

# HISTOPATHOLOGY PATTERN OF CARCINOMA OF THYROID IN MULTINODULAR GOITER

Muhammad Usman Shahid,<sup>1</sup> Muhammad Sarwar,<sup>2</sup> Muhammad Saad Faisal,<sup>3</sup> Maria Jabbar<sup>3</sup>

## ABSTRACT

**Background:** Universally, it is considered that risk of carcinoma thyroid is low in multinodular goiter (MNG) as compared to solitary nodule and hence is overlooked in many cases. **Objective:** To determine the frequency of thyroid carcinoma and document its histopathology patterns among patients with MNG undergone through thyroidectomy. **Methodology:** In this cross sectional study, retrospective medical records of 100 operated cases of thyroidectomy, for MNG from 1<sup>st</sup> January 2012 to 31<sup>st</sup> January 2018, in Surgery Department of Sharif Medical City Hospital, Lahore and Services Hospital Lahore, were analyzed. Demographics, FNAC reports, types of surgery and histopathology reports were reviewed and analyzed. Data was entered in SPSS version 20. **Results:** This study included 88 (88%) females and 12 (12%) male, with a mean age of  $41.29 \pm 5.94$  years. Carcinoma thyroid was present among 3 (3%) patients. Histopathology pattern of malignancy among these patients was follicular in 2 (66.7%) patients and papillary in 1 (33.3%) patients. Inadequacy of FNAC for detection of thyroid cancer was seen in 1 (1%) patient. Total thyroidectomy was performed in 85 (85%) patients, total thyroidectomy with neck dissection in 1 (1%) patient, subtotal in 13 (13%) patients and a re-do total thyroidectomy in 1 (1%) patient. **Conclusion:** Low frequency of thyroid cancer was observed among patients with MNG, but it was not negligible. This also obviates the need for undue total thyroidectomy as observed in our study. Inadequacy of FNAC for detection of thyroid cancer in MNG was also low, hence reliable.

**Keywords:** Carcinoma Thyroid, Multinodular goiter, Histopathology pattern, FNAC

## INTRODUCTION

The thyroid gland is an endocrine gland of extreme importance meant to regulate the metabolism rate hence controlling body growth.<sup>1</sup> Enlargement in size of thyroid gland is labeled as goiter, which may be a solitary nodule, diffuse or multinodular, associated with non-toxic or toxic status of thyroid function.<sup>2,3</sup> The prevalence of palpable goiter in middle aged women of Western world is 10-30%. The advancement and increase in use of diagnostic modalities like ultrasonography and thyroid scan, the prevalence has increased upto 30-70% of the adult population.<sup>4</sup>

Multinodular goiter (MNG) is considered, a benign disorder of thyroid gland. However, it may be associated with presence of thyroid carcinoma, which in most of the cases is detected on histological specimen.<sup>3</sup> The overall incidence of malignancy in multinodular goiter is 4-17%.<sup>5,6</sup>

In case of thyroid swelling, there is always emphasis to rule out the possibility of thyroid carcinoma preoperatively. Clinical assessment of multinodular goiter is based on physical examination of thyroid gland that may help in detecting any malignancy but is of limited value. Iodine uptake thyroid scan, ultrasonography of the gland and fine needle aspiration cytology (FNAC) can also play an important role. FNAC is the modality of choice but in case of multinodular

goiter, it may not be able to collect sample from malignant nodule, even ultrasonography guided FNAC may not help.<sup>7,8</sup>

Carcinoma of thyroid is uncommon accounting for only 1% of all human tumors. Annual incidence of thyroid cancer is 0.5 to 10:100,000 person's worldwide.<sup>8</sup> The prevalence of carcinoma is lower in multinodular goiter (MNG) than in solitary nodule (STN).<sup>9</sup> Malignancy is seen in only 0 to 11% of patients with MNG and is usually an incidental finding in thyroidectomy specimens, and in 3 to 33% of patients with STN.<sup>10</sup>

In Pakistan, thyroid cancer is responsible for 1.2% cases of all malignant tumors and studies from this region have reported papillary thyroid cancer to constitute 57% to 89% of all thyroid malignancies.<sup>11</sup>

