

**A study on clinical and histopathological evaluation of multinodular goitre.**

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**Abstract**

**Introduction:** Goiter is a nonspecific enlargement of the thyroid gland which is clinically or radiologically distinct from the surrounding thyroid gland. Thyroid nodules present either due to growth and fusion of localized colloid-filled thyroid follicles or as discrete adenomas or cysts. Thyroid nodules may be single or multiple and multinodular goiter (MNG) is characterized as a clinicopathological entity with an increase in the volume of the thyroid gland with the formation of nodules. FNAC or histological examination are required for final diagnosis by morphological and histological examination of the lesions, as other diagnostic techniques are reported to be less sensitive in diagnosing thyroid lesions. This study, therefore, compares the

clinical characteristics of patients with MNG in relation to the histopathological results and correlates different factors which interfere in the appropriate diagnosis and management.

**Aims and objectives:** To evaluate and compare the clinical characteristics and pathological features of multinodular goitre in relation to their histopathological results.

**Materials and methods:** This is a prospective observational study done from June 2021 to August 2022. All the patients with Multinodular goiter had undertaken a detailed clinical history and thorough clinical examination according to preset proforma. All the patients were investigated routinely and underwent a prior FNAC. These patients underwent surgery and the

excised thyroid specimen was sent for Histopathological examination. Patients were discharged after removing the sutures and were asked to come for follow-up.

### **Results**

**Age:** Most of the study participants in the present study were found to be in the age group of 41 – 50 years followed by 51 - 60 years.

**Gender:** In the present study, a higher prevalence of MNG was observed in females (76%) compared to males (24%). The ratio of females to males was 3.16:1.

**Clinical presentation:** Neck swelling was the universal presenting complaint in the present study (100%) followed by pain (44%), Palpitations (22%), hoarse voice (20%), tremors (12%), dyspnea (10%) and increased appetite (4%).

**Lobes involved:** All the cases of neck swelling were multinodular in nature in the present study. Both the lobes were involved in 42(84%) patients, right lobe in 7(14%) cases and left lobe in 1(2%) case.

**Functional Status:** Only 5 (10%) cases were found to be hyperthyroid and the remaining 45 cases (90%) were having a normal thyroid level in the present study.

**Duration:** Most of the patients in this study presented within a period 1 to 5 years (74%) followed by 22% of the patients within < 1-year duration, only 4% (2) gave a history of > 5 years duration.

**FNAC findings:** In the present study, cases with cytological findings of Multinodular goitre were evaluated. The reason for some of them to be biopsy-proven malignancy may be attributed to cause that sampling of FNAC might have been taken from only dominant nodules.

**Histopathological findings:** Most of the cases of MNG were found to be benign (78%) in the present study,

among the cases declared as malignant (22%). Among malignant cases, papillary carcinoma was found to be the most common (81%) followed by follicular carcinoma (18.1%). Hashimoto's Thyroiditis was detected in 2 cases.

**Operative procedure:** Total thyroidectomy was the most common operative procedure performed (84%) in the present study, followed by Hemithyroidectomy (16%)

**Incidence of malignancy in MNG:** In this study, 22% of the cases were found to be malignant and the rest of 78% cases were benign.

**Concomitant incidence of Toxic MNG with malignancy:** In our study, out of 5 cases of Toxic MNG in a total of 50 cases of MNG – 3 cases were reported to have malignancy and this was noted to be a significant result.

**Conclusion:** Though FNAC is a very useful diagnostic tool in MNG, it is not a gold standard tool for diagnosing malignancy in MNG. Malignancy is seen as a surprise in the postoperative period in histopathology reports.

**Keywords:** Multinodular Goitre, Thyroid, FNAC, Histopathology

### **Introduction**

Goiter is a nonspecific enlargement of the thyroid gland which is clinically or radiologically distinct from the surrounding thyroid gland (1). Thyroid nodules present either due to growth and fusion of localized colloid-filled thyroid follicles or as discrete adenomas or cysts. Nodules less than 1cm are not clinically palpable. The incidence of palpable nodules is reported to be 1% in men and 5% in women. With increasing age, there is an increased frequency of occurrence of palpable as well as non-palpable thyroid nodules (2).

Thyroid nodules may be single or multiple and multinodular goiter (MNG) is characterized as a clinicopathological entity with an increase in the volume of the thyroid gland with the formation of nodules. The annual incidence of MNG in nonendemic regions is found to be in between 0.1% to 1.5% and the prevalence ranges between 4 to 6%. Women and the elderly are reportedly more prone to developing a nonendemic goiter (3). Most of the thyroid nodules are benign but it was reported that 5% of the total account for thyroid cancers.

