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Research Article

Multi-Nodular Thyroid Goitre Over a 10-Year Period in Hospital Universiti Sains Malaysia; Is Iodine Deficiency Addressed Adequately in Kelantan, Malaysia?

*Nor Hayati Othman**

Department of Pathology, Universiti Sains Malaysia, Malaysia

Abstract

Background: This study was aimed to determine the trend and prevalence of this disease from 2006 to 2015.

Methods: The data of patients suffering from multinodular goitre from 2006 to 2015 was retrieved from the record office of Hospital Universiti Sains Malaysia (HUSM). The patients were mapped to the residential addresses classified under the ten districts of Kelantan to determine. Those with residential areas outside Kelantan were listed under 'Others'. The data were analysed using SPSS Statistics package version 17.

Results: A total of 589 cases of multinodular goitre were seen over this ten year period. Of these 492 (83.5%) were from Kelantan. The youngest was 14 and the oldest was 87. The mean age was 42 years old. Female to male ratio was 10:1. For those patients from Kelantan, majority were from the Kota Bharu 242/492 (49.2%) (p=0.00).

Conclusion: Multinodular goitre is still a prevalent disease in Kelantan. Iodine deficiency needs to be addressed. Thyroid cancer prevalence in iodine deficient areas is increasing in the world including the state of Kelantan in Malaysia. Intervention is inexpensive, by iodizing table salts.

Keywords: Multi-nodular goitre; Kelantan; Iodine deficiency; Trend 10 years; HUSM

Introduction

The incidence of clinical thyroid goitre is increasing globally [1]. It 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 (Figure 1) [2]. In Sarawak population living along the Ai River has one of the highest prevalence of goitre associated with iodine deficiency at a prevalence rate of 99.5% [3]. In Kelantan, the incidence of multi-nodular goitre is high at 31.4% in coastal/lowland areas to 45.0% in the inland areas [4]. The overall urinary iodine excretion is lower than normal at 57 µ/day regardless they live on high land or low land indicating these people are chronically iodine deficient [5]. Mean urinary iodine concentration was 3.36 microg/100 ml among children in Sarawak [6]. The mean urinary iodine excretion of non-goitre patients is 137.2 µg/l to 138.8 µg/l [7]. Urinary iodine excretions showed a significant increase after oral iodized oil intervention is effective in reducing thyroid size [8]. In nearly all countries, the best strategy to control iodine deficiency is iodization of table salts [9]. Iodized salt implementation significantly increased urinary iodine secretion in one aborigine's community in Malaysia [10].

Iodine is an essential trace element required for production of thyroid hormones which is important for normal brain and other organs development [11]. Iodine deficiency can lead to goitre and

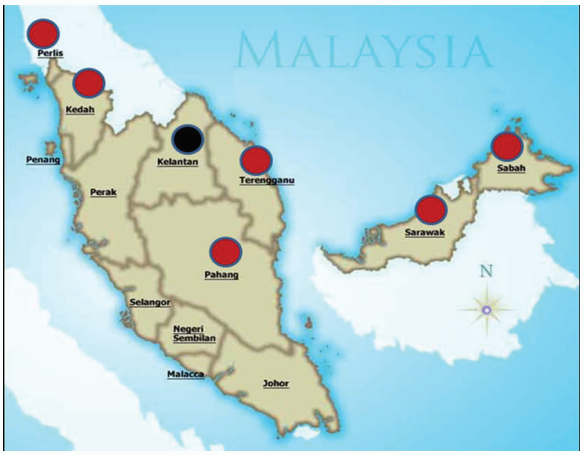

Figure 1: Map of Malaysia indicating states with high incidence of goiter (red and black circles). The black circle indicates the state which has the highest prevalence.

