Int. j. pathol 2014; 12(2): 59-62

Original Article

Size and Duration of Multinodular Goiter Predicts Its Toxicity

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Abstract

Objective: To evaluate the status of thyroid function in large multinodular goiters of more than 20 years duration.
Study design: Prospective, observational study
Place and duration of study: Department of Medicine Abbas Institute of Medical Sciences (AIMS) Muzaffarabad. The study included data from Jan 2011 to Dec 2012.
Materials and Methods: Patients with large multinodular goiters (MNG) of more than 20 years duration were evaluated for status of thyroid function. Operational definitions as large and moderate size goiters were described. 47 patients, who had large or moderate size goiter for more than 20 years, fulfilled the inclusion criteria for this study. These were evaluated for status of thyroid function.
Results: 96% of patients with large or moderate size goiter of more than 20 years were hyperthyroid.
Conclusion: A large goiter of more than 20 years duration should be investigated and managed with the suspicion of thyrotoxicosis.
Keywords: Goiter, Multinodular Goiter, Toxic Goiter, Iodine deficiency, Thyroid stimulating hormone.

Introduction

A multi-nodular goiter is enlarged thyroid gland that contains multiple thyroid nodules of various sizes.[1] The Iodine deficiency is associated with occurrence of endemic goiter in certain geographic regions of subcontinent, China, Central regions of Asia and Africa.[2] The normal thyroid gland in healthy adults weighs 10-25 Grams.[3] In the absence of Iodine there is inadequate production of thyroid hormones. It leads to activation of normal endocrine positive feedback mechanism in the pituitary thyroid axis. There is increased release of Thyroid Stimulating Hormone (TSH) from the pituitary gland to compensate the decreased production of T3 and T4 from thyroid gland. Thyrotropin (TSH) stimulates thyroid growth and thyroid hyperplasia attempts to maintain homeostasis and a euthyroid state in the body.[4] Thus, goiter develops in a compensatory response to Iodine deficiency. This goiter is initially small and diffuse but due to asymmetrical growth of various follicles it becomes multinodular over time.[5] In the presence of Iodine deficiency and continued stimulation by TSH some nodules become autonomous. These autonomous nodules are independent of TSH stimulation and can cause thyrotoxicosis especially if Iodine deficiency is not severe.[6]

Iodine deficiency is well known in the region of Himalayan Mountains in subcontinent.[7] This highest mountain system on the earth extends 1,600-miles in an ellipse across southern Asia from the bend of the Indus River in the northwest to the Brahmaputra in the east. The Himalayan system, averaging 200 to 250 miles in width, separates northern Pakistan and India from the plateau of Tibet, in China.[8] There are parallel lower ranges besides the Greater Himalayas reaching two to three thousand meters known as the lower Himalayan. Azad Kashmir is in the north of Pakistan in the lower Himalayan region.[9]

Goiter is endemic in this area. As it is asymptomatic patients do not seek early medical advice and large goiters are observed in clinical practice. This study was based on the clinical observation that large and chronic goiters of more than 20 years tend to become toxic. This study was possible in this area due to endemic nature of the condition, perception

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of goiter not as a disease and fear of neck surgery especially in females.

Materials and Methods

Functional definitions: Large Goitre: A large goitre is defined as multinodular thyroid swelling protruding out of neck up to the chin of the patient or prominent swelling protruding out and hanging down over the sternal notch and upper end of sternum.

Moderate size goiter: It was defined as multinodular thyroid swelling covering front and sides of the neck and protruding out up to the level of chin.

Non probability consecutive sampling method was used for selection of patients.

Inclusion criteria: Patients with large or moderate size goiters of more than 20 years duration were included in this study.

Large Goiter

Moderate Goiter

Exclusion criteria: Patients who were not meeting the criterion for functional definition of a large or moderate size goiter and thyroid swelling of less than 20 years duration were excluded from the study.

Patients with large multinodular goiters of more than 20 years duration were evaluated in the department of medicine of AIMS. A specially designed study Performa was used for this study.

A detailed account of history was taken from the patient. The duration of goiter was determined as accurately as possible. This was assisted by close family members often by the spouse or children.

A visual description of thyroid was recorded and goiter was measured in maximum horizontal and vertical dimensions. A detailed physical examination was performed which also included clinical evaluation for thyrotoxicosis.

Thyroid function was assessed by combination of TSH and T_3 or TSH, T_3 and T_4. The other investigations included were Blood complete examination, Blood sugar, urea, Creatinine, lipid profile, urine routine examination, chest radiograph and ECG. Further evaluation of patients was based on the presence of co morbid conditions as dictated by the clinical condition of the patient.

