International Journal of Research in Medical Sciences
Palo S et al. Int J Res Med Sci. 2016 Jun;4(6):2319-2323
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20161807

Research Article

Prevalence of malignancy in multinodular goiter and solitary thyroid nodule: a histopathological audit

Seetu Palo[1]*, Debadutta Mishra[2]

[1]Department of Pathology, Maharajah's Institute of Medical Sciences, Vizianagram, Andhra Pradesh, India
[2]Department of Microbiology, Maharajah's Institute of Medical Sciences, Vizianagram, Andhra Pradesh, India

Received: 14 April 2016
Accepted: 09 May 2016

***Correspondence:**
Dr. Seetu Palo,
E-mail: seetu.pearl@gmail.com

ABSTRACT

Background: Thyroid malignancy has varied prevalence worldwide and it is traditionally believed that solitary thyroid nodules are more likely to be neoplastic than multiple nodules.
Methods: Histopathological analysis was conducted on 165 surgically resected thyroidectomy specimens of multinodular goiter (MNG) and 123 cases of solitary thyroid nodule (STN) in order to determine and compare the prevalence and the types of various thyroid malignancies.
Results: 28 of 165 MNG (17%) and 47 of 123 STN (38.2%) were associated with malignancy and the difference was statistically significant. Papillary thyroid carcinoma was the commonest malignancy observed in both the study groups.
Conclusions: We conclude that the prevalence of cancer was significantly higher in STN than MNG. But, since the prevalence of malignancy in MNG was also quite high, every effort should be made to pre-operatively identify any malignant focus in patients presenting with MNG.

Keywords: Thyroid malignancy, Multinodular goiter, Solitary thyroid nodule, Papillary carcinoma

INTRODUCTION

Thyromegaly can be the clinical manifestation of a wide spectrum of thyroid pathology, ranging from functional enlargements to immunologically mediated disorders to neoplastic lesions.

The major concern in such patients presenting with thyroid enlargement is to rule out the possibility of neoplastic disease. Although thyroid tumors account for only 1% of the overall human cancer burden, they represent the most common malignancy of the endocrine system.[1]

Thyroid neoplasms usually present as a solitary palpable nodule or multiple discrete nodules. Rarely, a patient may present with obvious metastatic disease without a clinically detectable primary lesion.

The incidence of thyroid malignancy varies from 0.9% to 13% worldwide.[2] It is traditionally believed that solitary thyroid nodules are more likely to be neoplastic than multiple nodules.[3-5]

However, in recent past, various studies have reported a rising incidence of malignancy even in multinodular goiter.[4-7] With this background, this study was undertaken to determine and compare the prevalence and the types of various thyroid malignancies clinically presenting as multinodular goiter and solitary thyroid nodule by histopathological examination of thyroidectomy specimens.

METHODS

A prospective analytical study was carried on the thyroidectomy specimens received in the Pathology Department of Victoria hospital and Bowring and Lady Curzon hospitals, attached to Bangalore medical college and research centre, between November 2012 to October 2014. Details of the patients' demographics, clinical presentation and diagnosis, results of Fine needle aspiration cytology (FNAC), ultrasonographic findings, gross features and biopsy results of the resected thyroid specimens were obtained from the patients' case files, operation registers, histopathology records and laboratory request forms. Cases with insufficient clinical details and cases of Grave's disease and Hashimoto thyroiditis were excluded from the study.

The hematoxylin and eosin (H&E) stained slides of the thyroidectomy specimens were analyzed by an independent pathologist. Histopathological diagnosis was considered as gold standard. Tumour typing was based on the 2004 World Health Organization histological classification criteria.[1]

For the purpose of analysis, the included cases were divided into two study groups: multinodular goiter (MNG) group, when more than one nodule was detected on clinical examination and Solitary thyroid nodule (STN) group, when there was clearly only a single palpable nodule. The data was collected on a pre-designed excel sheet and statistical analysis was done using SPSS version 16. Percentages and means were calculated for quantitative variables. The statistical significance among different groups was determined using Chi square test. A p-value <0.05 was considered statistically significant.

