International Journal of Otorhinolaryngology and Head and Neck Surgery
Shahrear MK et al. Int J Otorhinolaryngol Head Neck Surg. 2024 Jun;10(3):294-298
http://www.ijorl.com
pISSN 2454-5929 | eISSN 2454-5937

DOI: https://dx.doi.org/10.18203/issn.2454-5929.ijohns20241324

Original Research Article

Frequency of lymph node metastasis in differentiated thyroid carcinoma

M. Khaled Shahrear[1]*, Muhammad M. Haque[1], Ashik Iqbal[1], M. Romena Khatun[2], Ali A. M. Nafis[1]

[1]Department of ENT, Rajshahi Medical College, Rajshahi, Bangladesh
[2]Department of Microbiology, Rajshahi Medical College, Rajshahi, Bangladesh

Received: 29 December 2023
Revised: 16 April 2024
Accepted: 29 April 2024

***Correspondence:**
Dr. M. Khaled Shahrear,
E-mail: shahrearkhaled@gmail.com

ABSTRACT

Background: Although lymphatic metastasis does not affect overall survival for patients with differentiated thyroid carcinoma, locoregional control can be improved with cervical lymphadenectomy. The major morbidity of neck dissection (ND) for the management of regional metastasis is spinal accessory (CN XI) dysfunction. To avoid this complication, some surgeon advocates limited ND. This study aimed to analyze the frequency of lymph node metastasis in differentiated carcinoma of the thyroid.
Methods: This cross-sectional observational study was conducted at the Department of Otolaryngology, Rajshahi Medical College Hospital, Rajshahi, and Department of Otolaryngology, Bangabandhu Sheikh Mujib Medical University (BSMMU), from July 2011 to Jun 2012. A total of 40 patients were selected as study subjects by simple random sampling technique. A descriptive analysis of data was carried out by using a statistical package for social science (SPSS) 22.0 for Windows.
Results: In this study, a majority 35 (87.5%) of the patients suffered from papillary carcinoma, followed by 5 (12.5%) follicular carcinoma It was found that 18 (51.43%) patients had lymph node metastasis from papillary carcinoma of the thyroid. 10 (55.56%), and 4 (22.22%) patients had right and left-sided lymph node involvement respectively. Bilateral involvement was found in 4 (22.22%) patients. The predominant site of metastasis was level-III (77.3%) followed by level-VI (63.64%) nodal metastasis.
Conclusions: This study concludes that metastasis in differentiated thyroid carcinoma is common. Lymph node metastasis is more common in papillary carcinoma than follicular carcinoma.

Keywords: Differentiated thyroid carcinoma, Lymph node metastasis, Solitary nodule

INTRODUCTION

Thyroid nodules are more common in women and increase in frequency with age. Though thyroid nodules are common, malignancy is uncommon, and the most common way to present as a solitary thyroid nodule.[1] Thyroid neoplasms represent almost 95% of all endocrine tumors, relatively uncommon and accounting for approximately 2.5% of all malignancies.[2] Malignant thyroid tumors can originate from any of the cellular components of the gland: follicular and parafollicular cells, lymphoid cells, and stromal cells. The vast majority are the follicular cell neoplasms of which papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC) are the commonest, collectively called differentiated thyroid carcinoma (DTC).[1] FTC occurs more commonly in areas of endemic goiter than PTC.[2] Exposure to ionizing radiation, endemic goiter, prolonged thyroid stimulating hormone (TSH) stimulation, and high iodine intake are important in the causation of thyroid malignancy.[1,2] The presence of a solitary thyroid nodule is also a risk factor

