Frequency of Malignancy in Multi-nodular Goiter: 
A Tertiary Care Hospital Experience

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Abstract

Objective: To determine the frequency and the types of thyroid carcinoma in multi-nodular goiter (MNG) by doing histopathological examination of thyroid resection specimens operated as benign thyroid disease.

Patients & Methods: This prospective case series was carried out at department of general surgery, Pakistan Institute of Medical Sciences, Islamabad from 01-Jan-2012 to 31-Dec-2014. Patients undergoing total, near total or subtotal thyroidectomy and lobectomy for multi-nodular goiter were included in the study. Detailed histopathological examination of all thyroid resection specimens was carried out.

Results: Amongst the 289 MNG cases which were studied, 23 (8%) cases contained malignant foci. Papillary carcinoma was the most common type of malignancy observed [17 (73.9 %) cases] followed by follicular carcinoma [3 (13.04 %) cases]. Mean age of patients with malignancy was 47.13 ± 8.8 years. Female dominance was present in malignant cases with a female to male ratio of 10.5:1.

Conclusion: The frequency of malignancy in multi-nodular goiter is quite significant in our region especially in females, thus all resected specimens should undergo histopathological examination and majority of patients should have initial total thyroidectomy as the correct surgical option. All the patients with multi-nodular goiter who have been treated conservatively need a close follow up for malignancy.

Key Words: Carcinoma, Malignancy, Multi-nodular goiter, Near total thyroidectomy, Subtotal Thyroidectomy, Total thyroidectomy.

Introduction

Thyroid disease commonly presents as multi-nodular goiter (MNG). Thyroid nodules have been reported to be found in 4-7% of the population on neck palpation and in 30-50% of the population by ultrasonography (USG). Dietary iodine deficiency has been associated with thyroid malignancy and northern areas of Pakistan are known for endemic iodine deficiency goiter and hence the high frequency of goiter in local population. Thyroid carcinoma has a reported frequency of 1.2 % in Pakistan, of all reported malignancies with more prevalence in females and a female to male ratio of 2.6:1. The frequency of the thyroid malignancy is reported between 0.9% to 13% from different parts of world.

MNG is usually considered a low risk for malignancy when compared with a solitary thyroid nodule. Frequency of malignancy ranging from 7 to 17 % has been reported in cases of MNG in different studies. Fine needle aspiration cytology (FNAC) has been instrumental in refining the management of solitary thyroid nodule whereas multiple nodules of MNG harboring a nodule of a carcinoma can’t be differentiated clinically or radiologically amidst other benign nodules with certainty. Frequency of thyroid carcinoma increases further if cases of occult carcinoma are also included. Exposure to ionizing radiation and accessibility to more sensitive diagnostic tests are also responsible for a global increase in the frequency of thyroid carcinoma.

Pakistan Institute of Medical Sciences, Islamabad is the tertiary care hospital of capital city of Pakistan. It caters to the local population of Rawalpindi and Islamabad and also for Northern Areas and Azad Jammu and Kashmir, where iodine deficiency is endemic since a long time. The objective of this study was to determine the frequency and the types of thyroid malignancies in multi-nodular goiter (MNG) by doing histopathological examination of thyroid resection specimens operated for clinically benign thyroid disease.

Patients and Methods

This prospective case series was carried out at the department of general surgery, Pakistan Institute of Medical Sciences, Islamabad from Jan 1st 2012 to Dec 31st 2014. Permission was obtained from the hospital ethical committee. Most of the patients were local or from Northern Areas of Pakistan and Azad Jammu and Kashmir. Histopathological data of patients of all ages and gender...
with clinical or sonological diagnoses of multi-nodular goiter (with or without thyrotoxicosis) undergoing total, near total or subtotal thyroidectomy and lobectomy were collected on a pre designed proforma after taking informed consent. Patients with pre-operative diagnosis of malignancy on FNAC, diagnosis or suspicion of malignancy on clinical examination or ultrasound/computed tomography (CT) scan, grave’s disease, recurrent goiter, metastatic cervical lymphadenopathy with occult primary and history of radiation to neck were excluded from the study. All the patients included in the study underwent a thorough clinical examination, biochemical investigations including the thyroid hormone assay and serum calcium levels, thyroid ultrasonography (USG) and indirect laryngoscopy to check for the vocal cord movements. FNAC was ordered only in cases with suspicious nodule i.e. hard, irregular nodules, rapidly growing or the presence of microcalcification, which was determined on the clinical examination or USG. A total number of 289 MNG patients fulfilled our inclusion criteria. These cases were evaluated on Hematoxylin and Eosin stained sections from paraffin embedded 10% buffered formalin fixed tissue blocks. Special stains and immunohistochemical analysis were performed whenever required.

The data were analyzed using International Business Machines Statistical Package for the Social Sciences (IBM SPSS) Version 21.0. Descriptive statistics were calculated as percentages, frequencies and means. The numerical data such as age were expressed as mean ± standard deviation while the categorical data such as the gender and histopathology were expressed as frequencies and percentages.

**Results**

In this prospective study we had 289 cases of multi-nodular goiter with a female to male ratio of 8:1.

**Figure 1: Age wise distribution of patients with MNG**

**Figure 2: Age wise distribution of cases with thyroid malignancy**

The frequency of malignancy in our study was 8 % (n=23) (Table 1). Amongst the 23 patients with carcinoma of the thyroid, 21 were females and 2 were males with a female to male ratio of 10.5:1. Amongst the 266 benign cases 236 were females and only 30 were males with a female to male ratio of 8:1. A greater part of the patients with MNG were in the 3rd (31%) and 4th (24%) decades of life as shown in Figure 1. Most frequent age for presentation of carcinoma of the thyroid was in 41-50 years (52 %) (Figure 2). Minimum age was 28 while maximum was 65 with a mean age of 47.13 ± 8.8.

