

## EVALUATION OF INCIDENCE OF MALIGNANCY IN MULTINODULAR GOITER

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**ABSTRACT:** Multinodular goiters are more often looked upon as potentially benign type. But the incidence of malignancy in MNG is on the rise. The objective of this study was to determine the incidence of malignancy in multinodular goiter. In this prospective study total 40 patient of thyroid swellings (MNG, STN & diffuse goitre) were seen in the M.K.C.G. Medical College Hospital, Southern Orissa, during August 2011- July 2013. Thyroid hormone profile and FNAC was done in all cases while, USG was done in 28 cases and all cases underwent surgery and subsequently histopathological examination. In our series 62.5% of patients were found to have MNG and 3 (12%) of them were found to harbor malignant lesions in their glands after histopathological studies.

**KEY WORDS:** Multinodular goiter, histopathology, malignancy.

**INTRODUCTION:** Nodular goitre is probably the most common endocrine problem in the world today generating enormous enthusiasm amongst the medical community of surgeons and physicians. Prevalence of nodular goiters is so common these days and varies considerably depending in large part on the iodine intake of population studied. However even in areas of adequate intake such as Framingham- Massachusetts study, the prevalence of nodular goitre was 4.2%. In another survey in England, Tunbridge et al found nodular goiters in 4.5% of men and 12.1% of women<sup>1</sup>.

The incidence of carcinoma was twice as much in males than females which signifies that males with MNG are at higher risk of malignancy than females as reported by Al-saleh, Al khatan<sup>2</sup>. Thyroid being the most frequently operated upon endocrine organ and significant prevalence of nodular thyroid diseases encompassing lot of controversies in its evaluation and management, has drawn the attention that every surgeon must know how best to diagnose and treat these patients

Amongst the nodular thyroid lesions that may be solitary thyroid nodule (STN) or multinodular goiter (MNG), the incidence of MNG is overlooked by simple physical examinations alone. Physical examination alone underestimates the incidence of MNGs. High resolution real time ultrasound and histopathological studies have been helpful in the demonstration of multiple small nodules, in many cases (40%), which was clinically detected as either STN or diffuse goitre. So multinodular goiters can be better evaluated and its incidence estimated more accurately by a combination of clinical examination, ultrasonogram, scintiscan, intra-operative findings, FNAC and histopathological studies.

Thyroid cancer is a relatively uncommon malignancy with an incidence of 9/1, 00, 000 populations comprising less than 1% of all malignancies<sup>3</sup>. Thyroid cancer makes an insignificant contribution to cancer deaths, responsible only 0.5% of all cancer deaths. Though uncommon cancer it stimulates many more controversies over evaluation and treatment, than its numbers would appear to warrant. Most of uncertainties concerning the treatment of thyroid cancer are due to the

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unique biological behavior of tumors. Perhaps no other group of human cancers has such a spectrum of lethality. At one end is papillary cancer (rarely kills a person) being indolent form and the potentially life threatening giant and spindle cell anaplastic cancer at the other end.

Common mode of presentation of thyroid cancer is as nodules, commonest being a solitary nodule, that is notorious for its higher incidence of malignancy. Multinodular goiters are more often looked upon as potentially benign type. But the incidence of malignancy in MNG is on the rise. The incidence of malignancy in various studies has been reported to be – 10% by C Cerci et al in 2007 <sup>4</sup>; 8 % by S.A. Abu-Eshy et al in 1995 <sup>5</sup>. Diagnosing malignancy in MNG pre-operatively has always been a problem. Alsorecurrence rate and mortality are also significantly higher in those of multinodular cancer than those with STN<sup>6</sup>.

In spite of its rarity it is significantly important because in most instances it is eminently treatable. Most patients with thyroid cancer have a good prognosis, but early diagnosis and appropriate treatment should result in an even better outcome. The patient's best chance of cure lies with the astute surgeon being alert to the possibility of diagnosis, through a combination of pre-operative clinical and biochemical findings and gross findings at operation.

This study was undertaken, as thyroid swellings of various natures are often seen in this part of our state. Solitary nodules are always viewed with suspicion of malignancy and batteries of investigations are carried out to arrive at the correct diagnosis. Same amount of concern is not taken into account in evaluating a MNG. Keeping in view the rising trend of thyroid malignancies, worldwide various authors have stressed for exclusion of malignancy in all forms of thyroid swelling, be it STN, diffuse or MNG. The aim of this study is to find out the incidence of cancer in the so called innocuous MNGs, which cannot be taken for granted as totally benign.

