

RESEARCH COMMUNICATION

Spectrum of Thyroid Lesions in Hospital Universiti Sains Malaysia Over 11-Years and A Review of Thyroid Cancers in Malaysia

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Abstract

Introduction: Endemic goitre is a major concern in many nations including Malaysia. Seven states in the country have been identified by Ministry of Health of Malaysia to have high incidence of goitre and one of these is Kelantan. **Methods:** This is a retrospective study over an 11-year period from 1994 to 2004 on all thyroid specimens submitted to the Pathology Department, Hospital Universiti Sains Malaysia (HUSM), in Kelantan. Epidemiological data were retrieved from the patients' records and pathology findings from the pathology reports. **Results:** During this period, Department of Pathology HUSM received a total of 1,486 thyroid specimens. The female to male ratio was 6:1 and the median age was 40.0 years. The duration of goitre ranged from one to 15 years. Histopathological examination showed 71.9 percent were non-neoplastic and 28.1 percent neoplastic lesions. The hospital-based incidence of nodular hyperplasia was 9.9 per 100,000 admitted patients per year. The hospital-based incidence of all types of malignant thyroid cancers was 3.5 per 100,000. The most common malignancy was papillary carcinoma (76.6 percent). The majority of the cancers (59.5 percent) occurred in a background of nodular hyperplasia. Thyroid cancers made up 4.9 percent of all cancers seen in HUSM. **Conclusion:** This study suggests that malignant thyroid lesions arising from multi-nodular goitre are high in a population living in an iodine-deficiency area.

Key Words: Thyroid diseases - multi-nodular goitre - thyroid cancer - papillary carcinoma - Malaysia

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Introduction

Endemic goitre is a major health concern in many parts of the world including Malaysia. Seven states in Malaysia; Sabah, Sarawak, Kelantan, Terengganu, Pahang, Perlis and Kedah are noted to have high incidence of goitre (Ministry of Health, Malaysia, 1998). In West Malaysia, the north-eastern region including Kelantan has a high incidence of multi-nodular goitre, with incidence of 31.4% in coastal/lowland areas to 45.0% in the inland areas (Mafauzy et al., 1995). The mean urinary iodine excretion of Kelantan population in the study done by Mafauzy et al (1995) was 57µg/day. The recommended dietary allowance of iodine is 150µg/day (children and adults). Urinary iodine concentration (UIC) represents a good approximation of iodine supply. The median urinary iodine concentration for normal people ought to be >100µg/l (Delange, 1998). In a study reported in 1996, histological examination of 300 consecutive cases of multi-nodular goitre specimens seen at Hospital Universiti Sains Malaysia (HUSM), 34% of them had malignant transformation (Madhavan and Othman, 1996); a high figure compared to international incidence of 4 to 17% (Murray, 1998).

The present study was conducted to investigate the

incidence of various thyroid diseases seen in Hospital Universiti Sains Malaysia (HUSM) over an 11-year period from 1994 to 2004 and to determine the incidence of thyroid cancers in Kelantan. In addition, a review of thyroid cancer in Malaysia is included.

Materials and Methods

All data pertaining to thyroid specimens seen in the department of pathology, HUSM from 1994 to 2004 were taken for analysis. The cytological diagnoses were obtained from the Cytology Registry and the histological diagnoses from the Histopathology [HPE] Registry. Epidemiological data and pathological findings were retrieved from these records. These data were scrutinized to avoid duplication in cases where repeat FNA (fine needle aspiration) procedure was done on the same patient. All patients were admitted through the specialists' clinics at the Hospital. In cases of cancer, the detail of the microscopic histological description was obtained.

The total number of cases for cytological and histopathological examination seen in the Pathology Department over the same 11 year period was noted. The data was analysed using SPSS version 11.5 for Windows.

