

THE FREQUENCY OF MALIGNANCY IN NODULAR GOITER - A SINGLE CENTER STUDY

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ABSTRACT

Objective: To find out the frequency of malignancy in nodular goiters.

Methodology: A total of 204 cases were studied in the department of ENT and Head and Neck Surgery, Hayatabad Medical Complex, Peshawar. The duration of this descriptive study was from June 1, 2008 to May 31, 2010. After taking informed consent, a detailed history was obtained. Clinical and laboratory investigations were carried out as an aid to diagnosis and determine the patients' fitness for surgery. Patients with nodular goiters were categorized into two categories i.e., Solitary thyroid nodule and multinodular goiter. Surgically resected thyroid specimens were examined histopathologically. The data was analyzed using SPSS 16.0 for windows to determine the frequency of malignancy in nodular goiter.

Results: Ages of the patients ranged from 17 to 84 years with a mean age of 37 ± 12.48 years. The male to female ratio was 1:3.5. 18.14% cases presented as solitary thyroid nodules (STN) and 81.86% as multinodular goiters (MNG). Out of the total 83.82% cases were benign and 16.18% cases were malignant. The prevalence of malignancy in multinodular goiter was 14.37% and in the solitary thyroid nodules as 24.32%. Papillary carcinoma was the commonest malignancy followed by follicular carcinoma.

Conclusion: The prevalence of cancer is significant in nodular goiters and these malignant tumours are usually of the papillary type. Solitary thyroid nodules have more chances of being malignant than multinodular goiter.

Keywords: Solitary Thyroid Nodule (STN), Multinodular Goiter (MNG), Thyroid Cancer.

This article may be cited as: Anwar K, Din G, Zada B, Shahabi I. The Frequency of Malignancy in Nodular Goiter - A Single Center Study. J Postgrad Med Inst 2012; 26(1): 96-101.

INTRODUCTION

Enlargement of thyroid gland is a common problem. Its true incidence is unknown though it is endemic in the northern areas of Pakistan especially in Swat, Dir and Chitral districts of Khyber Pakhtunkhwa^{1,2}. The most common cause of goiter formation is iodine deficiency. According to UNICEF (1998) report, 70% of the total population in Pakistan is at risk of iodine deficiency disorder. Other causes include heredity, neoplasia, inflammations, drugs and exposure to radiations.

Clinical thyroid cancer is uncommon, with an estimated incidence in various parts of the world as 0.5 to 10 cases per 100,000 populations. It accounts roughly for about 0.5% of all cancers in men and 1.5% of all cancers in women³. The most common types of thyroid cancers are differentiated, with papillary carcinoma accounting for 70%, follicular carcinoma 12% and the follicular variant of the papillary carcinoma 6% of all the thyroid cancers⁴. It may present either as a solitary nodule or as a dominant nodule in a multinodular goiter. In Pakistan, thyroid cancer accounts for 1.2% cases of all malignant tumors⁵.

The solitary thyroid nodule is a palpably discrete swelling within an otherwise normal gland on clinical examination. The prevalence of thyroid nodules ranges from 4% to 10% in the general adult population and from 0.2% to 1.2% in children⁶. The majority of clinically diagnosed solitary thyroid nodules are benign. However, the frequency of malignancy in solitary thyroid nodule may vary from 4.7-18.3%^{7,8}.

Longstanding multinodular goiter is known to undergo malignant transformation⁹. Traditionally patients with multinodular goiters have been considered less at risk of developing a thyroid

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Date Received: February 18, 2011

Date Revised: November 3, 2011

Date Accepted: December 3, 2011

cancer than those with solitary thyroid nodules. However recent studies show that the prevalence of malignancy in multinodular goiters (MNG) does not differ much from those with solitary thyroid nodules (STN)¹⁰.