**MATERIALS & METHODS:** The present study was taken to assess the incidence of malignancy in multinodular goiters in MKCG, Medical College and Hospital, Berhampur in patients with provisional diagnosis of thyroid goiters admitted to Departments of General Surgery and Endocrinology, during the period August 2011 to July 2013. This study comprises of patients of all age groups and both sexes, having goitre due to all possible causes. However this study excluded patients with post-operative recurrent thyroid swellings and patients who left the hospital before completion of the entire evaluation process as given in the Performa.

**METHODS:** After admission to hospital detailed history and thorough clinical examinations was carried out to reach the provisional diagnosis.

FNAC was done and in cases of thyroid cyst, fluid was aspirated and solution was sent to laboratory for centrifugation and slide preparation. Slides were stained by "papanicolaou's method"

**OPERATIVE NOTES:** Surgery was undertaken in those cases indicating for surgical intervention the thyroid was evaluated for presence of nodules intraoperatively. Depending upon the clinical and preoperative evaluation, lobectomy, hemi thyroidectomy and total thyroidectomy was undertaken and the specimen sent for histopathologic study.

**HISTO PATHOLOGICAL STUDY:** Tissue removed during operation was sent to histopathologist of M.K.C.G. medical college, Berhampur in 10% formal saline solution as preservative for histopathological study.

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The clinical history, biochemical investigation, USG scans, operative notes and pathological reports of each case was reviewed. The patients were classified according to the preoperative clinical diagnosis into those presenting with clinically STN, diffuse goitre and MNG. The preoperative diagnosis was based on clinical findings supported either by USG or isotope scan.

Subsequently the clinical diagnosis was correlated to the operative findings and histological examination of the specimen. Only patients with true multiple nodules by all those criteria were considered in order to determine the incidence of malignancy in MNG. Those data were compared to the reported incidence of malignancy in thyroid glands with confirmed STN and MNGs.

**OBSERVATION:** 40 patients of thyroid swellings (MNG, STN & diffuse goitre) were seen in the M.K.C.G. Medical College Hospital, Berhampur, during August 2011- July 2013.

Thyroid hormone profile and FNAC was done in all cases while, USG was done in 28 cases and all cases underwent surgery and subsequently histopathological examination.

The age and sex distribution of patients varied from 14-80 yrs. Sex incidence in the table shows that maximum numbers of patients were females (80.00%) and M: F ratio 1:4. The maximum number of patients was seen in between 31-40 yrs. of age which comprises 30% of all patients.

Neck swelling is the cardinal presenting feature in 95% cases. However, in 15. %, 10% & 7.5 % cases patients came to us for other symptoms like pain in swelling, rapid increases in size, hypothyroidism and cervical Lymph node enlargement respectively.

Clinically only 08 cases (20%) were decided as MNG and a vast majority (50%) presented as solitary nodule and diffuse swelling.

The consistency of the thyroid swellings was variable. Majority of the swellings were soft in consistency (52.63%) while 3.5% were cystic, 14.05% were hard, 17.54% had variegated consistency and 12.28% were firm in consistency.

Thirty five cases (92.5%) had swellings that were found to be mobile, 3 cases (7.5%) were fixed which were later found to be malignant.

The thyroid hormone profile and FNAC was done in all case. USG was done in 28 cases (70%) and histopathological study was done in all cases who underwent surgery i.e. 40 cases (100%). Majority of the patients (85%) were euthyroid, 4 cases (10%) were in hypothyroid state and 2 cases (5%) was in hyperthyroid state.

Type of lesion	No. of cases	% age
Colloid goitre	22	55.00
Adenoma	11	27.5
Follicular neoplasia	03	7.5
Suspicious lesion	01	2.5
Thyroiditis	01	2.5
Carcinoma (papillary)	02	5.0

Table – 1: Showing Results of FNAC (n= 40)

Table 6 shows the result of FNAC done in all 40 cases. Majority of cases were found to be Benign. Only 2 cases (5%) were detected as malignant (papillary carcinoma). One case was detected as suspicious lesion. 3 cases were detected as follicular neoplasia, later confirmed on histopathology

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Type of Goitre	No. of cases	% age
SN	18	45.00
MNG	16	40.00
Diffuse	06	15.00

**Table –2: Type of Goiter based on clinical and USG Scan (n=40).**

The above table-7 shows nodular pattern detected by USG and clinical examination. MNG were detected in 16 cases.

