Incidence of thyroid malignancy among goitrous thyroid lesions from the Sarawak General Hospital 2000–2004

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ABSTRACT

Introduction: Thyroid cancer is the most common among all endocrine malignancies. The worldwide prevalence of goitre in the general population is estimated at 4–7 percent and the incidence of malignancy in goitrous thyroid is about ten percent. It is postulated that goitrous thyroid is a precursor lesion to the development of malignant thyroid diseases. As Sarawak is a state well known for endemic goitre, this study focused on establishing the incidence of thyroid malignancy among goitrous thyroid swellings.

Methods: This study was a hospital-based retrospective study on the archived collection of the surgically-removed thyroid specimens from the Sarawak General Hospital, Malaysia. Cases were grouped into cancer and non-cancer groups. The cancer group included papillary thyroid carcinoma (PTC), PTC follicular variant, follicular carcinoma and anaplastic carcinoma (ANA).

Results: A total of 820 thyroid cases which underwent surgical removal in years 2000 to 2004 were collected. Of these, 143 (17.4 percent) were male and 677 (82.6 percent) female. It was observed that the highest prevalence of thyroid swelling cases occurred in the age group 41–60 years while the lowest prevalence occurred in the age group under 21 years, 371 (45.2 percent) vs. 31 (3.8 percent). By ethnicity, the Ibans and Malays were found to have a higher prevalence at 275 (33.5 percent) and 196 (23.9 percent), respectively, while the lowest prevalence was observed in Indians, 11 (1.3 percent). 55 cases (6.7 percent) were found to be cancerous and the rest (93.3 percent) were non-cancerous thyroid swellings. Histologically, the highest incidence of carcinoma was PTC (4.0 percent) and the lowest was ANA (0.2 percent).

Conclusion: Based on our observations, although goitrous thyroid swelling is quite a common problem in Sarawak, thyroid malignancy is not a major issue. Among thyroid malignancies, PTC is the most common histological type of malignancy.

Keywords: goitre, papillary thyroid carcinoma, thyroid cancer, thyroid malignancy

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INTRODUCTION

Thyroid cancer is a common malignancy with an apparent increasing incidence in a wide spectrum of clinical behaviour and therapeutic responsiveness. It is the most common among all endocrine malignancies. The worldwide prevalence of goitre in the general population is estimated at 4%–7% and the incidence of malignancy in goitrous thyroid is about 10%.[1] It was estimated in the United States in 2004 that there will be approximately 20,000 new cases, and 1,460 thyroid cancer deaths.[2] Among thyroid malignancies, papillary thyroid carcinoma (PTC) is the most common malignant tumour of the thyroid gland, accounting for 85% of all thyroid cancers.[3] An increased incidence of thyroid carcinoma has been noted in endemic goitre regions such as Columbia and Austria as well as in non-endemic goitre regions such as Iceland and Germany. It was also noted that follicular thyroid carcinoma (FCA) and anaplastic thyroid carcinoma (ANA) occurred more frequently in endemic goitre regions than in goitre-free areas. This implies that highly aggressive thyroid cancer prevails in countries with endemic goitre.[4,5]

According to the World Health Organisation (WHO), at least 1.6 billion people are at risk of iodine deficiency disorders (IDD). Among these, 655 million are affected by goitre, 27% of whom are in Southeast Asia, followed by the Western Pacific countries.[6] Based on the Ministry of Health, Malaysia biannual report, seven states are noted to have a high incidence of goitre, viz. Sabah, Sarawak, Kelantan, Terengganu, Pahang, Perlis and Kedah.[7-10] It is postulated that goitrous thyroid is a precursor lesion to the development of malignant thyroid diseases.[11-13] A study from one of the endemic goitre states in Malaysia revealed