for malignancy. The incidence of malignancy within a clinically apparent solitary thyroid nodule is approximately 10%.[1] The reported incidence of carcinoma in solitary nodules varies from 2-20%.[3,4] Lymph node metastasis carries an important prognostic value.[5] In DTC, lymph node metastasis was more common in papillary (35%) than follicular carcinoma (12.5%), but distant metastasis was more common in follicular (12.5%) than papillary carcinoma (3.70%).[6] DTC comprises approximately 90% of all thyroid cancers and carries an excellent long-term prognosis.[7] Recent studies have confirmed the incidence of nodal metastasis in PTC ranging from 60-65%.[5,8-10] Lymph node metastases in FTC occur less frequently but prefer to metastasize via veins to distant organs.[8,11] Metastasis in the central compartment is more common than in the ipsilateral and contralateral cervico-lateral compartment.[12] Regarding the level of involvement, the most frequently involved levels are II (52%), III (57%) and IV (41%).[13] There are several techniques to investigate thyroid carcinomas. About 80% of discrete swelling is "cold". Most nonfunctional or "cold" nodules are benign but as many as 20% may be malignant. The principal benefit of isotope scanning is to identify metastasis or residual local disease after total thyroidectomy for follicular carcinoma. Whole-body scanning can also be used to demonstrate metastasis but the patient must have no normal functioning thyroid tissue when the isotope is given because thyroid cancer can only very rarely compete with normal thyroid tissue in the uptake of iodine. Moreover, an ultrasound helps to measure tumor size, diagnosing multinodular goiters and excluding contralateral disease. Ultrasonography can also be used to evaluate complex cysts and can distinguish purely cystic nodules.[14,15] Increasing age, male gender, distant metastasis, extrathyroidal spread, and large tumor size, have all been shown to be more consistently linked to a worse prognosis.[3,16,17]

This study aims to detect the frequency of lymph node metastasis in differentiated carcinoma of the thyroid.

Objectives

General objective

General objective of the study was to detect the frequency of lymph node metastasis in differentiated carcinoma of the thyroid.

Specific objectives

Specific objectives of the study were to know the age and sex distribution of the study subjects, to see the educational status and occupation of the respondents, to observe the distribution of type of malignancy, to assess the symptoms on admission to the hospital of differentiated thyroid carcinoma, and to analyze the laterality of nodal involvement.

METHODS

This cross-sectional observational study was conducted at the Department of Otolaryngology, Rajshahi Medical College Hospital, Rajshahi, and Department of Otolaryngology, Bangabandhu Sheikh Mujib Medical University (BSMMU), from July 2011 to June 2012. All the patients having carcinoma thyroid with or without metastasis were considered as the study population. A total of 40 patients were selected as study subjects by simple random sampling technique as per inclusion and exclusion criteria.

Inclusion criteria

Patients with thyroid malignancy with or without metastasis, both male and female patients, and patients who were willing to give consent were included.

Exclusion criteria

Patients with thyroid disease, lymphoma, anaplastic and medullary carcinoma; patients with associated co-morbidities like hypertension, diabetes, bronchial asthma; and patients who did not give consent to participate in the study were excluded.

Patients undergo a thorough clinical examination of the ear, nose, throat, and head neck, including general examination, and important investigation. The findings of the clinical examination and results of the investigation have been recorded and plotted on the datasheet. Some data were collected from the patients by face-to-face interview. All data were collected using a pre-formed questionnaire. Collected data were analyzed using descriptive statistics. A descriptive analysis of data was carried out by using a statistical package for social science (SPSS) 22.0 for Windows. After analysis, the data were presented in tables and charts. Ethical clearance was taken from the ethical committee of BSMMU. Informed written consent was obtained from the participants.

RESULTS

In this study, a majority (35, 87.5%) of the patients suffered from papillary carcinoma, followed by (5,12.5%) follicular carcinoma (Table 1).

Table 1: Distribution of the type of malignancy in DTC (n=40).

Type of malignancy	N	%
Papillary	35	87.5
Follicular	5	12.5
Total	40	100

Among the papillary carcinoma highest (62.86%) number of cases were found in 3rd decade. Among the follicular carcinoma highest (40%) were found in the 5th decade. The

lowest age was 13 and the highest at 65 years of age. Male to female ratio was 1:2.5 in papillary and 1:5 in follicular carcinoma (Table 2).

