



Original Article

Risk of Thyroid Malignancy in Non-Toxic Multi-nodular Goitre: Experience in Rajshahi

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Abstract

Non-Toxic multi-nodular goitre is one of the common presentations of various thyroid diseases. A sizable portion of multi-nodular goitre turns into malignancy over time. This cross-sectional study was conducted in RMCH and different clinics of Rajshahi City to determine the incidence and types of various thyroid malignancies in non-toxic multi-nodular goitres. Among the total cases, 43% of the patients were in the age group of 31-40 years and majority (81%) of whom were female. 52% of the patients had a history of thyroid swelling for 1-5 years and 55% of the patients had goitre size ≤ 15 cm². Sub-total thyroidectomy was the commonest operation performed and all the resected specimens were sent for histopathological examinations, which demonstrates that 13% of the multi-nodular goitres had malignancies with papillary and follicular carcinoma ratio 5:1. This study did not reveal any significant association of malignancies with age and sex and goitre size also not influence the presence of malignancy. However, it was observed that the mean duration of thyroid swelling in patients who developed malignancy was significantly higher (8.6 years) than that of patients who did not experience any malignant change (5.7 years).

Key words : Thyroid malignancy, non-toxic, multi-nodular goitre.

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Introduction

Thyroid malignancy is a relatively rare tumour, but it represent the most frequent form of endocrine malignancy. It represent 01% of human neoplasias and its annual incidence is estimated worldwide from 0.5 to 10:100.000 in the world population.¹ Thyroid nodule have been reported to be found in 4% to 7% of the population and in 20% to 50% of population by ultrasonography.^{2,3,4} Multi-nodular goitre (MNG) had been traditionally thought to be at low risk malignancy as compared to a solitary nodule however various studies have reported a 7 to 17% incidence of malignancy in

MNG.^{5,6,7} The most common variety of malignancy which has been documented in the literature is papillary carcinoma, followed by follicular carcinoma and follicular variety of papillary carcinoma.^{8,9,10} Cases having high risk of malignancy can usually be indentified on clinical assessment and use of nuclear imaging modality. The exposure to ionizing radiation and the availability of more sensitive diagnostic tests may be possible explanation for a world wide increase in the incidence of thyroid cancer.¹¹

The present study was, therefore, an attempt to find out the incidence and types of various thyroid

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malignancies in multi-nodular goitre by doing histopathology of thyroid specimen. Also comparing demographic variables between patients of MNG with or without malignancies as well as to see whether the duration of swelling had any impact on malignant changes in multi-nodular goitre.

Material and Methods

This cross-sectional study was carried out in General surgery and ENT departments of Rajshahi Medical College Hospital and in the private clinics of Rajshahi City between January 2006 to October 2008. Total 100 patients of clinically non-toxic multi-nodular goitre were enrolled in this study, who underwent thyroid surgery. The inclusion criteria were clinically diagnosed cases of non-toxic multi-nodular goitre of any ages and either sexes. But patients having clinically non-toxic multi-nodular goitre in pregnant and lactating mothers, pre-operatively diagnosed thyroid malignancy, clinically solitary thyroid nodule and not in euthyroid state were excluded.

All the patients were subjected to FNAC to determine the malignancy. Then FNAC non malignant patients underwent different types of thyroidectomy (as indicated) and excised thyroid tissues were sent for histopathological examination to see how many of them harboured malignancies. Data were collected with the help of a structured questionnaire including all the variables of interest. Data were processed and analysed using computer software SPSS (Statistical Package for Social Science).

Result

Table 1: Patients demographics (n=100)

Age groups (years)	Male	Female	n (%)
11-20	1	5	6 (6%)
21-30	2	10	12 (12%)
31-40	7	36	43 (43%)
41-50	6	25	31 (31%)
51-60	2	3	5 (5%)
> 60	1	2	3 (3%)
Total	19	81	100 (100%)

Out of 100 cases, majority of the patients were in the 4th (43%) and 5th (31%) decades of life. The age ranged from 14-76 years. (Mean age \pm SD = 35.50 ± 10.12). 81% of the patients were female and remaining 19% were male. Female : male = 4.26:1.

Table 2 : Duration of illness (n=100)

Duration	n (%)
≤ 5	52 (52%)
> 5	48 (48%)
Total	100 (100%)

At presentation 52% of the patients had been suffering from MNG for 1-5 years, while remaining 48% for more than 5 years. The lowest and highest duration of illness were 1 and 28 years respectively.

Table 3: Findings of MNG (n=100)

Goitre shape	n (%)
Unilateral nodular	33 (33%)
Bilateral nodular	15 (15%)
Butterfly shaped nodular	52 (52%)
Goitre size	
$\leq 15 \text{ cm}^2$	55 (55%)
$> 15 \text{ cm}^2$	45 (45%)
Goitre consistence	
Firm	59 (59%)
Varigated	29 (29%)
Hard	12 (12%)

Most of the patients had butterfly shaped nodular goitre (52%), 55% patients had goitre sizes $\leq 15 \text{ cm}^2$ and most of the goitres were found firm in consistence (59%).