Cases having high risk of malignancy can usually be identified on clinical assessment and the use of modern imaging modalities. These techniques, however, are unable to differentiate reliably between benign and malignant. Fine needle aspiration cytology (FNAC) is capable of doing so when there is a solid mass in relation to the gland but is less reliable when the mass is cystic¹¹. FNAC is routinely carried out in nodular goiter as part of pre operative evaluation and planning of definitive treatment.

Unsuspected, occult carcinoma is not a very rare finding encountered in thyroid gland and ranges between 7-15%^{12, 13}. Therefore, it is not rare for the surgeons to find malignancy in thyroid biopsy specimens resected to treat apparently a benign lesion. This usually necessitates a second major operation in the form of total thyroidectomy in a shorter span of time with its inherent risks. The study aims to help identify patients at risk and determine the magnitude of the problem in a tertiary care hospital setting.

METHODOLOGY

This descriptive study was conducted in the Department of ENT and Head and Neck Surgery, Hayatabad Medical Complex Peshawar, a tertiary care hospital. The study was conducted from June 1, 2008 to May 31, 2010. A total of 204 cases were included in the study through non-probability consecutive sampling.

Sample size was calculated using WHO software for sample size determination and assuming 17% proportion of malignancy in goiters, 95% confidence interval and 4.9% margin of error.

All those cases of goiters undergoing excision/incision biopsy of the thyroid gland were included in the study while known cases of thyroid malignancy presenting for follow up or patients having goiters but were not fit for surgery were excluded from the study.

A total of 204 cases fulfilling the required criteria were included in the study. After taking informed consent, a detailed history was obtained. Patients were examined clinically with particular emphasis on looking for clinical signs and symptoms of malignancy. Besides giving consideration to the age and gender of the patient, a suspicion of malignancy was placed on thyroid nodules when there was history of rapidly enlarging nodule, pain, difficulty in breathing, the

presence of enlarged neck nodes, change of voice and family history of thyroid cancer.

Morphological classification of goiter was used for the purpose of initial clinical examination to identify solitary thyroid nodules and multinodular goiters. Final diagnosis was based only on histopathological examination of the biopsy specimens. The biopsy specimens were reported by different pathologists from different laboratories.

Laboratory investigations were carried as an aid to diagnosis and determine the patients' fitness for surgery. Haematological investigations like Full Blood Count with Erythrocyte Sedimentation Rate, serum T3, T4 and TSH estimation, BT, CT, Blood Sugar and Urea Levels, Serum Creatinine, Serum Calcium Levels, Serum Electrolytes Estimation, Liver Function Tests and Serum thyroglobulin levels were estimated in all cases which turned out to be malignant on cytology. Similarly, Urological investigation like Urine Routine Examination; Cardiopulmonary investigations like ECG, X-Ray Chest and Echocardiography; Imaging studies like Ultrasonography with Doppler Studies of neck vessels and Histopathological investigation like Fine Needle Aspiration Cytology (FNAC) were carried out.

On the basis of history, clinical examination and laboratory investigations appropriate surgery was chosen. The types of surgery included hemithyroidectomy, subtotal thyroidectomy, near total thyroidectomy, total thyroidectomy and incision biopsy. A partial surgery was converted into total thyroidectomy when the biopsy result showed malignancy. For the purpose of analysis, Nodular goiter was categorized as; 1. Solitary Thyroid Nodule (STN) when there was a single nodule palpable in the gland on clinical examination and 2. Multinodular Goiter (MNG) when more than one nodule was detected on examination. Final diagnosis was made on the basis of histopathological examination of the resected specimens. The biopsy findings were categorized as either benign or malignant. The information was recorded on a proforma and the results were analyzed.

The data regarding various variables like age, gender and the type of malignancy was analyzed using SPSS 16.0 for windows. The frequency of malignancy in STN and MNG was determined. Chi-square test was applied and p-value was determined to know the significance of difference in malignancy in STN and MNG.