The incidence of carcinoma has been increasing with time. It is estimated that there has been estimated increase of up to 6 folds. Exposure to ionizing radiation, changing levels of iodine nutrition and advancement in diagnostic modalities are purposed to cause it.<sup>3,12,13</sup>

In our clinical settings, thyroidectomy is routinely offered to the patients with multinodular goiter for cosmetic reasons or pressure symptoms.<sup>14</sup> The chances of thyroid carcinoma are overlooked as it is considered to be more common in solitary nodule. The literature showed that multinodular goiter is not out of risk of thyroid carcinoma.<sup>15-19</sup> However, the frequency and patterns of malignancy are variable in

1. RHC RenalaKhurd, District Okara, Pakistan.

2. Quaid-e-Azam Medical College, Bahawalpur, University of Health Sciences, Lahore, Pakistan.

3. Sharif Medical and Dental College, Lahore, University of Health Sciences Lahore, Pakistan.

**Correspondence:** Dr. Muhammad Saad Faisal, Assistant Professor of Surgery, Sharif Medical and Dental College, Lahore, Pakistan.

**Email:** saadi206@yahoo.com

**Phone:** +923214722111

**Received:** 13-09-2018

**Accepted:** 25-08-2018

different parts of the world.<sup>20-22</sup> These highlight the need to ascertain the frequency and pattern of carcinoma in patients with multinodular goiter in our setup. Therefore, this study was conducted in order to determine that how common thyroid carcinoma is among patients with multinodular goiter and document its pattern in a tertiary care surgical unit of a government sector teaching hospital of Pakistan.

## METHODOLOGY

In this cross sectional study, we retrospectively reviewed the data of 108 patients with multinodular goiter who underwent thyroidectomy from a period of 1<sup>st</sup> January 2012 to 31<sup>st</sup> January 2018 at department of Surgery of Services Hospital Lahore and Sharif Medical City Hospital. We excluded 8 patients with incomplete data. All the information was collected from medical records of the patients. Our objective was to determine the frequency of carcinoma of thyroid from histopathology records of all the patients with multinodular goiter necessitated for thyroidectomy and to describe the pattern of malignancy among those patients. We included only those patients in whom multinodularity was diagnosed on physical examination (palpable thyroid gland that moved on deglutition and presence of multiple nodules on thyroid surface) and confirmed on either ultrasonography scan or thyroid scan. Demographic data was also collected. Thyroid function tests reports were also noted. All the patients were euthyroid before surgery. FNAC reports were also traced and findings were observed. Indications for thyroidectomy were also recorded which included cosmetic grounds, compression symptoms, thyrotoxicosis, or suspected FNAC slides i.e. atypia, follicular, papillary, or Hurthle cells. Histopathology reports were also checked for the diagnosis of thyroid carcinoma which was confirmed if the reports were consistent with findings of malignancy i.e. the presence of atypical cells, or unequivocal cytology or the presence of cells specific to malignancy (i.e. Hurthle cells, or Orphan Annie Nuclei)] of the resected thyroid tissue after surgery. The patients in whom the cytology was found consistent with any of the above histopathology were labeled as positive for malignancy. If the report turns as positive for thyroid carcinoma, the pattern of malignancy was noted (i.e. papillary carcinoma;

follicular carcinoma; medullary carcinoma; anaplastic carcinoma and undifferentiated malignant carcinoma). Statistical analysis was done using by SPSS 20. Quantitative data like age (in years) were described as means and standard deviation. The qualitative data that included gender (male/ female), presence or absence of thyroid carcinoma (yes/no) and pattern of thyroid carcinoma (i.e. papillary carcinoma; follicular carcinoma; medullary carcinoma; anaplastic carcinoma and undifferentiated malignant carcinoma) were described as frequency and percentage.

## RESULTS

We reviewed the medical records of 108 patients, of which 8 were excluded due to incomplete data. Among the 100 patients included in the study, the mean age of the patients was  $41 \pm 5$  years [range 23 – 55]. There were 26 (26%) patients of age range of 20 – 30 years, 39 (39%) patients of age range of 31 – 40 years, 31 (31%) patients of age range of 41 – 50 years, 4 (4%) patients of age range of 50 – 60 years.

