

Original Research Article

Frequency of nodal metastasis in differentiated thyroid carcinoma

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ABSTRACT

Background: Thyroid cancer is the most common endocrine malignancy. Moreover, within thyroid cancer, differentiated thyroid carcinoma (DTC) is the most common variety, with the incidence rising over the past decade. Often, most of the cases present with multicentric disease and presenting with lymph node metastases at the time of diagnosis. Nodal metastasis has prognostic importance, and it may guide surgeons regarding further management. Considering this scientific fact, the study was performed to see the frequency of lymph node metastasis in DTC among the patients admitted to a tertiary care hospital.

Methods: This cross-sectional study was conducted in the department of otolaryngology and head-neck surgery, Sher-E-Bangla Medical College Hospital, for 9 months after the acceptance of the protocol. A total of 50 patients (in all age groups) who attended the relevant department due to thyroid malignancies were approached and interviewed. Thorough history taking, physical examination, and relevant investigation were done and recorded into separate case record forms. Informed written consent was taken from each subject. Following collection, data were coded and inputted into statistical software. Data analysis was done with SPSS 21 according to the objective of the study. Data were presented in the form of tables, and charts.

Results: Among the 50 patients, the mean age of the patients was 47.86 ± 15.69 SD (years) with minimum and maximum ages of 14 and 78 years respectively. The male-female ratio was 1:4 (20% male vs 80% female). Papillary carcinoma was the most frequent (88%) followed by follicular (10%). Nodal metastasis was most common in the papillary variety, about 54.55% of cases, whereas 20% were present in the follicular variety. The majority of the patients underwent total thyroidectomy with neck dissection (90%) and the remaining cases were managed by lobectomy (10%).

Conclusions: This study concluded that nodal metastasis was present in 54.55% of cases of papillary carcinoma.

Keywords: Nodal metastasis, Carcinoma, Thyroid gland, Papillary, Follicular

INTRODUCTION

The common way to present thyroid carcinoma is as a solitary thyroid nodule. Thyroid nodules are more common in women and increase in frequency with age, but malignancy is not so common and the most common way to present is as a solitary thyroid nodule. Thyroid

neoplasms represent almost 95% of all endocrine tumors, relatively uncommon, and account for approximately 2.5% of all malignancies.¹ A malignant thyroid tumor can originate from any of the cellular components but the vast majority are the follicular cell neoplasms of which papillary thyroid carcinoma (PTC) and follicular thyroid carcinoma (FTC) are the commonest, collectively called

DTC. FTC occurs more commonly in areas of endemic goiter than PTC.¹ 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 to 20%.²⁻⁵ Papillary carcinoma accounts for 60% of all cases of thyroid malignancies. It can occur in all age groups. Frequent age incidence is 3rd to 4th decade of life, typically present as a nodule in the thyroid and virtually the only thyroid cancer of children. FTC occurs between 50-59 years, but seldom below the age of 30. It accounts for 10-20% of thyroid malignancy, most commonly present as a solitary thyroid nodule or a long-standing multinodular goiter (MNG).¹⁻³ The thyroid gland has a rich lymphatic network. The lateral aspect of the gland drains into the middle and lower (levels III and IV) and those of the posterior triangle (level V). The more medial aspect of the gland drain to the anterior compartment neck node (level VI) and then to the upper mediastinum (level VII). Level I and II are less involved.^{3,6} In DTC, lymph node metastasis is more common in papillary (35%) than follicular carcinoma (12.5%), but distant metastasis is more common in follicular (12.55) than papillary carcinoma (3.70%). Lymph node metastasis carries an important prognostic value of thyroid carcinomas.⁷ Recent studies have confirmed that the incidence of nodal metastasis in PTC ranges from 60-65%.⁷⁻¹⁰ Lymph node metastasis in FTC occurs less frequently but prefers to metastasize via veins to distant organs.^{8,11,12} Metastasis in the central compartment is more common than in the ipsilateral and contralateral lateral compartments.¹³ The most frequently involved lymph node lateral groups are III (57%), and IV (41%).¹⁴ The incidence of thyroid cancer continues to rise worldwide and is often attributed to the increased use of diagnostic imaging and surveillance. Even though the incidence is rising steadily, mortality from thyroid cancer has changed minimally over the past five decades.¹⁵ Most thyroid cancers show biologically indolent phenotypes and have an excellent prognosis with survival rates of more than 95% at 20 years although the recurrence or persistent rate is still high.¹⁶ Differentiated thyroid cancer is the most common thyroid cancer, accounting for more than 95% of cases.¹⁷ Under the category of well-differentiated thyroid cancers are papillary thyroid cancer, follicular thyroid cancer, and Hurtle cell thyroid cancer. Poorly differentiated thyroid cancer is a more aggressive follicular-derived thyroid cancer than differentiated thyroid cancer.¹⁵ The majority of differentiated thyroid cancers (DTC) are usually diagnosed at an early stage, during a routine checkup, or more increasingly as an incidental finding of neck ultrasonography (US). In these cases, the presence of clinically apparent nodal metastases is uncommon. That being said, multiple studies have shown that the incidence of occult lymph node metastases may reach up to 60%, but this microscopic disease has no prognostic value in patients with DTC.¹⁸ The associated cervical lymph node metastasis with an increased recurrence rate, a more aggressive DTC, and low operative and

