A CLINICAL, BIO-PATHOLOGICAL STUDY OF MULTINODULAR GOITRE IN REWA REGION, MADHYA PRADESH

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ABSTRACT

BACKGROUND
Multinodular goitre is the most prevalent thyroid gland biochemical change and pathology. Multinodular goitre is a condition with various clinical presentations. Although, the majority are benign, the incidence of occult malignancy in multinodular goitre varies from 1.2% to 16.66%. Accurate preoperative diagnosis of malignancy is therefore very important for appropriate management of the patient with multinodular goitre.

MATERIALS AND METHODS
This is a descriptive study of 23 patients attended in outpatient department and inpatient department with multinodular thyroid swelling from July 2015 to February 2016 at the Otorhinolaryngology Department, Gandhi Memorial and Sanjay Gandhi Memorial Hospitals, Shyam Shah Medical College, Rewa (MP). After registration of patients, a detailed history was taken and thorough clinical examination was carried out, which was entered in the proforma. All the patients underwent routine investigations, thyroid profile, x-ray and FNAC. Multinodular goitre specimen were sent for histopathological examination (HPE). 15 age and sex matched healthy control group were compared for thyroid profile.

RESULTS
23 patients were selected for our descriptive study. Mean age for benign lesion was 39.5 years and for the malignant lesion was 33.5 years. Two peak incidences for malignant lesions were noted. Greater peaks for age groups are between 21-30 years with 50% of all cases of malignancy. Female-to-male ratio for malignancy was 0.8:1. The average duration of symptom for malignancy was 2.46 years and for benign was 4.38 years. There was one false positive and one false negative FNAC result. Histopathology showed 8.69% patients had malignancy. Multinodular goitre (86.95%) was the most common diagnosis histopathologically among benign diseases. Papillary carcinoma was the most common malignant lesion. The overall sensitivity of fine needle aspiration cytology in multinodular goitre in our study was 80%. Thus, FNAC and thyroid profile are very good diagnostic tools preoperatively.

CONCLUSION
Multinodular goitre is the commonest thyroid disease in Rewa (MP), more common in males with chief complaints of symptomless swelling in front of the neck. The malignancy rates were slightly higher in males compared to females. 86.95% of the multinodular goitre were benign and 8.69% were malignant. Papillary carcinoma was the most common malignancy. FNAC and thyroid profile are a very good diagnostic tool for detection of multinodular goitre preoperatively.

KEYWORDS
Multinodular Goitre; Fine Needle Aspiration Cytology; Thyroid Profile and Thyrotoxicosis.


BACKGROUND
The thyroid gland is a bilobed structure situated in the lower anterior neck. It has two endocrine functions: secretion of thyroid hormones namely thyroxine (T4) and triiodothyronine (T3) from follicular cells and calcitonin from parafollicular or C cells. The thyroid hormones ensure the metabolic demands of the tissues of the body. They are also essential for normal growth and maturation at cell level. Calcitonin is released rapidly in response to elevated levels of circulating calcium ensuring levels do not fluctuate wildly and thereby helping prevent hypo and hypercalcaemia. Enlargement of the thyroid gland is the most common manifestation of the thyroid disease. The enlargement may be either generalised or localised, which again may be toxic or non-toxic. Nodular goitre occurs both endemically, mainly related to iodine deficiency when goitre prevalence in every age group within a population is more than 5% and sporadically when this number is 5% or less. Goitre is very common in many parts of the world and was recognised long before the thyroid gland itself. Goitre was recognised by Chinese and Europeans living in Alps since BC. Chinese seem to have used burnt sponge and seaweed for its treatment since 1600 BC. In the Indian “Ayurvedic” medicine, it came into existence in 1400 BC and lasted until 400 AD. Goitres are mentioned by the designation “gala-ganda” and are described in detail. Diseases of thyroid gland, especially multinodular goitre due to deficiency of iodine is prevalent in India. India has the world’s biggest goitre belt in

