

MULTINODULAR GOITER VS. SOLITARY THYROID NODULE: A CLINICOPATHOLOGICAL COMPARISON

Asmatullah¹, Fazal-I-Wahid², Qaisar Khan¹, Muhammad Riaz Khan¹

ABSTRACT

Objective: To compare the clinicopathological features of multinodular goiter and solitary thyroid nodule in a tertiary care hospital.

Material and Methods: This prospective cross sectional study was carried out in the department of ENT, Head and Neck Surgery, KGMC/HMC, Peshawar, Pakistan from June 2012 to May 2014. All the patients were evaluated pre-operatively in terms of detailed history, thorough clinical examination and relevant investigations. Thyroidectomy was performed according to the pre-operative and per-operative findings, nature and extent of the disease in all patients. The data were collected on a proforma and analyzed using SPSS version 17. Chi square test was applied keeping P value of < 0.05 as significant.

Results: Out of 130 patients included in this study 40 (30.7%) were male and 90 (69.2%) were female with male: female ratio of 1: 2.2. Age of the patients ranged from 17-65 years, with mean age of 46.47 +S.D 5.27 years. Majority of the patients i.e. 66 (50.7%) were in the age group 41-59 years followed by 40 patients(30.7%) in the age group of 21-40 years. There was no significant difference in the age and gender among these patients (P=0.112, P=0.990). Out of 130 patients 67(51.5%) were having multinodular goiter while 63(48.5%) had solitary thyroid nodule. The commonest clinical features were anterior neck swelling (100%), followed by cervical lymphadenopathy (6.9%).Papillary and follicular carcinomas were the commonest findings on FNAC and histopathology with no significant difference between multinodular goiter and solitary thyroid nodules.

Conclusion: There is no difference between the age and gender and incidence of thyroid malignancy between the patients with multinodular goiter and solitary thyroid nodules. Papillary and follicular carcinomas are the commonly occurring thyroid carcinoma.

Key Words: Multinodular goiter, Solitary thyroid nodule, Thyroid malignancy.

INTRODUCTION

Although thyroid carcinoma (TC) is a rarely occurring tumour in human being, still it is the commonest tumour among the endocrine glands. It is estimated as 1% of human neoplasias, with a global incidence of 0.5–10 per 100,000 persons in world population annually. The incidence of carcinoma in the multinodular goiter (MNG) is reported as 5 to 10 percent. It is a general belief that incidence of carcinoma in solitary thyroid nodule is more than MNG, but however there is no statistically significant difference in the incidence of thyroid

carcinoma between MNG and solitary thyroid nodule as proved by post-operative histopathological examination of the thyroidectomy specimen.¹ The known risk factor for development of thyroid carcinoma is ionizing radiation as ascertained by the drastic increase in thyroid cancer incidence in the inhabitants suffered from the Chernobyl accident of 1986, especially in the pediatric population. More over the presence of solitary thyroid nodule, exposure to prolonged stimulation by elevated TSH and genetic predisposition also contribute in the development of thyroid cancer.²The reason for so called “thyroid cancer epidemic” could not be established. However it may be either due to easy availability of sophisticated screening tests across the globe, increase in the diagnosis of occult carcinoma or “incidentalomas” or increase in exposure to radiation.

Majority of thyroid malignancies arise from thyroid follicular cell and are classified into three major classes; papillary thyroid carcinoma (PTC), follicular thyroid carcinoma (FTC) --- Differentiated thyroid carcinoma, and anaplastic thyroid carcinoma (ATC) --- undifferentiated thyroid carcinoma. The differentiated thyroid carcinomas possess some similarities in the management but there are differences in diagnostic, therapeutic and prognostic characteristics. The other types include medullary thyroid carcinoma (MTC), which arises from

¹ Department of ENT, Head and Neck Surgery Khyber Girls Medical College, Hayatabad Medical Complex, Peshawar-Pakistan.

² Department of ENT, Head and Neck Surgery Post-graduate Medical Institute, Lady Reading Hospital, Peshawar-Pakistan.

