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Original Article

Nodule Size and Fine Needle Aspiration Cytology (FNAC): A Suitable Choice in Early Diagnosis of Thyroid Malignancy

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Abstract

Background: Thyroid nodules have been found a very common clinical problem and the size of the nodules including FNAC considered a choice of diagnosis. This study was an attempt to explore the options to be considered suitable in early diagnosis of said malignancy toward improved quality of life.

Objective: This study is designed to explore thyroid examination features, nodule size with type and sub-type of cancer, nodule size and FNAC findings including histopathological diagnosis of thyroid lesions in particular.

Methods: This was a descriptive cross sectional study conducted from November 2015 to April 2016 in Combined Military Hospital Dhaka and Dhaka Medical College Hospital. 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.

Results: Out of 100 evaluated nodules, 19 (19%) were cancerous, demonstrating no graded increase in risk beyond the 2 cm threshold. When malignant, the proportion of papillary carcinoma decreased (nodules, 1.0-1.9 cm, 100%, of cases; 2.0-2.9 cm, 100% ; 3.0-3.9 cm, 80%; ≥ 4cm, 0%) [p< 0.02], while follicular carcinoma increased (1.0-1.9 cm, 0%; 2.0-2.9 cm, 0%; 3.0-3.9 cm, 20%; ≥ 4 cm, 66.7%) [p< 0.02] as nodules enlarged.

Conclusion: FNAC findings have found suitable for early diagnosis and prognosis of different types of thyroid malignancies. However, increasing nodule size, large, hard and fixed nodule, palpable lymph nodes, hoarseness of voice, as clinical parameters may provide clues for a suspected malignancy. A mass awareness program would have been beneficial for the population towards early diagnosis and intervention in improving quality of life.

Keywords: Thyroid malignancy, Nodule size, FNAC

Introduction

Thyroid nodules are one of the commonest endocrine problems in the world. In general, a nodule of 1 cm diameter is detectable by palpation. A discrete swelling in an otherwise impalpable gland is termed isolated or solitary, whereas the preferred term is dominant for a similar swelling in a gland with clinical evidence of generalized abnormality. About 70% of discrete thyroid swellings are clinically isolated and about 30% are dominant[1].Thyroid gland and its enlargement were known since the time of Hippocrates. The thyroid gland was described by Galen in 160-200 AD and more completely by Vesalius in 1543 (the Fabrica). It was named as such by Thomas Wharton in 1946 presumable because of its association with thyroid cartilage (Greek- *thyreoeides*, shield-shaped).[2] The gland was previously referred to as the 'laryngeal gland'. First successful thyroidectomy operation, on record, appears to have been performed in 952 AD by Albucasis (AD 936-1013), the Moorish physician and surgeon of Andalusia 29. Thyroid nodule could be benign or malignant. The importance of solitary thyroid nodule lies in the significant risk of malignancy compared with other thyroid swelling. The incidence of thyroid malignancy within a clinically solitary thyroid nodule varied widely in the literature i.e. from 10- 23.7%.[3] Iodine deficiency is the main cause of goiter development in Bangladesh.[4] In Bangladesh, the highest prevalence rate of goiter is in the district of Rangpur and Jamalpur and the range varies from 21-30%.[5] It is postulated that goitrous thyroid is a precursor lesion to the development of malignant thyroid disease. The world wide incidence of malignancy in goitrous thyroid is about 10%[6]. Detail history and physical examination alone is often not enough practically to make a proper diagnosis. Common employed diagnostic tools regarding final diagnosis and subsequent management are thyroid hormone assay, thyroid scan, ultrasonography (USG) and fine niddle aspiration cytology (FNAC). Serum TSH measurement is the initial step to exclude hyper or hypo functioning nodule. The thyroid scan is helpful in determining whether a solid nodule is functioning (warm or hot) or non functioning (cold). Hot solitary nodules are rarely malignant but there is about 20%

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chance of malignancy in cold nodules[1]. USG can differentiate between solid and cystic lesions but unfortunately there are no sonographic criteria at present that reliably distinguish benign from malignant nodule.[7] But sonographic findings of microcalcifications, hypoechogenicity, absence of a halo, and irregular nodular margins all increase cancer risk.[8] 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, with an accuracy approaching up to 98%.[9-11] However, FNAC is associated with a 0-7% false positive and 1-11% false negative rate.[12] FNAC is also unable to distinguish a benign follicular or Hurthle cell carcinoma, and persistently nondiagnostic results account for up to 20% of FNACs.[13] Tumour size is known to be an important prognostic factor in patients with malignant disease. Patient with differentiated thyroid cancer ≥4 cm in size have a higher risk of recurrence and mortality and, as a result, total thyroidectomy is recommended. The significance of nodule size in initial evaluation and management of patients is unclear. Some authors have reported that increased nodule size confers an increased risk of malignancy.[14-21] Other authors have not found nodule size to be an independent predictor of malignancy.[22-25] FNAC is now well established as first line diagnostic test and confers several advantages including the prevention of unnecessary thyroidectomies and the detection of earlier-stage thyroid cancer.[26-28]

