Histomorphologic spectrum of thyroid lesions in surgically treated thyroid specimens

Haque WS\textsuperscript{a}, Yasmin S\textsuperscript{b}, Islam SMJ\textsuperscript{c}, Giti S\textsuperscript{d}

Abstract

Background: Diseases involving thyroid gland are myriad—they span from functional to goiterous which again can be non-neoplastic or neoplastic. The pattern and prevalence of these disorders depend on various factors like age, sex, ethnicity and geographic location of residence. The aim of the present study was to determine the pattern of thyroid lesions in surgically resected thyroid specimens.

Methods: This retrospective study was conducted at Department of Histopathology of Armed Forces Institute of Pathology (AFIP), Dhaka, Bangladesh. All thyroidectomy specimens received in the Department of Histopathology over the period from 1\textsuperscript{st} January 2018 to 30\textsuperscript{th} June 2019 were included in the study. Data including age, sex and histopathological diagnosis were collected from the records and histopathology slides of all cases were reviewed to verify diagnosis. Data were then analyzed by standard statistical methods.

Results: A total of 377 specimens were collected, 301 specimens were from females and 76 from males (female to male ratio 4.01:1). The age ranged from 13 years to 82 years (mean 38.44±12.89 years). Nodular goiter (274, 72.62%) was the commonest thyroid lesion; other benign lesions included follicular adenoma (18) and Hashimoto thyroiditis (17). Overall malignancy was 18.03% (68). Papillary carcinoma (61, 89.70%) constituted majority of the malignant neoplasms. Other malignant neoplasms included follicular carcinoma (3 cases including 1 case of Hurthle cell carcinoma), anaplastic carcinoma (2) and medullary carcinoma and non-Hodgkin lymphoma 1 each.

Conclusion: Our study revealed that the prevalent form of thyroid diseases is nodular goiter that mostly affects females. Papillary carcinoma is the commonest malignancy of thyroid gland which also predominantly affects females.

Key words: thyroid, histopathology, non neoplastic, neoplastic, nodular goiter, papillary carcinoma

Introduction

Disorders of thyroid manifest as enlargement of thyroid gland (goiter) or alterations in its hormonal levels or both.\textsuperscript{1} The prevalence and spectrum of thyroid disorders depend on factors like age, sex, ethnic origin and geographic location.\textsuperscript{2} Thyroid disorders are four times more in females than in males.\textsuperscript{3,4} They are endemic in mountainous regions, where the soil, water and food contain little iodine.\textsuperscript{5} Thyroid lesions range from non-neoplastic to neoplastic. Nodular goiter (NG) is the commonest cause of thyroid enlargement followed by thyroid tumors.\textsuperscript{6} Most of the tumors are benign in nature. Overall, the incidence of thyroid malignancy is low, constituting only 0.5-1.0% of all cancers and 3.3-17% of all thyroid diseases.\textsuperscript{7} Among thyroid malignancies papillary carcinoma (PTC) is the most common malignant neoplasm followed by follicular carcinoma (FTC), medullary carcinoma (MTC), anaplastic carcinoma (ATC) and non-Hodgkin lymphoma (NHL).\textsuperscript{8}

Virtually any disease of the thyroid can present as thyroid swelling. The prevalence of goitreous swelling of thyroid is quite common, about 4% to 7% of the adult population has a clinically palpable thyroid enlargement; on the other hand, prevalence of thyroid nodule found incidentally on ultrasonography is 19% to 67%.\textsuperscript{4}
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Haque WS et al

For the purpose of clinical management, diagnosis of thyroid disease relies on a thorough clinical examination, ultrasonographic examination, fine needle aspiration cytology (FNAC) of the enlarged gland, hormonal evaluation and thyroid scan. Main indications of surgical treatment of thyroid swelling are malignancy or indeterminate cytology in FNAC and/or suspicious history and clinical findings. Indications of thyroidectomy also include patients with symptomatic goiters e.g. with pressure symptom, or cosmetic problem. Histopathological examination gives a definitive diagnosis in surgically removed thyroid.