Type of goitre	No. of cases	Percentage
SN	12	30
MNG	25	62.5
Diffuse	03	7.5

**Table – 3: Table showing Operative & histopathological findings (n= 40)**

The above table-8 shows that the number of multinodular goiters increased postoperatively after histological confirmation, as some cases diagnosed to be SN or diffuse goitre were found to be MNGs, but none of the case diagnosed preoperatively as MNGs proved otherwise. The sex distribution of 25 cases of MNGs shows a female preponderance. (84%). Male to female ratio is 1:4.2.

Age in years	Benign	Malignant
<20	01	-
21-30	02	-
31-40	08	-
41-50	05	01
>51	06	02
Total	22 (88.00%)	03 (12.00%)

**Table – 4: Showing results of histopathological Studies of case detected as MNGs (n=25)**

The above table-10 shows the result of histopathological studies of 25 cases detected as MNG by clinical, USG, and histopathology. 22 cases (88.00%) presented as benign lesions, only 3 cases (12.00%) presented as malignant lesion. One case in the age 41- 50 year found to be a suspicious lesion in FNAC was confirmed to be papillary carcinoma. Two cases in age group more than 50 years were detected as follicular neoplasia in FNAC was confirmed to be follicular carcinoma. Histopathology in other cases was consistent with FNAC.

The histological subtypes of carcinomas detected in MNGs 66.67% (2 cases) were found to be of papillary type, and 33.33 % (one case) was found as follicular carcinoma.

**DISCUSSION:** A long standing and hitherto unresolved issue is whether MNG is surgically associated with carcinoma. The diagnosis of malignancy in solitary nodule is easy, made by different methods like surgical excision of palpable nodules or aspiration biopsy. But the incidence of malignancy in MNG puts some diagnostic and therapeutic dilemmas.

This study was based on prospective and retrospective clinicopathological analysis of thyroid malignancies or cancer presenting as thyroid nodules in those having other morphological form during the period August 2011 to July 2013.

**History and physical exam:** Numerous historical features are relevant in evaluation of thyroid nodules. A family history of benign thyroid diseases is reassuring, as the prevalence of benign goitre in patients with family history of benign thyroid disease is 4 fold greater than prevalence of malignant nodules in those with family history of benign disease<sup>7</sup>.

The age and sex incidence of thyroid nodules in our study is comparable with the study conducted by other authors, Anwer K et al 2012<sup>8</sup>, Fukunoga et al 1975<sup>9</sup> and Abu-eshy et al<sup>10</sup>.

38 patients out of 40 presented with swelling on the anterior aspect of neck of variable duration ranging from 6 months to 3 years. Their patients were diagnosed to have thyroid nodules when they were investigated for other symptoms.

Symptoms of either thyrotoxicosis or hypothyroidism are important in the evaluation of nodular thyroid diseases although most of our patients (85.00%) were euthyroid. Nodules found in patients with abnormal thyroid function should not be dismissed without investigations. As with history, physical examination though important, is not sufficient for a thorough evaluation of nodular thyroid diseases. Though fixed, firm, hard nodules are suspicious for cancer; they are neither sufficiently sensitive nor specific regarding the presence of cancer as reported by Shimaoka et al 1962<sup>11</sup>. Similarly finding of cervical lymphadenopathy in 3 cases (7.5%) indicated the presence of thyroid cancer, However it is not specific for malignancy (Hamming J. et al 1990)<sup>12</sup>. Small goiters in adolescents are not necessarily pathologic and upto 1/3<sup>rd</sup> cases spontaneously regress and are thought to be simple adolescent goiters. However goiters which enlarge, fail to regress, or contain discrete nodules should be treated with suspicion the presence of a multi nodular goitre, especially one with dominant nodule, does not militate against the diagnosis of thyroid cancer<sup>7</sup>.

**Investigation:** Most of the patients with thyroid nodules either benign or malignant were euthyroid with normal serum concentration of TSH, T3 and T4.