Results

A total number of 47 patients fulfilled the inclusion criterion of large Multinodular goiter (Table-1). 45 patients (96%) were found hyperthyroid while only two patients (4%) were euthyroid (Table-2). No patient was hypothyroid with large or moderate size MNG. The majority of patients 45 (96%) were female (Table-3). The number of male patients was two (4%).

Table 1. Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Duration	47	20.00	40.00	27.0426	6.90922
Age	47	37.00	70.00	54.7447	6.98591
TSH	47	.00	1.44	.0741	.24053
T3	47	1.04	27.60	4.6909	4.90534
T4	20	5.50	43.20	14.9345	10.40773
Valid N (list wise)	20				

Table 2. Status of Thyroid Function

Thyroid Function	Frequency	Percent
Hyperthyroid	45	95.7
Euthyroid	2	4.3
Total	47	100.0

Table 3. Gender distribution

Gender	Frequency	Percent
Male	2	4.3
Female	45	95.7
Total	47	100.0

The maximum duration of goiter in this study was 40 years while the minimum period was 20 years. The average duration of goiter was twenty seven years (Table-1). The large

goiter was found in 45% of patients while it was of moderate size in 55% on the basis of functional definition of goiter (Table-4).

Table 4. Size of Multinodular Goiter

Size on MNG	Frequency	Percent
Large	21	44.7
Moderate	26	55.3
Total	47	100.0

No patient had previous evaluation for thyroid status. None of these patients had eye signs (lid lag, lid retraction and exophthalmos) of thyrotoxicosis. Atrial fibrillation was found in majority of patients (76%).

The evaluation of thyroid function showed marked suppression of TSH (< 0.004 IU/ml) in these patients. The level of T3 was above its normal limits and its value was modestly high. It was less than two fold higher than the upper limit of normal in majority of cases.

Discussion

Multinodular goiter is endemic in the sub Himalayan Mountains of subcontinent. It is well established fact that toxic Multinodular goiters are found in elderly patients and are extremely rare before 40 years of age.[10] However, there is no established relationship between duration and size of MNG and development of its toxicity. In this study we examined the clinical behavior of large and moderate size goiters of more than 20 years duration.[11] This study was possible in this area due to endemic nature of condition and attitude of population towards this disease. The female population considers neck surgery as dangerous and is reluctant for thyroid surgery. They normally cover their neck with clothes (Dopatta) or with some ornaments so they have little cosmetic reasons to seek advice. In the absence of any symptoms or discomfort these goiters gradually increase in size over several years. Here we encounter with huge goiters in patients coming to hospitals for co morbid conditions and no complaints of thyroid. They successfully hide large MNGs as they go unnoticed on superficial observation. This study was possible due to all these social and personal factors and endemic nature of disease in this part of the world.

We found that predominant large majority were female patients. The other significant finding was tendency of MNG to become toxic after 20 years. In fact the actual duration of goiter is more than this period. This is the time of noticeable presence of almost this size of goiter. We found that 96% of moderate and large size goiters according to our functional classification are toxic after 20 years. The mean duration of goiter in our study was 27 years.

Rieu M and colleagues found 75% prevalence of subclinical hyperthyroidism in Multinodular goiters. This high prevalence was found in patients presenting with non toxic multinodular goiters with normal base line thyroid function tests.[12]

Multinodular goiter progressively increases in size over several years and in the due course of time thyroid function may progress from TSH dependent condition to autonomy and then overt thyrotoxicosis.[13] The pathogenesis at molecular level leading to ultimate autonomy of increased functioning tissues has not yet been fully understood in MNG. It is believed to be TSH receptor mutations in hyper functioning nodules of Multinodular goiter. There are increased chances of these mutations in large MNGs if they persist for several years.[14]

There is a linear relationship between the size and duration of the goiter as large MNGs gradually increase in size over several years. However, converse relationship does not exist as prolong duration may only result in small goiters. There is no reported study in our knowledge to explore the size and duration of MNG with its toxicity. In this small study we found a very convincing evidence of this relationship. A large goiter of more than 20 years duration becomes toxic in 96% of cases. 4% of large goiters of more than 20 years duration (average duration 27 years) remain euthyroid.

Importance of study: The presence of this size of large goiters is negligible in developed world and in areas with availability of good health care services. However, a large majority of world's population in Asia and Africa is still deprived of basic health care services. This study will help to provide guidelines for primary health care physicians in endemic areas of Multinodular goiter. A large goiter of more than 20 years duration should be investigated and managed with the suspicion of toxicity.

Limitation of study: It was a small study in endemic area. The exact underlying pathophysiology of toxic transformation of MNG is still not fully understood. There are several factors contributing to it along with size and duration of the goiter. This finding needs to be confirmed in a larger study.

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