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the Sub-Himalayan region with nearly 55 million cases are estimated to be suffering from endemic goitre. Currently, no less than 140 million people are estimated to be living in goitre endemic regions of the country.\(^5\)

Multinodular goitre is the most prevalent thyroid pathology characterised by unilateral or bilateral thyroid growth with morphologically and/or functionally transformed follicles. Diseases of thyroid gland, especially multinodular goitre due to deficiency of iodine are prevalent in India. Multinodular goitre occurs up to 13 percent of adults depending upon the population studied.\(^6\) Nodular goitres are more common in men than in women and the nodularity increases with increasing age. Thyroid nodules can be detected by palpation in 8 percent of men and 2 percent of women. Multinodular goitre is a condition with various clinical presentations. The manifestation varies from a simple symptom like swelling to compressive symptoms like dysphagia and dyspnoea. The treatment for multinodular goitre varies in accordance to the clinical manifestation of the disease. Thus, it is necessary to understand the various manifestations of the disease and to treat it accordingly. The evaluation and management of patients with multinodular goitre represents a much more difficult problem in the clinical setting than solitary nodule. Neither a well-formulated nor a simple procedure is available for the management of multinodular goitre. Although, the majorities are benign the incidence of occult malignancy in multinodular goitre varies from 4 to 17 percent.\(^6\)

The first reliable description of successful thyroidectomy dates back to the tenth century when Albucasis under opium sedation removed a large goitre of a man who was seated with a bag around his neck to catch the blood.\(^7\) The leading thyroid surgeons at the second half of the nineteenth century were Theodor Kocher (1841 - 1917) of Bern, a scholarly and meticulous surgeon and Theodor Billroth (1829 - 1894) of Vienna, a great extrovert and fast operator. Both European Surgeons performed thousands of thyroidectomies with progressively better results. At the turn of century, Thomas Dunhill Peel described near total thyroidectomy for thyrotoxicosis.\(^8\)

Multinodular goitre refers to an enlargement of the thyroid with deformation of the normal parenchymal structure by the presence of nodules. These nodules vary considerably in size, morphology and function. In areas without endemic goitre, it is often referred to as sporadic nontoxic goitre. Multinodular goitre usually develops in an already enlarged thyroid independent of the cause of hyperplasia. Sometimes for decades many multinodular goitres enlarge and some develop subclinical hyperthyroidism and subsequently present as toxic multinodular goitre.\(^9\)

FNAC and Bio-pathological analysis are used in association with clinical features, but there are drawbacks of each technique and the final answer to the problem is still elusive. The present study is undertaken to evaluate usefulness of clinical features, FNAC and Bio-pathological analysis in managing thyroid nodule.

**MATERIALS AND METHODS**

A descriptive study was done in Department of Otorhinolaryngology, Gandhi Memorial and Sanjay Gandhi Memorial Hospital, Rewa (MP). Written informed consent was taken from every patient before start of the study.

**Objectives of Study**

Our main objectives of study are to find out of multinodular goitre in Rewa region, Madhya Pradesh. Finding of FNAC diagnoses in multinodular goitre and also of serum thyroid profile variation when compared with normal healthy individuals.

The studies comprised of 23 patients who were selected from the outpatient and inpatient Department of Otorhinolaryngology after confirmation of multinodular goitre. The study was carried out for a period of eight months from July 2015 to February 2016.

**Inclusion Criteria**

Once the clinical diagnosis for multinodular goitre and pre-deposition factors were made after screening of various examinations such as thyroid profile, histopathology and FNAC, then patients undergo treatment and management.

**Exclusion Criteria**

1. Those patients who do not consent are excluded.
2. Patients below 05 years and above 70 years of age were excluded.
3. Pregnant patients were excluded.
4. Investigation of x-ray and USG were excluded and only used for confirmation of nodular area of thyroid.