The aim of the study is to evaluate the histologic spectrum of these surgically treated thyroid specimens sent of AFIP- a tertiary care health facility which receives samples not only from various army hospitals but also from different civil hospitals of the country.

Methods

This retrospective study was done at Department of Histopathology, Armed Forces Institute of Pathology (AFIP), Dhaka, Bangladesh over a period of 18 months (from 1st January 2018 to 30th June 2019). The materials for this study consisted of the slides and paraffin embedded blocks of all the thyroidectomy specimens received in the Histopathology Department of AFIP. Total 377 thyroidectomy specimens received during the study period were analyzed. The thyroidectomy specimens included lobectomy, partial thyroidectomy, subtotal thyroidectomy and total thyroidectomy. All biopsies had been fixed in 10% buffered formalin, routinely processed for paraffin embedding, then microtome sectioned at 5µm and stained with Haematoxylin and Eosin (H&E). Special histochemical stains and immunohistochemistry (IHC) were performed whenever required.

All thyroidectomy specimens irrespective of age, gender and demographic habitat were included in the study. For each case, the laboratory request form and duplicate copy of the histological report were retrieved and relevant clinical information such as age, sex and the histological type of thyroid disease were extracted.

Histopathology slides of all cases were reviewed to verify diagnosis. The lesions were classified based on their main histological diagnostic features into NG, inflammatory and neoplastic lesions. The neoplastic lesions were classified according to the World Health Organization (WHO) histological classification of thyroid tumors. The data was subsequently analyzed and presented.

Results

A total of 377 thyroidectomy specimens were examined. The specimens received ranged from total thyroidectomies to lobectomies. There were 301(%) females and 76(%) males (female to male ratio 4.01:1). The age ranged from 13 years to 82 years. Maximum number of thyroid lesions were seen in 31-40 years age group (104, 27.58%), and in 21-30 years age group (100, 26.52%) followed by fifth decade (79, 20.96%). No case was found in our study in children less than 10 years of age and only one case was found in more than 70 years age group; this case was represented by a 82 years old female with histological diagnosis of NG.

Histopathological spectrum of all thyroid lesions and age and sex distributions of benign thyroid lesions are presented in Table I and II respectively. NG was the most common non-neoplastic thyroid lesion (274, 72.67%) followed by follicular adenoma (FA), (18, 4.77%) and Hashimoto thyroiditis (HM) (Figure 2), (17, 4.50%). All 17 patients with HM are female.

<table>
<thead>
<tr>
<th>Table I</th>
<th>Histopathological spectrum of lesions of thyroidectomy specimens (N=377)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Histopathologic diagnosis</td>
<td>Frequency</td>
</tr>
<tr>
<td>Benign lesion</td>
<td></td>
</tr>
<tr>
<td>Nodular goiter</td>
<td>274</td>
</tr>
<tr>
<td>Follicular adenoma</td>
<td>18</td>
</tr>
<tr>
<td>Hashimoto thyroiditis</td>
<td>17</td>
</tr>
<tr>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>Malignant lesion</td>
<td></td>
</tr>
<tr>
<td>Papillary carcinoma</td>
<td>61</td>
</tr>
<tr>
<td>Follicular carcinoma</td>
<td>3</td>
</tr>
<tr>
<td>Anaplastic carcinoma</td>
<td>2</td>
</tr>
<tr>
<td>Medullary carcinoma</td>
<td>1</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>377</td>
</tr>
</tbody>
</table>
Among the 377 thyroid lesions, there were 68 (18.03%) malignant neoplasms; which included 62 cases of PTC (Figure 3), 3 cases of FTC -including one case of Hurthle cell variant of FTC (Figure 4 & 5), 2 cases of ATC (Figure 6), 1 case of MTC (Figure 7 & 8) and 1 case of NHL (Figure 9). Figure 1 shows age and sex distribution of PTC. Maximum numbers of PTC were seen in age group 31-40 years (20 cases) and 19 cases were found in 21-30 years age group. A good number of PTC were found in age group 11-20 years with 8 cases which constituted about 34% of the total thyroid lesion in this age group where as in other age group it ranged from 11.39% in age group 41-50 years to 20.19% in age group 31-40 years.

