# Clinicopathological profile of Papillary thyroid carcinoma in a tertiary cancer hospital in Nepal

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## Abstract

**Background:** Differentiated thyroid cancers (DTC), including papillary thyroid carcinoma (PTC), are on the rise. This study provides a detailed examination of PTC cases in a tertiary care cancer hospital in Nepal, aiming to understand its clinical characteristics and treatment patterns. We conducted a retrospective analysis of PTC, including demographics, features of tumor, and treatment modalities. **Methods:** A retrospective cross-sectional study assessed cases of PTC from January 2022 to December 2022. Patient data were collected and analyzed, focusing on demographics, tumor attributes, and treatment approaches. **Results**: Among 105 patients, females were predominant (female-to-male ratio 5.2:1), and ethnic diversity was observed. Most patients were from Lumbini Pradesh. The mean age was 40.78 years. Fine-needle aspiration cytology (FNAC) showed Bethesda VI as the most common classification. Primary treatment involved total thyroidectomy (76.25%). Classical PTC was the major histopathological variant (78.1%). Tumors were frequently located in the right lobe (55.25%). Unifocal tumors were prevalent (74.28%), with an average size of 2.74 cm. Lymph node metastasis occurred in 49.5% of patients. Intermediate-risk patients constituted the majority (53.5%). **Conclusion:** This study offers crucial insights into PTC's clinical spectrum in Nepal, aiding in tailored patient care strategies. The findings contribute to informed decision-making for enhanced treatment outcomes.

***Keywords***: papillary thyroid carcinoma, clinicopathological characteristics, demographic profile, treatment modalities

## Introduction

The incidence of differentiated thyroid cancers (DTC) is steadily increasing, primarily comprised of papillary thyroid carcinomas (PTC), along with follicular and Hurthle variants.[1] Thyroid cancers constitute around 10% of head and neck cancers in Nepal.[2] Despite salt iodization efforts, the

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surge in thyroid cancers remains partially unexplained, showing distinct patterns among genders, ages with higher rates among younger women.[3,4]

PTC are discovered on routine examination as a asymptomatic neck mass.[5] A study in 2002 noted a 2.4-fold rise in thyroid cancer incidence from 1973 to 2002, mainly the tumors ≤1 cm, actually attributed to improved detection by imaging.[6] Guidelines from the American Thyroid Association (ATA) suggest tailored surgeries, however depending on disease characteristics and patient preferences, the treatment team may opt for total thyroidectomy to facilitate Radio Iodine Ablation (RIA) therapy or to enhance follow-up.[7]

Based on the 2004 World Health Organization classification, aside from the most prevalent classic PTC type, there exist 15 other subtypes some of which are highly aggressive such as tall cell variant conferring risk of mortality.[8] PTC generally shows a favorable prognosis, but specific factors like age, metastasis, and tumor size influence outcomes and disease severity assessment.[9,10,11] The clinical difficulty lies in promptly distinguishing patients who require aggressive treatment from those with a slow-developing course.[12]

By conducting this study, we can identify any unique characteristics of PTC in the Nepalese population, such as age-specific incidence, gender distribution, stage at diagnosis, presence of metastasis which will enhance our understanding of the disease's characteristics and contribute to the advancement of clinical practice.

## Methods

This study was a retrospective cross-sectional analysis held at the Unit of ENT – HNS of BPKMCH. Case notes of pathologically confirmed PTC diagnosed from January 01, 2022, to December 31, 2022, were analyzed. Incomplete records, missing data, and other types of thyroid cancers were excluded. Patient information covered demographics, symptoms, surgeries, and treatments. Details like age, gender, location, tumor features, metastasis, ATA risk, and TNM staging were collected. SPSS version 22 was used to analyse the data.

## Results

The study consisted of 105 patients diagnosed with Papillary thyroid carcinoma. Regarding patient demographics, the male-to-female ratio was found to be 1:5.2 in our study. Analysis of patient ethnicities revealed the majority of the patients (29) to be Chettri (27.6%). In order of decreasing frequencies other ethnicities included Brahmins (16.2%), Madhesis (14.3%) and Magars (12.4%). Newars, Dalits and Tharus were 7.6% each followed by Gurungs (6.7%). The majority of patients in our study were from Pradesh 5 (Lumbini Pradesh) which comprised 28.5%.

