

Biochemical Status and Cytopathological Profile of Patients Presenting with Multinodular Goiter

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Abstract:

Background: Objective of the study was to evaluate the biochemical status and cytopathological profile in multinodular goiter.

Materials and Methods: 50 patients with multinodular goiter were selected consecutively. Multinodularity was confirmed by ultrasonography and scintiscan of the thyroid gland. Hormonal assays of serum T_3 , T_4 and TSH was done for biochemical status evaluation. Fine needle aspiration cytology (FNAC) was done to evaluate the cytopathological profile of the MNG patients.

Results: The patients had a female preponderance with a male to ratio of 5.25:1. Biochemical status evaluation revealed that sixty percent presented with euthyroid features followed by those of hyperthyroidism (16%). The distribution of hypothyroid, subclinical hypo- and hyper- thyroid patients were equal (8% each). Among the clinical and subclinical hyperthyroids there was Jod Basedow. The cytological profile of multinodular goiter showed that two were malignant (found by open biopsy after surgery) and four had suspicious cytology.

Conclusion: Though relatively benign, risk of malignancy in multinodular goiter should not be undermined and FNAC should be included in the initial diagnostic procedures during work up of a multinodular goiter.

Keyword: Multinodular goiter, Hyperthyroidism, Hypothyroidism, Malignancy, FNAC, Scintigram

Introduction:

Goiter is one of the commonest presentations of thyroid disorders in Bangladesh. Prevalence of goiter has been 4-10% of the general population upon neck examination and upto 50% of autopsy cases. ¹Biosynthetic defects, iodine deficiency, autoimmune diseases and nodular diseases can each lead to goiter through different mechanisms. Depending on the population studied, MNG occurs in up to 12% of adults. ² MNG is more common in women than men and increases in prevalence with age. The incidence of goiter in women is 1.2-4.3 times as great as that in men. ³

It is more common in iodine-deficient regions but also occurs in regions of iodine sufficiency, reflecting multiple genetic, autoimmune, and environmental influences on the pathogenesis. In a multinodular goiter, nodules grow at varying rates and secrete thyroid hormone 'autonomously', thereby suppressing TSH-dependent growth and function in the rest of the gland. Ultimately, complete suppression of TSH occurs in about 25% of cases, with T_4 and T_3 levels often within the normal range (subclinical thyrotoxicosis) but sometimes elevated (toxic multinodular goitre). ⁴ Opinions differ as to whether the nodules represent multiple adenomas or focal hyperplasia. Therefore multinodular goiter patients are usually diagnosed with thyrotoxic features or

with features of compression of surrounding structures. The incidence of occult malignancy in multinodular goiter varies from 4 to 17 percent. ⁵ In accordance with published works, the histopathological type of carcinoma more frequently associated to MNG was shown to be the papillary (62.5%). ⁶ Malignancy was significantly commoner in females with simple nodular goiter than those with multinodular goiter and generally occurred at a significantly older age. ⁷

Materials and Methods:

Fifty (50) patients presenting with clinically apparent multinodular goiter, irrespective of their biochemical thyroid status, were included in this study. Multinodular goiter was confirmed by ultrasonography and scintiscan ("hot" or "cold" or irregular patchy concentration) of thyroid gland. In all cases, serum T_3 , T_4 and TSH was done to evaluate the biochemical status and FNAC was done to identify malignant or suspicious malignant cases. Detailed history was recorded with special attention to age, sex, residence, symptoms with durations, drug history, history of irradiation and history of goitrogen intake. Thorough physical examination including meticulous examination of thyroid gland, cervical lymph nodes, eyes for other signs of thyroid disorder and neurological examinations were done to reach the diagnosis. Clinically thyroid status was evaluated.

A structural questionnaire was filled up for each patient after taking informed consent. Results and observations were tabulated and studied.