**Table I: Distribution of patients on FNAC report. (n=100)**

Pattern of FNAC Report		Patients	
		No.	%
Colloid nodular goiter		71	71
Hashimoto's Thyroiditis		8	8
Adenomatous goiter		18	18
Suspected Cytology	Follicular	1	1
	Papillary	1	1
Inconclusive		1	1
<b>Total</b>		<b>100</b>	<b>100</b>

**Table II: Distribution of patients by pattern of malignancy. (n=100)**

Pattern of Histopathology Report	Frequency	
	No.	%
Colloid nodular goiter	76	76
Hashimoto's Thyroiditis	6	6
Follicular adenoma	15	15
Follicular carcinoma	2	2
Papillary carcinoma	1	1

There were 12 (12%) male patients and 88 (88%) female patients in the study. Preoperative FNAC reporting pattern is described in table I. On postoperative histopathology reporting, thyroid carcinoma was present in 3 (3%) patients. Histopathology distribution is described in table 2. Among all carcinomas, follicular was most common

variant present in 2 (66.7%) patients and papillary being present in 1 (33.3%) patients. Both of the two patients who were suspected as thyroid malignancy were positive for thyroid carcinoma on histopathology while in one patient with colloid cytology, FNAC could not detect malignancy and malignancy was proven on histopathology. So, in adequacy of FNAC for detection of carcinoma was seen in 1 (1%) case. This patient had a redo surgery (Total thyroidectomy). Total thyroidectomies were performed in 85 (85%) patients, total thyroidectomy with neck dissection in 1 (1%) patient, subtotal thyroidectomies were performed in 13 (13%) patients, while a re-do total thyroidectomy followed by subtotal dissection needed to be done in 1 (1%) patient. Two (2%) patients with proven thyroid malignancies were in age group 30 – 40 years and one in age group 41 – 45 years. All the malignancies were present in females.

## DISCUSSION

Thyroid enlargement when present is of concern to detect its etiology. One of the special interest is in detection of malignancy in thyroid gland. Once it is a solitary nodule, a higher frequency of malignancy is suggested. The case is not different for multinodular goiter either.<sup>16,17,18</sup> Literature suggests a variation among different authors.<sup>16-22</sup> In our study, we could detect carcinoma in only 3% patients which is quite lower than previously reported studies.<sup>23-26</sup>

In our study, the mean age of the patients was 41±5 years. We observed the presence of MNG in all age groups. However, majority of patients (39%) were in age group 30 – 40 years. This observation was similar to Amudhan J, et al,<sup>1</sup> who observed that MNG was present in all age groups and majority (32%) of the patients were in age group 30 – 40 years. They documented that in their study, the mean age was 42 years. In our study, majority of the patients were female (88%). In study by Amudhan J, et al,<sup>1</sup> 94% patients were female and in Zambudio et al,<sup>19</sup> in which 89% patients were female. So, it can be observed that multinodular goiter is seen frequently among female with a mean age around 40 years and in more common among adults of age 30 – 40 years.

On FNAC reports, the most common pattern was colloid nodular goiter (71%), while hashimoto's

thyroiditis and adenomatous also contributed. Only two slides showed suspected cytology. This observation is comparable to study by Amudhan et al,<sup>1</sup> who showed that colloid cytology was seen among 64%, hashimoto's thyroiditis in 22% and malignancy in 4% patients. FNAC in thyroid disorders is mainstay of the diagnostic pathway. It is routinely done as is readily available, safe and reliable, cost effective.<sup>2</sup> In case of thyroid nodules, its sensitivity ranges from 80-90%, and specificity upto 100%.<sup>22</sup> For detection of carcinoma, the inadequacy of FNAC was 1%, while Honda U documented and inadequacy of 5.06%.<sup>22</sup> In previous studies, the inadequacy was seen variably among 0 to 25%.<sup>22,23</sup>

In literature, various authors have documented variable figures about thyroid carcinomas among patients with multinodular goiter. In a study by Memon W, et al,<sup>13</sup> which was performed on 140 patients, the thyroid carcinoma was found in 15 patients (7.6%). Of those malignant cases papillary carcinoma was found in 6 (75%) cases, follicular and anaplastic carcinoma in one (12.5%) cases each.<sup>13</sup>

In a study by Cerci C, et al,<sup>24</sup> among 170 patients with multinodular goiter, the frequency of malignancy among these patients was 12.2% confirmed on histopathology findings. This frequency is much higher than ours i.e. 3%. Moreover, like our study, they revealed that papillary carcinoma was the most common (61.1%). In our study, the frequency of papillary cancer was 33.3%.