radioiodine-related morbidity support an aggressive approach for the management of thyroid carcinoma with lymph node metastasis. This study aimed to detect the frequency of lymph node metastasis in DTC.

Objectives

General objective

General objective was to find out the frequency of lymph node metastasis in DTC.

Specific objectives

Specific objectives were to find out the association of lymph node metastasis with the histologic type of DTC, to assess the level of lymph node metastasis in DTC and to assess the relationship between the size of the tumor and lymph node metastasis.

METHODS

This cross-sectional study was conducted in the department of otolaryngology and head-neck surgery, Sher-E-Bangla medical college hospital, for 9 months after the acceptance of the protocol. Total of 50 patients (in all age groups) who attended the relevant department due to thyroid malignancies were approached and interviewed. The purposive sampling method was used in this study. A semi-structured questionnaire containing a few items of questions regarding socio-demographic information (e.g., age, gender, resident, marital status, occupation, monthly income, level of education, etc.) and relevant information about comorbidity. Thorough history taking, physical examination, and relevant investigation were done and recorded into separate case record forms. The patients were requested to perform hormonal analysis, USG, and thyroid scans. Moreover, they were requested to perform FNAC, CT scan, or MRI to confirm malignancy and/or inflammatory lesions. Thyroid scans were also done in relevant cases when necessary. To estimate the association for categorical variable chi-square (χ^2) test was considered. In all cases, data analysis was done with a 95% confidence interval with a 5% acceptable error. The significance level was set when the p was less than 0.05. Following collection, data were coded and inputted into statistical software. Data analysis was done with SPSS 21 according to objective of the study. Data were presented in the form of tables, and charts. Informed written consent was taken from each subject. Ethical clearance was taken from the institutional Ethical committee of Sher-E-Bangla medical college hospital, Barisal before starting the study. All information was collected confidentially with complete respect to the patient's wish and without any force or pressure.

Inclusion criteria

All patients having DTC (based on history, clinical examination, FNAC report, and histopathological report)

and patients who had given consent to participate in the study were included in study.

Exclusion criteria

Patients with benign thyroid disease, lymphoma, medullary and anaplastic carcinoma and who did not give consent to participate in the study were excluded.

RESULTS

A total of 50 patients with DTC met the inclusion criteria within the study period. The mean age of the patients was 47.86±15.69 years with minimum and maximum ages of 14 and 78 years respectively. The highest frequency of thyroid cancer was found between 40 to 49 years of age (26%) (Table 1).

Table 1: Age distribution of patients (n=50).

