the category 'suspicious' is included in malignant group because of the effect on surgical decision. Diagnostic accuracy of FNAC has been done by comparing it with histopathology as gold standard. FNAC showed 93% accuracy, 84.21% sensitivity, 95.1% specificity with positive predictive value (PPV) 80% and negative predictive value (NPV) of 96.3% (table-07).

Table- 7. Accuracy of FNAC in diagnosis of malignancy (n=100)

		Histopathology		
		Positive	Negative	Total
FNAC	Positive	16 (TP)	04 (FP)	20

	Negative	03 (FN)	77 (TN)	80
	Total	19	81	100
Sensitivity	84.21%			
Specificity	95.1%			
Accuracy	93%			
PPV	80%			
NPV	96.3%			

Note: TP- True positive, FP- False positive, TN- True negative, FN- False negative, PPV- positive predictive value, NPV- negative predictive value

DISCUSSION

Thyroid disease is more common in female than male (M:F= 1:3.2) including both benign and malignant nodule. In this study, mean age of thyroid swelling is 42 (± 11.1) and 39.3 (± 11.37) for benign and malignant cases respectively. In these series peak incidence of the disease and male to female ratio is comparable to other study.[12] The exact cause of increased nodule formation more in female is not known. Recent studies suggest that estrogen increases the thyroid binding globulin which binds more T_3 and T_4 and thus decreases serum thyroxin level. Low blood level of thyroxin increases production of TSH which is responsible for the hyperplasia and hypertrophy of the gland thyroid gland among female.[1,13] The likelihood of malignancy increases with cervical lymph node which has been supported by the work of Alexopoulou O, et al and Guido M Sclabas, et al.[3,14] We have also found cervical lymphadenopathy among 03 (15.8%) cases out of 19 malignancy. The identification of reliable malignancy predictors among more prevalent thyroid nodules are of great importance in guiding therapeutic strategy. Increased nodule size confers to an increase risk of malignancy.[1] The mean nodule size in our study was larger for malignant nodules in compare to benign nodules (2.8 vs 2.2 cm). We have found statistically significant (P <0.004) low malignancy rate in small nodules (1.0 to 1.9 cm) in compare to larger one (≥ 2 cm). These results are closer to the study results of McHenry C R et al and Kamran S C et al.[15,16] The proportion of papillary carcinoma decreased (1.0-1.9 cm, 100%; >4cm, 0%) while follicular and other carcinoma increased (1.0-1.9 cm, 0%; ≥4 cm, 66.7%) as nodules enlarged, which correlates with the work of Kamran S C et al.[16] Papillary carcinoma is largely predetermined at its inception and is not influenced by growth or cellular expansion. In contrast, follicular carcinoma is much more likely in larger nodules.[17] FNAC remains the most important investigation for selection of modalities of treatment for patients with nodular thyroid disease whether treated by surgery or can be followed up clinically. FNAC findings of present study (benign- 80, malignant- 11 and suspected malignant- 09 cases) are comparable to previous studies.[12] FNAC has confirmed 77 (96.25%) benign cases out of 80 and 11 (100%) out of 11 patients with malignancy. When co-related with histopathological diagnosis in 100 cases FNAC showed accuracy of 93%, sensitivity of 84.21% and specificity of 95.06%. These values are closely comparable to other studies.[12,14,18] In this study, false negative result of FNAC was in 03% and false positive in 04% cases. Previous study have shown that false negative rate of thyroid FNAC ranges between 2% - 4%.[1,19] False positive results FNAC are rare as observed in a case series by the Mayo clinic (only 01 of 221 cases).

Similar findings has also been observed by P Caraci et al series and others.[12,20] In this series high false positive result was produced because suspicious FNAC result was considered as malignant due to its influence in surgical decision making. As because FNAC is highly sensitive and specific test, it is now considered as first line diagnostic tools for evaluation of thyroid nodules to prevent unnecessary thyroidectomies and detection of earlier-stage thyroid cancer.[21]