The mean age of patients was 40.78±13.04 years (range: 9-72) and specifically the mean age of female patients was 40.22 years. There were 88 female and 17 male patients in our study. (Table 1)

**Table 1. Female age distribution in PTC (n = 88)**

| Females | No. of patients | Percentage (%) |
|---|---|---|
| More than 55 years | 12 | 13.6 |

| | | |
|---|---|---|
| Less than 55 years | 66 | 86.4 |
| Total | 88 | 100 |

FNAC emerged as a cornerstone for accurate diagnosis, with most tumors classified as Bethesda VI type in 62%, Type V in 27.6% and Type IV in 10.4%. In terms of treatment, 76.25% of patients underwent total thyroidectomy with or without neck dissection, while 14.25% underwent hemithyroidectomy. (Table 2). Surgery performed for PTC as shown in (Table 2). TT - Total Thyroidectomy, CCND - Central Compartment Neck Dissection, ND - Neck Dissection

**Table 2. Type of Surgery performed for PTC (n=105)**

| Surgery | Number of patients | Percentage (%) |
|---|---|---|
| TT | 31 | 29.5 |
| TT with CCND | 33 | 31.5 |
| TT with CCND and Lateral ND | 16 | 15.25 |
| Hemithyroidectomy | 15 | 14.25 |
| Completion Thyroidectomy | 10 | 9.5 |
| Total | 105 | 100 |

Histopathological variants of PTC showed the classical type to be most prevalent (78.1%). (Table 3)

**Table 3. Histopathological types of PTC (n=105)**

| Variant | Number of patients | Percentage (%) |
|---|---|---|
| Classical | 82 | 78.1 |
| Follicular | 15 | 14.3 |
| Micropapillary | 8 | 7.6 |
| Total | 105 | 100 |

Regarding tumor characteristics, most tumors were in the right lobe (55.25%), followed by the left lobe (35.25%), and a smaller proportion being bilateral (9.5%). The majority of the tumors were unifocal (74.28%) and fewer patients had multifocal tumors (25.72%). (Table 4)

**Table 4. Sex and Multifocality**

| Particulars | | Tumor Focality | | Total | *p-value |
|---|---|---|---|---|---|
| | | Multi | Uni | | |
| Sex | F | 18 | 70 | 88 | <0.001 |
| | M | 9 | 8 | 17 | |
| Total | | 27 | 78 | 105 | |

*Chi-square test

The average tumor size was 2.74±1.39, with a range of 0.7 cm to 8 cm. There was a dominance of lesions falling within the T2 range (57.1%). (Table 5)

**Table 5. Tumor(T) staging of PTC (n=105)**

| T Stage | Number of patients | Percentage (%) |
|---|---|---|
| T1a | 8 | 7.6 |
| T1b | 22 | 21 |
| T2 | 60 | 57.1 |
| T3 | 11 | 10.5 |
| T4A | 4 | 3.8 |
| Total | 105 | 100 |

Lymph node metastasis, common in PTC, was seen in 52 patients (49.5%), with central compartment involvement in 36 patients (34.25%) and lateral compartment involvement in 16 (15.25%). Among the 27 patients who had multifocal tumors, central node was positive in 15 patients. (Table 6)

As per the American Joint Commission of Cancer, Tumor Node Metastasis (AJCC TNM) Staging, majority of patients that is 93, were Stage I (88.5%). Stage II had 7.5% followed by Stage III (3%) and Stage IVB (1%) which was the least and consisted of a patient with bilateral lung metastasis.

Table 6: Tumour Focality and Central node status

| Particulars | | Tumour Focality | | Total | *p-value |
|---|---|---|---|---|---|
| | | Multi | Uni | | |
| Central node (pN1a) | Node negative | 12 | 57 | 69 | <0.0001 |
| | Node positive | 15 | 21 | 36 | |
| Total | | 27 | 78 | 105 | |

*Chi-square test

| **Table 7. Risk stratification in PTC (n=105)** | | |
|---|---|---|
| Risk group | Number of patients | Percentage (%) |
| High risk | 7 | 6.5 |
| Intermediate risk | 56 | 53.5 |
| Low risk | 42 | 40 |
| Total | 105 | 100 |

On risk stratification, the majority of the patients fell in the Intermediate risk group (53.5%) (Table 7). Among the overall patients, Radioactive iodine ablation was received by 32 (30.5%) patients.