RESULTS

A total of 204 cases were included in the

study. Histopathological results of specimens for analysis were available in all the cases. The ages of the patients ranged from 17 to 84 years with a mean age of 37 ± 12.48 years. The male to female ratio was 1:3.5. The age and gender distribution of patients is shown in Table 1. Rapid increase in longstanding goiter followed by enlargement of neck nodes were the most frequent clinical features observed. Thirteen (6.37%) patients were found to have pain in their goiters on initial assessment. The majority of these patients (n=9) had pain appearing in the past 3 months whereas the same number of patients had their neck nodes enlarged in the previous 6 months. Twelve patients had rapid increase in the size of goiter for 3-6 months. (Table 2 & 3) Thirty seven cases (18.14%) presented as solitary thyroid nodules and 81.86% (n=167) as multinodular goiters. Out of the total

83.8% (n=171) cases were benign and 16.2% (n=33) were malignant. The frequency of malignancy in multinodular goiter was 14.4% (n=24) as compared to 24.3% (n=9) in the solitary thyroid nodules. (Table 4).

There was high frequency of malignancy in solitary thyroid nodules as compared to multinodular goiters, although it was not statistically significant with p-value=0.137. Follicular carcinoma was the commonest malignancy encountered in solitary thyroid nodules. Papillary carcinoma was more frequent in multinodular goiters. (Table 5). However with respect to the frequency of papillary and follicular carcinomas in STN and MNG, this difference is statistically insignificant (p-value =0.129). No case of medullary or anaplastic carcinoma was noted in the solitary thyroid nodules.

Table 1: Age and Gender Distribution of the Patients

		Sex		Total
		Male	Female	
Age	<=30	12 (5.9%)	62 (30.4%)	74 (36.3%)
	31-50	26 (12.7%)	80 (39.2%)	106 (52.0%)
	51-70	5 (2.5%)	17 (8.3%)	22 (10.8%)
	> 70	0	2 (1.0%)	2 (1.0%)
Total		43 (21.1%)	161 (78.9%)	204 (100%)

Table 2: Features Suggestive of Thyroid Malignancy on Initial Assessment

Clinical Features	No. of Patients	Percent of total
Rapid increase in longstanding goiter	20	9.80%
Enlarged neck nodes	18	8.82%
Pain	13	6.37%
Rapidly enlarging nodule	7	3.43%
Vocal cord paralysis	5	2.45%
Difficulty in breathing	3	1.47%

Table 3: Duration of Symptoms in Patients Presenting with Thyroid Malignancies

Clinical Features	1-3 Months	3-6 Months	6-12 Months
Rapid increase in longstanding goiter	3	12	5
Enlarged neck nodes	7	9	2
Pain	9	2	2
Rapidly enlarging nodule	2	4	1
Change of voice	4	1	0
Difficulty in breathing	3	0	0

Table 4: Type of Goiter and Distribution of Histopathological Nature

			Histopathological Nature		Total
			Benign	Malignancy	
Type of goiter	STN	Count	28	9	37
		% within Type of goiter	75.7%	24.3%	100.0%
	MNG	Count	143	24	167
		% within Type of goiter	85.6%	14.4%	100.0%
Total		Count	171	33	204
		% within Type of goiter	83.8%	16.2%	100.0%

STN = Solitary Thyroid Nodule; MNG = Multinodular Goiter

Table 5: The Nature of Malignancy in Nodular Goiter

	Type of carcinoma	Type of goiter		Total
		STN	MNG	
Malignancy	Papillary	4	16	20
		12.1%	48.5%	60.6%
	Follicular	5	4	9
		15.2%	12.1%	27.3%
	Anaplastic	0	3	3
		.0%	9.1%	9.1%
	Medullary	0	1	1
		.0%	3.0%	3.0%
Total		9	24	33
		27.3%	72.7%	100.0%

STN= Solitary Thyroid Nodule; MNG= Multinodular Goiter

DISCUSSION

Thyroid carcinoma is a relatively rare tumour, but it represents the most frequent form of cancer of the endocrine glands. Multinodularity of goiter should no longer be considered an indicator of probable benign disease. The primary challenge in the management of nodular goiter is to rule out malignancy. Solitary or multiple nodules which produce pressure symptoms or become cosmetically unacceptable are readily treated by thyroidectomy. Those nodules which are suspected of malignancy are similarly best treated by surgery.