Address for correspondence:

Dr. Asmatullah

Associate Professor,
Department of ENT, Head & Neck Surgery
KGMC/HMC, Peshawar, KPK, Pakistan
Mobile No: 0300-8155335
E-Mail: drasmatent@yahoo.com

calcitonin secreting 'C' cell, malignant lymphomas and sarcomas⁴. PTC is the most commonly occurring cancer of thyroid gland, however FTC and ATC are considered to be more common in the endemic goiter areas. Hence highly aggressive thyroid carcinomas are more prevalent in countries with endemic goiter like Pakistan⁵. The treatment choice for Differentiated thyroid carcinoma is surgical resection of the tumor with or without the addition of radioactive iodine ablation. Neck dissection may be accompanied if there is spread of the tumor to surrounding lymph nodes.⁷ Well differentiated thyroid carcinomas have good prognosis where as ATC carries very bad prognosis. Thyroid carcinoma can affect any age, but it is rare in children less than 10 years of age. Females can be affected more than males by thyroid carcinoma, with reported ratio of 3:1, which support the importance of hormonal factors in etiology of TCs.⁸

As goiter is endemic in our region, so a large number of patients are presenting to our hospital with MNG or solitary thyroid nodule. Sometimes goiters are hugely enlarged either due to negligence on the part of the patients or due to patients' residence in far flung areas with no health care facilities in the vicinity of patient.

The aim of this study was to determine the frequency, types, clinical features and any significant difference by histopathological examination of thyroid malignancy between patients with MNG and solitary thyroid nodule.

MATERIALS AND METHODS

This prospective cross sectional study was carried out in the department of ENT, Head & Neck Surgery, KGMC/HMC, Peshawar, Pakistan from June 2012 to May 2014 (02 years). A total of 130 patients of any age and either gender with euthyroid goiter subjected to surgery were enrolled in the study. Patients diagnosed as Grave's disease, Hashimoto's thyroiditis, hyper or hypothyroidism and those not willing for enrollment in the study were excluded. Study was started after getting ethical approval from hospital ethical committee. Well informed consent was taken from each patient explaining risks, benefits, associated complication and prognosis of the procedure along with publication of the data and pictures if needed. All the patients were evaluated pre-operatively in terms of detailed history. Each patient was thoroughly interrogated regarding the duration, presentation, progression of goiter and any other symptom favoring malignant transformation of the goiter. Thorough clinical examination was performed and biochemical investigations specifically thyroid hormones assay was done in every patient. Neck ultrasonography and FNAC was performed in all these patients. Thyroidectomy was performed if the patient was euthyroid, while those with hyper or hypothyroidism were treated medically prior to surgery till they became euthyroid. All the patients were operated under general

anesthesia with endotracheal intubation. Thyroidectomy was performed according to the pre-operative and per-operative findings, nature and extent of the disease. Every patient was put on injectable broad spectrum antibiotics and analgesics. All the resected specimens were sent for histopathology study and final diagnosis was based on histopathology report. The data were collected on a pre-designed proforma and statistical analysis was done using SPSS version 17. Frequency and percentages were calculated for qualitative variables while mean \pm standard deviation was calculated for quantitative variables. Chi square test was applied keeping P value of ≤ 0.05 as significant.