## Discussion

This study gives insight into various aspects of patient demographics, tumor characteristics, treatment modalities, and prognostic markers, contributing to a deeper understanding of PTC within our patient population. In our study, the gender distribution revealed a male-to-female ratio of 1:5.17, which closely resembled the findings of Rao et al, who reported a ratio of 1:5.[13] Correspondingly, other studies conducted by Carcangiu et al and Heitz et al unveiled ratios of 1:2.6 and 1:3.1, respectively.[14,15]

Upon categorizing patients based on their ethnic backgrounds, the majority belonged to the Chettri community (27.6%), followed by Brahmins (16.2%), Madhesis (14.3%) and Magars (12.4%) respectively. Geographical diversity seemed to play a role, with a concentration of patients hailing from the western region of Nepal, particularly Lumbini Pradesh (Pradesh 5) which constituted 28.6%. This phenomenon might be correlated with inadequate iodine consumption, a known factor linked to an increased risk of thyroid cancer.[16]

The mean age of our patient cohort stood at 40.78 years (range: 9-72), closely paralleling the Italian study's mean age of 41.3[14]. Among female patients, the mean age was 40.22 years, akin to the findings by Joshi et al[17], whereas another study by Dorairajan reported a lower mean age of 32 years among females.[18] The potential contribution of hormonal and reproductive factors in females to the development of this malignancy, as indicated by previous research, might offer insights into the higher prevalence of thyroid carcinoma in females.[19,20,21] The peak incidence of PTC was observed in the 4th to 6th decade of life, mirroring the findings of Catana et al[22], substantiating the significance of patient age in prognosis.

The diagnostic role of fine-needle aspiration cytology (FNAC) in precise and timely management strategies for thyroid cancers was underscored. Most tumors were classified as Bethesda VI (61%), followed by types V (26.6%) and IV (12.5%), aligning well with the study by Sarita et al, where Bethesda VI accounted for 57.6% of cases.[23]

In the context of treatment, our study revealed that 76.25% of patients underwent total thyroidectomy with or without neck dissection, whereas 14.28% underwent hemithyroidectomy. This trend deviated from the study by Joshi et al, where 64.29% of patients underwent total thyroidectomy.[17] The study conducted by Doraijan et al had more patients in the TT group that is 82.24%, however hemithyroidectomy (17.75%) was similar to our study.[18] The preference for total thyroidectomy in this study potentially stems from its association with improved outcomes since conservative surgery gave rise to a high rate of recurrence which adversely affectes survival.

Numerous histopathological variants of PTC with distinct prognostic significance were identified. The classical variant (CVPTC) was the most prevalent (78%), followed by the follicular variant (14.3%) and the micropapillary variant (PMC) (7.6%). These prevalence proportions mirrored those of the study by Karkuzhali et al, where CVPTC accounted for 68.7%. [24] The study also had one case of tall cell variant which was absent in ours however, a unique instance of PTC and minimally invasive follicular carcinoma coexistence was noted in our study, which was seen in a 72 years female with multifocal T2 lesion echoing a similar finding by Plauche et al.[25]

Incidence of PMC in our research was higher compared to an Indian study[13], yet notably lower than the study conducted by Roti et al., which reported an incidence of 28.8%.[26] This variance could potentially be explained by the broader recognition of PMCs, facilitated by enhanced diagnosis through high-resolution ultrasounds.

Concerning tumor localization, most tumors were situated in the right lobe (55.25%), followed by the left lobe (35.25%), and a smaller proportion in bilateral locations (9.5%). This was similar to the study conducted by Joshi et al wherein 52.85% had disease in the right lobe.[17]

Multifocality was noted in 25.72% of tumors, in par to Feng's study in which multifocality was seen in 24.7%.[27] Multicentricity is a marker of worse prognosis and a study showed that it had higher propensity for nodal and distant metastasis.[14] In our study multifocality was seen in 11 male patients that was significantly high in comparison to the females ($p<0.0001$).(Table 4) This was in par with the study by Karkuzhali et al[24], which showed that there was association between centricity of tumors and gender, however study by Kawaura M et al showed that there was no correlation.[28] There was also a significant relation between multifocality and central node metastasis in our study as in a study by Al Atif et al.[29](Table 6)

Histopathologically, the average tumor size was 2.74±1.39, ranging from 0.7 cm to 8 cm,

like a study in India wherein majority of tumours fell in the T2 category.[30]

