

Proportion of Thyroid Malignancy in Simple Multi-nodular Goiter: A Prospective Observational Study in Rajshahi Medical College Hospital

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Abstract

Background: Thyroid swelling is a common clinical problem throughout the world. Most of the swellings are benign but some are malignant. Epidemiologically ascertained risk factors for thyroid carcinoma are ionizing radiation, presence of thyroid adenoma and multi-nodular goiter.

Objectives: To determine the proportion and type of thyroid carcinoma in simple multi-nodular goiter after surgical resection on histopathological basis.

Materials and methods: This prospective observational study was carried out in the Department of Surgery and Otolaryngology and Head neck surgery of Rajshahi Medical College Hospital from January 2015 to December 2016. The study population consisted of 200 patients who were diagnosed as a simple multi-nodular goiter. Among them 60 samples were from surgery and 140 samples from Head neck and otolaryngology wards. All the patients were admitted through OPD with routine plus investigations specific to thyroid including thyroid profile, ultrasonography of neck, FNAC of dominant nodule before being subjected to surgery.

Results: Among 200 cases which were included in this study 22 (11%) containing foci of malignancy. Incidence of malignancy commonly occurs in females, papillary carcinoma is being the commonest entity.

Conclusion: The incidence of malignancy in simple multi-nodular goiter in this study was 11% that is quite high. So, people should be educated and encouraged to attend the thyroid clinics for proper evaluation and early diagnosis of malignancy.

Keywords: Multi-nodular goiter, Solitary thyroid nodule, Thyroid malignancy, FNAC.

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Introduction

Thyroid swelling is a common clinical problem throughout the world. This is also an important clinical problem in Bangladesh. Most of the swelling are benign but some are malignant. Epidemiologically ascertained risk factors for thyroid carcinoma are ionizing radiation, presence of thyroid adenoma and multi-nodular goiter. In published reports, the incidence of carcinoma varies from 7% to 17% (Simple multi-nodular goiter 10.58% Toxic Multi-nodular goiter (9%).¹

The annual incidence of thyroid cancers is about 3.7 cases per 1000000 populations and the female male ratio is 3:1.¹ The overall mortality rate in patient suffering from carcinoma in multi-nodular goiter should be low because most are in a low risk category; however older patients have more aggressive disease with a worse prognosis. The most common presenting symptom is a thyroid swelling and a 5 year history is not uncommon in differentiated growth. Enlarge cervical lymph nodes, recurrent laryngeal nerve paralysis is very suggestive of locally advanced diseases.

Thyroid nodule is probably one of the commonest endocrine problems in the world. The frequency of thyroid nodule increases throughout life.¹ In a study lifetime risk of developing a thyroid nodule was estimated 5 to 10%.² A nodule may be solitary thyroid nodule or dominant nodule of multi-nodular goiter which is due to focal anatomical

lesions, such as thyroid cyst, adenoma or malignancy.³ Multi-nodular goiter is a clinicopathological entity characterized by an increased volume of the thyroid gland with formation of nodules. Multi-nodular goiter is common in endemic regions with low iodine in the soil, such as countries in the mountainous areas in South East Asia, Latin America and Central Africa. The world Health Organization reported a worldwide iodine deficiency rate 9.8-56.9% and total goitre prevalence of 4.7-37.3% by year 2003.⁴

In the United States, clinically apparent nodules are present in 4-7% of about population and more common in women than men.⁵ The incidence of malignancy varies from country to country and with the changing methods of evaluation. A long standing unresolved issue is whether multi-nodular goiter is significantly associated with malignancy. Multi-nodular goiter has been traditionally thought to be at a low risk for malignancy as compared to solitary thyroid nodule.⁶⁻⁹ However, various studies have reported a 7 to 17% incidence of malignancy in multi-nodular goiter.^{8,10,11}

There has been controversy in the literature about the risk of thyroid cancer in patients with multi-nodular goiter. Initially, studies suggested that the patients with simple multi-nodular goiter, toxic nodular goiter carried a lower risk of thyroid cancer than patients with only a single thyroid nodule. However, recent studies suggested a higher risk cancer in these patients (10-20%).¹²

The objective of this study was to determine the incidence and the types of various malignancies in simple multi-nodular goiter by FNAC findings and by doing clinical examination, the histopathological examination of thyroidectomy specimens.

Materials and Methods

This prospective observational study was carried out in department of Surgery and Otolaryngology and Head neck surgery of Rajshahi Medical College Hospital from January 2015 to December 2016. The study population consisted of 200 patients who were diagnosed as a simple multi-nodular goiter. Patients with simple multi-nodular thyroid diseases above 13 years age of both sexes, euthyroid clinically and bio-chemically were included in the study. The size of the sample was 200 of which 60 from surgery and 140 were from Head Neck and Otolaryngology wards. For collection of sample, we used random sampling technique.