**Table II** Age and sex wise distribution of patients with benign thyroid lesions (N=309)

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Nodular goiter</th>
<th>Follicular adenoma</th>
<th>Hashimoto thyroiditis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>11-20</td>
<td>4</td>
<td>13</td>
<td>0</td>
</tr>
<tr>
<td>21-30</td>
<td>5</td>
<td>66</td>
<td>2</td>
</tr>
<tr>
<td>31-40</td>
<td>7</td>
<td>64</td>
<td>2</td>
</tr>
<tr>
<td>41-50</td>
<td>19</td>
<td>43</td>
<td>1</td>
</tr>
<tr>
<td>51-60</td>
<td>14</td>
<td>27</td>
<td>0</td>
</tr>
<tr>
<td>61-70</td>
<td>4</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>&gt;70</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>53</td>
<td>221</td>
<td>7</td>
</tr>
</tbody>
</table>

**Figure 1** Age and sex wise distribution of papillary carcinoma (N=61)

**Figure 2** Hashimoto thyroiditis. Lymphocytic infiltrates forming numerous lymphoid follicles with germinal centers in thyroid (H&Ex40). Inset shows prominent Hürthle cell metaplasia of thyroid follicular cells (H&Ex400).

**Figure 3** Papillary carcinoma. Neoplastic papillae having fibrovascular core (H&Ex100). Inset depicting nuclear overlapping, ‘orphan Anne’ like nuclei and nuclear grooving- nuclear characteristics of papillary carcinoma (H&Ex400).
Histomorphologic spectrum of thyroid lesions in surgically treated thyroid specimens

Figure 4 Follicular carcinoma. Neoplastic follicles showing ‘mushroom like’ (arrow) capsular invasion (H&Ex100).

Figure 5 Hürthle cell variant of follicular carcinoma. Neoplastic follicular cells are having abundant eosinophilic cytoplasm (H&Ex100) and showing ‘mushroom like’ capsular invasion (arrow). Inset (H&Ex400).

Figure 6 Anaplastic carcinoma. Spindled highly anaplastic cells forming fascicles with areas of necrosis (arrow) (H&Ex100, inset- H&Ex400)

Figure 7 Medullary carcinoma. Solid proliferation of round to polygonal cells having granular cytoplasm (H&Ex100). Abundant amyloid deposition (arrow) in the stroma is also present.

Figure 8 Medullary carcinoma. A. Congo red stained section highlighting amyloid (arrow), B. Apple green birefringence of amyloid in polarized microscopy. C & D. Immunohistochemistry for carcinoembryonic antigen (CEA) and calcitonin- neoplastic cells are positive.

Figure 9 Non-Hodgkin lymphoma (Diffuse large B cell lymphoma). Diffuse proliferation of large lymphoid cells (H&Ex40). Inset shows immunohistochemistry for CD20 - the neoplastic cells are positive.
Discussions
Occurrence of thyroid diseases varies according to different geographical areas, age and sex and both neoplastic and non neoplastic diseases of thyroid are common all over the world.\textsuperscript{11,12} Solitary nodules are about 4 times more common in women than in men and occur more often in people who live in iodine deficient geographic location.

Benign lesions in the present study were 81.96\% and malignant neoplasms 18.03\%. Similar findings are found in the study done by Sreedevi AR et al in India, Hussain N et al in Pakistan and Othman HN in Malaysia; but a strikingly high incidence of thyroid malignancy (61.57\%) is found in study done by Beigh A et al in India.\textsuperscript{6,12-14} Thyroid diseases have historically been known primarily to affect the female sex. In our study female representation was 79.84\% in thyroidectomies. Similar female representations are found in study carried out by Rahman MA et al at Dhaka, Bangladesh and Sreedevi et al. in India; even more female predominance is found in studies done by Joseph E et al in India and by Solomon R et al in Keno, Nigeria.\textsuperscript{2,8,15,16} In the present study the commonest age group presenting with thyroid disorders was in the 3\textsuperscript{rd} to 5\textsuperscript{th} decade while study carried out by Ramesh VL et al found age incidence to be commonest in 3\textsuperscript{rd} to 5\textsuperscript{th} decade and Jagadale K et al found commonest age in the 4\textsuperscript{th} to 6\textsuperscript{th} decades.\textsuperscript{17,18}