Table 2: Age distribution of differentiated carcinoma: (n=40).

Variables	Papillary (35 patients)		Follicular (5 patients)	
	N	%	N	%
Age (years)				
11-20	3	8.57	0	0.0
21-30	22	62.86	0	0.0
31-40	3	8.57	1	20.0
41-50	2	5.71	2	40.0
51-60	5	14.29	1	20.0
61-70	0	0.0	1	20.0
Gender				
Male	10	28.57	0	0.0
Female	25	71.43	5	100.0

In this series, 22 (55%) subjects resided in rural areas (Figure 1).

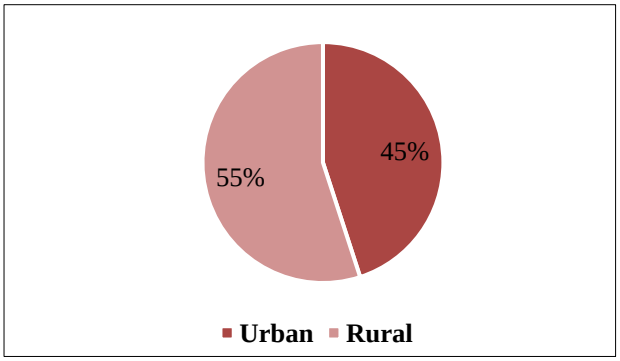

Figure 1: Distribution of patients according to residents (n=40).

In the present study, a majority (39.0%) of the patients had primary level education, followed by (30.0%) secondary level (Figure 2).

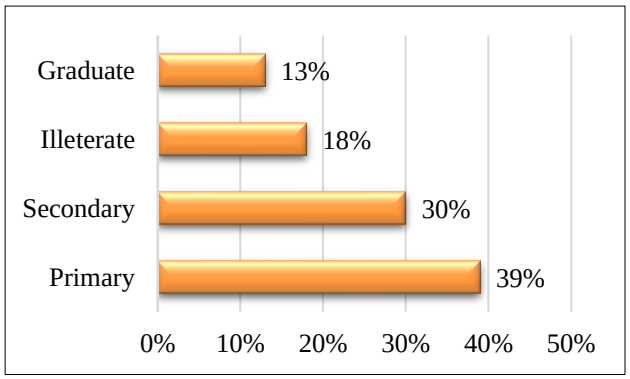

Figure 2: Educational status of the study subjects (n=40).

The commonest symptom for seeking medical admission was swelling in the neck (lymph node swelling included), which was present in 39 (97.5%) cases.

Symptoms of distant metastasis and dyspnoea were present in 3 (7.5%) and 1 (2.5%) case respectively (Table 3).

Table 3: Symptoms on admission to hospital of differentiated thyroid carcinoma (n=40).

Symptoms	N	%
Swelling in the neck	39	97.5
Dyspnea	1	2.5
Symptoms of distant metastasis	3	7.5

18 patients were FNAC positive and none were found to be FNAC negative (Table 4).

Table 4: FNAC finding of neck node in DTC (n=18).

N	FNAC (+ve) malignancy	FNAC (-ve) malignancy
18	18	0

It was found that 18 (51.43%) patients had lymph node metastasis from papillary carcinoma of the thyroid (Table 5).

Table 5: Distribution of lymph node metastasis in DTC (n=40).

Types of malignancy	N	Patients with nodal metastasis (n)	Metastasis (%)
Papillary	35	18	51.43
Follicular	5	0	0.0

It was observed that 10 (55.56%), and 4 (22.22%) patients had right and left-sided lymph node involvement respectively. Bilateral involvement was found in 4 (22.22%) patients (Table 6).

Table 6: Laterality of nodal involvement in DTC (n=18).