Laboratory methods:

Serum T₃, T₄ and TSH estimation: The serum T₃, T₄ and TSH were measured by highly specific radioimmunoassay method. The normal ranges of these hormones in our laboratory is 60-150 nmol/L for serum T₄, 1-3 nmol/L for serum T₃ and 0.5-5.0 mIU/L for TSH.

FNAC: FNAC was done from the nodules directly and sent for cytopathology.

Results

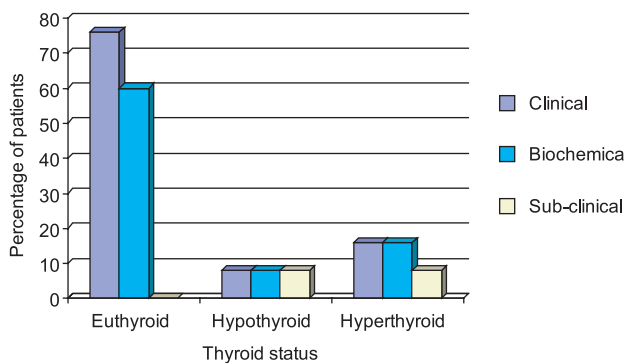
A total number of 50 cases of multinodular goiter were studied in this series. The ages at presentation ranged from 11 to 70 years. The majority (52%) of them were between 30 and 49 years. Out of 50 cases, 42 were females with a female to male ratio of 5.25:1

Table-I

Duration of goiters in patients with multinodular goiter in the context of various thyroid status and conditions

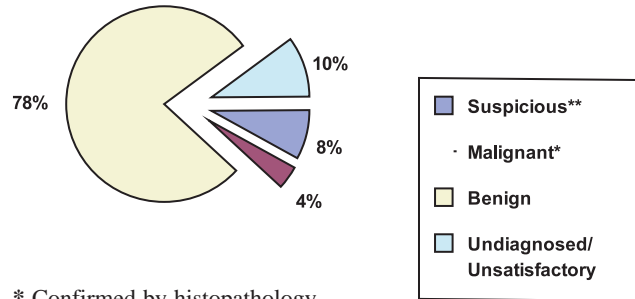
Thyroid status/ condition	Duration in years
Euthyroid	9.5 ± 9.8
Hypothyroid	3.4 ± 3.9
Hyperthyroid	4.38 ± 8.1
Malignant	2.16 ± 1.83
Suspicious	1.9 ± 2.43

The malignant and suspicious (according to cytopathology) cases had the mean duration at presentation of about 2 years (SD ± 2 years). The hypothyroid and hyperthyroid cases fall in between the two groups mentioned- the hypothyroids presented earlier than the hyperthyroids (Table-I).



* One of them was Jod-Basedow
 ** Two of them were Jod-Basedow

Fig.-1: Clinical and biochemical status of MNG patients (n=50)



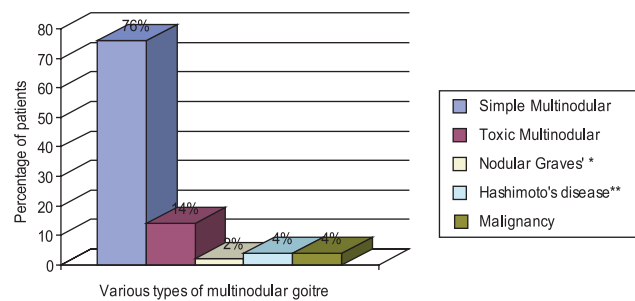
* Confirmed by histopathology
 ** Report as follicular cells and some atypical cells

Fig.-2: Cytopathological evaluation of MNG (n=50) by FNAC

Figure 1 represents comparison between clinical and hormonal profile. Here study of hormonal status revealed that thirty eight (76%) of patients of the studied series were clinically euthyroid but 30 (60%) of them were biochemically euthyroid. Eight patients (16%) were both clinically and biochemically hyperthyroid while the rest four (8%) patients were clinically and biochemically hypothyroid. Of the eight patients who were clinically euthyroid but biochemically not, four (8%) were subclinical hypothyroid while the rest four (8%) were subclinical hyperthyroid. Two of the subclinical hyperthyroid and one of the hyperthyroid patients had the history of excessive intake of iodide followed by development of hyperthyroidism (at least biochemically) and thus belonged to Jod-Basedow.