The various causes that are implicated in the etiopathogenesis of MNG are dietary deficiency of iodine, impairment in the synthesis of thyroid hormone (dyshormonogenesis), consumption of goitrogens, previous irradiation of thyroid, increased kidney iodine clearance, presence of antibodies to the thyroid plasma membrane antigens, referred to as thyroid stimulation immunoglobulins and also due to genetic influences.

The clinical spectrum starts initially from a euthyroid state into evident hyperthyroidism with increased levels of T3 and T4(4). Multinodular nontoxic goiter is found to be the most prevalent form of Goiter presenting as a unilateral or bilateral enlargement of the thyroid gland with clinical Euthyroidism (5). An appropriate diagnosis and effective management of MNG requires a good understanding of the anatomical and surgical knowledge along with the physiological and medical aspects, and a proper histopathological diagnosis.

The initial workup and evaluation apart from clinical examination includes the use of thyroid function tests, ultrasound scanning, and also radioisotope scanning for detecting heterogeneous thyroid tissue (4). FNAC or histological examination are required for final diagnosis by morphological and histological examination of the

lesions, as other diagnostic techniques including clinical examination are reported to be less sensitive in diagnosing thyroid lesions (6).

Although FNAC is considerably accurate and cost-effective, it has a 3% chance of giving false-negative results, and 25% of the results would be nondiagnostic (7). To increase the diagnostic accuracy, histological examination is essential and helps in arriving at a specific diagnosis. Not only for this reason but also due to the deep-seated location of a suspicious nodule or nondominant nodule being missed out during cytological evaluation, which results in the suboptimal treatment of the patient, histological examination is required.

This study, therefore, compares the clinical characteristics of patients with MNG in relation to the histopathological results and correlates different factors which interfere in the appropriate diagnosis and management. Evaluation of clinical findings and correlation with histopathological examination will reveal a representative investigation of choice and help in further management of the patient.

### **Aims**

To evaluate and compare the clinical characteristics and pathological features of multinodular goitre in relation to their histopathological results.

### **Objectives**

1. To study the clinical presentation and the corresponding histopathological features in multinodular goitre.
2. To compare histopathological reports along with clinical findings in multinodular goitre.
3. To estimate the incidence of malignancy in cases with multinodular goitre.

## Materials and methods

- Study Design: Observational prospective hospital-based study.
- Study Setting: Patients admitted to the General surgery department, NRI Institute of Medical Sciences, Chinakakani, Mangala Giri, Andhra Pradesh.
- Study Period: 1 year (June 2021 to August 2022).
- Study Population: Randomly selected patients presenting with Multinodular Goitre.
- Sample Size: 50 patients

All the patients with Multinodular goiter had undertaken a detailed clinical history and thorough clinical examination according to preset proforma. All the patients were investigated - thyroid function test, an x-ray of the neck antero posterior and lateral views and chest X-ray, ultrasound neck, ENT examination, complete blood analysis, urine analysis, blood sugar and urea estimation, serum creatinine, blood grouping and typing.

All patients underwent a prior FNAC. These patients underwent surgery and the excised thyroid specimen was sent for Histopathological examination. Patients were discharged after removing the sutures and were asked to come for follow-up. Postoperative thyroid profile was done in 3rd week of postoperative period.

## Inclusion Criteria

- Patients above 18 years of age.
- Patients with Multinodular Goitre undergoing surgery.
- Patients consenting for the study.

## Exclusion Criteria

- Patients with solitary nodular goitre.
- Patients with diffuse hyperplastic goitre.
- Patients who are not willing to get operated.

## Variables studied

- A) Age
- B) Gender
- C) Clinical Presentation
- D) Lobes Involved
- E) Functional Status
- F) Duration
- G) FNAC Findings
- H) Histopathological Findings
- I) Operative Procedure
- J) Incidence of Malignancy in MNG
- K) Concomitant Incidence of Toxic MNG with Malignancy