Materials and Methods

This was a descriptive cross sectional study conducted from November 2015 to April 2016 in Combined Military Hospital Dhaka and Dhaka Medical College Hospital. All hospital admitted Patients with nodular goiter cases treated surgically during the study period were selected purposively. Total 100 cases were taken for the study where 67 from Combined Military Hospital Dhaka and 33 from Dhaka Medical College Hospital. Cases having thyroid nodule less than 1 cm and not agreed were excluded. Ethical issues were dealt adequate. Nodule size was measured by Ultrasonography. Solitary nodules or dominant nodules in multi nodular goiter greater than 1 were biopsied. FNAC slides were evaluated by Cytopathologist of Armed Forces Institute of Pathology. After thyroidectomy, histopathological data were used to estimate the actual nodule size and predictive role of FNAC was evaluated in comparison with histopathology. Data were recorded in data collection sheet and analyzed by SPSS (Statistical Package for Social Science) version 16 for windows.

Results

Table 1: Distribution of cases by age and sex (n=100)

Features	Benign (n=81)	Malignant (n=19)	P value
Age	42.0±11.13	39.3±11.37	0.348
Sex - M:F (24:76) Ratio -1:3.2	18:63	6:13	0.390
	1:3.5	1:2.16	

P value reached from Chi-square test, *=significant

Table 1 illustrates that the age of the patients were ranged from 21 to 69 years and mean age was 42 ± 11.3 and 39.3 ± 11.37 years for benign and malignant cases. Sex incidence showed female predominance.

Table 2: Distribution of cases by thyroid examination features (n=100)

Features		Benign (n=81)	Malignant (n=19)	P value
Thyroid function status	Euthyroid	66(81.5%)	14(73.7%)	0.876
	Hyperthyroid	7(8.5%)	2(10.5%)	
	Hypothyroid	3(3.7%)	1(5.3%)	
Neck swelling		81(100%)	19 (100%)	-
Mean nodule size (cm)		2.24(±.83)	2.84(±.99)	*0.007
Nodule character	Solid	51(63%)	11(58%)	0.882
	Cystic	9(11%)	2(10.5%)	
	Mixed	21(26%)	6(31.5%)	

P value reached from Chi-square test, *=significant

Table 2 showed that majority of the patients were in euthyroid state. Mean nodule size was larger for malignant versus benign nodules (2.8 ± .99 cm vs 2.24 ± .83 cm). Clinically 03 (3%) patients had cervical lymphadenopathy. Out of 100 nodules 62 (62%) were solid, 11 (11%) cystic and 27 (27%) mixed in nature.

Table 3: Distribution of cases by size of nodule and type of cancer (n=100)

Nodule size	Total nodule	Benign type	Malignant type	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%)	
	(n=40)			
2.0-2.9 cm	23	17 (73.9%)	6 (26.1%)	0.528^{ns}
3.0-3.9 cm	11	6 (54.5%)	5 (45.5%)	
≥ 4 cm	6	4 (66.7%	2 (33.3%)	

P value reached from Chi-square test, *=significant, ns=Not significant.

Table 3 illustrated that Thyroid nodule 1.0-1.9 cm in diameter

provides base line cancer risk (10%). The overall prevalence of cancer in nodules 2.0 to 2.9 cm was 26.0%, in nodules 3.0 to 3.9 cm was 45.5% and in nodules ≥ 4 cm was 33.3%.

Table 4: Distribution of cases by nodule size and thyroid cancer subtype (n-19)

Nodule size	Total	Type of thyroid carcinoma			P value
		Papillary	*Follicular*	*Other/ anaplastic*	
1.0-1.9 cm	6	6(100.0%)	0	0	0.02*
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%)	

P value reached from Chi-square test, *=significant

Table 4 showed that increased nodule size was associated with a lower proportion of papillary carcinoma (p< 0.02). In contrast, the proportion of follicular or other carcinoma increased as diameter increased.

Table 5: Distribution of cases by nodule size and FNAC (n=100)

FNAC findings	Thyroid nodule size, cm				Total no (%)
	1.0-1.9	2.0-2.9	3.0-3.9	≥ 4.0	
Non malignant/ Benign	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

Table 5 showed that 68 (68%) were found non malignant/benign, 12 (12%) cellular follicular lesion, 11 (11%) malignant and 09 (9%) suspicious.