The majority of the multinodular goiters had benign cytology (88%). Two cases (4%) had malignant cytology. Four cases (8%) had suspicious cytology having some atypical cells while those cases which were undiagnosed or unsatisfactory at first FNAC became ultimately proved to be of benign nature (Fig.-2).

Considering the biochemical and cytopathological nature, goiters were classified into 5 types- simple multinodular, toxic multinodular, nodular Graves', Hashimoto's disease and



* Of the eight toxic multinodular goiters, one was a case of "nodular Graves' disease"
 ** Both of them were clinically and biochemically hypothyroid

Fig.-3: Different types of MNG (n=50)

cancer. In this study, the majority (76%) of patients were of simple multinodular while the minority (2%) was of nodular Graves' (Fig.-3) which was included in toxic multinodular goiter. Of the four cases of suspicious cytology (Fig.-2) mentioned earlier, two belonged to simple multinodular while the nodular Graves' and one of the Hashimoto's disease were the other two.

Discussion:

All the 50 cases of multinodular goiter studied in this series were selected from a thyroid clinic of a tertiary referral centre where patients of different thyroid disorders are referred from all parts of Bangladesh. The age incidence of the population ranged from 11 to 70 years- the majority being in the 4th and 5th decades of life. Since the natural history goes like that the iodine deficiency related disorders gradually evolve from simple diffuse goiter and toxic solitary nodule through simple multinodular goiter to toxic multinodular goiter, it is natural that patients of multinodular goiter will present in their late decades of life. The age incidence of multinodular goiter found in this series conforms to those found by Alam et al.⁸ Frequency of multinodular goiter declined after fifth decade. In several other studies, the frequency of nodular goiter increases with age and they are usually observed among adults and elderly subjects, but in severe endemic areas goiter may be found in preadolescents. In these studies, solitary thyroid nodule and multinodular goiter were not considered separately.⁹

Female to male ratio of 5.25:1 conforms well to other studies and also with that of simple goiter since multinodular goiter derived from simple goiter having the same female to male ratio.^{10, 11}

Majority of patients had been aware of goiter for many years and the long duration of euthyroid multinodular goiter at presentation was due to their asymptomatic nature of illness. This reasoning is further strengthened by the earlier presentation by patients of toxic or hypothyroid multinodular goiter as they were symptomatic (Table-I). This delayed presentation of multinodular goiter (the majority being euthyroid multinodular) conforms to other studies.^{4, 8, 10, 12}

Cytopathological evaluation of nodules of multinodular goiter by FNAC revealed that 4% of cases are malignant which conforms well to the fact that more than 60 percent of aspirates are benign, 5% are malignant and the remainder is in the suspicious or indeterminate group.¹³ The incidence of malignant disease in series in which all patients with suspicious lesions underwent operation ranged from 15 to 40 percent.¹³ No effective method has been found to evaluate lesions that are suspicious or indeterminate according to

FNAC. Large needle biopsy and cutting needle biopsy yield results and have accuracy rates that are similar to those of FNAC, but they have more side effects.¹⁴

Conclusion:

Multinodular goiter, one of the iodine deficiency related disorders, is an important health hazard of the iodine deficient parts of the world such as Bangladesh. Multinodular goiter is usually euthyroid, presents in elderly patients with a predilection for females.

Patients with multinodular goiter have a significant chance of developing thyroidal malignancy contrary to the general belief that malignant change in multinodular goiter is very very rare. Therefore, FNAC should be included in the initial diagnostic procedures for evaluation of all clinically suspected multinodular goiters.

Conflict of Interest: None

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