RESULTS

Out of 130 patients registered in this study 40 (30.7%) were male and 90 (69.2%) were female with male: female ratio of 1:2.2. Age of the patients ranged from 17-65 years, with mean age of $46.47 \pm S.D 5.27$ years. Among these patients, 67 (51.5%) patients possessed multinodular goiter (MNG), while 63 (48.5%) patients had solitary thyroid nodule (STN). Majority of the patients i.e. 106(81.5%) presented in the age group 21-59 years i.e. 13 male (10%), 27 female (20.8%) with mean age of $33.21 \pm S.D 3.11$ years in age range 21-40 years, while 19 male(14.6%), 47 female(36.1%), with mean age of $46.38 \pm S.D 5.28$ years in the age range 41 to 59 years had MNG and STN respectively. There was no statistically significant difference in the age and gender among these patients ($P=0.112$, $P=0.990$) (Table 1). The commonest clinical features noted were anterior neck swelling in all the patients (100%), followed by cervical lymphadenopathy in: 6.9%, 4.6% and dysphagia in 8.5%, 1.5% in patients with MNG and STN respectively. Besides other features dysphagia and cervical lymphadenopathy were found more in the patients with MNG, with statistically significant difference ($P= 0.004$, $P=0.032$) (Table 2). Pre-operative ultrasonography and FNAC were performed in all patients. Mean size of nodule was $4.33\text{cm} \pm SD 1.12\text{cm}$ (range ≤ 1.0 - $\leq 4.0\text{cm}$). The commonly found nodule was ≥ 4.0 in 66 patients (50.7%) with MNG and in 33 patients (25.4%) with STN. So nodule of size ≥ 4.0 cm was more common in patients with MNG with significant difference ($P=0.012$). The commonest FNAC findings were PTC and FT (23/130, 17.7%), (15/130, 11.5%) in patients with MNG and (28/130, 21.5%), (7/130, 5.3%) in patients with STN respectively. PTC and FTC were also the commonest findings on histopathology (30%), (13.1%) and (20%), (16.2%) in patients with MNG and STN respectively with no significant difference between MNG and STN. (Table 3). The commonest surgical procedures performed in this study were total thyroidectomy followed by completion thyroidectomy 13.1%, 8.5% in patients with MNG and 16.2%, 11.5% in patients with STN respectively with no statistically significant difference ($P=0.321$, $P=0.411$). The commonest post-operative complication was seroma formation 6.9%

Table 1: Age and Gender wise distribution of patients (n= 130).

Age	MNG(67)				STN(63)				Total	%	P Value
	Male	%	Female	%	Male	%	Female	%			
< 20	1	0.8	3	2.3	-		2	1.5	6	4.6	0.501
21-40	6	4.6	11	8.5	7	5.4	16	12.3	40	30.7	0.112
41-59	11	8.5	25	19.2	8	6.1	22	16.9	66	50.7	0.990
> 60	4	3.1	6	4.6	3	2.3	5	3.8	18	13.8	0.311
Total	22	16.9	45	34.6	18	13.8	45	34.6	130	100	

Table 2: Clinical features observed in patients with MNG and STN (n=130).

Clinical Features	MNG(67)		STN(63)		P value
	Frequency	%	Frequency	%	
Anterior neck swelling	67	100	63	100	0.121
Dysphagia	11	8.5	2	1.5	0.004
Dyspnea	4	3.1	1	0.8	0.010
Dysphonia	3	2.3	4	3.1	0.331
Pain	1	0.8	-	-	0.000
Weight Loss	2	1.5	4	3.1	0.211
Hoarseness	3	2.3	3	2.3	0.000
Cervical Lymphadenopathy	9	6.9	6	4.6	0.032
Signs of hyperthyroidism	4	3.1	2	1.5	0.211
Signs of hypothyroidism	6	4.6	3	2.3	0.322

Table 3: Ultrasound, FNAC and histopathology findings in this study (n= 130).

Investigations		MNG(67)		STN(63)		P Value
		Frequency	%	Frequency	%	
	Nodule size (cm)					
	< 1.0	-	-	9	6.9	0.020
	1.0-3.9	1	0.8	21	16.2	0.003
	>4.0	66	50.7	33	25.4	0.012
FNAC	PTC	23	17.7	28	21.5	0.133
	FT	15	11.5	7	5.3	0.053
	MTC	6	4.6	4	3.1	0.101
	ATC	4	3.1	6	4.6	0.101
	SCC	2	1.5	1	0.8	0.200
	Colloid Nodule	11	8.5	14	10.8	0.511
	Inconclusive	5	3.8	3	2.3	0.402
Histopathology	PTC	39	30	26	20	0.213
	FTC	17	13.1	21	16.2	0.111
	MTC	7	5.4	10	7.7	0.322
	ATC	3	2.3	4	3.1	0.772
	SCC	1	0.8	-	-	0.000

Table 4: Types of surgery and complications observed in this study (n=130).