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***Corresponding author:** Nor Hayati Othman, Department of Pathology, Universiti Sains Malaysia, 16150 Kubang Kerian, Kelantan, Malaysia, Tel: +609 7676948/+60123232091; Fax: +609 7672351; E-mail: hayatikb@usm.my

myriad other medical disorders [12]. The mechanism by which the thyroid gland adapts to an insufficient iodine supply is to increase the trapping of iodide as well as the subsequent steps of the intrathyroidal metabolism of iodine leading to preferential synthesis and secretion of triiodothyronine (T_3) [13]. On histology, the thyroid tissue changes are nodules of thyroid epithelium hyperplasia due to stimulation by TSH (Thyroid stimulating hormone) while in other areas there are large thyroid follicles containing colloid. Over years some of these large colloid-filled follicles would rupture leading to haemorrhage. Haemorrhage incites acute and later chronic inflammatory response. Healing is seen and bands of fibrous tissue are seen scattered throughout the glands. The flowchart of how goitre develops is depicted in Figure 2. The gross appearance is irregular nodules of enlarged thyroid glands termed multi-nodular goitre. Continued increased secretion of TSH over years is ultimately responsible for the development of goitre [13].

We have earlier conducted an eleven year study (from 1994-2004) study on the spectrum of thyroid lesions seen in Kelantan [2]. This current study is done as follow-up to previous study, to determine the trend of goitre seen in Hospital Universiti Sains (HUSM) from 2006 to 2015 and mapped them against the residential addresses to determine which communities which are most affected.

Methodology

Registry of patients diagnosed with multinodular from year 2006 to 2015 were obtained from the medical record office of Hospital Universiti Sains Malaysia (HUSM). The data was carefully scrutinized to delete duplicate or more entry in the list. Variables extracted for each year were diagnosis, age, gender, district where the patients come from (residential addresses) and concomitant diseases such as diabetes mellitus, cancer and other diseases if present. The district names are Kota Bharu, Bachok, Gua Musang, Jeli, Kuala Krai, Machang, Pasir Mas, Pasir Puteh, Tanah Merah and Tumpat according to the geographical/administrial divisions of the state. From these data, the frequency of the goitre was mapped to geographic locations. Those who have residential addresses outside Kelantan were listed under 'Others'.

The data were analysed using IBM SPSS statistics version 17 for Windows. The level of significance was set at $p<0.05$.

Results

General results

There were a total of 589 patients clinically diagnosed as goitre observed in the 10 year period between 2006 to 2015 of which 557/589 (94.6%) were Malays, 29/589 (4.9%) were Chinese and 3/589 (0.5%) from other races. The trend of this disease is displayed in Figure 3. There were 492/589 (83.5%) patients whose residential addresses were from Kelantan while the rest were from out of Kelantan state. Those whose residential addresses were in Kelantan, majority of them were from Kota Bharu; 242/492 (49.2%) ($p<0.05$) (Figure 4). There were only 45 males and the female to male ratio is 10:1. The age range was from 14 to 87 years and the mean age was 42.34 (16.435) years (Figure 5). Fifteen of the patients (2.6%) have died; due to diabetes 4/589 (0.7%), hypertension 2/589 (0.3%) and other causes 9/589 (1.5%) (Table 1).

Discussion

This study shows multi-nodular goitre due to iodine deficiency is still high. In the study from the same hospital covering 1994 to 2004, it was highlighted that the iodine deficiency needs to be addressed [2]. The overall proportion of the households in Malaysia using adequately iodised salt as recommended by Malaysian Food Act 1983 of 20 ppm to 30 ppm is only 6.8% (95% CI: 5.1, 9.0) [14]. Almost half of the states in Peninsular Malaysia still have large proportion of urinary iodine level <100 µg/L [14]. Iodine deficiency causes goitre. If the iodine supply to the thyroid is only moderately low, the gland may compensate by a number of mechanisms to maintain sufficient thyroid hormone production. Over years, this compensation may lead to nodular hyperplasia leading to multinodular goitre (MNG) (Figure 1) [15]. Seventy-five percent of people with goitre live in less developed countries where iodine deficiency is prevalent [16].