In another study by Wani KA, et al,<sup>25</sup> 108 patients of thyroid malignancy were studied for the pattern of the malignancy. The commonest observed thyroid malignancy was papillary carcinoma (48.15%), followed by follicular carcinoma (37.04%), anaplastic carcinoma (7.41%), medullary carcinoma (5.55%) and malignant lymphoma (1.85%). Their observation also differs from our results. In our study, follicular variant was the most common, but in their study, papillary carcinoma was the most common thyroid malignancy unlike our study. In another study by Gandolfi, et al, the thyroid malignancy was found in 13.7% of all cases of multinodular goiter,<sup>5</sup> Woolner et al,<sup>26</sup> also reported papillary carcinoma in 61.1%, follicular carcinoma in 17.7%, anaplastic carcinoma in 14.7% and medullary carcinoma in 6.5%. Mofti et al observing higher incidence of thyroid malignancies (29%) in a study of 158 patients.<sup>14</sup> In contrast to other studies, we find a low frequency of thyroid carcinoma among patients with multinodular goiter. However,

Amudhan et al,<sup>1</sup> also found a low frequency of thyroid cancer i.e. 4% only.

In our study, we observed an increased tendency of performing total thyroidectomies (85%) as compared to subtotal thyroidectomies (14%) among surgeons. This high tendency of performing total thyroidectomy has also been observed by Amudhan et al,<sup>1</sup> who performed total thyroidectomy among 88% patient and subtotal thyroidectomy among 12% patients. This increasing trend of doing total thyroidectomy among surgeons may be related to the high anxiety of thyroid carcinoma being present. Although, it better prevents patient from re-do surgery or recurrence, it puts the patient more at risk of parathyroid or recurrent laryngeal nerve damage. However, seeing our results, subtotal thyroidectomy may be encouraged if there is no other concern except malignancy. We also noted a positive influence of FNAC in detection of carcinoma. FNAC showed only 1% inadequacy. This study had some limitations. This was a retrospective analysis in a limited population.

## CONCLUSION

The frequency of thyroid carcinoma among patients with multinodular goiter is low but not negligible. Importance should be given to FNAC in MNG which shows a very low inadequacy in detection of carcinoma. Surgeons must reconsider performing subtotal thyroidectomy instead of total thyroidectomy in case of multinodular goiter for better surgical outcome.