Age (years)	N	Percentages (%)
<20	3	6
20-29	5	10
30-39	13	26
40-49	9	18
50-59	9	18
60-69	6	12
70-79	5	10

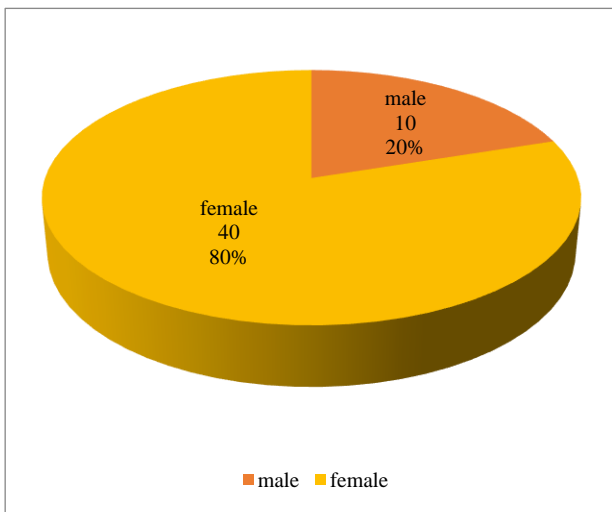


Figure 1: Gender distribution of patients (n=50).

Our study shows female dominance with a male-to-female ratio of 1:4. Mean ages of the two separate genders were 44.10±13.32 years and 48.80±16.24 years respectively (Figure 1).

Table 2: Histological diagnosis of cancer (n=50).

Histological type	N	Percentages (%)
Papillary	45	90
Follicular	5	10
Total	50	100

The majority of the thyroid malignancy was histological of papillary variant (90%) followed by follicular (10%) (Table 2).

Table 3: Size of the thyroid tumor of a different variety (n=50).

Size of tumor (cm)	The histological type of DTC, N (%)		Total, N (%)	Chi-square, p value
	Papillary	Follicular		
<1	3 (6.82)	0	3 (6)	10.37, 0.796
2-3	10 (22.73)	1 (20)	11 (22)	
3-4	14 (31.82)	3 (60)	17 (34)	
>4	18 (27.27)	1 (20)	19(38)	
Total	45 (100)	5 (100)	50 (100)	

At the time of diagnosis, the majority of the papillary (31.82%) and follicular (60%) tumors were 3-4 cm in diameter. There is no significant difference in size according to histological type (p=0.7960) (Table 3).

Table 4: Relation between tumor size and nodal metastasis (n=50).

Size of tumor (cm)	Number of thyroid cancer	Metastasis		Chi-square, p value
		N	%	
<1	3	0	0	18.236, 0.001
2-3	11	1	9.1	
3-4	17	9	52.94	
>4	19	15	78.94	

Thyroid tumors of this study were found to tend to be metastasized when they become large. (78.94%) of the tumor metastasis occur when the size is >4 cm. These findings were significant statistically (p=0.001) (Table 4).

Table 5: Frequency of nodal metastasis (n=50).

Histological type	Metastasis		Total	Chi-square, p value
	N	%		
Papillary	24	54.55	44	3.164, 0.206
Follicular	1	20	5	
Total	25	50	50	

More than half of papillary carcinoma metastasized to lymph nodes (54.55%). On the other hand, 20% of follicular variety did cause nodal involvement (Table 5).

DISCUSSION

Although the prognosis of well-DTCs with localized disease is excellent, in situations with regional disease or distant metastasis, survival is dependent on age.¹⁹ In two studies by Ito et al both among cases of papillary and follicular thyroid carcinoma, there was higher disease-specific survival among younger patients, although this

