

PREVALENCE OF THYROID CARCINOMA IN CLINICALLY DIAGNOSED MULTINODULAR GOITRE IN A TERTIARY CARE CENTRE- A RETROSPECTIVE DESCRIPTIVE STUDY

Premlal Ayyappan Prasanna¹, Rishikesan Nair Kavsthubham Venugopalan Nair², Resmi Madhusoodanan Santhakumar³

¹Associate Professor, Department of Plastic Surgery, Government Medical College, Thiruvananthapuram.

²Associate Professor (CAP), Department of General Surgery, Government Medical College, Thiruvananthapuram.

³Junior Resident, Department of Community Medicine, Government Medical College, Thiruvananthapuram.

ABSTRACT

BACKGROUND

Multinodular goitre is a very common, usually benign thyroid disorder, but sometimes occurrence of malignancy is reported as a histopathological surprise. Longstanding multinodular goitre has been suggested as a predisposing factor, since areas with iodine deficiency related endemic goitre have a high incidence of follicular carcinoma. In this study, we have evaluated the prevalence of incidental or occult carcinoma and thyroiditis in thyroidectomies performed for clinically benign multinodular goitres. We also attempted to find if a more radical approach is needed in the management of clinically benign multinodular goitres.

In this study, we aimed to identify the prevalence of carcinoma and thyroiditis clinically and on fine needle aspiration cytologically looking benign multinodular goitres. This study also intended to identify the relation of Sex, Age and Duration of illness from thyroid carcinoma.

MATERIALS AND METHODS

This is a retrospective descriptive study of patients with clinically and ultrasonographically proved multinodular goitre treated in one year. Fine Needle Aspiration Cytology proved malignancy is excluded from the study population. All the thyroidectomy specimens were pathologically studied and correlated with clinical findings.

RESULTS

Out of 303 patients, 90.4% (274) were females and 9.6% (29) were males. 50.8% were below 40 years and 49.2% were above 40 years. Duration of illness is 1 - 20 years. 64.4% were pathologically Benign Multinodular goitre only. 8% was having malignancy along with Multinodular goitre, of which 7.3% was papillary carcinoma and 0.7% was Follicular carcinoma.

CONCLUSION

It is found that prevalence of carcinoma in clinically multinodular goitres is 8%, which was not detected by Fine Needle Aspiration Cytology. No correlation with duration of illness. Incidence of Papillary Carcinoma is more in clinically benign Multinodular goitres than Follicular Carcinoma against what is said in Western literature.

KEYWORDS

Multinodular Goitre, Papillary Carcinoma, Follicular Carcinoma, Thyroiditis, Thyroidectomy.

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BACKGROUND

Enlargement of thyroid or goitre is the most common manifestation of thyroid disease.¹ Diffuse and multinodular goitre reflect impaired synthesis of thyroid hormone, most often caused by dietary iodine deficiency. Impairment of thyroid hormone synthesis leads to compensatory rise in serum TSH level, which in turn causes hypertrophy and hyperplasia of thyroid follicular cells and ultimately gross enlargement of thyroid gland. This compensatory increase in functional mass of the gland is able to overcome the hormone deficiency ensuring euthyroid state. The degree of thyroid enlargement is proportional to the level and duration of thyroid hormone deficiency.^{2,3}

With time, recurrent episodes of hyperplasia and involution combine to produce irregular enlargement of thyroid termed multinodular goitre. Virtually, all long-standing simple goitre convert into multinodular goitre.⁴ They may be nontoxic or may induce thyrotoxicosis (toxic multinodular goitre). Multinodular goitre may produce the most extreme thyroid enlargement and may be mistaken for neoplastic involvement than any other form of thyroid disease. Because they derive from simple goitre, they occur in sporadic and endemic forms, having the female preponderance distribution and presumably the same origins but affecting older individuals because they are late complications.^{5,6}

It is believed that multinodular goitre may arise because of the variation among follicular cells in response to external stimuli, such as trophic hormones. If some cells in a follicle have a growth advantage, perhaps because of intrinsic genetic abnormalities similar to those that give rise to adenomas, those cells will develop into clones of proliferating cells. This may result in the formation of a nodule whose continued growth can be autonomous without an external stimulus.⁷ Consistent with this model both monoclonal and

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Corresponding Author:

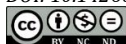
Dr. Premlal Ayyappan Prasanna,

"Nriithya", Trwa-S, Thaliyal,

Karamana P.O., Thiruvananthapuram.