Surgery	MNG(67)		STN(63)		P value
	Frequency	%	Frequency	%	
Total thyroidectomy	17	13.1	21	16.2	0.321
Completion thyroidectomy	11	8.5	15	11.5	0.411
Subtotal thyroidectomy	18	13.8	6	4.6	0.020
Near total thyroidectomy	14	10.8	17	13.1	0.425
Total thyroidectomy+ Neck dissection	7	5.4	4	3.1	0.193
Complications					
Seroma formation	9	6.9	5	3.8	0.222
Neck hematoma	5	3.8	3	2.3	0.124
Transient Hypocalcaemia	4	3.1	4	3.1	0.000
Transient vocal cord palsy	6	4.6	2	1.5	0.827
Persistent hypoparathyroidism	2	1.5	3	2.3	0.897
Persistent unilateral vocal cord palsy	2	1.5	1	0.8	0.398
Persistent bilateral vocal cord palsy	1	0.8	0	-	-

and 3.8% in patients with MNG and STN respectively with no significant difference (Table 4).

DISCUSSION

Goiter being endemic in our region, a significant number of people suffering from goiter may be harbouring thyroid malignancy. Long standing goiter is more prone to develop malignancy due to prolonged stimulation by elevated TSH. The incidence of malignancy in MNG is of the order of 5% to 10% and is similar to that in a solitary thyroid nodule, which is the most common way of presentation of thyroid malignancy. Although thyroid malignancy may affect people in any age, however people in middle or advanced age are suffered more. In this study age of the patients ranged from 17-65 years, with mean age of 46.47 +S.D 5.27 years and majority of patients were in the age range of 21-59 years of life, which is corresponding with report of Niazi⁹ with age range of 8 years to 90 years, and maximum number of thyroid malignancies (106 cases, 62.35%) were seen in the 21-50 years age group. Likewise in Shah's study¹⁰ the mean age of patient was 52 years (range 22-87) and most (69%) were > 45 years of age. Thyroid malignancy is more common in female around the world. We found female predominance in this study with male: female ratio of 1: 2.2, which simulates the study of Goldust¹¹ who observed that out of 356 patients, 100 (28%), were male and 256 (72%) were female with male: female ratio 1:2.5. The reason for this female dominance is not established yet. Distribution of goiter in this study was that MNG and STN were found in 51.5% and 48.5% patients respectively with no statistically significant difference in age and gender between these two groups. This result is comparable to the work of Nanjappa¹² who found that among 175 patients, 77(44%) presented with MNG, of which 68 (88.3%) were female and 9 (11.7%)

male, while 98 patients (56%) presented as STN, of which 92 (93.9%) were female and 6 (6.1%) male. In this study only 14 patients (8%) with MNG and 23 patients (13.1%) with STN had thyroid malignancy. There was no significant difference among these two groups of patients (P=0.543, P= 0.262).

The commonest clinical features noted were anterior neck swelling in all the patients (100%), followed by cervical lymphadenopathy in 6.9%, 4.6% and dysphagia in 8.5%, 1.5% in patients with MNG and STN respectively with significant difference in clinical features between the two groups (P=0.04), which is in agreement with work of Tarrar¹³ who noted anterior neck swelling 100%, palpable cervical lymphadenopathy 6.67% and dysphagia in 5% of patients. Similarly Larijani¹⁴ also reported that neck mass was the commonest presentation (68%) in patients with goiter followed by dysphonia 9%, dysphagia 3% and lymphadenopathy was the least common (2%). Goldust¹¹ also reported that neck mass was the most prevalent symptom (88.2%), while pain was the least common symptom (8.9%), with no significant difference between the male and female (P=0.32, P=0.08).

Pre-operative sonography showed that nodule was > 4.0 in 66 patients (50.7%) with MNG and in 33 patients (25.4%) with STN. Thus nodule of size > 4.0 cm was more common in patients with MNG with significant difference (P=0.012), which is in conformity with the study of Shah¹⁰ where nodule of size > 4.0 cm was 53%. The commonest FNAC findings were PTC and FT (23/130, 17.7%), (15/130, 11.5%) in patients with MNG and (28/130, 21.5%), (7/130, 5.3%) in patients with STN respectively, which is in accordance with Tarrar's study having PTC the commonest finding on FNAC. While result of this study differs from Bagga's¹⁵ report who