All cases of multinodular goitre underwent through aspiration of sample with sterile needle to collect and send for histopathological microscopy. Blood samples were collected aseptically. Blood was allowed to clot; samples were centrifuged at 2000 rpm for 10 minutes at room temperature. Serum was separated and was stored at -20°C until the analysis to minimise non-specific variability of all parameters. The analysis of thyroid stimulating hormone (TSH), thyroxine T\(_4\) (T\(_4\)) and tri-iodothyronine T\(_3\) hormone (T\(_3\)) were done by using enzyme linked fluorescence assay (ELISA) technique. Then the patients were treated surgically and were followed up by medical treatment. All cases of multinodular goitre and predisposing factors were examined in detail and sent for radiographic examination; x-ray of the patients and USG. Data of thyroid profile in the text and tables were reported as the Mean ± SD. Comparison of thyroid profile among control subjects and subclinical hypothyroid patients were performed by the student’s t-test for unpaired data using the software SPSS version 16.

Later multinodular goitre treatment was started which was followed up for a minimum period of six months for observing clearance or recurrence of the disease. During this period, patients were advised to avoid bad habits such as smoking and alcohol drinking.
al examination and subjected to preoperative discussion and preparation. FNAC. This allows better investigation and wiser confirm the diagnosis of the thyr varous thyroid diseases. There is an increasing tendency to FNAC has been proven a very useful tool in diagnosis of Multinodular goitre is the most prevalent thyroid pathology. It presents with regarding a possible malignancy being extremely common. Multinodular goitre is the most prevalent thyroid pathology. It presents with various clinical features. Thyroid is an important and popular site for fine needle aspiration cytology. FNAC has been proven a very useful tool in diagnosis of various thyroid diseases. There is an increasing tendency to confirm the diagnosis of the thyroid cancer at first consultation by FNAC. This allows better investigation and wiser preoperative discussion and preparation.

DISCUSSION
Thyroid swelling is a common complaint presenting in the Otorhinolaryngology outpatient department with anxiety regarding a possible malignancy being extremely common. Multinodular goitre is the most prevalent thyroid pathology. It presents with various clinical features. Thyroid is an important and popular site for fine needle aspiration cytology. FNAC has been proven a very useful tool in diagnosis of various thyroid diseases. There is an increasing tendency to confirm the diagnosis of the thyroid cancer at first consultation by FNAC. This allows better investigation and wiser preoperative discussion and preparation.

RESULTS

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Type Multinodular Goitre</th>
<th>Our Study</th>
<th>Comparison of Multinodularity with other Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Benign disease</td>
<td>86.95</td>
<td>83.33, 90.5, 90.5, 64</td>
</tr>
<tr>
<td>2</td>
<td>Malignant</td>
<td>8.69</td>
<td>16.66, 12, 6</td>
</tr>
<tr>
<td>3</td>
<td>Suspicious</td>
<td>4.34</td>
<td>3.8, 6.7%, 12</td>
</tr>
<tr>
<td>4</td>
<td>Thyroid cyst</td>
<td>4</td>
<td>--, 1.2, --</td>
</tr>
<tr>
<td>5</td>
<td>Hyperplastic nodule</td>
<td>--</td>
<td>7.6, --</td>
</tr>
<tr>
<td>6</td>
<td>Haemorrhagic nodule</td>
<td>2</td>
<td>--, 1.2, --</td>
</tr>
<tr>
<td>7</td>
<td>Hashimoto’s</td>
<td>2</td>
<td>3.8, 5, 18.25</td>
</tr>
<tr>
<td>8</td>
<td>Follicular neoplasm</td>
<td>2</td>
<td>5.1, 15, 4.3</td>
</tr>
</tbody>
</table>

Table 1. Thyroid Swelling Percentages on the Basis of various FNAC Diagnoses and their Comparison with Other Authors