group was more susceptible to regional and distant recurrences.^{20,21} Cervical lymph node metastases are common and are reported to be present in 50% of patients with DTC.²²⁻²⁵ There were 40 (80%) women with a mean age of 48 years and 10 (20%) men with a mean age of 44 years. A total of 15 (37.5%) women and 4 (40%) men were younger than 45 years. A study conducted at McGill university, Montreal, Quebec, Canada in 2014 named “Is age associated with risk of malignancy in thyroid cancer?” by Do et al showed a similar result which is further supported by two other studies, “Thyroid carcinoma pattern presentation according to age” by Giradi and “Incidence of metastatic well-differentiated thyroid cancer in cervical lymph nodes” by Wang et al in two completely different set-ups.²⁶⁻²⁸ A study of 988 patients by Kwong et al.” The influence of patient age on thyroid nodule formation, multinodularity, and thyroid cancer risk” found the highest incidence of thyroid cancer in the 4th and 5th decade of life.²⁹ Our findings are in concert with this result which is reinforced by an earlier study.³⁰ The thyroid cancer group included papillary (86.5%) and follicular (10.0%) cancers after histopathological examination in the series of Stansifer et al, “Modifiable risk factors and thyroid cancer” conducted in the university of Nebraska medical center, Omaha, Nebraska, and USA.³¹ Similar frequencies of various histopathological types of thyroid malignancy were observed in many other past and recent studies.^{27,29,30,32} The incidence of histological subtypes of our series was in tandem with those of previous works. The rate of lymph node metastasis in the entire group of tumors, ranging from 3-4 cm in size, was 17% (9 patients). When we looked only at tumors more than 3 cm in size, the proportion with nodal spread was 48%, with statistically significant p value (p=0.001) indicating that size did affect the rate of lymph node metastasis which is contrary to Reddy et al and Koo et al but matched with Kasai and Sakamoto.³³⁻³⁵ who found a more significant difference in the frequency of lymph node metastases concerning the primary size, 13% of tumors 0.5 cm or less and 95% of those >0.5 cm. Our study demonstrates that papillary carcinomas are more prone to be metastasized than follicular counterparts (54.55% vs 20%) but the relationship was not significant. Gradient et al and Wang et al reported similar results.^{27,28} A study was done in Rome where 1503 patients were treated for DTC was observed. Papillary carcinoma was found in 93% and follicular carcinoma in 7% of the cases; ipsilateral metastases were detected in 63 patients (82%) and bilateral metastases in 14 cases (18%). The pathological T-staging was: pT1 22%, pT2 31%, pT3 9% and pT4a 38%. Nodal cervical metastases in the lateral neck were studied considering the number of N+, involved levels, and evidence of nodal extra-capsular spread (ECS). The mean number of metastatic nodes was 6.2 per patient (ranging between 1 and 43). The mean number of cervical levels involved was 2 (from 1 to 5) per patient. In the present series, 45% had more than 3 metastatic nodes and 22% had ECS in one or more lymph nodes. A total of 8 out of 14 patients with bilateral metastases

presented multiple neoplastic nodules in the thyroid. Concerning the histology variant, patients with follicular carcinoma developed 69% of recurrences after 6 years, vs. 18% with papillary carcinoma. Considering cervical nodal involvement, bilateral metastases were detected in 29% of cases, when the tumor was located bilaterally in the gland and in 13% of cases with a unilateral location. In only one case was the metastasis found contra laterally to the tumor. At clinical follow-up, distant metastases (DM) were observed in 8 out of 77 cases (10%) and nodal recurrences (NR) in 5 out of 77 (6%). As far as concerns the sub-group of 8 patients with DM, 5 had > 3 metastatic nodes and >1 metastatic level involved. ECS was found in 7 out of 8 cases with DM and in 3 out of 5 patients with NR.³⁶

Limitations

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

Differentiated thyroid cancer, which includes papillary and follicular histology, is a common malignancy and is increasing in incidence. It carries a favorable prognosis compared to other cancers. There has been much debate undergone by endocrinologists and surgeons about the prognostic importance of nodal metastasis. Although there is no consensus, nodal metastasis is seemed to be a poor prognostic indicator and has been associated with an increased recurrence rate. As it helps to plan further treatment modalities, the study was designed to reveal the frequency and pattern of nodal metastasis in DTC in Bangladeshi adults. In this study, papillary carcinoma was the most common among differentiated carcinoma followed by follicular carcinoma, and the frequency of nodal metastasis was about one-third of all cases.

Recommendations

Larger studies involving larger sample sizes and long-term follow-up of patients may help to provide a more complete picture of the state. A larger randomized control trial should be designed based on this baseline study. In case of nodal metastasis in clinical setup, papillary carcinoma should be suspected.

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