found papillary carcinoma 66.67%, follicular tumour 64.6% and medullary carcinoma 33.33%. The frequency of thyroid malignancy was greater in Basharat¹⁶ study i.e. papillary carcinoma (60.0%), medullary carcinoma (20.0%) and anaplastic carcinoma (20.0%). The commonest tumours among thyroid carcinomas are papillary and follicular carcinoma all over the world. In this study histopathology findings were PTC and FTC: (30%), (13.1%) and (20%), (16.2%) in patients with MNG and STN respectively with no significant difference between MNG and STN. Likely Larijani¹⁴ found the frequencies of tumor types as papillary (9.7%), follicular (8.8%), anaplastic (7.9%) and medullary (3.6%). However our results were at variance from Niazi⁹ study where tumours frequency was papillary 68.23%, follicular 14.11%, medullary 6.47 and anaplastic 5.88%. In Goldust¹¹ study histopathological findings were that PTC was the most common tumour (n=281; 78.9%), followed by FTC (n=35; 10%) and the least common was MTC (n=18; 5.1%). Similarly in Bukhari's study¹⁷ papillary carcinoma was 90.2%, medullary was second most common (4.5%) and follicular carcinoma was least common (2%).

Surgery is the treatment of choice for differentiated thyroid carcinoma and total thyroidectomy is the commonly performed surgery as we noted in our study that total thyroidectomy followed by completion thyroidectomy was 13.1%, 8.5% in patients with MNG and 16.2%, 11.5% in patients with STN respectively with no statistically significant difference (P=0.321, P=0.411), which is coinciding with report of Goldust¹¹ who observed that total thyroidectomy was 30%, lobectomy 3.3% and radical neck dissection with total thyroidectomy was 64%. However regarding thyroid surgery our results differs from Ahmed¹⁸ research work, who described that total thyroidectomy was 4%, completion thyroidectomy 4%, lobectomy 2% and subtotal thyroidectomy 4%. Similarly Bilimoria¹⁹ also found that total thyroidectomy was the commonest (82.9%) surgery. The commonest post-operative complication was seroma formation 6.9% and 3.8% in patients with MNG and STN respectively with no significant difference. Our complications are different from Al-Amri²⁰ study who noted death (0.07%), nerve palsy (7.35%), hypoparathyroidism (0.07%) and recurrence of thyroid cancer (8.8%). The complications of thyroid surgery of our study are also supported by Karamanakos²¹ results where hematoma was 1.3%, wound infection 0.3% and permanent hypoparathyroidism 4.8%. In Khanzada's²² study commonest complication of thyroid surgery was hypocalcaemia (10.7%).

CONCLUSION

It is concluded that although there is no difference between the age and gender, diagnostic outcome and incidence of thyroid malignancy between the patients with multinodular goiter and solitary thyroid nodules, however there is significant difference between the

clinical features of these two groups. Papillary and follicular carcinomas are the commonly occurring thyroid carcinoma.