MNG remains as one disease of interest in the state of Kelantan as it is fairly common. We did similar study from 1994 to 2004 and during those periods there were a total of 1,068 MNG cases from Hospital

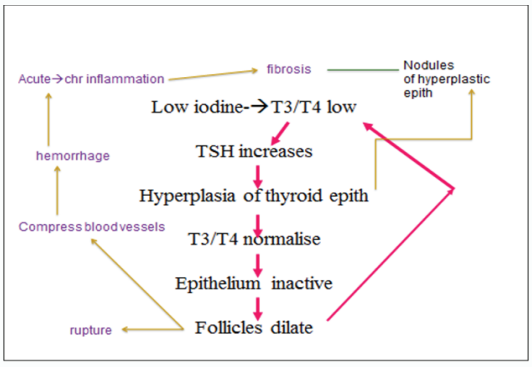

Figure 2: The flowchart showing how multi-nodular goitre develops after prolonged iodine insufficiency. Legends: T3: triiodotyronine, T4: thyroixine. TSH: thyroid Stimulating Hormone. Chr: Chronic, epith: epithelium.

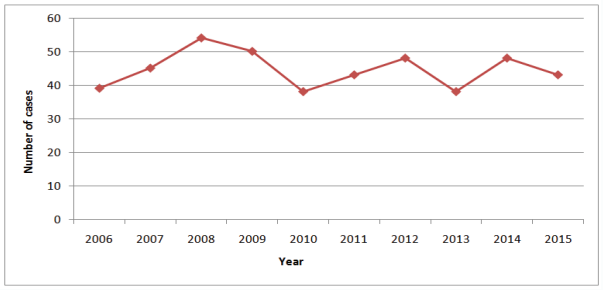

Figure 3: The number of multi-nodular goitre cases seen in Hospital Universiti Sains Malaysia from 2006 to 2015.

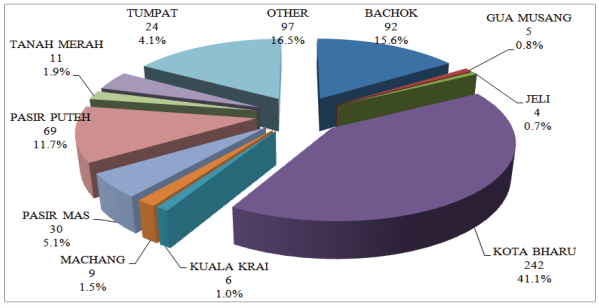

Figure 4: The proportion of goitre seen in Hospital Universiti Sains Malaysia from 2006 to 2015 according to districts of Kelantan. 'Others' is for patients who reside out of Kelantan.

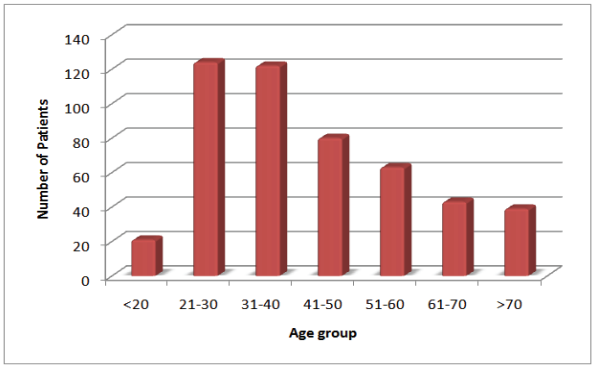

Figure 5: The number of goitre case seen in Hospital Universiti Sains Malaysia from 2006 to by age groups.

Table 1: The number of multi-nodular goitre cases with other diseases seen in Hospital Universiti Sains Malaysia from 2006 to 2015.