Table 4: Histopathological findings (n=100)

HPE Findings	n(%)
Benign multi-nodular goitre	81 (81%)
Papillary carcinoma	10 (10%)
Follicular adenoma	04 (04%)
Follicular carcinoma	02 (02%)
Hurthle cell carcinoma	01 (01%)
Chronic thyroiditis	02 (02%)
Total	100 (100%)

Among the total cases, 13% (papillary carcinoma 10%, follicular 02% and hurthle cell carcinoma 01%) of cases were malignant, while remaining 87% were non-malignant.

Table : 5 Comparison of demographic features between groups (n=100)

Demographic characteristics	Diagnosis		P- Value
	Non-malignant (n=87)	Malignant (n=13)	
Age			0.865
≤ 35	49 (56.3)	7 (53.8)	
> 35	38 (43.7)	6 (46.2)	
Sex			0.647
Male	16 (18.4)	3 (23.0)	
Female	71 (81.6)	10 (77.0)	

Data were analyzed using **Chi-Square (χ^2) Test**. Neither of the age groups and sexes tends to be associated with harbouring malignancy significantly in non-toxic multi-nodular goitre.

Table 6 : Comparison of duration of illness between groups (n=100)

Status of MNG	Duration of illness (years)		P- Value
	Mean	SD	
Non-malignant (n=87)	5.7	4.1	0.024
Malignant (n=13)	8.6	4.2	

Data were analyzed using **Student's t-Test** and data are presented as **mean** and **SD**. Patients who developed malignancy had significantly higher duration of illness than those who did not develop malignancy.

Table 7: Comparison of goitre size between groups (n=100)

Goitre size cm ²	Diagnosis		P- value
	Non-malignant (n=87)	Malignant (n=13)	
≤15	48 (55.2%)	7 (53.8%)	0.691
>15	39 (44.8%)	6 (46.2%)	

Data were analyzed using **Chi-square (χ^2) Test**. Size of the goitre was almost indistinctly distributed between malignant and non-malignant multi-nodular goitre.

Discussion

Multi-nodular goitre (MNG) is defined as the palpation of multiple discrete nodules in the enlarged thyroid gland. Etiology and pathogenesis of MNG is not very clear. A mild dietary deficiency of iodine, slight impairment of hormones synthesis, increased iodide clearance from the kidney and presence of thyroid stimulating immunoglobulins have been suggested as the various causes.¹²

Globally, incidence of thyroid cancer has increased by up to five-fold during the past 60 years.¹³ The annual incidence of thyroid cancer varies considerably in different registries and is increasing in some European countries, USA and Canada.¹⁴ There are several possible reasons for the increase in thyroid cancer, including ionizing radiations, sex hormones, iodine deficiency and other factors but the findings are inconsistent.^{15,16}

Multi-nodular goitre is the commonest indication for thyroidectomy in endemic iodine-deficient regions. Pre-operative evaluation for thyroid cancer by means of FNAC is difficult in multi-nodular goitre owing to the presence of multiple nodules and thyroid cancer is frequently an unexpected post-operative findings.¹⁷ Traditionally, patients with MNG have been considered at lower risk of malignancy than those with solitary nodule. However, the literature review has shown that the incidence of malignant tumors in patients with solitary nodule does not differ much from those with MNG.^{17,18}

In this study 100 patients with MNG were studied. The highest frequency was 43(43%) cases in 31-40 years which is correlated with study of Rahman,¹⁹ Sattar.²⁰ Male and female ratio was 1:4.26 in our study. In a study done by Pdamallu²¹ MNG was found to be higher in female (88%) compared to that of males (12%). Female preponderance is seen in all other studies.

This ratio was shown 1:5 by Rahman,¹⁹ 1:4 by Welkar.²²

MNG is a risk factor for epidemiologically ascertained thyroid malignancy.²³ Epidemiologically studies have demonstrated the incidence of malignancy in patient with MNG was higher than the incidence of general population.²³ Histopathological analysis in this study showed that benign MNG was present in 87 (87%) cases and malignant thyroid lesion in 13 (13%) cases. This is consistent with the figures from various international studies. Benzarti et al in Tunis found a 9.5% incidence of malignancy in MNG²⁴ whereas Alagic et al reported an 8% incidence of malignancy in MNG in his study.²⁵ Prades et al from France however reported quite a high incidence i.e 12.25%.²⁶

There appears to be general agreement in all these studies that papillary carcinoma is the predominant malignancy in MNG. In this study, papillary carcinoma was the most common thyroid malignancy. This is consistent with figure from various national and international studies.²⁷

In this study we did not find any significant association of malignancies with either age groups or sexes. Nor did it find any significant association of malignancy with size of the swelling. Some studies however, reported malignancy to be significantly commoner in female and generally occurred at a significantly older age. However, it was observed that mean duration of thyroid swelling in patients who developed malignancy was significantly higher (8.6 years) than those who did not so (5.7 years). Mathai²⁸ et al found a longer duration of thyroid swelling (9.11 years) in patients who had MNG with malignancy, as opposed to patients who had only MNG (5.48 years).

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