RESULTS

Table 1: Age and gender-wise distribution of cases in MNG and STN group.

Age (in years)	MNG group (n=165)			STN group (n=123)		
	M	F	T	M	F	T
<20	1	3	4	0	3	3
21-40	6	90	96	3	83	86
41-60	8	47	55	6	22	28
>60	3	7	10	1	5	6
Total	18	147	165	10	113	123

Key: M-Male; F-Female; T-Total

A total of 288 thyroidectomy specimens, meeting the inclusive criteria, were analyzed. Of these, 165 (57.3%) patients presented with multiple nodules (MNG group), while 123 (42.7%) patients presented with a solitary palpable nodule (STN group). The overall age and gender distribution of all these cases is depicted in Table-1. The commonest clinical presentation was anterior neck swelling in all the patients (100%), followed by pain (10% cases in MNG group, 18.7% cases in STN group) and dysphagia (7.2% cases in MNG group, 12.2% cases in STN group). None of these patients had a history of neck irradiation or a family history of a thyroid malignancy.Data of pre-operative ultrasonography and FNAC results were available in all cases and are stated in Table 2. Ultrasonography revealed that most of the thyroid nodules in MNG patients were of larger size as compared to that of the STN group at the time of presentation. Mean size of nodules was 3.98 cm in the MNG group and 2.56 cm in the STN group. According to FNAC results, more number of malignant cases belonged to the STN group.

Table 2: USG and FNAC findings of the cases in MNG and STN group.

Investigation			MNG group (n=165)	STN group (n=123)
USG	Nodule size (in cm)	<2.0	0	19
		2.1 – 4.0	93	89
		4.1 – 6.0	64	13
		>6.0	8	2
FNAC	Colloid nodule		11	10
	Adenomatous nodule		6	20
	Multinodular goitre		128	0
	Follicular neoplasm		2	54
	Papillary carcinoma		14	39
	Medullary carcinoma		1	0
	Inconclusive		3	0

Key: USG- Ultrasonography; FNAC- Fine needle aspiration cytology.

Table 3: Histopathological findings in MNG and STN group.

Histo-pathologic diagnosis		MNG group (n=165)	STN group (n=123)
Benign	Pure MNG	116	0
	Colloid Nodule	11	10
	Adenomatous nodule	8	30
	Follicular adenoma	2	36
	Total	137(83%)	76(61.8%)
Malignant	cPTC	11	22
	mPTC	10	0
	FVPTC	6	20
	FTC	0	5
	MTC	1	0
	Total	28(17%)	47(38.2%)

Key: cPTC- Classical variant of papillary thyroid carcinoma; mPTC- Papillary thyroid microcarcinoma; FVPTC- Follicular variant of papillary carcinoma; FTC- Follicular Carcinoma of thyroid; MTC- Medullary carcinoma of thyroid.

Post-operative histopathological analysis revealed 28 (17%) cases in the MNG group and 47 (38.2%) cases in the STN group had malignant focus. Papillary thyroid carcinoma (PTC) was the commonest malignancy observed in both the study groups (Table 3). Five cases of follicular carcinoma and one case of medullary carcinoma were found in exclusively in STN group and MNG group respectively. No other histological type of thyroid cancer was encountered in this study. In the benign spectrum, follicular adenoma was the commonest lesion.

Table 4: Prevalence of malignancy in STN in the present study and as reported by various authors.

Various studies	Prevalence of malignancy (in percentage)
Present study	38.2
Tai et al[14]	36.6
Anwar et al[15]	24.3
Nanjappa et al[13]	23.5
Satihal et al[16]	20.0
Abu-Eshy et al[17]	15.2
Asmatullah et al[18]	13.1
Ramchandraiah et al[19]	13.0
Sudarshan Babu et al[20]	8.0
Golder et al[21]	8.0

Table 5: Prevalance of malignancy in MNG in the present study and as reported by various authors.