REFERENCES

1. Watkinson JC, Gilbert RW. Surgery for benign thyroid disease. In Stell & Maran's Textbook of Head and Neck Surgery and oncology. Fifth edition. Hodder Arnold 2012; 22:406-421.
2. Srilatha B, Hima Bindu A, Soumya D Epidemiology and Treatment for Thyroid Cancer. J Cancer Sci Ther. 2011; 17:1-6. doi:10.4172/1948-5956.S17-011.
3. Sinna EA, Ezzat N. diagnostic accuracy of fine needle aspiration cytology in thyroid lesions. Journal of the Egyptian National Cancer Institute. 2012; 23:63-70.
4. Pang HN, Chen CM. Incidence of Cancer in Nodular Goitres. Ann Acad Med Singapore 2007; 36:241-3.
5. Happa HMB, Gopinathan S, Rana RS, Raid GPRS, Shetty GH, Shetty AH et al. The Incidence of Malignancy in Multi-nodular Goitre: A Prospective Study at a Tertiary Academic Centre. Journal of Clinical and Diagnostic Research. 2012; 6(2): 267-70.
6. Brown RL, De Souza JA, Cohen EEW. Thyroid Cancer: Burden of Illness and Management of Disease. J Cancer 2011; 2: 193-99. doi:10.7150/jca.2.193.
7. Htwe TT. Thyroid malignancy among goitrous thyroid lesions: a review of hospital-based studies in Malaysia and Myanmar. Singapore Med J 2012; 53(3) : 159-63.
8. Iranmanesh P, Puztaszeri M, Robert J, Meyer P, Schiltz B, Saowski SM et al. Thyroid Carcinoma in Hot Nodules: Review of the Literature. World J Endoc Surg 2013;5(2): 50-54.
9. Niazi S, Arshad M, Bukhari MH. A Clinicopathological Study of Thyroid Cancers at King Edward Medical University / Mayo Hospital, Lahore. ANNALS 2011; 17(3): 268-76.
10. Shah MD, Conrad A, Ahmed A, Eski S, MacMillan C, Freeman JL. Decision Making for the Extent of Thyroidectomy in the Patient with Atypical Cytologic Results. Arch Otolaryngol Head Neck Surg. 2010; 136(12):1177-80.
11. Goldust M, Sokouti M, Montazeri V, Fakhrajoo A, Samankan S. A clinical epidemiologic study of thyroid carcinoma in patients under 25 years old in Tabriz, Iran (1995-2010). JPMA 2012; 62:1265- 68.
12. Nanjappa N, Mohanty A, Arou TT, Smile RS, Kotasthane D. Thyroid Carcinoma (Tc) in Nodular Goitre. Thyroid Disorders Ther 2012, 1:115. doi:10.4172/2167-7948.1000115.
13. Tarrar AM, Wahla MS, Ilyas S, Khan OU, Waqas A, Raza A. Solitary thyroid nodule; Frequency of malignancy at Combined Military Hospital Rawalpindi. Professional Med J 2010; 17(4):598-602.
14. Larijani B, Aghakhani S, Khajeh-Dini H and Jalili RB. Clinico-pathological Features of Thyroid

- Cancer as Observed in Five Referral Hospitals in Iran. *Acta Oncologica*. 2003; 42(4):34-37. DOI: 10.1080/02841860310001547
15. Bagga P K, Mahajan N C. Fine needle aspiration cytology of thyroid swellings: How useful and accurate is it? *Indian J Cancer* 2010; 47:437-42.
 16. Basharat R, Bukhari MH, Saeed S, Hamid T. Comparison of Fine Needle Aspiration Cytology and Thyroid Scan in Solitary Thyroid Nodule. *Pathology Research International* .2011; 9:2-9. doi:10.4061/2011/754041.
 17. Bukhari U, Sadiq S. Histopathological Audit of Goiter: A Study of 998 Thyroid Lesions. *Pak J Med Sci* 2008; 24(3):442-6.
 18. Ahmed M, Aurangzeb, Abbas S, Boota M, Ashfaq M, Rashid AZ et al. Should We Routinely Expose Recurrent Laryngeal Nerve(s) During Thyroid Surgery? *Journal of the College of Physicians and Surgeons Pakistan* 2013, Vol. 23 (3): 186-89.
 19. Bilimoria KY, Bentrem DJ, Ko CY, Stewart A, Winchester D, Talamonti MS et al. Extent of Surgery Affects Survival for Papillary Thyroid Cancer. *Ann Surg*. 2007; 246(3): 375–84. doi: 10.1097/SLA.0b013e31814697d9.
 20. Al-Amri AM. Pattern of Thyroid Cancer in the Eastern Province of Saudi Arabia: University Hospital Experience. *Journal of Cancer Therapy*, 2012; 3: 187-191
 21. Karamanakos SN, Markou KB, Panagopoulos K, Karavias D, Vagianos CE, Scopa CD et al. Complications and risk factors related to the extent of surgery in thyroidectomy. Results from 2,043 procedures. *HORMONES* 2010, 9(4):318-325.
 22. Khanzada TW, Samad A, Memon W, Basant Kuma B. Post thyroidectomy complications: The Hyderabad experience *J Ayub Med Coll Abbottabad* 2010; 22(1): 65-68

ONLINE SUBMISSION OF MANUSCRIPT

It is mandatory to submit the manuscripts at the following website of KJMS. It is quick, convenient, cheap, requirement of HEC and Paperless.

Website: www.kjms.com.pk

The intending writers are expected to first register themselves on the website and follow the instructions on the website. Author agreement can be easily downloaded from our website. A duly signed author agreement must accompany initial submission of the manuscript.