Table 6: Distribution of cases by nodule size and histopathological diagnosis (n=100)

Histopathological diagnosis		Thyroid nodule size, cm				Total N=100 (%)
		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

Table 6 showed that 81 (81%) patients were benign. Among them 63 (77.8%) had nodular goiter, 10 (12.3%)) follicular adenoma, and 08 (9.9%)) thyroiditis. The remaining 19 (19%) were diagnosed as malignant. About 15 (78.9%) patient had papillary carcinoma, 3 (15.8%) follicular carcinoma and 1 (5.3%) anaplastic carcinoma.

Discussion

This analysis of 100 cases with clinically relevant thyroid nodules provides the assessment of thyroid nodule size and FNAC findings for malignancy. This study also reflects thyroid examination features, nodule size with type and sub-type of cancer, nodule size and FNAC findings including histopathological diagnosis of thyroid lesions.

The age incidence of thyroid swelling ranges from 21 to 69 years and mean age 42 ± 11.13 and 39.3 ± 11.37 for benign and malignant cases respectively. Male to female ratio is approximately 1:3.2. Thyroid disease is more common in female than male including both benign nodule and malignancy. In these series peak incidence of the disease and male to female ratio is comparable to other studies.[29,30,31]

The study cases presented with neck swelling. Among 19 malignancy 03 (15.8%) have cervical lymphadenopathy (p<.005). The mean nodule size was larger for malignant versus benign nodules (2.8±.99 cm vs 2.24±83 cm) (p<.007). The likelihood of malignancy increases with larger nodule and presence of cervical lymph node. This statement supports the work of Guido M Sclabas, et al and Alexopoulou O, et al.[14,18]

However thyroid nodules 1.0 to 1.9 cm in diameter provided baseline cancer risk (10.0% risk of cancer). The overall prevalence of cancer in nodules 2.0 to 2.9 cm was 26%; in nodules 3.0 to 3.9 cm, 45.5%; and in nodules ≥ 4.0 cm, 33.3%. The primary influence of this association was the low malignancy rate in nodules 1.0 to 1.9 cm. This was statistically significant (*P*<.004). When comparing nodules 2.0 to 2.9 cm, 3.0 to 3.9 cm, or ≥4.0 cm, no difference in malignancy rate was demonstrated (*P* < .528). This suggests a possible threshold effect. These results are closer to the results of McHenry C R et al and Kamran S C et al where they were unable to demonstrate a significant relationship between increasing nodule size with risk of thyroid malignancy.[32]

In this study nodule size was compared with the type and distribution of thyroid malignancy, discordance was detected. Increasing nodule size was associated with a lower proportion of papillary carcinoma in contrast with the proportion of follicular or other carcinomas, increased linearly as diameter increased (*P*< .02). The proportion of papillary carcinoma decreased (nodules, 1.0-1.9 cm, 100%, of cases; 2.0-2.9 cm, 100%; 3.0-3.9 cm, 80%; > 4cm, 0%,) while follicular carcinoma increased (1.0-1.9 cm, 0%; 2.0-2.9 cm, 0%; 3.0-3.9 cm, 33.3%; ≥ 4 cm, 66.7%) as nodules enlarged, which correlates well with the work of Kamran S C et al and McHenry C R et al.[32,33]

Results of fine needle aspiration cytology were negative for malignancy in 80 (80%) cases, positive for malignancy in 11 (11%) cases and in 09 (09%) cases were suspicious, which are comparable to the works of others [29,30,31].
In this series histological diagnosis was available in all the cases. Total 81 (81%) patients were benign. Among them 63 (77.8%) were histologically proved as nodular goitre, 10 (12.3%) follicular adenoma, 08 (9.9%) thyroiditis and remaining 19 (19%) were malignant. This result is close to the observation of M.K Islam et al and Kabir A D M [29,30].

Conclusion

The identification of options to be considered suitable in early diagnosis of thyroid malignancies are of great importance in guiding therapeutic strategy, especially because thyroid nodules are becoming more and more prevalent. FNAC findings have found suitable for early diagnosis and prognosis of different types of thyroid malignancies yet increasing nodule size, large, hard and fixed nodule, palpable lymph nodes, hoarseness of voice, as clinical parameters may provide clues for a suspected malignancy as well. A mass awareness program among high risk population about the consequence of thyroid malignancy may have been considered to enhance their knowledge about this cancer and its prognosis. Measures can be taken towards its early detection and intervention in order to improve the quality of life in deed.

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