E-mail: drpremlal@gmail.com

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polyclonal nodules coexist within the same multinodular goitre, the latter presumably having arisen owing to acquisition of a genetic abnormality favouring growth. Mutation in proteins of TSH signalling pathway that lead to constitutive activation of this pathway have been identified in a subset of autonomous thyroid nodules. With uneven follicular hyperplasias, generation of new follicles and uneven accumulation of colloid, tension and stresses are produced that lead to ruptures of follicle and vessels followed by haemorrhages, scarring and sometimes calcifications. The scarring adds to the tension and in this cyclical manner nodularity appears. Moreover, the preexisting stromal framework may enclose areas of expanded parenchyma contributing to the nodularity.^{8,9,10,11}

About 4% to 7% of the population has nodular thyroid disease. Approximately, 4% of these nodules are malignant and account for about 1% of all cancers. The female-to-male ratio of thyroid nodules is 6.5: 1.5.^{12,13}

Around 2000 patients are admitted in all surgical units of Medical College, Trivandrum every year for thyroid surgery. Of this, more than half are admitted with multinodular goitre.

Multinodular goitre is a very common, usually benign, thyroid disorder. However variable and sometimes surprisingly high occurrence of malignancy has been reported in many a surgical series.^{14,15,16} Multinodularity of goitre should no longer be considered an indicator of probable benign disease. Longstanding multinodular goitre has been suggested as predisposing factor in some cases, since areas with iodine deficiency related endemic goitre have a high incidence of follicular carcinoma.^{17,18,19,20}

Multinodular goitre cannot be considered as a condition predisposing to cancer, but it may harbour a cancer. Since neoplastic transformation is a multistep process that results in a continuous spectrum from the normal (physiological) state to a fully established neoplasm.^{21,22}

Thyroid Carcinoma (TC) is a relatively rare tumour, but it represents the most frequent form of cancer of the endocrine glands. Epidemiologically ascertained risk factors are ionising radiation, the presence of thyroid adenoma and Multinodular Goitre (MNG).^{23,24,25,26}

The incidence of thyroid carcinoma in thyroiditis and multinodular goitre has been debated and the possibility of autoimmune and immunological mechanisms in the aetiopathogenesis of carcinoma, particularly papillary type stimulating lymphocytic infiltration has been suggested. Histologically, it is difficult to differentiate lymphocytic infiltrate surrounding thyroid carcinoma from lymphocytic thyroiditis. It is still unclear whether thyroiditis is induced secondarily by thyroid carcinoma or thyroiditis predisposes thyroid gland to development of carcinoma.^{2,27,28,29,30}

The present study is an attempt to evaluate the prevalence of incidental or occult carcinoma and thyroiditis in thyroidectomies performed for benign nodular thyroid disease. The type of carcinoma associated with benign nodular disease and the duration of the nodular disease is also taken into consideration. Another factor which is of importance in this study is the fact that clinically solitary nodules may actually be a dominant nodule in a multinodular goitre.^{31,32} The study also attempts to find if a more radical approach including a change from subtotal to total or near total thyroidectomy decreased the rate of subsequent completion thyroidectomy for occult carcinoma.^{33,34,35,36,37}

MATERIALS AND METHODS

This is a retrospective descriptive study of patients with clinically and ultrasonographically proved multinodular goitre diagnosed and treated in all surgical units of Medical College, Trivandrum during a period of 1 year from January 2008 to December 2008. Each patient's symptoms and signs, investigations, treatment given and histopathology report were entered in the proforma with details of clinical examination in relation to the thyroid swelling. All patient's basic investigations like complete haemogram, blood sugar, blood urea, serum cholesterol, routine urine examination, chest x-ray, ECG, radiograph of neck, thyroid function tests, tissue diagnosis obtained by Fine Needle Aspiration Cytology (FNAC) were taken for analysis.^{38,39,31} Ultrasonogram of neck was done in most of the patients.⁴⁰ All the patients underwent surgery, either hemithyroidectomy, subtotal thyroidectomy or near total/total thyroidectomy^{41,42,43} and all operated specimens were subjected to detailed histopathological examination in the Department of Pathology, Medical College, Trivandrum. All histopathology reports were taken and analysed.^{44,45,8,46}

Study participants were patients with clinically diagnosed multinodular goitre who underwent surgery in all surgical units of Medical College, Trivandrum. Patients diagnosed to have toxic goitre and FNAC-proven thyroiditis and malignancy were excluded from the study. So, only clinically and cytologically-proven multinodular goitre were included.

Preoperative and post-operative complications were analysed. All observations were analysed and compared with other studies.