<table>
<thead>
<tr>
<th>Sl. No.</th>
<th>Thyroid Profile Parameters</th>
<th>Normal Healthy Persons (n=15)</th>
<th>Multinodular Goitre Patients (n=23)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Thyroid stimulating hormone (TSH: µIU/mL)</td>
<td>02.13-03.44</td>
<td>07.31-10.13</td>
<td>8.45±0.616</td>
</tr>
<tr>
<td>2</td>
<td>Thyroxine (T4: µg/dL)</td>
<td>06.13-10.02</td>
<td>0.91-04.80</td>
<td>2.54±0.99</td>
</tr>
<tr>
<td>3</td>
<td>Tri-iodothyronine (T3: ng/dL)</td>
<td>80-105</td>
<td>93.73±7.76</td>
<td>25-44</td>
</tr>
</tbody>
</table>

Table 2. Significance of various Thyroid Profile Parameters in Multinodular Goitre

Note: P<0.0001; extremely statistically significant.

In our study, twenty-three patients presenting with multinodularity of the thyroid gland without obvious clinical evidence of malignancy were studied and evaluated in terms of history, clinical examination and subjected to relevant investigations. The age ranged from 20 years to 63 years with an average of 38.66 ± 9.6 years. The most common age group having high multinodular goitre intensity was 31–40 years. This is in accordance with various studies mentioned below. According to study by Yaarubi et al on 136 patients with multinodular goitre, the mean age was 39 ± 13 years with an age range from 5 to 85 years.(13) According to Khalid et al, the mean age of presentation of multinodular goitre is 32.2 ± 11.58 years with a range of 13 to 90 years. In retrospective, consecutive analysis by Hee-Nee Pang and Chung-Ming Chen, the mean age of patients with nodular goitres was 48 years. Our study also falls within these limits. Our study showed 2 peak incidences for malignant lesions, a greater peak for age group between 21-30 years with 50% of all cases of malignancy. Another peak for the age group of 41-50 years was noted with 33.33% of all malignant cases. This was not statistically significant with our study.

It was observed in the current study, out of 23 cases 20 (86%) were males and 03 (14%) were females. The female-to-male ratio for malignancy was 0.8:1. In females, 88.37% of the multinodular goitres were benign in nature and 11.63% were malignant. In males, 85.72% of multinodular goitres were benign and 14.28% were malignant. Overall, 86.95% of all malignancies were found in both females and males. Thus, most of the multinodular goitres were benign irrespective of the sex. The malignancy rates were slightly higher in males as compared to females. There was no statistically significant difference between the two sexes in relation to malignancy. Study by Hee-Nee Pang and Chung-Ming Chen showed that 79.1% with nodular goitres were females. In the retrospective study by Gandolfi et al on 58 cases of multinodular goitre 08 (13.7%) cases were malignant, 05

Note: Needle tip placement (bright spot) in solid portion of nodule.

Figure 1. Ultrasound-Guided Fine Needle Aspiration of a Complex Nodule

Note: Needle tip placement (bright spot) in solid portion of nodule.

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The patients complained of pain or discomfort in the throat (19) and swelling. The majority of patients with benign disease had symptoms for 1 - 2 years (21). Thus, the study correlates with these values. Present study shows that the duration of symptoms before seeking medical attention varies from 15 days to 6 years. 10 (42%) patients had symptom for 1 year to 2 years. The mean duration of the symptom being 1 year (3.99%). Also 06 (27.27%) of the patients with benign thyroid disease had symptom for 1 - 2 years and 05 (20.45%) had symptoms for 2 - 5 years. Thus, majority of the patients with benign disease had symptoms for 1 - 5 years. An average duration of symptom for benign disease being 4.26 years. According to a study by Khalid et al, the average period before seeking help was 4 years. (14) Our study shows similar results.