All the patients were admitted through OPD with routine plus investigations specific to thyroid including thyroid profile, USG of neck, FNAC of dominant nodule before being subjected to surgery. All FNAC examinations were carried out through Rajshahi Medical College and Hospital. All the patients underwent different thyroid operations ranging from hemi thyroidectomy, Subtotal thyroidectomy and total thyroidectomy. Histopathology of operated specimen was the main criteria for diagnosis of malignancy.

Results

Based on findings the results are presented in the form of tables as follows:

Table 1: Age and Sex distribution of simple multi-nodular goiter (n=200)

Age (Years)	Male	Female	Total (%)
11-20	0	8	04
21-30	4	32	18
31-40	24	76	50
41-50	12	16	14
51-60	16	4	10
61-70	0	8	04
Total	56	144	100

Table 1 shows that, highest frequency (50%) was in 31-40 years and highest frequency was in female in same group.

Table 2: Clinical presentation of patients in multi-nodular goiter. (n=200)

Symptoms	Number of patients	Percentage (%)
Swelling anterolateral aspect of the neck	200	100
Pressure Symptom (Dyspnoea)	12	6
Voice Change	0	0
Multinodular goitre with cervical lymphadenopathy	12	6

Table 2 shows that all patients (100%) present with swelling in anterolateral aspect of the neck. Dyspnoea was 6% and palpable cervical lymph nodes were 6%. No other reasons were detected for cervical lymphadenopathy.

Table-3: Durations of simple multi-nodular goiter and number of malignancy: Thyroid nodules. (n=200)

Duration of goiter	Number of Patients	Percentage (%)	Number of Malignancy
<2 yr	24	12	0
2-4 yr	88	44	8
5-7 yr	28	14	4
8-10 yr	20	10	4
11-13 yr	32	16	4
>13 yr	8	04	2

Table 3 shows that the highest frequency of thyroid nodules (44%) was in duration 2-4 years.

Table 4: Preoperative FNAC examination of study group in Simple multi-nodular goiter (n=200)

FNAC Findings	Number of Patients	Percentage (%)
Nodular goitre	128	64%
Adenomatous goitre	30	15%
Colloid goitre	10	5%
Papillary carcinoma	14	7%
Follicular neoplasms	8	4%
Thyroiditis	10	5%
Total	200	100%

Table 4 shows the result of FNAC examination done in all 200 cases. Majority of cases were found to be benign. Only 14 cases (7%) were detected as malignant (papillary carcinoma). cases were detected as follicular neoplasia among them 4 cases later confirmed as malignant on histopathology.

Table 5: Histopathological findings of the study group in simple multi-nodular goiter (n=200)

H/P findings	Number of patients	Percentage (%)
Multinodular goitre	162	81%
Adenomatous goitre	12	06%
Medullary carcinoma	02	01%
Papillary carcinoma	14	07%
Follicular carcinoma	04	02%
Follicular adenoma	04	02%
Anaplastic carcinoma	02	01%
Total	200	100%

All patients underwent histopathology, majority of which were benign thyroid lesions. 22 cases were found as malignant.

Table 6: Tissue histopathology with age and sex presentations in simple multi-nodular goiter as malignancy. (n=22)

Type of Malignancy	Number of patients	Age (Years)	Male	Female
Papillary carcinoma	14 (63.64%)	30-50	2	12
Follicular carcinoma	4 (18.18%)	40-60	2	2
Anaplastic carcinoma	2 (09.09%)	70	2	0
Medullary carcinoma	2 (09.09%)	40-60	2	0
Total	22/200(11%)	-	8(36.36%)	14 (63.63%)

Table-6 shows that, carcinoma are more frequent in female

as others benign thyroid diseases.

Table-7: Incidence of thyroid malignancy in simple multi-nodular goiter. (n=11)

Malignant	Non Malignant	Total	Proportion of Malignancy (%)
22	178	200	11 (%)
z=2.03, p0.05			

Table 7 shows that the proportion of malignancy in simple multi-nodular goiter was 11%. Out of 200 patients with simple multi-nodular goiter 22 were malignant. All patients clinically and biochemically were in euthyroid state. There was statistically significant difference between the finding of this study and the findings from reported study (z=2.03, P<0.05 with 95% CI)

Table 8: Histological pattern of malignancy in simple multi-nodular goiter. (n=22)

Histopathological patterns	Number of Malignant patient	Primary carcinoma percentage (%)	Secondary Metastasis
Papillary carcinoma	14	63.64	10
Follicular carcinoma	4	27.27	4
Anaplastic carcinoma	2	9.09	0
Medullary carcinoma	2	9.09	0

Table 8 shows highest proportion of primary and secondary metastasis of thyroid carcinoma in multi-nodular goiter and highest frequency was papillary carcinoma in simple multi-nodular goiter. Among 22 malignant patients 14(63.63%) were diagnosed in metastasis stage.