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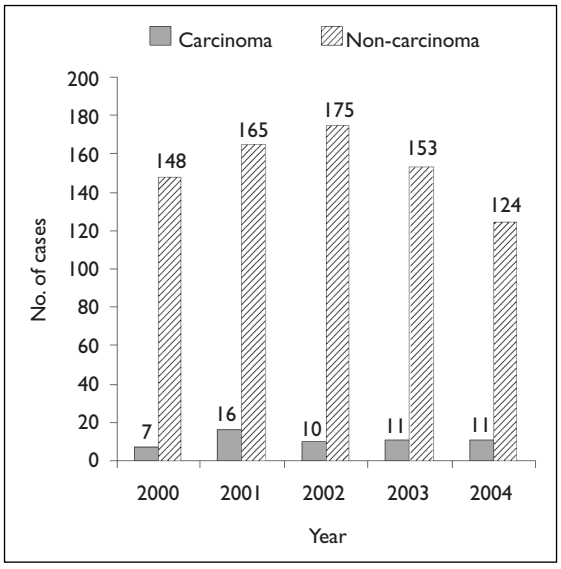

Fig 1. Prevalence of thyroid carcinoma vs. non-carcinoma detected by year.

a high prevalence of 34% of goitrous thyroid lesions harbouring malignancy.[14,15] As Sarawak is one of the states with a high incidence of endemic goitre, this study aimed at observing the incidence of thyroid malignancy among the incidence of goitrous thyroid swellings.

METHODS

This study was a hospital laboratory-based retrospective study on the archived collection of sections and wax blocks from the Sarawak General Hospital, Malaysia. Cases included all consecutive thyroid glands removed by surgery. Clinically-diagnosed goitre patients, irrespective of age, gender and race, undergoing total or partial thyroidectomy were included in this study, while non-goitrous thyroid cases, e.g. thyroglossal cysts, were excluded. The clinical data of each patient, such as age, gender, race and clinical diagnosis, was obtained from the histopathological examination request form. Slides were thoroughly reviewed and grouped into cancer and non-cancer cases. New sections were prepared from the appropriate wax blocks when necessary; this was performed only on ten cases where the old slides were lost.

The cases were reviewed by three pathologists (JW, GKS and TTH) without being aware of the previous results. All the reviewed slides matched the original diagnosis and there was no discrepancy. Sections were cut in 4–5 μm thickness on which routine haematoxylin and eosin staining sections were prepared. Microscopy was done under the Olympus BH-2 microscope using the scan for screening and the high-dry magnifying lens for detailed morphological examination. Lesions observed in the cancer group were PTC, PTC follicular variant (PTCFV), FCA and ANA. The non-cancerous lesions comprised follicular adenoma (FA), Hürthle cell adenoma (HA), nodular goitre (NG), toxic goitre (TG) and Hashimoto's thyroiditis (HT).

For the diagnosis of FA, colloid-filled follicles having uniform-appearing epithelial cells together with a well-confined capsule formation were identified. Careful observations to exclude malignancy and to differentiate from NG were performed. In HA, the lesions composed of cells with abundant eosinophilic cytoplasm and small regular nuclei were taken into account. For NG, thyroid nodules containing colloid-rich follicles lined by flattened, inactive epithelium were noted. TG was diagnosed by the presence of crowded glands and follicles lined by tall columnar epithelia. The enlarged epithelial cells project into the lumens of the follicles and the scalloped appearance of the edges of the colloid are diagnostic. In HT, the thyroid parenchyma with a dense active lymphocytic infiltration are diagnostic.[16]

The diagnostic criteria applied for PTC were the characteristic nuclear appearances, such as ground glass nuclei, grooved nuclei and nuclear pseudo inclusions. For FCA, either a vascular or capsular invasion was looked for. Sufficient slides were prepared for the relevant cases to confirm the FCA diagnosis. Those observed to have characteristic nuclear features (as in PTC), but without vascular or capsular invasions were classified as PTCFV. For ANA, cells showing marked nuclear pleomorphism and hyperchromatism were identified. Classification of cancer was done via the standard WHO histological classification for thyroid cancers.[17] Sigma Stat for Windows version 2.0 (Jandel Corporation, San Rafael, CA, USA) was used as a software for data collection and for the descriptive analysis of the variables. Statistical significances were calculated by chi square test and Fisher's exact test. The Statistical Package for Social Sciences version 13.0 (SPSS Inc, Chicago, IL, USA) was also applied where appropriate.