Laterality	N	%
Unilateral		
Right	10	55.56
Left	4	22.22
Bilateral	4	22.22

18 patients (22 neck dissections) had a total of 65 lymph node involved levels from II to VI. The most frequently involved levels are II (50%), III (77.3%), IV (54.55%), V (27.27%), and VI (63.64%).

Multiple levels of involvement are common (Table 7).

Table 7: Level of lymph node involvement (n=18).

Level	Right neck (%)	Left neck (%)	Total (%)
I	0	0	0
II	8 (44.45)	3 (16.67)	11 (50)
III	13 (72.22)	4 (22.22)	17 (77.3)
IV	8 (44.45)	4 (22.22)	12 (54.55)
V	4 (22.22)	2 (11.11)	6 (27.27)
VI	11 (61.11)	3 (16.56)	14 (63.64)

DISCUSSION

The age of patients in differentiated thyroid carcinoma in this series ranges from 13 to 65. years. Irrespective of sex maximum number of patients (62.86%) were found in the age group of 21-30 years in papillary carcinoma and 41-50 years (40%) in follicular carcinoma. Therefore, the peak incidence of the disease is in the 3rd decade in papillary and the 5th decade in follicular carcinoma. One study done in Bangladesh reported the highest number of patients present in 4th decade both in papillary and follicular carcinoma.[18] Whereas, in another study, it is the 5th decade for papillary and the 6th decade for follicular carcinoma.[1] Among forty patients thirty were female and ten were male. Females are more commonly affected than males and the male-female overall ratio was 1:3, for papillary it was 1:2.5, and for follicular it was 1:5. In other series, male-female ratio was 1:2.5.[19] The commonest symptom for seeking medical admission of differentiated thyroid carcinoma was swelling in the neck (lymph node swelling included). Regarding the histological type of differentiated thyroid carcinoma, 35 patients (87.5%) had papillary and 5 (12.5%) had follicular carcinoma in this series. Papillary type was more common than follicular type in differentiated thyroid carcinoma. Relative incidence in other studies were 73.33%, 80%, 60%, 75.3% for papillary and 26.67%, 10%, 20%, 24.62%.[1,18,20,21] FNAC findings showed that its accuracy is 94.23% in papillary carcinoma (33 reported positive, 1 benign, and 1 suspicious), but FNAC cannot differentiate follicular adenoma and carcinoma. Which correlates with other literature.[21] 18 patients with papillary carcinoma (51.43%) and no patients with follicular carcinoma (0%) had lymphatic metastasis. Nodal metastasis is common in papillary carcinoma in this series. A study stated that bilateral spread to neck nodes is found in about 8% of papillary carcinoma which is 22.22% in this study.[19] This may be due to lack of consciousness, and late seeking of medical measure. Multiple nodal metastasis either unilateral or bilateral were usually found at surgery. Patterns of neck node metastasis in the present study were 0% in level I, 50% in level II, 77.3% in level III, 54.55% in level IV, 27.27% in level V, and 63.64% in level VI. Lymph node metastasis was more common in the lateral neck from level II to IV. Of them most common was level III. Sivanandan et al found a progression in metastasis frequency from level I (3.75%) to III (65%), with a slight decrease at level IV (56.3%) in their study of 75 patients.[22] Pingpank et al reported a similar trend in their 44 patients, with the highest rates at levels III (76.4%) and IV (58.8%).[23] Kupferman's 39 patients showed an increase from level I (14%) to II (52%), with a subsequent decrease at level V (21%).[24] In a larger cohort of 167 patients, Lee et al observed an increase from level II (55.5%) to a peak at level III (80.6%), then a decrease at level V (16.8%).[25] Roh et al's study on 52 patients had the lowest frequency at level I (3.7%) and the highest at level VI (84.6%), with levels II and III being equal (72.2%).[26] A second study by Kupferman with 70 patients found an even distribution at levels III and IV (62%) but higher at level VI (77%).[27] Farrag et al's 53 patients had no data for level I but showed a decrease from level III (66%) to V (40%).[28] These findings illustrate that nodal positivity in DTC is generally higher at levels III and IV, with some variation across studies. This finding represents lymphatic metastasis following the usual lymphatic drainage of the thyroid gland. This pattern of nodal involvement correlates with other previous studies.