**Discussion**

The thyroid is the largest of the endocrine glands and definitely the most common site of all primary endocrine cancers. The frequency of the thyroid malignancy is reported between 0.9% to 13% from different parts of the world. There is evidence that frequency of thyroid carcinoma has risen in the last three decades as reported by studies from all over the world. Increased sampling of resected specimens by pathologists is suggested as one of the causes of increase in frequency of occult papillary carcinomas. The increase has largely been attributed to heightened medical surveillance and the use of improved diagnostics but there are suggestions to explore other factors. Some environmental carcinogens in the industrialized lifestyle maybe affecting thyroid as well as the
Table 2: Comparison with local studies showing frequency of thyroid malignancy (%)

<table>
<thead>
<tr>
<th>Literature Review</th>
<th>Frequency of CA</th>
<th>Papillary CA</th>
<th>Follicular CA</th>
<th>Anaplastic CA</th>
<th>Medullary CA</th>
<th>Hurthle Cell CA</th>
<th>Mean Age (yrs)</th>
<th>F:M</th>
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<tbody>
<tr>
<td>Our Study</td>
<td>8.0</td>
<td>73.90</td>
<td>13.04</td>
<td>-</td>
<td>8.69</td>
<td>4.34</td>
<td>47.13</td>
<td>10.5:1</td>
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<tr>
<td>Hanumanthapa</td>
<td>10</td>
<td>60</td>
<td>20</td>
<td>-</td>
<td>10</td>
<td>10</td>
<td>-</td>
<td>5.6:1</td>
</tr>
<tr>
<td>Khan</td>
<td>9.5</td>
<td>57.89</td>
<td>21.05</td>
<td>15.78</td>
<td>5.36</td>
<td>-</td>
<td>33.5</td>
<td>5.3:1</td>
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<tr>
<td>Memon</td>
<td>7.6</td>
<td>75</td>
<td>12.5</td>
<td>12.5</td>
<td>-</td>
<td>-</td>
<td>52.0</td>
<td>7:1</td>
</tr>
<tr>
<td>Ul Haq</td>
<td>2.92</td>
<td>33.3</td>
<td>33.3</td>
<td>23.81</td>
<td>-</td>
<td>9.5</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Moosa</td>
<td>3.0</td>
<td>66.6</td>
<td>33.3</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>33.42</td>
<td>-</td>
</tr>
<tr>
<td>Ahmad</td>
<td>5.7</td>
<td>66.6</td>
<td>33.3</td>
<td>-</td>
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<td>-</td>
<td>-</td>
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<tr>
<td>Soomro</td>
<td>7.37</td>
<td>71.4</td>
<td>14.43</td>
<td>14.43</td>
<td>-</td>
<td>-</td>
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<td>6:1</td>
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<tr>
<td>Anwar</td>
<td>14.37</td>
<td>66.6</td>
<td>16.66</td>
<td>12.5</td>
<td>4.16</td>
<td>-</td>
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increased exposure to the medical radiations is a likely risk factor. Thyroid cancer mortality is approximately 0.5 cases per 100,000.

An enlarged thyroid gland with multiple distinct nodules on palpation is labeled as a multi-nodular goiter (MNG). Multiple factors are implicated in the etiopathogenesis of MNG including mild dietary deficiency of iodine, increased iodide clearance from the kidneys, slight impairment of hormone synthesis, and the presence of thyroid stimulating immunoglobulins. About 50.5% of the solitary nodules clinically felt on palpation are essentially component of the multi-nodular goiter. Cosmetic reasons, compressive symptoms, toxicity and suspicion of malignancy are the usual causes for offering surgical management to MNG patients. FNAC is a quick and cheap investigation with established importance in the assessment of thyroid nodules but a negative FNAC is by no means confirmatory of a benign disease in cases of MNG.

In our study we have observed an 8% frequency of malignancy as an incidental finding in patients undergoing surgical management for MNG. Benzarti et al in Tunis observed a 9.5% frequency of malignancy in MNG, while Sarajevo gave 8% frequency of malignancy in MNG. Prades et al from France have reported fairly high frequency of 12.2%. Papillary carcinoma is the most commonly reported carcinoma in literature followed by follicular carcinoma.

In Our study the frequency of thyroid malignancy in MNG was 8% and this finding is comparable to the findings reported in international and national literature. Females have a higher frequency of MNG as well as carcinoma which is comparable to other studies. Furthermore carcinoma increases in frequency with advancing age.

Evidence has suggested to do detailed histopathological examination of all thyroid resection specimens to detect any foci of malignancy. Recent studies in literature have advocated total thyroidectomy as a primary surgical option for multi-nodular goiter in expert hands as it removes the disease process completely, allows better control of postoperative therapy, lowers local recurrence rates and avoids the substantial risks of surgery for completion thyroidectomy. Limitation of our study is that it is a single center study.

**Conclusion**

Frequency of malignancy in multi-nodular goiter is quite significant in our region especially in females. In our opinion all specimens should undergo histopathological examination and majority of patients should have initial total thyroidectomy as the correct surgical option. All the patients with multi-nodular goiter who have been treated conservatively need a close follow up for malignancy.

**Conflict of interest**

This study has no conflict of interest declared by any author.

**References**