Various studies	Prevalence of malignancy (in percentage)
Nanjappa et al[13]	18.2
Present study	17.0
Ullah et al[22]	15.0
Anwar et al[15]	14.4
Hussain et al[23]	14.35
Baloch et al[24]	14.0
Vittal et al[25]	12.5
Prades et al[26]	12.2
Nadeem et al[27]	10.2
Hanumanthappa et al[28]	10.0
Benzarti et al[29]	9.5
Bhuiyan et al[30]	8.9
Abu-eshy et al[17]	8.0
Koh et al[31]	7.5
Awati sm[32]	5.0

DISCUSSION

The incidence of thyroid malignancy has been on a rise during the past 60 years.[3,8] It has been proposed that the availability of more sensitive diagnostic tools might be responsible for the increasing incidence.[3,9] High-resolution ultrasound and FNAC are useful investigation modalities. Ultrasonograghic features suggestive of malignancy in thyroid nodules are micro calcifications, hypo echogenicity, irregular margins or absent halo sign, solid lesion and intraocular vascularization.[10] FNAC is increasingly become an indispensible investigation tool in thyroid pathology with varying sensitivity and specificity.[11]The final diagnosis, however, rests upon post-operative histopathological examination of the surgically removed thyroid gland.

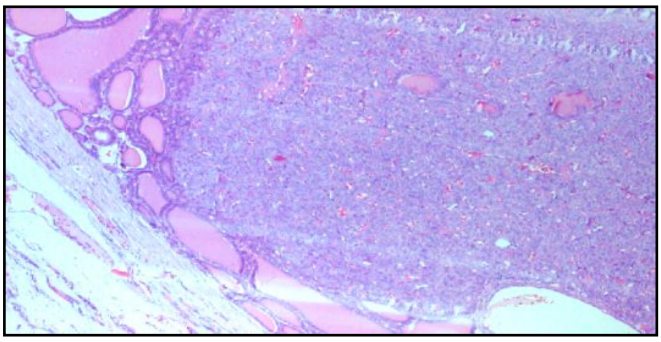

Figure 1: Histopathological picture of an occult papillary micro-carcinoma in a multinodular goiter (H & E, 40x).

In our study, FNAC findings correlated well with postoperative histopathological findings of most of the excised specimen. FNAC proved to be more sensitive in picking up malignancy in the STN group. All cases of papillary thyroid micro-carcinoma (mPTC) in MNG were missed by FNAC (Figure 1). Hence, a negative FNAC report does not necessarily exclude the possibility of an occult carcinoma, especially in MNG, because the degree of error in sampling the appropriate area is greater.[4] Sensitivity can be increased by multiple aspirations from different sites and USG-guided FNAC.

In our study, a striking female predominance was noted in both the study groups. Majority of the patients were in the 3rd and 4th (58% in MNG group and 78% in STN group) decade of life. In the MNG group, malignancy was found in 15 males and 13 of females. Malignancy was found in 8 males and 39 females in the STN group. The mean age of patients who had malignancy was slightly higher than those who had benign lesion. Similar observations were made by Pang and Chung and Nanjappa BA et al.[12,13]

Upon histopathological examination, the frequency of malignancy was higher in STN group (38.2%) as compared to MNG group and it was statistically significant (p-value < 0.05). Various other investigators have reported similar higher percentage of malignancy in STN (Table 4). But, as demonstrated in our study, it should be also noted that the prevalence of malignancy in MNG not as meager as it was traditionally believed. We noted malignant focus in 17% of cases of MNG. In recent times, other investigators too have noted a rise in the prevalence of malignancy in cases of MNG (Table 5).

Classical type papillary thyroid carcinoma (cPTC) is known to be the commonest thyroid malignancy and we

observed the same. 11 cases of cPTC were found in MNG group and 22 cases were encountered in the STN group. Follicular variant of papillary thyroid carcinoma (FVPTC) was the next common histological type that we observed in our study. Out of 6 cases of FVPTC found in the MNG group, 2 cases showed multifocality on histopathology. All cases of follicular carcinoma (Figure 2) presented itself as solitary thyroid nodule.