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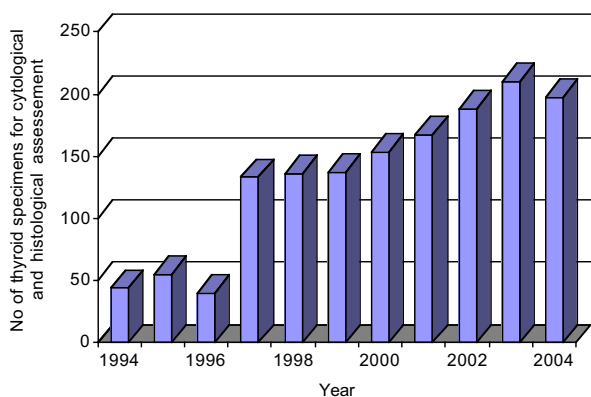


Figure 1. The Number of Thyroid Samples Received in the Pathology Laboratory, HUSM 1994 – 2004

The hospital-based incidence for common thyroid diseases was calculated based on the number of thyroid disease confirmed histopathologically over the number of patients attending the outpatients specialists clinics at HUSM during the same period multiply by 100,000. This figure was divided by eleven (the duration of the study period) to give a yearly incidence.

Results

A total of 1486 thyroid specimens were received by Department of Pathology HUSM from 1994 to 2004. Majority 1167/1486 (78.5%) had prior FNA before surgical removal. During the same period, a total of 20,381 cytological and 37,926 histological samples were seen in the same laboratory, making thyroid specimens 2.5% of the total samples examined. Four hundred and ninety seven (497) patients had both cytological assessment followed by histological confirmation. The number of patients attending the specialist clinics to HUSM over the 11-year period was 294,328 patients.

The number of thyroid samples received each year is depicted in Figure 1. The age of the patients ranged from 12 to 85 years. Sixty nine records (4.6%) did not state the age of the patients. The mean age was 40.9 years (SD14.6) and the median age was 40.0 years. The female to male ratio was 6:1. The duration of goitre ranged from one to

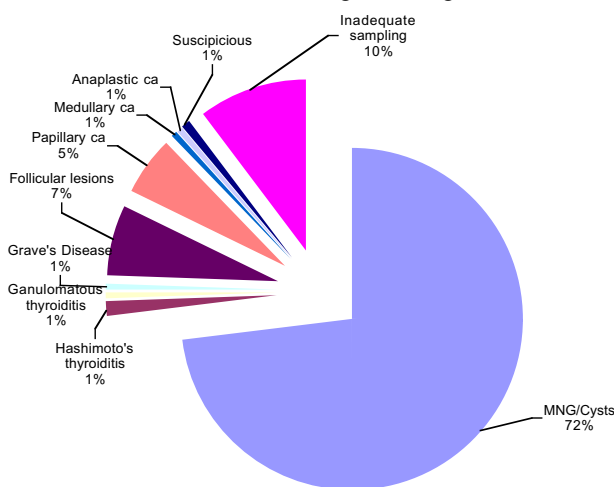


Figure 2. The Diagnoses Made By Fine Needle Aspiration Cytology for Thyroid Cases Seen in HUSM; 1994 – 2004

Table 1. The Hospital-based Incidences of Various Thyroid Diseases per 100,000 Admitted Patients seen in HUSM; 1994 to 2004

| | |
|-----------------------------------|------|
| Multinodular goitre/colloid cysts | 9.9 |
| Graves's Diseases | 0.5 |
| Thyroiditis | 0.3 |
| Follicular lesion | 1.1 |
| Thyroid Malignancies n=111 | 3.5 |
| Papillary carcinoma -76.6% | 2.6 |
| Follicular carcinoma -18.9% | 0.6 |
| Hurtle cell carcinoma -1.8% | 0.1 |
| Medullary carcinoma -0.9% | <0.1 |
| Anaplastic carcinoma-2.7% | <0.1 |

15 years.

Multi-nodular goitre, also termed nodular hyperplasia, was the most common diagnosis made by cytology; 852 (73.0%) and by histology; 322(64.8%). Neoplastic diagnoses were made in 166(14.1%) cases by FNA and 147(28.1%) by HPE. All neoplastic cases diagnosed by cytology had histology confirmation. The various diagnoses made from aspiration cytology is shown in Figure 2.