Diagnosis	Frequency (%)
Multinodular goitre only	443 (75.2%)
Multinodular goitre with non-thyroid cancer	11 (1.9%)
Multinodular Goitre with diabetes mellitus	132 (22.4%)
Multinodular goitre with other diseases	3 (0.5%)

Universiti Sains Malaysia [2], average about 97 cases annually. In this current study covering 2006 to 2015 we recorded a total of 589 or about 60 cases annually. The number seems to decrease but the trend appears to plateau however the frequency is still considered high. The other explanation on lower number of MNG cases seen now is probably not truly reflecting a true decline. Most patients with goitre are asymptomatic other than cosmetic complaints. They will seek treatment once compression or other symptoms manifest. Furthermore unlike thyroid cancers which get referred to referral hospitals like Hospital Universiti Sains Malaysia (HUSM), cases of mild to moderate goitre may be seen in Hospital Kota Bharu or other peripheral hospitals.

Animal experiments have demonstrated a clear increase in incidence of thyroid epithelial cell cancers after prolonged iodine deficiency [17]. We have also observed increasing number of thyroid cancer secondary to iodine deficiency in our institution over the years [15].

The female to male ratio our patients in this study are 10:1. This is much higher than seen in other endemic countries [18-20]. Women are at higher risk of becoming iodine deficient due to higher needs in pregnancy. Kelantan women in general are multiparous thus requiring higher level of iodine in nutrition [21]. Improvement in iodine status of the population results in lowering of goitre size [22]. The situation in Kelantan is akin what is seen in India where prevalence of goitre is high among females due to continued demand for pregnancy and childbirth [23]. Iodine supplementation has been shown to increase urinary iodine excretion indicating positive response to interventional treatment [24]. After seven years of instituting iodized salt in the community with moderately iodine deficient the urinary iodine secretion becomes normal and goitres regress [24]. The optimal level of iodine intake to prevent thyroid disease may be around the recommended daily iodine intake of 150 µg [25].

In this study, we saw majority of patients were from Kota Bharu district (41.2%) which is considered lowland in Kelantan thus expected to be of lesser iodine deficient compared to those from highlands such as from districts of Gua Musang, Kuala Krai or Jeli. There is inverse relationship between urinary iodine excretion and thyroid volume, meaning the lower the urinary excretion of iodine, the bigger the size of the goitre [26]. In Europe, goitre occurs when the urinary iodine is below 10 µg/dl [26]. There are also studies where researchers have found discrepancy in thyroid volume measured by ultrasound (size of goitre) and the corresponding level of iodine excretion in the urine [27].

Iodine deficiency is also associated with poor socio-economic status. According to Department of Statistics Malaysia, the socio-economic status of Kelantan is lowest at 42.4%. Iodized salts are more expensive than commonly used rock salts. The addition of iodine to table salts or iodine supplementation has greatly eliminated the problem of iodine deficiency [28]. In Malaysia, prenatal mothers are given iodized salts to be taken till they deliver however the treatment is not carried out once the women deliver the babies.

There are other causes of goitre [29]. Excessive intake of cassava and goitrogen-containing plants such as cabbage and rapeseeds can contribute to goitre [30]. Consumption of cassava conferred a four-fold risk of developing goitres among the aboriginal children in Ulu Langat, Selangor [31]. In countries that are iodine-deficient, avoidance of ingestion excessive goitrogens is a fair advice.

Iodine deficiency needs to be addressed as there are a myriad of clinical disorders related to it [32]. There is increasing evidence that chronic iodine deficiency may lead to cancer [19]. "Cold" thyroid nodules are 2.5 times more frequent in patients coming from iodine deficient areas compared to control [33]. Follicular and anaplastic carcinomas are the cancers commonly associated, at three times more frequent than control [33].

Conclusion

Multinodular goitre is still a prevalent disease in Kelantan. Iodine deficiency needs to be addressed. Pregnant mothers are given iodized salts but treatment stops after the mothers deliver the babies. Thyroid cancer prevalence in iodine deficient areas is increasing in the world including in the state of Kelantan in Malaysia. Intervention by iodizing table salts is inexpensive.

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