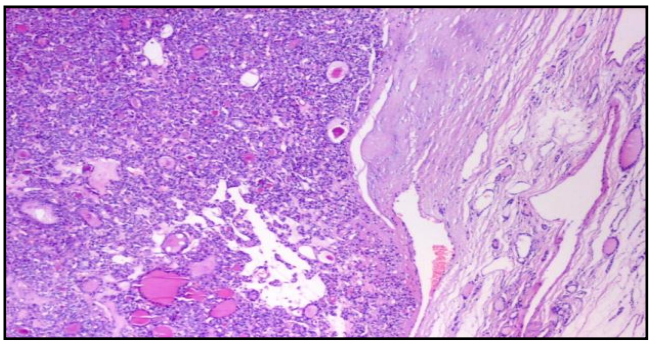

Figure 2: Histopathological picture of a case of follicular carcinoma (H & E, 40x).

Interestingly, all cases of mPTC were encountered exclusively in the MNG group and all were missed on pre-operative FNAC evaluation.

mPTC is defined as a papillary carcinoma of the thyroid that is less than 10 mm in diameter. Such cases of mPTC and cystic PTC can be missed on FNAC and in such scenario; ultrasound-guided fine-needle aspiration cytology is advisable. In our series, we came across two cases of cystic PTC, one presented as MNG and other as STN.

CONCLUSION

We conclude that the prevalence of malignancy was significantly higher in STN than MNG, with cPTC being the most common histological subtype. But, the prevalence of malignancy in MNG was also quite high and cannot be underestimated. It would be practically wise to keep this in mind while evaluating patients with MNG and ample effort should be made to pre-operatively identify any malignant focus, so that appropriate therapeutic protocol can be planned.

ACKNOWLEDGEMENTS

Authors would like to express their gratitude to Dr. Raghupathi A R, Dr. Dayananda SB, and Dr Nirmala CP, Department of Pathology, Bangalore Medical college and research institute for their valuable support and suggestions.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. DeLellis RA, Williams ED. Tumours of thyroid and parathyroid. In: DeLellis RA, Lloyd RV, Heitz PU, Eng C edts. Pathology And Genetics. Tumors of endocrine organs. World Health Organization Classification of Tumors. Lyon, France: IARC Press; 2004:49-56.
2. UI Haq RN, Khan BA, Chaudhry IA. Prevalence of malignancy in goitre: a review of 718 thyroidectomies. J Ayub Med Coll Abbottabad 2009;21(4):134-6.
3. Memon W, Khanzada TW, Samad A, Kumar B. Incidence of thyroid carcinoma in multi-nodular goitres. Rawal Med J. 2010;35(1):65-7.
4. Gandolfi PP, Frisina A, Raffa M, Renda F, Rocchetti O, Ruggeri C, et al. The incidence of thyroid carcinoma in multi-nodular goitre: a retrospective analysis. Acta Bio Medica Ateneo Parmense. 2004;75:114-7.
5. Pedamallu R, Pedamallu SB, Rama Rao K, Pedamallu CS. Incidence of occult carcinoma in multi-nodular goitre which was diagnosed on the basis of the histopathological findings. Internet J Surg. 2008;17:1.
6. Cole WH. Incidence of carcinoma of the thyroid in nodular goitre. Semin Surg Oncol. 1991;7(2):61-3.
7. Sachmechi I, Miller E, Varatharajah R. Thyroid carcinoma in the single cold nodules and in the cold nodules of multi-nodular goitres. Endocr Pract. 2000;6(1):110-2.
8. Whelan SL, Parkin DM, Masuyer E. The patterns of cancer in five continents. IARC Sci Publ. 1990;102:152-3.
9. Cerci C, Cerci SS, Eroglu E, Dede M, Kapucuoglu N, Yildiz M, et al. Thyroid cancer in toxic and non-toxic multi-nodular goitre. J Postgrad Med. 2007;53:157-60.
10. Rago T, Vitti P. Role of thyroid ultrasound in the diagnostic evaluation of thyroid nodules. Best Pract Res Clin Endocrinol Metab. 2008;22(6):913-28.
11. Lokhande R ,Gedam BS, Shah Y, Kale V, Tandon M, Ansari I. The accuracy of ultrasonography and fine needle aspiration cytology in the diagnosis of nodular goitre: A prospective analysis of fourty two cases. IJBAR. 2015;6(1):43-6.
12. Pang HN, Cheng CM. Incidence of cancer in nodular goitres. Ann Acad Med Singapore. 2007;36: 241-3.
13. Nanjappa BAN, Mohanty A, Aroul TT, Smile SR, Kotasthane D. Thyroid Carcinoma (Tc) in Nodular Goitre. Thyroid Disorders Ther. 2012;1:115. doi:10.4172/2167-7948.1000115.
14. Tai JD, Yang JL, Wu SC, Wang BW, Chang CJ. Risk factors for malignancy in patients with solitary thyroid nodules and their impact on the management. J Can Res Ther. 2012;8:379-83.
15. Anwar K, Din G, Zada B, Shahabi I. The frequency of malignancy in nodular Goiter: a single center study. JPMI. 2012;26(1):96-101.