Diagnostic Workup

In the study, the following investigations were done in all patients which includes blood routine examination, urine routine examination, blood sugar, blood urea, serum creatinine, plain x-ray neck, chest x-ray, indirect laryngoscopy and Fine Needle Aspiration Cytology.^{47,48,49} Most of the patients had done ultrasonogram of neck.⁵⁰ All the patients had their thyroid function tests- T3, T4 and TSH done before and after surgery.^{51,52,53}

Radionucleotide scanning was not done for any patient due to non-availability of the facility in our hospital.^{54,55,56} Fine needle aspiration cytology represents a reliable method of providing tissue diagnosis and has been done for all patients and subjects with FNAC-proven malignancy were excluded from the study.

RESULTS

Out of 303 patients studied, 274 were females (90.4%) and 29 were males (9.6%) [Table 1]. Out of this 154 was below age of 40 years (50.8%) and 149 was above the age of 40 years (49.2%) [Table 1] with a range of 20 years to 72 years. The total duration of illness ranged from 1 year to 20 years; 227 patients were having a duration of < 5 years (74.9%), 69 patients were between 5 - 10 years (22.8%) and 7 were having above 10 years' duration (2.3%) [Table 1]. Near Total/ Total Thyroidectomy was the most common surgical procedure performed (n= 177, 58.4%). Hemithyroidectomy was done for 8 patients (2.6%) and subtotal thyroidectomy was done for 118 patients (38.9%) [Table 1].

Multinodular goitre/ Nodular colloid goitre was the most common finding in histopathology (n= 195, 64.4%). Multinodular goitre with cellular nodule was the report obtained for 40 patients (13.2%) and Multinodular goitre with thyroiditis was obtained for 44 patients (14.5%). Other reports included Multinodular goitre with papillary carcinoma (n= 22, 7.3%) and Multinodular goitre with follicular carcinoma (n= 2, 0.7%). So, the total number of malignancies reported was for 24 patients; (22 papillary carcinoma + 2 follicular carcinoma), a total of 8% (Table 2).

Out of the patients reported to have multinodular goitre (n= 195), 22 were men (11.3%) and 173 were women (88.7%) [Table 3]. Among the patients having multinodular goitre with cellular nodule (n= 40), two were men (5%) and 38 were women (95%), and among patients having multinodular goitre with papillary carcinoma two were men (9.1%) and 20 were women (90.9%). Both the patients with multinodular goitre with follicular carcinoma were women. Of the 44 patients having multinodular goitre with thyroiditis, 3 were males (6.8%) and 41 were females (93.2%) [Table 3]. Of the 195 patients having multinodular goitre alone, 98 patients (50.3%) are < 40 years and 97 patients are > 41 years of age (49.7%) [Table 3]. Of the 40 patients having multinodular goitre with cellular nodule 23 (57.5%) were < 40 years and 17 (42.5%) patients were > 40 and among 22 patients having multinodular goitre with papillary carcinoma 11 were < 40 years (50%) and 11 were > 41 years of age (50%) [Table 3]. Both the patients having multinodular goitre with follicular carcinoma both were below 40 years. Of the 44 patients having multinodular goitre with thyroiditis 20 (45.5%) were < 40 years and 24 (54.5%) were > 40 years (Table 3).

Of the 195 patients having multinodular goitre alone 5 patients underwent hemithyroidectomy (2.6%), 72 patients underwent subtotal thyroidectomy (36.9%) and 118 patients underwent near total/ total thyroidectomy (60.5%) [Table 4]. Of the 40 patients having multinodular goitre with cellular nodule 2 patients underwent hemithyroidectomy (5%), 16 patients underwent subtotal thyroidectomy (40%) and 22

patients underwent near total/ total thyroidectomy (55%). Of the 22 patients having multinodular goitre with papillary carcinoma 1 patient underwent hemithyroidectomy (4.5%), 9 patients underwent subtotal thyroidectomy (40.9%), 12 patients underwent near total/ total thyroidectomy (54.5%). Of the 2 patients having multinodular goitre with follicular carcinoma, one underwent subtotal thyroidectomy (50%) and other underwent near total thyroidectomy (50%). Of the 44 patients having multinodular goitre with thyroiditis, 20 patients underwent subtotal thyroidectomy (45.5%) and rest 24 underwent near total/ total thyroidectomy (54.5%) [Table 4].