NG is the most common among thyroid disease. Iodine deficiency and genetic factors are the two most important environmental factors that influence development of NG.\textsuperscript{19} It accounted 72.65\% (274) cases in our study, representing the most common pathologic lesion. This is similar to studies by Tsegaye B et al and Ashwini K et al.\textsuperscript{1,20}

HM is the commonest cause of hypothyroidism in iodine non-deficient regions of the world. It is an autoimmune disease and shows distinct female preponderance with majority of the patients over 40 year of age.\textsuperscript{19,21} It presents as diffuse firm thyroid enlargement, sometimes accompanied by signs of tracheal or esophageal compression and rarely with a dominant nodule.\textsuperscript{1} Histologically it is characterized by extensive lymphocytic infiltrates forming germinal centers, with admixed plasma cells. The thyroid follicles becomes atrophic and follicular cells show prominent Hürthle cell change.\textsuperscript{21,22} HM constituted 17 cases (4.50\%) in our study. All 17 patients of HM were female. The average age was 40.88±9.27 years with most patients belonging to 4\textsuperscript{th} decade. Similar findings are seen in study done by Darwish AH et al in Bahrain, where all the patients were female with mean age of 42 years. On the other hand Joseph E et al found 32 female and 5 male patients of HM in their study done in Kerala, India.\textsuperscript{7,2}

Commonest malignant neoplasm in our study was papillary carcinoma PTC. PTC is the most common malignant thyroid tumor, representing 85\% to 90\% of differentiated thyroid carcinomas, and occurs across all ages; women are affected four times more commonly than men.\textsuperscript{19,21,22} In the current study PTC accounted for about 91\% of all malignancies with female to male ratio of 3.42:1. Similar high percentage of PTC is also seen in studies done by Albasri A et al in Al Madinah region of Saudi Arabia and Beigh A et al in Srinagar, India.\textsuperscript{14,23} It was the most common malignant thyroid lesion and constituted 85.14\% of the malignant lesions in the study done by Beigh A et al and represented 87.8\% of all thyroid malignancies in study done by Albasri A et al. In fact this high frequency of papillary carcinoma among all thyroid carcinomas corroborate with the recent increased trend of papillary carcinoma diagnosis among malignant thyroid tumors world wide.\textsuperscript{14} In our study out of 62 cases 53 were classical papillary carcinoma and 9 were follicular variant.

FTC account for 5\% to 15\% of primary thyroid cancers and are more common in women.\textsuperscript{21} In the current study the second most common type of malignancy was FTC (4.41\%). There were total 3 cases and all of them were minimally invasive, showing capsular invasion only. None of these showed distant metastasis at the time of presentation.

ATC are undifferentiated tumors of the thyroid follicular epithelium, accounting for less than 5\% of thyroid tumors and usually presents in elderly patients. In the current study there were 2 cases of ATC, one was an elderly male of 70 years and the other was a 55 years old female. Both cases were sarcomatoid variant histologically. Medullary carcinomas of the thyroid are neuroendocrine neoplasms derived from the parafollicular cells, and account for approximately 5\% of thyroid neoplasms. In our study there was only a single case of medullary carcinoma presenting with classic histologic features. The patient was a 57 yr old female patient.
Primary non Hodgkin lymphomas (NHL) of thyroid are uncommon. Most cases of primary NHL of the thyroid are seen in adult or elderly females. In our case the patient is a 53 yr old female presented with diffuse large B cell lymphoma (DLBCL) in thyroid.

**Conclusion**

Our study echoed with the historical fact that thyroid diseases primarily affect the female sex - be it benign or malignant. It reveals that the prevalent form of thyroid diseases is nodular goiter. Papillary carcinoma is the commonest malignancy of thyroid gland which also predominantly affects females. It appears that papillary carcinoma was a bit more frequently diagnosed malignancy in our study.

**Conflict of interest**: Nothing to declare.

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