16. Satihal SN, Palled ER. A study of various clinical presentation of solitary thyroid nodule at tertiary care center. IJRTSAT. 2014;10(2):30-2.
17. Abu-Eshy SA, Khan AR, Khan GM, al-Humaidi MA, al-Shehri MY, Malatani TS. Thyroid malignancy in multinodular goitre and solitary nodule. J R Coll Surg Edinb. 1995;40:310-2.
18. Asmatullah, Wahid FI, Khan Q, Khan MR. Multinodular goiter vs. solitary thyroid nodule: a clinicopathological comparison. KJMS. 2014;7(2):206-11.
19. Ramchandraiah C, Sadgunachary R, Vijayabhargav. Incidence of malignancy in solitary nodule of thyroid. Indian journal of applied research. 2016;6(2):703-7
20. Sudarshan Babu KG, Shantharam L. A clinicopathological study of solitary nodule of thyroid. IJSR. 2014;3(4):307-9.
21. Golder S, Satpathy SN, Pandhy RK, Panigrahi R, Ghata S. A clinicopathological study of solitary thyroid nodule. J Pharm Biomed Sci. 2015;05(03):233-7.
22. Ullah I, Hafeez M, Ahmad N, Muahammad G, Gandapur S. Incidence of thyroid malignancy in multinodular goiter. J Med Sci. 2014;22(4):164-5.
23. Hussain N, Anwar M, Nadia N, Ali Z. Pattern of surgically treated thyroid disease in karachi Biomedica. 2005;21:18-20.
24. Baloch MN, Aslam T, Maher M. Rational for near total thyroidectomy. Pak J Surg. 2007:23:177-9.
25. Vittal S, Kumar KB, Chandrasekharan M, Suchitra V, Jeevarathinam R. Thyroid surgery: indian experience. Indian J Surg. 1993;55:183-7.
26. Prades JM, Dumollard JM, Timoshenko A, Chelikh L, Michel F, Estour B, et al. Multi-nodular goitre: surgical management and histopathological findings. Eur Arch Otolaryngol. 2002;259:217-21.
27. Nadeem K, Akhtar N, Tarar JM. Thyroid malignancy in multi nodular goiter; incidence, a retrospective study in southern punjab. Professional Med J. 2013;20(4):587-90.
28. Hanumanthappa MB, Gopinathan S, Rithin Suvarna R, Rai G, Shetty G, Shetty A, 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):267-270.
29. Benzarti S, Miled I, Bassoumi T, Ben Mrad B, Akkari K, Bacha O, et al. Thyroid surgery (356 cases): the risks and complications. Rev Laryngol Otol Rhinol. 2002;123(1):33-7.
30. Bhuiyan MMZU, Machowski A. Nodular thyroid disease and thyroid malignancy: experience at polokwane mankweng hospital complex, limpopo province, South Africa. SAMJ. 2015;105(7):570-2.
31. Koh KB, Chang KW. Carcinoma in multinodular goitre. Br J Surg. 1992;79:266-7.
32. Awati SM. A study of clinical evaluation and management of multinodular goiter. Int J Sci Stud. 2014;2(8):41-5.

Cite this article as: Palo S, Mishra D. Prevalence of malignancy in multinodular goiter and solitary thyroid nodule: a histopathological audit. Int J Res Med Sci 2016:4:2319-23.