## REFERENCES

- Amudhan J, Vijay A, Latha G, Anandan H. Clinicopathological Study on Multinodular Goiter: A Prospective Study. *Int J Sci Stud* 2017;5(1):83-85.
- Nurunnabi ASM, Alim A, Sabiha M, Manowara B, Monira K, Shami A. Weight of the Human Thyroid Gland – A Postmortem Study. *Bangladesh Journal of Medical Science* 2010;9:44-48.
- Pedamallu R, Pedamallu SB, Rao KVR, Pedamallu CS. Incidence of occult carcinoma in multinodular goiter using histopathological findings. *The Internet Journal of Surgery* 2008;17:1.
- Järhult J, Vedad R. A Conservative Approach Is Reasonable in Patients with Non-Toxic Goitre: Results from an Observational Study during 30 Years. *Eur Thyroid J* 2014;3:240-244
- Gandolfi PP, Frisina A, Raffa M, Renda M, Rocchetti O, Ruggeri C, Tombolini C. The incidence of Thyroid Carcinoma in Multinodular Goiter:retrospective analysis. *ACTA Bio MedicaAteneoParmense* 2004;75;114-117.
- Rehman AU, Iodhi S, Anwar MI. Histopathological Evaluation of 432 Cases of Goiter. *ANNALS* 2009;15:54-56.
- Alam M, Qureshi H, Jan QA. Accuracy of fnac as a diagnostic modality in the management of solitary thyroid nodule. *J Med Sci* 2010;18:94-96.
- Cappelli C, Castellano M, Pirola I, Cumetti D, Agosti B, Gandossi E, Rosei EA. The predictive value of ultrasound findings in the management of thyroid nodules. *QJM* 2007;100:29-35.
- Tollin SR, Mery GM, Jelveh N. The use of fine needle aspiration biopsy under ultrasound guidance to assess the risk of malignancy in patients with multinodular goiter. *Thyroid* 2000;10:235-241.
- Collins SL. Thyroid cancer: controversies and etiopathogenesis, In: Flak SA (eds) *Thyroid disease: Endocrinology, surgery, Nuclear Medicine, and Radiotherapy* 2nd ed, Lippincott – Raven, Philadelphia 1997;495-564.
- Mulaudi TV, Ramdial PK, Madiba TE, Callaghan RA. Thyroid carcinoma at King Edward VIII Hospital, Durban, South Africa. *East Africa Med J* 2001;78:252-255.
- Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973-2002. *JAMA* 2006;295:2164-2167.
- Memon W, Khanzada TW, Samad A, Kumar B. Incidence of thyroid carcinoma in multinodular goiters. *Rawal Medical Journal* 2010;35:65-67.
- Mofti AB, Al Momen AA, Suleiman Si, Jain GC, Assaf, HM. Experience with thyroid surgery in Security Forces hospital, Riyadh. *Saudi Med J* 1991;12:504-506.
- Abdulkareem FB, Banjo AA, Elesha SO. Histological Review of Thyroid Lesions: A 13-year Retrospective Study (1989-2001). *Niger Postgrad Med J* 2005;12:210-214.
- Enewold L, Zhu K, Ron E, Marrogi AJ, Stojadinovic A, Peoples GE, Devesa SS. Rising thyroid cancer incidence in the United States by demographic and tumor characteristics, 1980-2005. *Cancer Epidemiol Biomarkers Prev* 2009;18:784-791.
- Cerci C, Cerci SS, Eroglu E, Dede M, Dapucuoglu N, Yildiz M. Thyroid cancer in toxic and non-toxic multinodular goiter. *J Postgrad Med* 2007;53:157-160.
- Pandey P, Dixit A, Mahajan NC. Fine needle aspiration of the thyroid: A cytohistologic correlation with critical evaluation of discordant cases. *Thyroid Res Pract* 2012;9:32-9.
- Zambudio AR, Rodriguez J, Riquelme J, Soria T, Canteras M, Parrilla P. Prospective study of postoperative complications after total thyroidectomy for multinodular goiters by surgeons with experience in endocrine surgery. *Ann Surg* 2004;240:18-25.
- Cappel RJ, Bouvy ND, Bonjer HJ, Muiswinkel JM, Chadha S. Fine needle aspiration of thyroid nodules: how accurate it is and what are the causes of discrepant cases? *Cytopathology* 2001;12:399-405
- Arul P, Masilamani S. A correlative study of solitary thyroid nodules using the Bethesda system for reporting thyroid cytopathology. *J Can Res Ther* 2015;11:617-22
- Handa U, Garg S, Mohan H, Honda NU, Nagarkar N. Role of fine needle aspiration cytology in diagnosis and management of thyroid lesions: A study on 434 patients.

- Journal of Cytology 2008;25(1):13-7.
23. Muratli A, Erdogan N, Sevim S, Unal I, Akyuz S. Diagnostic efficacy and importance of fine-needle aspiration cytology of thyroid nodules. *J Cytol* 2014;31:73-8.
24. Cerci C, Cerci SS, Eroglue E, Dede M, Dapucuoglu N, Yildiz M. Thyroid cancer in toxic and non-toxic multinodular goiter. *J Postgrad Med* 2007;53:157-160.
25. Wani KA, Mustafa G, Wani RA, Hussain Z, Arif SH, Malik AA, Nisar A. Choudhary. Clinical study of neoplastic thyroid swellings with particular reference to surgical management. *JK-Practitioner* 2007;14:19-21.
26. Woolner LB, Beahrs OH, Black BM, Moconahey WM, Keating. Classification and prognosis of thyroid carcinoma: A study of 885 cases observed in 30 years period. *Am J Surg* 1961;102:354-387.

**Article Citation:** Shahid MU, Sarwar M, Faisal MS, Jabbar M. Histopathology pattern of carcinoma of thyroid in multinodular goiter. *JSZMC* 2018;9(3): 1434-1438.