In conclusion, the study presented highlights the age-dependent prevalence of DTC, particularly noting that papillary carcinoma peaks in the third decade, while follicular carcinoma peaks in the fifth decade of life. Women are disproportionately affected by DTC, with a male-to-female ratio of 1:3, emphasizing a significant gender disparity in disease incidence. The predominant histological type is papillary carcinoma, accounting for 87.5% of cases in this series, corroborating the higher likelihood of lymph node metastasis compared to follicular carcinoma. Lymphatic spread was most frequently observed in lateral neck levels, with the highest concentration at level III. These findings on nodal involvement and the spread of DTC are consistent with other studies and underline the pattern of lymphatic drainage from the thyroid gland, emphasizing the importance of vigilant monitoring and management strategies tailored to the metastatic tendencies of DTC.

Limitations

The study was conducted in two hospitals with a small sample size for a short duration. So, the results may not represent the whole community.

CONCLUSION

This study concludes that metastasis in differentiated thyroid carcinoma is common. Lymph node metastasis is more common in papillary carcinoma than follicular carcinoma.

Recommendations

This study provides important insight that may guide the management plan of metastatic lymph nodes in differentiated thyroid carcinoma. Moreover, further studies should be conducted involving a large sample size and multiple centers to get robust data.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Watkinson JC, Gaze MN, Wilson JA. Tumors of the thyroid and parathyroid glands, Stell and Maran's Head Neck Surgery. 4th Edition. Butterworth Heinemann. 2000: 459-463.
2. Flint PW, Haughley BH, Lund VJ. Cummings Otolaryngology-Head and Neck Surgery. 5th edition. Volume 2010;2:1750-61.
3. Kendal IW, Condon RE. Prediction 0f malignancy in solitary thyroid nodules. Lancet. 1969;293:1071-3.
4. Psarras A, Papadopoulos SN, Livadas D, Pharmakiotis AD, Koutras DA. The single thyroid nodule. Br J Surg. 1972;59:545-8.
5. Wada N, Duh QY, Sugino K, Iwasaki H, Kameyama K, Mimura T, et al. Lymph node metastasis from 259 papillary thyroid microcarcinomas: frequency, pattern of occurrence and recurrence, and optimal strategy for neck dissection. Ann Surg. 2003;237(3):399-407.
6. Azim MA, Salam KS, Khan JA, Hussain MA. Metastasis in differentiated carcinoma. Mymensing Med J. 2010;19(4):497-503.
7. Shaha AR. Implications of prognostic factors and risk groups in the management of differentiated thyroid cancer. Laryngoscope. 2004;114:393-402.
8. Lin X, Zhu B, Liu Y, Silverman JF. Follicular thyroid carcinoma invades venous rather than lymphatic vessels. Diagn Pathol. 2010;5:8.
9. Roh J, Park J, Park CI. Total thyroidectomy plus neck dissection in differentiated papillary thyroid carcinoma patients: Pattern of nodal metastasis, morbidity, recurrence, and postoperative levels of serum parathyroid hormone. Ann Surg. 2007;245:604-10.
10. Ito Y, Jikuzono T, Higashiyama T, Asahi S, Tomoda C, Takamura Y, et al. Clinical significance of lymph node metastasis of thyroid papillary carcinoma located in one lobe. World J Surg. 2006;30:1821-8.