Soft tissue radiography of neck and xeroradiography are not useful predictors of the histology of thyroid nodule, as neither of these investigations are sufficiently sensitive or specific to predict the histologic feature of the nodules. Investigations like thermography and angiography also lack the diagnostic accuracy to differentiate benign from malignant lesions<sup>13</sup>. Neither CT nor MRI can distinguish between malignant or benign nodule but both are useful in evaluating the extension of substernal, retrotracheal diseases, regional metastasis, adenopathy and obliteration of tissue planes by tumours<sup>13</sup>. A radiological evaluation of chest should be obtained with evaluation of nodular diseases to search for metastatic disease as advised by most of the surgeons.

High frequency real time USG examination of thyroid is an important investigative tool in detection of thyroid nodules. USG can detect nodules as small as 1 mm but cannot reliably predict the malignancy. Ultrasound examination of thyroid adds to the evaluation determined by isotope scan, as it can readily diagnosed unsuspected multinodularity and distinguish a solid lesion from a cystic one. In our study 8 cases (20%) presented clinically as MNG, later on 8 more cases detected by USG and were found to have multinodular goiter, and finally 25 cases of MNG were detected after histopathological examination. So the attempt to determine sonographic criteria for MNG have not

fully been successful, but ultrasound of thyroid is mandatory in thyroid goiters. Although USG is not of value for histological examinations of thyroid nodule, it is of extreme assistance to surgeons in demonstrating unexpected presence of a multinodular gland, thyroid cyst and location of a mass either intra or extrathyroidal, for screening of high risk patients and for assisting difficult FNAC.

The prevalence of malignancy in cold or warm nodule is not insignificant approaching 12%. Because of its limited sensitivity and specificity it can be no longer recommended as a primary or sole diagnostics option in the evaluation of thyroid malignancy.

The reliance on clinical examination and USG is inaccurate in identifying neoplastic thyroid nodules whereas FNAC has been shown to be a simple, accurate, easy and cost effective technique of screening patients of high risk for thyroid malignancy and suspicious thyroid nodules. The requirements for successful FNAC are skillful palpation, aspiration of sufficient material, adequate smear preparation, and skillful pathological evaluation. In our series (Table 13) shows the distribution of cytological diagnosis. However the FNAC findings were later confirmed by histopathological studies (4 papillary, 1 follicular neoplasm and one suspicious lesion are confirmed to be malignant)

MNG and Malignancy: The controversial issue whether MNG is significant associated with carcinoma or not, depends on several factors which includes but not limited to the following.

- Method of diagnosis; whether surgical excisions or aspiration biopsy
- Expertise in interpretation of aspiration biopsy.
- Care in microscopic section.
- The ambiguity in pathogenesis MNG.

Therefore considering above facts a nodule harboring malignancy in MNG cannot be distinguished clinically or radiologically but can be assessed by FNAC and histopathology in combination.

9 of our patients with SN and diffuse goitre under clinical and USG examination were found to have additional nodules at operation and by histopathological examination. This is not surprising since the sensitivity of clinical examination in detecting thyroid nodules is reported to be low. In fact the sensitivity of clinical examination, USG and scintiscan was calculated to be around 44%.

We believe like other that true diagnosis of MNG should be based on clinical examination, USG, scintiscan, intraoperative findings and confirmation of histopathological studies. In our series 62.5% of patients were found to have MNG and 3 (12%) of them were found to harbor malignant lesions in their glands after histopathological studies, which is comparable with other studies.

Preoperative frozen section examination of suspected lesions is debatable but not very helpful investigation in case of MNG because of the cost of the procedure and the incurred additional anesthetic and operative procedure. Do not justify its routine use. When carcinoma is found in excised specimen postoperatively, the remaining tissue can be ablated by radioactive iodine or repetitive surgery.

However the incidence of carcinoma was twice as much in males than females which signifies that males with MNG are at higher risk of malignancy than females as reported by other authors<sup>2</sup>. In this series we could not corroborate the significance of sex distribution as we had 2 females and 1 male with a ratio of 2:1 as the number of cases studied is very less and duration of study was short from our study. The type of carcinoma was classified according to WHO pattern of

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classification. Papillary carcinoma was the commonest type, accounted for 66.67% in our study, and one (33.33) of our patient had follicular type. This prevalence of papillary carcinoma in MNG is similar to that reported by many authors<sup>6,7</sup>. None of our patient had anaplastic carcinoma, which supports the observation of extreme varieties of such tumor in Indian population with MNG.