Variable	Group	No. of Patients (n=303)	%
Age	Up to 40 years	154	50.8%
Sex	Female	274	90.4%
Duration in Years	<5	227	74.9%
	5-10	69	22.8%
	>10	7	2.3%
Management Given	Hemithyroidectomy	8	2.6%
	Subtotal Thyroidectomy	118	38.9%
	Near Total/ Total Thyroidectomy	177	58.4%

Table 1. Demographic Data, Duration of Illness and Surgical Procedure Performed

Histopathological Report	No. of Patients	Percentage
Multinodular goitre/ nodular colloid goitre	195	64.4%
Multinodular goitre with cellular nodule	40	13.2%
Multinodular goitre with papillary carcinoma	22	7.3%
Multinodular goitre with follicular carcinoma	2	0.7%
Multinodular goitre with thyroiditis	44	14.5%

Table 2. Histopathological Diagnosis of Study Participants

Category	Histopathological Report					P value
	Multinodular Goitre/ Nodular Colloid Goitre (n=195)	Multinodular Goitre with Cellular Nodule (n=40)	Multinodular Goitre with Papillary Carcinoma (n=22)	Multinodular Goitre with Follicular Carcinoma (n=2)	Multinodular Goitre with Thyroiditis (n=44)	
Male	22	2	2	2	3	
Female	173	38	20	0	41	
<40 yrs.	98	23	11	2	20	
>41 yrs.	97	17	11	0	24	

Table 3. Demographic Factors associated to Histopathological Diagnosis

Surgery Done	HPR	Frequency	%
Hemithyroidectomy	MNG	5	62.5%
	MNG with Cellular Nodule	2	25%
	MNG with papillary carcinoma	1	12.5%
	MNG with follicular carcinoma	0	-
	MNG with thyroiditis	0	-
Subtotal Thyroidectomy	MNG	72	61%
	MNG with Cellular Nodule	16	13.5%
	MNG with papillary carcinoma	9	7.6%
	MNG with follicular carcinoma	1	0.8%
	MNG with thyroiditis	20	16.9%
Near Total/Total Thyroidectomy	MNG	118	66.6%
	MNG with cellular nodule	22	12.4%
	MNG with papillary carcinoma	12	6.7%
	MNG with follicular carcinoma	1	0.5%
	MNG with thyroiditis	24	13.5%

Table 4. Surgical Procedures performed and Histopathological Diagnosis

DISCUSSION

In this study, prevalence of carcinoma in clinically multinodular goitre was found to be 8%. All these patients studied were subjected to Fine Needle Aspiration Cytology before surgery and none of them was reported to be malignant even though Fine Needle Aspiration Cytology was thought to be much sensitive to diagnose papillary carcinoma thyroid. This may be attributed to the fact that FNAC obtained were not from the involved areas. Of the 8% of malignancies detected, 7.3% was papillary carcinoma and 0.7% was follicular carcinoma and the result is comparable with those from various studies but different from studies in Western literature.

Among the patients with multinodular goitre with papillary carcinoma, 90.9% were females and 9.1% were males which shows a significant female preponderance.

Among the patients with multinodular goitre with follicular carcinoma, 100% were females.

13.2% of patients operated were having a cellular nodule in histopathology and 14.5% of patients were having thyroiditis co-existing with multinodular goitre. 93.2% of patients having thyroiditis were females and 6.8% were males.

When age group is taken into account, there is no much difference in occurrence of malignancy between the age groups < 40 or > 40.

We could not find out any correlation of malignancy with duration of illness. But in Western literatures, it has been stated that longstanding multinodular goitres has greater association with follicular carcinoma thyroid.

Among those patients with multinodular goitre with papillary carcinoma being operated, hemithyroidectomy was done for 4.5%, 41% of the patients had subtotal thyroidectomy and 54.5% of patients had near total/total thyroidectomy done.

Of the patients reported to have MNG with follicular carcinoma, 50% had subtotal thyroidectomy done and 50% had total thyroidectomy done.

CONCLUSION

The following conclusions were reached at the end of this study after comparing and analysing the data collected-

1. The prevalence of malignancy in multinodular goitre in the study group was 8%.
2. 7.3% of the study group had papillary carcinoma and 0.7% of the study group had follicular carcinoma showing an increased prevalence of papillary carcinoma compared to follicular carcinoma in multinodular goitres.
3. The prevalence of the thyroiditis noted in the study, population was 14.5%.
4. A definite female preponderance was found in malignant changes and 83% of the malignancy reported was females.
5. No correlation between duration of illness and prevalence of malignancy in multinodular goitre could be noted in this study. Hence, occult malignancy can occur in tumours with short duration also. So surgery should not be delayed thinking that it is benign disease.
6. There is no statistically significant difference in prevalence of malignancy among different age groups in the study.
7. Considering the high prevalence of malignancy in clinically benign multinodular goitre, near total/ total thyroidectomy could be the appropriate surgery of choice, since the patients undergoing hemithyroidectomy or subtotal thyroidectomy will have to be subjected to completion thyroidectomy if the histopathology report comes as malignant.

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