From the 147 cases diagnosed to be neoplastic by HPE, 111 (75.5%) were malignant. The peak age of patients with malignancy was from 30-49 years old. Majority of the cancer was papillary carcinoma (76.6%). The hospital-based incidence of papillary carcinoma was 2.6 per 100,000 admitted patients and follicular carcinoma was 0.6 per 100,000 (Table 1). The female to male ratio was 5.2:1. HPE showed 66/111 (59.5 %) of the cancers arose from pre-existing nodular hyperplasia. All except two were papillary carcinoma. From 1994 to 2004 pathology laboratory HUSM made diagnoses of cancer in 2251 cases (Figure 3). The average percentage of HPE confirmed thyroid cancers seen was 4.9% of total cancers. The percentage ranged from 1% to 7.5%. The annual hospital-based incidence of thyroid diseases seen in HUSM over the 11-year period is as shown in Table 1.

Discussion

Reported studies on thyroid cancers in Malaysia are few. The early hospital-based reports of Malaysian thyroid cancer incidence were reported by Marsden in 1958 and

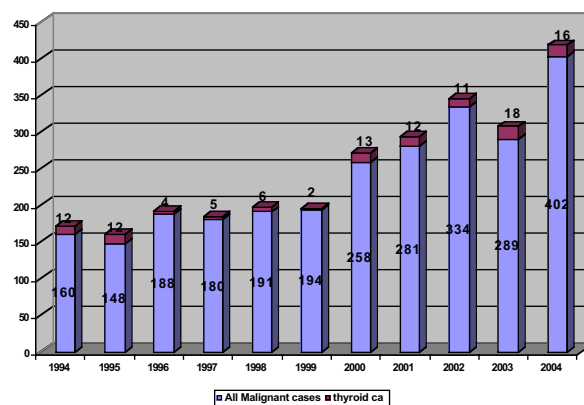


Figure 3. The Frequency of Cancer of Thyroid Compared to All Malignant Cases Diagnosed In Pathology Department, HUSM 1994 – 2004

by Lim in 1962. The incidence of the cancer was 2.1% in the Marsden series based on total 4,650 cancer cases seen in Institute of Medical Research (IMR) and 3.6% in the Lim's series based on 1047 cancer cases seen in Hospital Kuala Lumpur (HKL). Armstrong reported the incidence as 2.4% (out of 368 total cancer cases) in the same hospital in 1979. These were biased figures as they were derived from centres which managed cancer patients and did not reflect the incidence of the disease in the population. A more recent report was that by Abdullah (2002), which was also conducted in Kuala Lumpur. Unlike these studies, ours was conducted outside Kuala Lumpur, in the state of Kelantan which was noted previously (Mafauzy et al., 1995) to have a high rate of iodine deficiency. Thyroid cancer makes up 4.9% of all cancers in our series implying that the incidence of this cancer is slightly higher than the figures noted earlier. However it is still generally low; less than 5% of all cancers regardless of the states in Malaysia.

Hospital Universiti Sains Malaysia (HUSM) is one of the 2 major hospitals in the state of Kelantan catering for 1.5 million populations. The hospital-based incidence in our series could be crudely projected to population-based incidence by having Kelantan population at risk (1.5 million) as the denominator in the calculation, giving the population-based incidence of thyroid cancer 0.7 per 100,000.

The National Cancer Registry (NCR) of Malaysia in 2003 stated the population-based incidence of this cancer was 2.5 per 100,000 (Lim and Halimah, 2003) Elsewhere in Asia the incidence of thyroid cancer is also low (Shah et al., 1999; Yeole, 1999). In France, data from 8 French Cancer Registries over the period 1925 -1997 studied by Colonna et al showed that the incidence of thyroid cancer increased exponentially, 6.2% per year in men and 8.1% per year in women (Colonna et al., 2002). In the past three decades incidence rate have been increasing in most developed countries. We are also seeing a gradual rise but we think it could be due to the introduction of FNA in our hospital since 1989 which could pick up early lesions. The peak age seen in our data is similar to the data from National Cancer Registry; 30-49 years. The female to male ratio was 6:1, higher than the ratio stated in the National Cancer Registry of Malaysia; 2.8:1 (Lim and Halimah, 2003)

World Health Organization (WHO) in its report on world cancer incidence, identified Malaysia to have a higher age-standardized incidence of thyroid cancers in women (<23.2 per 100,000) compared to the neighbouring countries (<4.4 per 100,000 population) (Stewart and Kleihues, 2003) We are not sure how WHO obtained such figure as that from NCR is much lower.