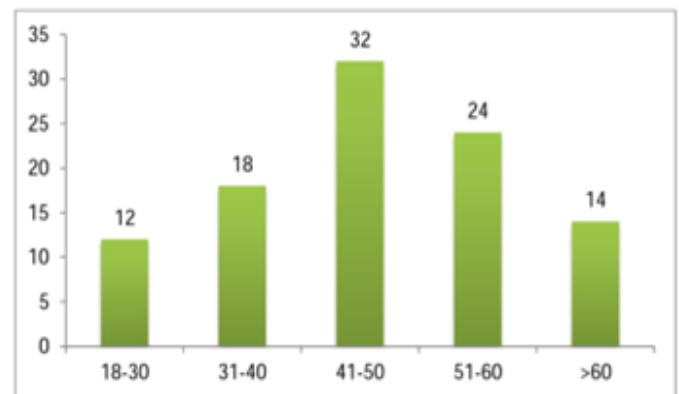
## Results

### Age

The majority of the study participants were in the age group of 41-50 years (32%) followed by 51-60 years (24%) in the present study. The patients with age >60 years were around 14% and the frequency of patients in the age group 18-30 years was 12%.

Graph 1:

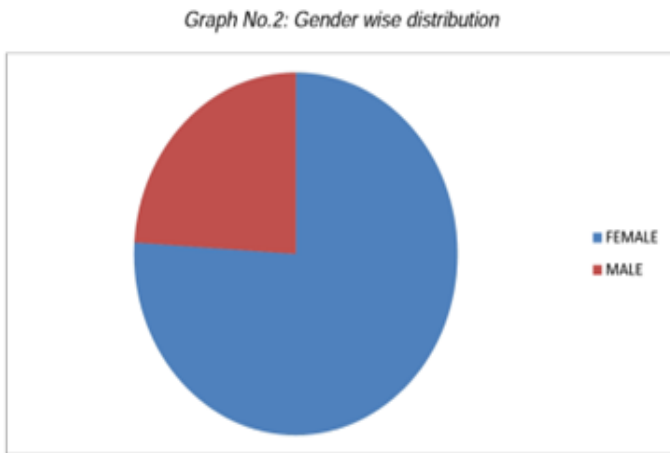
Graph No.1: Age-wise distribution



### Gender

Females were the most prominent gender (76%) in this study compared to males (24%). The male to female ratio was found to be 1:3.16.

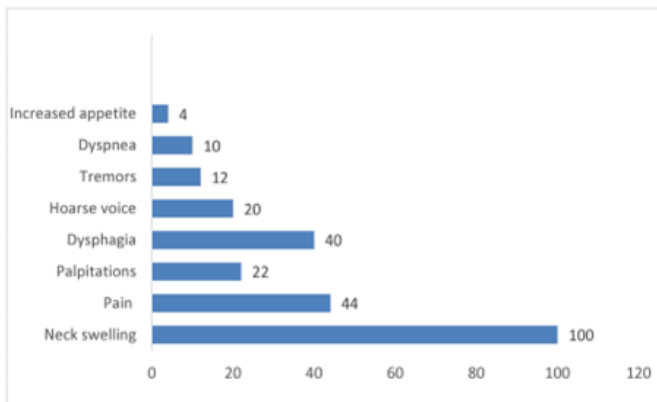
Graph 2:



### Clinical Presentation

The primary reason for the visit to the hospital in all the patients was due to swelling in the front of neck. Around 44% of the patients complained of associated pain, other frequent complaints include Dysphagia (40%), Palpitations (22%), hoarse voice (20%), tremors (12%), dyspnea (10%), and increased appetite (4%).

Graph 3:



### Duration

Most of the patients complained that they had the presenting symptoms for a period between 1 to 5 years (74%). Followed by 22% with < 1-year duration and 4% gave history of > 5 years.

Table 1:

Duration	No.	%
<1 year	11	22
1 -5 years	37	74
> 5 years	2	4
Total	50	100

### Lobe Involved

The surface of the neck swelling was multinodular in all of the cases (100%). A higher frequency (88%) of patients was found to have both lobes involved. In 14% of the patients, the right lobe was involved and in 2% the left lobe.

Table 2:

Lobes involved	No.	%
Both lobes	42	84.0
Left lobe	1	2.0
Right lobe	7	14.0
Total	50	100

### Functional Status

Only 5 (10%) cases were found to be hyperthyroid and 45 (90%) cases were having normal thyroid levels.

Table 3:

Clinical finding	No.	%
Normal	45	90.0
Hyperthyroid	5	10.0
Total	50	100

### FNAC Findings

In the present study all of the cases were reported to be multinodular goiter. These cases were eventually subjected to histopathological examination for further diagnosis and evaluation.