Limitations of The Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

Risk of thyroid malignancy has been found significant among larger nodule (≥2 cm) in comparison to smaller nodule. FNAC is a highly sensitive, specific, and accurate initial diagnostic test for evaluation of thyroid malignancy. A benign FNAC diagnosis should be viewed with caution as false negative results do occur and these patients should be followed up clinico-radiologically for any progression that will require repeated FNAC and/or surgery.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. *Krukowski Z H. The thyroid and parathyroid glands. In: William NS, Balstrode CJK, O'Connel, Bailey & Love's Short Parctice of Sugery. 26th Edittion. Arnold, London, 2013: 750*
2. *Watkinson JC, Gaze MN, Wilson JA. Tumours of thyroid and parathyroid gland. In: Stell and Maran's Head Neck Surgery, 4th Edition. Butterworth Heinemann, 2000: 458-484*
3. *Alexopoulou O, Beguin C, Buysschaert M, et al. Predictive factor of thyroid carcinoma in non-toxic multinodular goiter. Acta Clin Belg 2004; 59: 84 – 89*
4. *McCoy KL, Jabbour N, Ogilvie JB, et al. The incidence of cancer and rate of false-negative cytology in thyroid nodules greater than or equal to 4 cm in size. Surgery 2007; 142: 837– 844*
5. *Sippel RS, Elaraj DM, Khanafshar E, et al. Tumor size predicts malignant potential in Hürthle cell neoplasms of the thyroid. World J Surg 2008; 32: 702–707*
6. *Sahin M, Gursoy A, Tutuncu B, et al. Prevalence and prediction of malignancy in cytologically indeterminate thyroid nodules. Clin Endocrinol 2006; 65: 514–518*
7. *Cooper DS, Doherty GM, Haugen BR, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid 2009; 19: 1167–1214*
8. *Porterfield JR, Grant CS, Dean DS, et al. Reliability of benign fine needle aspiration cytology of large thyroid nodules. Surgery 2008; 144: 963-969*
9. *Ogilvie JB, Piatigorsky EJ, Clark OH. Current status of fine needle aspiration for thyroid nodules. Adv Surg 2006; 40: 223–238*
10. *Rosen JE, Stone MD. Contemporary diagnostic approach to the thyroid nodule. J Surg Oncol 2006; 94: 649–661*
11. *AACE/AME Task Force on Thyroid Nodules. American Association of Clinical Endocrinologists and Associazione Medici Endocrinologi medical guidelines for clinical practice for the diagnosis and management of thyroid nodules. Endocr Pract 2006; 12: 63–102*

12. *Caraci P, Aversa S, Mussa A et al. Role of fine-needle aspiration biopsy and frozen section evaluation in the management of thyroid nodules. British Journal of Surgery 2002; 89: 797-801*
13. *Ganong WF. The thyroid gland. In: Ganong WF, Review of Medical Physiology. 23rd edition. MC Graw-Hill, USA. 2010: 301-313*
14. *Scalabas GM, Staerkel GA, Shapiro SE, et al. Fine-needle aspiration of the thyroid and correlation with histopathology in a contemporary series of 240 patients. Am J Surg 2003; 186: 702–710*
15. *McHenry CR, Walfish PG, Rosen IB. Nondiagnostic fine needle aspiration biopsy: a dilemma in management of nodular thyroid disease. Am Surg 1993; 59: 415-419*
16. *Kamran SC, Marqusee E, Kim MI, et al. Thyroid nodule size and prediction of cancer. J Clin Endocrinol Metab 2013; 98: 564-570*
17. *Christopher RM, Eun SH, Rhoderick NM, et al. Is nodule size an independent predictor of thyroid malignancy? J. Surgery 2008; 144: 1062-1069*
18. *Chao CT, Lin JD, Chao HH, et al. Surgical treatment of solitary thyroid nodules via fine needle aspiration biopsy and frozen section analysis. Annals of Surgical Oncology 2007; 14: 712-718*
19. *Godinho-Matos L, Docjan G, Kurtz A. Contribution of fine needle aspiration cytology to diagnosis and management of thyroid disease. J Clin Pathol 1992; 45: 391-395*
20. *Young AE. The thyroid gland. In: Burnand KG, Young AE, The New Aird's Companion in Surgical Studies. 3rd edition. Harcourt Brace & Co Ltd, London 2005: 457-483*
21. *Amrikachi M, Ramzy I, Rubenfeld S, et al. Accuracy of fine needle aspiration of thyroid: a review of 6226 cases and correlation with surgical or clinical outcome. Arch Pathol Lab Med 2011; 125: 484*