The world literature is full of reports with a wide range of figures for prevalence of malignancy in goiters. It is difficult to determine the true incidence of malignancy in nodular goiter in our country because of lack of a national database. However, the histopathologic distribution

of differentiated thyroid cancer is comparable to international literature, as has been reported from Pakistan by various authors.

The frequency of malignancy in nodular goiter in our study was 16.18%. Our findings are comparable to those of Baloch MN and colleagues who in their study of 521 thyroidectomy specimens found malignancy in 14% of cases¹⁴. However Mofti et al observed a much higher incidence of thyroid malignancies (29%) in a study of 158 patients¹⁵. A rather lower prevalence rate of 11% in goiters was reported by Memon W and colleagues¹⁶. In a recent study conducted at the Jinnah Postgraduate Medical Centre in Karachi, the frequency of thyroid malignancy was found to be 15.33% in a series of 998 cases¹⁷. In a similar study at the JPMC, Karachi, the authors found malignancy in 14.35% of the surgically resected thyroid specimens¹⁸. In yet another study conducted

at hospitals in Rawalpindi/Islamabad, the authors have reported a much lower prevalence of malignancy (2.92%) in goiters with equal proportion for both papillary and thyroid carcinomas (33.3% each)¹⁹. Possible reasons for such a wide variations in the prevalence of malignancy in nodular goiters may be iodine deficiency, heredity, sex hormones, use of drugs, exposure to ionizing radiations and referral of selected cases to tertiary care hospitals.

Ríos A and colleagues in a study of 672 multinodular goiters found a prevalence of malignancy in 9% of their cases²⁰. In a study conducted in a single centre in Singapore, the authors reported malignancy in 21.2% cases whereas in a retrospective analysis of 361 thyroid specimens in Saudi Arabia, the authors found 8% of MNG and 15.2% of STN were associated with malignancy^{21,22}. In a retrospective analysis of a larger series of 819 cases in Yemen, Al-Jaradi M and colleagues found malignancy in 21% of patients operated for goiters²³.

In our study the frequency of malignancy in solitary thyroid nodules was 24.3% as compared to 14.34% in multinodular goiters. These finding support recent published reports suggesting that there is no statistically significant difference between incidence of thyroid carcinoma in patients with a solitary nodule and those with multinodular goiter. This possibly may be due to the fact that 50% of solitary nodules found on palpation are actually part of multinodular goiters^{10, 24}.

There appears to be general agreement in all these studies that papillary carcinoma is the predominant malignancy in nodular goiters. In this study, papillary carcinoma was the most common thyroid cancer observed followed by follicular carcinoma. This is consistent with figures from various national and international studies.

CONCLUSION

The prevalence of cancer is significant in nodular goiters and these malignant tumours are mostly of the papillary type. Solitary thyroid nodules have more chances of being malignant than multinodular goiter. It would be prudent to keep the high incidence of thyroid cancer in mind during the assessment and investigation of patients with nodular goiters and every effort should be made to identify nodules with malignant potential.

Limitations of the study

The study was conducted in tertiary care hospital settings where mostly selected patients are received for treatment. These, therefore, do not reflect the magnitude of the problem. Also, the sample was not representative of a specific

population. The patients belonged to various parts of Khyber Pakhtunkhwa and whole of Afghanistan. So any risk factor for development of goiter and thyroid malignancy in a specific population are difficult to identify. Moreover, due to the small sample, the results of this study cannot be generalized.

Grant Support, Financial Disclosure and Conflict of Interest

None Declared

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CONTRIBUTORS

KA conceived the idea, GD and BZ did the data collection and literature search, IS provided guidance and supervision during the study.