### Histopathological Findings

On histopathological examination multinodular goiter (74%) was the most common type of lesion noted followed by papillary carcinoma in 9 (18%) cases. Follicular variant of papillary was seen in 3 (6%) cases, multinodular goiter with cystic areas of calcification was seen in 2 cases (4%) and follicular carcinoma and Hashimoto’s disease was seen in 2 cases (4%) each. Other findings observed in a single patient were, follicular adenoma and papillary microcarcinoma. In one patient it was found that left lobe has papillary carcinoma and the right lobe was having a follicular adenoma. A total of 11 cases (22%) were found to be malignant in the present study.

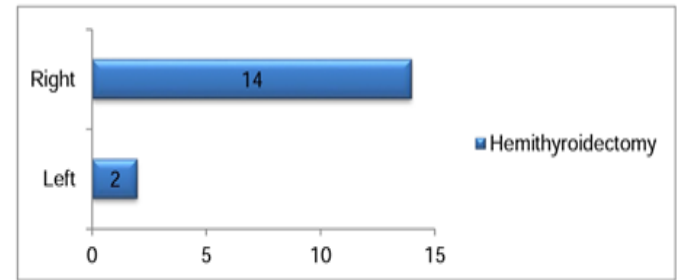
Table 4:

S.No.	HPE finding	No.	%
1.	Multinodular Goiter	34	68.0
2.	Multinodular Goiter with cystic areas of calcification	2	4.0
3.	Hashimoto's Thyroiditis	2	4.0
4.	Follicular Adenoma	1	2.0
5.	Follicular Carcinoma	2	4.0
6.	Follicular variant of papillary	3	6.0
7.	Papillary carcinoma	4	8.0
8.	Papillary microcarcinoma	1	2.0
9.	Left Papillary carcinoma and Right Follicular adenoma	1	2.0
	Total	50	100

### Operative Procedure

Total thyroidectomy is the most common operative procedure performed (84%) in the present study, followed by Hemithyroidectomy (8%).

Graph 5:



### Discussion

#### A) Age

Most of the study participants in the present study were found to be in the age group of 41 – 50 years followed by 51 - 60 years. “Bremer and Moll Night” on analysis of 1280 cases of MNG, quoted in a western analysis that, the maximum incidence was seen between 40-49 years. These results are similar to our results.

#### B) Gender

In the present study, a higher prevalence of MNG was observed in females (76%) compared to males (24%). The ratio of females to males was 3.16:1.

Congruent to the findings observed in the present study, Anwar K et al (2011) (8) also reported a similar higher prevalence of MNG in females, where out of the 204 cases included in the study, 161 were female with a female to male ratio of 3.5:1 which is almost comparable to the results obtained in the present study.

#### C) Clinical presentation

Neck swelling was the universal presenting complaint in the present study (100%) followed by pain (44%), Palpitations (22%), hoarse voice (20%), tremors (12%), dyspnea (10%) and increased appetite (4%).

Similar to these findings Amudhan J et al (2017) also found that swelling was present in all the study subjects (100%) and in this study it was observed that swelling



was associated with pain in 48% of the cases. 44% of the patients reported pressure symptoms in this study (9)

#### **D) Lobes Involved**

All the cases of neck swelling were multinodular in nature in the present study. Both the lobes were involved in 42(84%) patients, right lobe in 7(14%) cases and left lobe in 1(2%) case. Similarly, a higher number of patients with multi locularity (82%) was reported by Atha vale et al (2019) (10). In a study of 100 cases conducted by Asok an M et al, both lobes are involved in 88(88%) cases, right lobe was involved in 7(7%) cases and left lobe in 5(5%) cases was involved (11).

#### **E) Functional Status**

Only 5 (10%) cases were found to be hyperthyroid and the remaining 45 cases (90%) were having a normal thyroid level in the present study.

Altae MA et al (2009) reported that 73.2 % of the cases were found to be euthyroid in their study around 24% were hyperthyroid and only 3.4% cases were found to be hypothyroid (12).

#### **F) Duration**

Most of the patients in this study presented within a period 1 to 5 years (74%) followed by 22% of the patients within < 1-year duration, only 4% (2) gave a history of > 5 years duration.

Sanjeev a KK et al (2015) in their study reported that majority of the patients i.e., 82% presented within 5 years of duration. Only 5% of the patients were reported to be presented with duration of above 10 years. These results are consistent with the observations made in the present study (13).

#### **G) FNAC findings:**

In the present study, cases with cytological findings of Multinodular goitre were evaluated. The reason for some

of them to be biopsy-proven malignancy may be attributed to cause that sampling of FNAC might have been taken from only dominant nodules.

In a study done by Sanjeev a KK et al (2015) 73% of the patients were found to have nodular or colloidal goiter, followed by lymphocytic thyroiditis in 14 % of the cases, papillary hyperplasia in 10%, and follicular neoplasia in the remaining 8% of the cases (13).