In our study all 100% of patients presented with thyroid swelling, of which 36% did not have any symptoms other than swelling. Thus, most of the multinodular goitre presented as asymptomatic swelling. Also 32% had toxic symptoms and 18% of the patients complained of pain or discomfort in the neck. Pressure symptom like dysphagia were present in only 12% of the patients. Hypothyroid symptoms were present in all patients. Study by Hee-Nee Pang and Chung-Ming Chen showed that most of the multinodular goitres were asymptomatic. 6.7% complained of painful nodules, 6.0% patients noted hoarseness of voice and another 6.0% gave a history of dysphagia. (15) According to Khalid et al, dyspnoea was the most common symptom (20.5%) followed by thyrotoxic symptoms in 18.9%, dysphagia in 16.6%, pain in 8.2%, hypothyroid symptom in 6% and hoarseness in 5.2% of the patients. (14)

Subclinical hypothyroidism is the term used to describe patients with normally decreased thyroxine and triiodothyronine and raised thyroid stimulating hormone concentration who do not have symptoms. (16) Mild-to-modest elevations in patients with normal T4 and T3 levels indicate impaired thyroid hormone reserves and incipient hypothyroidism (subclinical hypothyroidism). Large population studies have suggested that the prevalence of subclinical hypothyroidism is much higher in women than men and increases with age. In the Whickham survey, TSH levels above 6 mIU/ L were approximately three times more common in females (7.5%) than in males (2.8%) and occurred more frequently in females over 45 years of age. TSH levels also showed a progressive increase with age in women, but not in men. (17) Progression to hypothyroidism was noted to be more common in those with initial TSH value greater than 10 mIU/ L and in those with positive anti-thyroid antibodies. (20) Huber et al found that basal TSH, thyroid reserve (increase in T4 and T3 after TRH stimulation) and the presence of antimicrosomal antibody are important prognostic factors for the development of overt hypothyroidism. (21)

Present study shows that in the duration of symptom before seeking medical attention, serum TSH increased significantly (8.455 ± 0.616 μIU/mL). Thyroxine (T4) and triiodothyronine (T3) were decreased significantly (2.544 ± 0.99 μg/dL) and (34.70 ± 5.72 ng/dL) respectively. The study is also not according to the findings of Ladenson et al, who have also considered TSH test as a criterion for the diagnosis of thyroid dysfunction, especially in cases of minimal thyroid failure (subclinical hypothyroidism). (22 - 23) The study has inconsistency with the findings of Evered et al have been investigated that in case of mild hypothyroidism serum TSH also have been observed high and the values of T3 and T4 have remained in normal range. Such studies would be helpful to understand the prevalence of diffuse goitre in different subjects and will also suggest the measures to minimise the goitre associated with its onset. (24) CONCLUSION

It can be concluded that multinodular goitre is the most common thyroid disease with a diverse aetiology. Multinodular thyroid disease is perhaps the commonest of all thyroid disorders in clinical practice worldwide. It is highly prevalent in iodine deficient areas and possibly has its inception in adolescence or puberty. Nodules larger than 1 cm may be detected by palpation. Genetic heterogeneity of normal follicular cells and acquisition of new inheritable qualities of replicating cells are the primary factors for nodular disease. The goitre may well give rise to local discomfort and may in case of large goitres cause mechanical obstruction of the upper airway. Progressive autonomous function of thyroid nodules can cause overt thyrotoxicosis in multinodular goitre patients. Even more frequently, patients develop subclinical thyrotoxicosis with its potential for osteoporosis and atrial fibrillation. Finally, thyroid cancer is present in approximately 86.95% of multinodular goitre patients, which is comparable to the risk in solitary thyroid nodules.

Management of multinodular goitre patients by clinicians is not uniform. Differences in the availability and cost of the various biochemical tests as well as the accessibility of the imaging methods and treatment options without doubt play a significant role in this setting. After serum TSH measurement, FNAC is the diagnostic test most often employed. Prevalence of diffuse goitre may be dependent on the extent of hormonal irregular functioning, specifically normal and abnormal thyroid stimulating hormone levels.

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