11. Shaha AR, Shah JP, Loree TR. Patterns of nodal and distant metastasis based on histologic varieties in differentiated carcinoma of the thyroid. Am J Surg. 1996;172:692-4.
12. Goropoulos A, Karamoshos K, Christodoulou A, Ntitsias T, Paulou K, Samaras A, et al. Value of the cervical compartments in the surgical treatment of papillary thyroid carcinoma. World J Surg. 2004;28:1275-81.
13. Kupferman ME, Patterson M, Mandel SJ, Li Volsi V, Weber RS. Patterns of lateral neck metastasis in papillary thyroid carcinoma. Arch Otolaryngol Head Neck Surg. 2004;130:857-60.
14. Seifert P, Freesmeyer M. Preoperative diagnostics in differentiated thyroid carcinoma. Nuklearmedizin-Nuclear Med. 2017;56(06):201-10.
15. Lin JH, Chiang FY, Lee KW, Ho KY, Kuo WR. The role of neck ultrasonography in thyroid cancer. Am J Otolaryngol. 2009;30(5):324-6.
16. Shaha AR, Shah JP, Loree TR. Risk group stratification and prognostic factors in papillary carcinoma of the thyroid. Ann Surg Oncol. 1996;3:534-8.
17. Mazzaferri EL, Jhiang SM. Long-term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. Am J Med. 1994;97:418-28.
18. Alauddin M, Joarder MAH. Management of thyroid carcinoma experience in Bangladesh. Indian J Otolaryngol Head Neck Surg. 2004;56(3):201-5.
19. Gleeson M, Browning GG, Burton JJ, Clerk R, Hibbert J, Jones NS, et al. Scott- Browns otolaryngology, 7th Edition. 2009;314-67.
20. Sinha NK, Alam MM, Akaiduzzaman DGM, Alauddin MA. The pattern of metastasis in differentiated thyroid carcinoma. Bangladesh J Otorhinolaryngol. 2009;15(2):60-8.
21. William NS, Bulstrode CJK, O'Connel PR. The thyroid and parathyroid glands. Bailey and Love's Short practice of surgery. 25th Edition. Hodder Arnold, London. 2008;771-806.
22. Sivanandan R, Soo KC. Pattern of cervical lymph node metastases from papillary carcinoma of the thyroid. Br J Surg. 2001;88(9):1241-4.
23. Pingpank JF Jr, Sasson AR, Hanlon AL, Friedman CD, Ridge JA. Tumor above the spinal accessory nerve in papillary thyroid cancer that involves lateral neck nodes: a common occurrence. Arch Otolaryngol Head Neck Surg. 2002;128(11):1275-8.
24. Kupferman ME, Patterson M, Mandel SJ, LiVolsi V, Weber RS. Patterns of lateral neck metastasis in papillary thyroid carcinoma. Arch Otolaryngol Head Neck Surg. 2004;130(7):857-60.
25. Lee J, Sung TY, Nam KH, Chung WY, Soh EY, Park CS. Is level IIb lymph node dissection always necessary in N1b papillary thyroid carcinoma patients? World J Surg. 2008;32(5):716-21.
26. Roh JL, Kim JM, Park CI. Lateral cervical lymph node metastases from papillary thyroid carcinoma: pattern of nodal metastases and optimal strategy for neck dissection. Ann Surg Oncol. 2008;15(4):1177-82.
27. Kupferman ME, Weinstock YE, Santillan AA, Mishra A, Roberts D, Clayman GL, et al. Predictors of level V metastasis in well-differentiated thyroid cancer. Head Neck. 2008;30(11):1469-74.
28. Farrag T, Lin F, Brownlee N, Kim M, Sheth S, Tufano RP. Is routine dissection of level II-B and V-A necessary in patients with papillary thyroid cancer undergoing lateral neck dissection for FNA-confirmed metastases in other levels. World J Surg. 2009;33(8):1680-3.

Cite this article as: Shahrear MK, Haque MM, Iqbal A, Khatun MR, Nafis AAM. Frequency of lymph node metastasis in differentiated thyroid carcinoma. Int J Otorhinolaryngol Head Neck Surg 2024;10:294-8.