#### **H) Histopathological findings**

Most of the cases of MNG were found to be benign (78%) in the present study, among the cases declared as malignant (22%). Among malignant cases, papillary carcinoma was found to be the most common (81%) followed by follicular carcinoma (18.1%). Hashimoto's Thyroiditis was detected in 2 cases, one of which also had to coexist MNG. The incidence of malignancy was higher among males (18%) compared to females (4%) in the present study.

In a study of 3233 patients conducted by K Apostolou et al (14), out of 1026 malignant cases 917(89.4%) cases were papillary carcinoma. Atha vale et al (2019) in their study reported a similar pattern of higher number of benign MNG in 67% of the ses, 22% were found to be colloid type of goiter. In their study there was higher number of cases of follicular carcinoma (6%) followed by papillary carcinoma (2%) and one case of medullary carcinoma was also detected (10).

#### **I) Operative procedure**

Total thyroidectomy was the most common operative procedure performed (84%) in the present study, followed by Hemi thyroidectomy (16%) – 14% right hemi thyroidectomy and in 2% cases left hemi thyroidectomy was performed in our study. In 8 hemi thyroidectomy performed cases, one case i.e., one right

hemi thyroidectomy was reported as follicular adenoma rest all other hemithyroidectomy cases were reported as Multi nodular goiter. In a study of 100 cases by Asokan M et al Total and near-total thyroidectomy was done in 69% of cases, subtotal thyroidectomy was done in 19%, and hemi thyroidectomy (12%)- right hemi thyroidectomy in 7% and left hemi thyroidectomy in 5% of cases (11).

#### **J) Incidence of malignancy in MNG**

In this study, 22% of the cases were found to be malignant and the rest of 78% cases were benign.

Rahman MM et al (2014) (15) reported that the incidence of malignancy in MNG cases was 3.87% in their study.

Altae MA et al (2009) (12) observed in their study that the incidence of thyroid tumors was 11% and in those which were malignant are 5.5%. Contrastingly in some studies relatively higher rates of incidence of malignancy were noted.

#### **K) Concomitant incidence of Toxic MNG with malignancy**

In our study, out of 5 cases of Toxic MNG in a total of 50 cases of MNG – 3 cases were reported to have malignancy and this was noted to be a significant result.

In a study conducted on 179 patients by Pacini, 7.5% of patients with toxic MNG had malignancy (16).

In 2014 a similar study was conducted by Preece et al. In a study conducted by Cerci et al (17), out of 294 patients the incidence of malignancy in TMNG was seen in 9% cases, and non-toxic MNG it was seen in 10.58% cases. But there was no significant difference in incidence of malignancy between the two groups.

#### **Conclusion**

Iodine deficiency, Radiation, genetics, enzyme deficiencies, certain drugs, and other dietary factors have been implicated in the causation of MNG. Autonomy of growth and Autonomy of function are responsible for clinical picture of MNG. In this study, Multinodular goiter was found to be most common in the age group of 40-50 years with least age being at 20years and the maximum age of occurrence is at 75 years. The prevalence of MNG was more common in females compared to males. Malignancy is most commonly seen in males.

The most common presentation is swelling in the front of neck and is associated with pain in majority of the cases. Both lobes were involved in most of the cases and when a single lobe is involved right lobe is mostly involved. MNG can present as hyper thyroid, hypo thyroid but presents mostly in euthyroid state depending on the overall functional status of the thyroid gland. Hyper thyroidism is seen in 10% of the cases. It occurs in Multi nodular goiter, during the natural evolution of the disease and the patient must be treated to attain a euthyroid state before surgery otherwise it may result in a dreadful complication called Thyroid storm. Among malignant cases, most common one was Papillary carcinoma followed by follicular carcinoma.

Though FNAC is a very useful diagnostic tool in MNG, it is not a gold standard tool for diagnosing malignancy in MNG. Malignancy is seen as a surprise in the postoperative period in histopathology reports. The indication of surgery includes suspicion of malignancy or malignancy, hyperthyroidism, pressure symptoms, cosmesis. Total thyroidectomy was the most common surgical procedure performed, as in most of the cases



both lobes are involved with the disease process. But when only single lobe is involved Hemithyroidectomy was performed as an alternative option with caution in mind at chance of future recurrence and occurrence of malignancy in recurred disease and necessity of regular follows with both the nodular status of left-over or insitu lobe and thyroid functional status.

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