RESULTS

A total of 820 consecutive goitrous thyroid cases for surgical intervention were collected within five years, from January 2000 to December 2004. These included 143 (17.4%) male subjects and 677 (82.6%) female subjects. The age group for the highest incidence of thyroid swelling was in the 41–60 year age group with 371 cases (45.2%), followed by 352 cases (42.9%) in the 21–40 year age group, 66 cases (8.1%) in the > 60 years age group, and 31 cases (3.8%) in the age group < 21 years. By ethnicity, the Ibans and Malays were found to

Table I. A demographic characteristic of the study population with goitrous thyroid swelling.

Variable	No. (%)
Gender	
Male	143 (17.4)
Female	677 (82.6)
Total	820 (100.0)
Age group (years)	
≤ 20	31 (3.8)
21–40	352 (42.9)
41–60	371 (45.2)
> 60	66 (8.1)
Total	820 (100.0)
Ethnicity	
Iban	275 (33.5)
Malay	196 (23.9)
Bidayuh	172 (21.0)
Chinese	116 (14.2)
Indian	11 (1.3)
Others	50 (6.1)
Total	820 (100.0)

Table II. Histopathological diagnosis of thyroid lesions.

Diagnosis	No. (%)
Malignant thyroid lesions	
Papillary thyroid carcinoma	33 (4.0)
Papillary thyroid carcinoma follicular variant	6 (0.7)
Follicular carcinoma	14 (1.7)
Anaplastic carcinoma	2 (0.2)
Total malignant cases	55 (6.7)
Non-malignant thyroid lesions	
Follicular adenoma	144 (17.6)
Hurthle cell adenoma	4 (0.5)
Nodular goitre	577 (70.4)
Toxic goitre	33 (4.0)
Hashimoto thyroiditis	7 (0.9)
Total non-malignant cases	765 (93.3)
Total of all cases	820 (100.0)

have highest prevalence at 275 (33.5%) and 196 (23.9%), respectively, and the lowest prevalence was the Indians, 11 (1.3%) (Table I).

Among those cases with thyroid swellings, only 55 cases (6.7%) were found to be cancerous lesions and the remaining 765 cases (93.3%) were non-cancerous thyroid swellings. Fig. 1 shows the incidence of thyroid cancer and non-cancer cases by year. The highest cancer incidence was observed in year 2001 (8.8%) and the lowest in year 2000 (4.5%), although the prevalence of non-cancerous cases were similar in all five years. Among all thyroid lesions, PTC had the highest incidence at 33 cases (4.1%), followed by FCA 14 (1.7%), PTCFV 6 (0.7%), and the lowest incidence was ANA 2 (0.2%). In the non-malignant lesions, NG had the highest incidence at 577 cases (70.3%), followed by FA 144 (17.6%). There was no statistical significance between the subgroups of age and ethnicity ($p > 0.05$) (Table II). Table III shows the incidence of thyroid malignancy among goitrous swellings by demographical variables. Male subjects showed a higher incidence (11.9%) than female subjects (5.6%) and this difference was statistically significant ($p = 0.01$).

DISCUSSION

The problem of iodine-deficiency induced goitrous thyroid swelling is one of the world's most important health problem, and this is also true in Malaysia.[9,10] The Universal Salt Iodization programme was meant to be a major slogan to solve this problem. While focusing on this issue, it is the duty and responsibility of healthcare professionals to be aware of the consequences of increased iodine intake which could probably result in either iodine-induced thyrotoxicosis or thyroid cancers.[18] Thyrotoxicosis is transient and of less significance, while thyroid cancer requires early detection and treatment.[18] From our observation in this five-year study, only 55 (6.7%) cancer cases were detected out of the 820 goitrous thyroid cases. This figure is lower than that noted by Pacini and DeGroot in 2001, where they observed the incidence of thyroid malignancy among goitrous thyroid cases to be as high as 10%.[1] A higher incidence of cancer at 26.4% was also observed in a three-year study done in Myanmar.[19] Thus, although Sarawak has a high prevalence of goitrous enlargement, the incidence of thyroid malignancy is not as high as the other comparative studies.