Papillary carcinoma was the most common cancer in our series 76.6% of total thyroid cancers. This finding is comparable with findings of other authors (Burgess et al., 2000; Bal et al., 2001; Levi et al., 2002; Verkooijen et al., 2003; Burgess; 2002). In general this cancer is often not associated with iodine deficiency. There are reports in which thyroid cancers are associated with iodine deficiency; however they are from countries in which the populations were also exposed to radiation (Szybinski et

al., 2003; Niedziela et al., 2004).

Multi-nodular goitre also termed nodular hyperplasia has been cited in the literature as an associated factor of thyroid cancer, particularly papillary carcinoma (Sachmechi et al., 2000; Gandolfi et al., 2004). In a study involving consecutive thyroid specimens removed for long standing multi-nodular goitre, Madhavan and Othman (1996) found microcarcinoma in 34% ; much higher than what is cited in the literature. A subsequent study by Omar et al from the same laboratory using RET and p53 by immunohistochemistry found 22.7% of nodular hyperplasia expressed RET protein, indicating a role in the genesis of thyroid cancer (Omar and Othman, 2003; Omar et al., 2004). It is a known fact that goitre prevalence is high in iodine-deficient areas.

Is iodine deficiency an associated factor in thyroid malignancy? Animal experiments have demonstrated a clear increase in incidence of thyroid epithelial cell carcinomas after prolonged iodine deficiency (Feldt-Rasmussen, 2001). Iodine deficiency is recognized as a public health problem worldwide including Malaysia. Since prevalence of goitre is high in iodine-deficient states and goitres have been known to be a risk factor in thyroid malignancy, we could speculate that iodine deficiency is a risk factor in cancer development. This equation is not straight-forward. It cannot be assumed that iodine deficiency alone is a risk factor for cancer development. In certain other iodine-deficient countries such as Poland and Belarus, the population were also exposed to nuclear radiation (Szybinski et al., 2003; Mahoney et al., 2004; Niedziela et al., 2004) In these countries, children who are chronically deficient in iodine are at greater risk to develop thyroid malignancies if they are further exposed to radiation. On the other hand, high thyroid cancer incidence is also reported in localities where there are no exposures to radiation (Larijani et al., 2003). Where there is no exposure to radiation, our series has demonstrated that thyroid cancer is high. In Iran, a country described as endemic for iodine deficiency, a high number of thyroid cancers was recorded in one year from 1998-1999 (Larijani et al., 2004). The excess relative risk of thyroid cancer was significantly associated with increasing thyroid radiation dose and was inversely associated with urinary iodine excretion levels (Shakhtarin et al., 2003). In those countries where iodine supplementation was given, the cancers are more of the differentiated type.

The population of Kelantan is in a state of chronic moderate iodine deficiency however they are not known to have exposure to radiation. The hospital-based incidence of colloid goitre seen in this study is high at 9.9 per 100,000 admitted patients and the hospital-based incidence of cancer is high at 3.5 per 100,000 admitted patients. Histopathological examination of the malignant thyroid tissues showed 59.5% of them had nodular hyperplasia implying that iodine deficiency could be a possible risk factor to thyroid malignancy in such setting. Such speculation is shared by Feldt-Rasmussen (2001). In our series except for 2 cases, those that had existing nodular hyperplasia were papillary carcinomas.

Kelantan is listed as one of the states in Malaysia having chronically moderate iodine deficiency. This study
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shows the most common thyroid disease seen at HUSM was multi-nodular goitre. Majority of thyroid cancers seen in this study had pre-existing nodular hyperplasia implying that prolonged goitre is a possible risk factor to thyroid malignancy in a backdrop of population with chronic iodine deficiency. To the best of our knowledge this is the first such study published from the north-eastern region of West Malaysia to the date of publication of this article.

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