**CONCLUSION:** In our series 62.5% of patients were found to have MNG and 3 (12%) of them were found to harbor malignant lesions in their glands after histopathological studies, which is comparable with other studies. We had 2 females and 1 male with a ratio of 2:1. Papillary carcinoma was the commonest type, accounted for 66.67% in our study, and one (33.33) of our patient had follicular type.

In this study the incidence of malignancy in MNG is found to be corroborating with the previous study but prevalent more commonly in female population.

### BIBLIOGRAPHY:

1. Tunbridge WMG, Evered DC, Hall R, Appleton D, Clark F, Bird T et al. The spectrum of thyroid disease in a community-The Wickham. *Clinical endocrinology* 1977; vol 7: p 481-3.
2. Al-saleh MS, Al-khatan KM. Incidence of carcinoma in multinodular goiter in Saudi Arabia. *J.R.Coll.surg.* 1994;p106-8.
3. Jameson JL, Weetman PA, Disorders of the thyroid glands In:Longo DL, Kasper DL, Jameson JL, Fauci AS, Hauser SL, Loscalzo J(Editors) *Harrisons principals of internal medicine* 18<sup>th</sup> edition, New York, Mc Graw Hill:2008, p2911-39.
4. Cerci C, Cerci SS, Eroglu O, Dede M, Kopucuoglu N, Yildiz M. Thyroid cancer in toxic and nontoxic multinodular goiter. *J Postgrad Med* 2007; 53: p157-60.
5. Abu-Eshy SA, Khan AR, Khan GM, Al-Humaidi MA, Al-Shehri MY, Malatani TS. Thyroid malignancy in multinodular goitre and in a solitary nodule. *J.R. Coll. Surg. Edinb* 1995; 40: p 310-12.
6. Kapur MM, Sarada AK, Bal S, Sood S. Carcinoma of thyroid, differential behaviour in solitary and multinodular goiter:*BJS* 1986;73; p894-5.
7. McCall A, Jarosz H, Lawrence AM, Paloyan E. The incidence of thyroid carcinoma in solitary cold nodules and in multinodular goiters. *Surgery*, 1986; 100(6):p1128-32.
8. Anower K, Din G, Zada B, Shahabi I. The frequency of malignancy in nodular goiter.*JPMI*, 2012; 26(1):p106.
9. Fukunaga FH, Yatani R. Geographic pathology of occult thyroid carcinomas.*Cancer* 1975 Sep; 36(3): p1095-1099.
10. Koh KBH, Chang KW. Carcinoma in multinodular goitre.*Br J Surg* 1992; 79(3): 266-267.doi: 10.1002/bjs.1800790328.
11. Shimaoka K, Badillo J, Joseph E, Sokal JE, Frank C, Marchetta, Clinical differentiation between thyroid cancer and benign goiter.*JAMA* 1962;181(3):p179-185.
12. Hamming JF, Gosling BM, Van Steenis GJ et al. The value of fine needle aspiration biopsy in patients with nodular thyroid disease divided into groups of suspicion of malignant neoplasm on clinical grounds. *Arch. Intern. Med.* 1990; 150(1):113-116.
13. Friedman M, Toriumi DM, Mafee MF. Problems in management of solitary nodule and diffuse goiter.*Am j surg*, 1988; 81(1):p45-46.

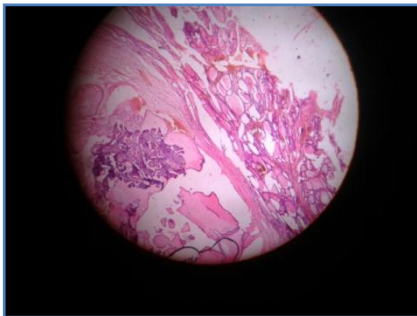
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**Fig.1: Clinical photograph of left sided multinodular goitre.**



**Fig. 2: Operative specimen of multinodular goitre.**



**Fig. 3: "Image no 3 showing microscopic picture of papillary thyroid cancer in multi nodular goitre."**

(Left side shows pattern of papillary malignancy, right side - colloid goitre component visualized.(10x)"

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