From the Myanmese study, it was observed that there was a high incidence of thyroid cancer in the age range between 21 and 60 years, in both follicular and papillary patterns.[19] For the study in Sarawak, it was found that a high prevalence of IDD was present among women of child-bearing age, i.e. 15–44 years, and the prevalence of the disorder ranged from 60%–90% depending on the area of study.[20-22] In our study, the prevalence of goitrous thyroid swelling was 42.9% and 45.2% in the age range 21–40 years and 41–60 years, respectively. However, the incidence of cancer was observed to be highest for the > 60 years (13.6%), compared to that for age groups 21–40 years (5.7%) and 41–60 years (6.2%). Although this finding is not statistically significant, a further study in age prevalence would be interesting in terms of explaining the immunity against malignancy in the elderly age group.

Regarding gender variation, we observed a significantly high incidence of cancer cases in male subjects, though the prevalence of goitrous lesions in male subjects was lower ($p = 0.01$). The possibility of a significantly higher chance of malignancy in males should be considered in this situation as there is a disparity

Table III. Prevalence of thyroid malignancy among goitrous swellings by demographic variables.

Sociodemographic variable	No. (%) of non-cancer cases	No. (%) of cancer cases	Total no. of cases	p-value
Gender				
Male	126 (88.1)	17 (11.9)	143	0.01*
Female	639 (94.4)	38 (5.6)	677	
Total	765 (93.3)	55 (6.7)	820	
Age group (years)				
≤ 20	28 (90.3)	3 (9.7)	31	NS
21–40	332 (94.3)	20 (5.7)	352	
41–60	348 (93.8)	23 (6.2)	371	
> 60	57 (86.4)	9 (13.6)	66	
Total	765 (93.3)	55 (6.7)	820	
Ethnicity				
Malay	179 (91.3)	17 (8.7)	196	NS
Iban	254 (92.4)	21 (7.6)	275	
Bidayuh	167 (97.1)	5 (2.9)	172	
Chinese	107 (92.2)	9 (7.8)	116	
Indian	10 (90.9)	1 (9.1)	11	
Others	48 (96.0)	2 (4.0)	50	
Total	765 (93.3)	55 (6.7)	820	

*p-value is statistically significant at < 0.05; NS: not significant

between male and female patients with thyroid cancers, according to Machens et al in 2006. They emphasised that an early diagnosis and treatment of thyroid cancer in male patients are needed because the cancer may behave more aggressively in men than in women, as there is a marked variation in the risk of hormone-dependent cancers found between males and females.[23,24] Regarding cancer incidence by year, it was observed that the highest cancer incidence was in the year 2001 (8.8%) and the lowest in year 2000 (4.5%). This was different from the study done in Myanmar where the incidence of cancer was increasing in subsequent years, possibility due to the increasing exposure to carcinogens.[19] We observed a similar result in Sugitani et al's study, where among thyroid malignancies, PTC is the most common histopathological type.[3] Although Sarawak is known to be an endemic area for iodine deficiency, the incidence of PTC was found to be higher than the other types of thyroid cancer, in contrast to findings by Riccabona in 1980 and Bikiri et al in 1998, that highly-aggressive thyroid cancers like FCA and ANA were more prevalent in countries with endemic goitre.[4,5] From our study, we did not observe any case of medullary carcinoma, although existing literature reports its presence in less than 5% of the total thyroid malignancy.[16]

As our study population was just limited to the collected cases in Sarawak General Hospital, the findings might not be reflective of the overall general population in Sarawak, even though Sarawak General Hospital represents the majority of specimens obtained from the whole of Sarawak. Nevertheless, we observed from our study that thyroid malignancy is not a major issue in Sarawak, although goitrous thyroid swelling is a common problem in this state. We also observed that among thyroid malignancies, PTC is the most common histological type of malignancy.

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