Discussion

Multi-nodular goiter is defined as the palpable multiple distinct nodules in the enlarge thyroid gland. The etiopathogenesis of multi-nodular goiter is not clear. The malignancy predominantly occurred in females, so hormonal influence may be considered to be the etiological factor for malignant changes in goiter. Majority of patients come from iodine deficient areas. Some patients presented with prolong history of goiter. These are the etiological factors known to induce malignancy.¹³ The presence of thyroid stimulating immunoglobulins has been suggested as the various causes.

Multi-nodular goiter is the commonest endocrine problem worldwide. The incidence of malignancy in the nodule varies from country to country. Appropriate surgical interventions can reduce the higher rates morbidity and mortality.

Thyroid nodules have been reported in 4% to 7% of the population on neck palpation and in 30%-50% of the population by ultrasonography.^{14,15,16} It has been observed that 50.5% of the solitary nodules which are felt on palpation are actually a part of the multi-nodular goiter.¹⁴ The appreciation of the nodules may be hampered by the presence of a short and thick neck.¹⁴ Even the experienced physicians may fail to detect the nodules when they are less than 1 cm in diameter.¹⁴

In multi-nodular goiter, surgery is offered for cosmetics, the compressive symptoms, toxicity and for the suspicion of malignancy. A long standing unresolved issue is whether multi-nodular goiter is significantly associated with malignancy or not. Multi-nodular goiter has been traditionally thought to be a low risk for malignancy as compared to a solitary nodule thyroid. However, various studies have shown that the risk is quite high in multi-nodular goiter also. A study which was conducted by Benzartiet al in Tunis found a 9.5% incidence of malignancy in multi-nodular goiter. Prades et al from France, however, reported quite a high incidence i.e. 12.2%.

In our study, the incidence of malignancy in simple multi-nodular goiter is 11%, which is comparable to local and international studies. Out of 200 cases 144 were females and 56 were males with M:F ratio was 1:2.6. There is predilection of multi-nodular goiter in females. Majority of patients with multi-nodular goiter in our study were in the range between 30-50 years, with maximum incidence in 3rd and 4th decade. The maximum incidence of malignancy in this study was analyzed in age range of 30-50 years which is comparable to literature.

In this study, malignancy predominantly occurred in females, so hormonal influence may be considered to be the etiological factor for malignant changes in goiter. Majority of patient come from iodine deficient areas.

A thyroid nodule should be viewed with suspicion if it is seen as a dominant nodule in the multi-nodular goiter, which is hard, irregular, fixed and rapidly increasing, seen along with cervical lymphadenopathy, recurrent laryngeal nerve palsy, extremes of age and the male sex. High frequency, real-time ultrasonography and fine-needle aspiration cytology (FNAC) are the indispensable tools which are used in the pre-operative evaluation of multi-nodular goiter for malignant foci. The important sonographic findings are suggestive of malignancy in the thyroid nodules, micro-calcifications, irregular margins of the nodules and a complex echogenecity. It has been postulated that the thyroid cancers would have manifested with more overt symptoms and signs of local invasion or metastasis by the time they had reached significant size.¹⁴ FNAC is the fast and inexpensive investigation which can be done to obtain cellular samples.¹⁴ A series of reviews have reaffirmed its importance in the assessment of the thyroid nodules. Ionizing radiation, iodine deficiency and other factors have been attributed for the increase in thyroid carcinoma, but these findings are inconsistent.¹⁷

However, a negative FNAC report does not exclude with certainty the possibility of a carcinoma, especially in multi-nodular goiter, where the error in sampling the right area is greater.¹⁸ FNAC of a suspicious nodule under ultrasonography guidances of great help¹⁹. Thyroid carcinomas account for 1% of all the malignancies and they are the most common endocrine tumors. The incidence of thyroid carcinoma varies considerably in different regions of the world. Globally, the incidence of thyroid carcinoma has increased by up to five-fold during the past 60 years.²⁰ Among malignancies, papillary carcinoma was found as the commonest malignancy (63.64%) followed by follicular carcinoma (18.18%) anaplastic carcinoma (9.09%) and medullary carcinoma (9.09%). This finding is consistent with the observation made in most of the literatures and international studies.²¹

Conclusion

Multi-nodular goiter is one of the common problems of the thyroid disease in all ages. Female is more commonly affected than male. The highest numbers were found in 30-40 years age group. The frequency of malignancy in this study was 11%. Among the malignancies papillary carcinoma was the most common (63.64%) followed by follicular carcinoma, anaplastic carcinoma and medullary carcinoma. Clinical importance of thyroid nodule is exclusion of malignancy. The risk of malignancy in simple multi-nodular goiter should not be underestimated as significant numbers of patients with thyroid malignancies present with simple multi-nodular goiter.

Limitations

Short duration of time for study as well as small samples were the major limitations. Thus it may not reflect the actual scenario for representing population in concern to the situation of malignancy in simple multi-nodular goiter.

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