PTC demonstrate a tendency for lymphatic spread and the occurrence of nodal metastasis in patients with PTC ranges from approximately 20 to 50 %.[31] It was detected in 49.5% of patients in our study with central compartment involvement overall in 34.25% and lateral compartment in 15.25%. This incidence largely fell within established ranges, though higher than those reported by Shrikhande et al and Chung et al, which stood at 36.5% and 26.5%, respectively.[32,33]

Risk stratification revealed the majority of patients falling into the intermediate-risk category (53.5%), followed by low-risk (40%) and high-risk (6.5%). This distribution diverged from a Nepalese study, where low-risk patients dominated at 62.85%, potentially accounting for the greater proportion of total thyroidectomy and radioiodine therapy in our study (30.5%) compared to that study.[17] Risk stratification's role in treatment planning and management strategy was underscored, emphasizing the potential need for adjuvant therapy.

The study bears several limitations, primarily stemming from its retrospective nature, potentially introducing biases due to data availability and collection. Being conducted at a single center, the findings might not be universally applicable. The sample size is relatively small, which could limit the representation of broader trends. Long-term impacts and extended follow-up data aren't explored. Lastly, the absence of a control group limits the ability to make comparative assessments.

## Conclusion

In conclusion, our study provides a detailed insight into the characteristics and trends of PTC within Nepal's tertiary cancer hospital. Females were predominantly affected, and the Chettri and Brahmin communities were prominently represented. FNAC emerged as a vital diagnostic tool, and total thyroidectomy was the preferred treatment. Classical PTC was the most common histopathological variant. Tumor features like laterality, size, and multifocality were assessed, revealing noteworthy correlations. The intermediate-risk group dominated risk stratification. These findings offer crucial guidance for tailored patient care, leading to improved treatment strategies and better outcomes.

## References

1. Murthy SP, Balasubramanian D, Anand A, Limbachiya SV, Subramaniam N, Nair V, Thankappan K, Iyer S. Extent of Thyroidectomy in Differentiated Thyroid Cancers—Review of Evidence. Indian Journal of Surgical Oncology. 2018 Mar;9:90-6.
2. Shrestha G, Siwakoti B, Mulmi R, Gautam D. Trend of Head and Neck Cancers in a National Tertiary Cancer Hospital of Nepal from 2012 to 2017. South Asian Journal of Cancer. 2021 Dec 31;10(04):236-40.
3. Sakoda LC, Horn-Ross PL. Reproductive and menstrual history and papillary thyroid cancer risk: the San Francisco Bay Area thyroid cancer study. Cancer Epidemiology Biomarkers & Prevention. 2002 Jan 1;11(1):51-7.
4. Haselkorn T, Stewart SL, Horn-Ross PL. Why are thyroid cancer rates so high in southeast asian women living in the United States? The bay area thyroid cancer study. Cancer Epidemiology Biomarkers & Prevention. 2003 Feb 1;12(2):144-50.
5. Gangadharan P, Nair KM, Pradeep VM. Thyroid cancer in Kerala. InThyroid cancer: an Indian perspective 1999.

6. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973-2002. Jama. 2006 May 10;295(18):2164-7.
7. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, Pacini F, Randolph GW, Sawka AM, Schlumberger M, Schuff KG. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association guidelines task force on thyroid nodules and differentiated thyroid cancer. Thyroid. 2016 Jan 1;26(1):1-33.
8. Ho AS, Luu M, Barrios L, Chen I, Melany M, Ali N, Patio C, Chen Y, Bose S, Fan X, Clair JM. Incidence and mortality risk spectrum across aggressive variants of papillary thyroid carcinoma. JAMA oncology. 2020 May 1;6(5):706-13.
9. Cady B, Rossi R. An expanded view of risk-group definition in differentiated thyroid carcinoma. Surgery. 1988 Dec 1;104(6):947-53.
10. Hay ID, Bergstralh EJ, Goellner JR, Ebersold JR, Grant CS. Predicting outcome in papillary thyroid carcinoma: development of a reliable prognostic scoring system in a cohort of 1779 patients surgically treated at one institution during 1940 through 1989. Surgery. 1993 Dec 1;114(6):1050-8.
11. Gabriel NH, James LC, Carl JD, Stephen BE, Elizabeth AM, Hope SR, Lawrence JS, Donald LW, David JW, Armando G. AJCC Cancer Staging Manual Eighth Edition, 1–50.
12. Lind P, Langsteger W, Molnar M, Gallowitsch HJ, Mikosch P, Gomez I. Epidemiology of thyroid diseases in iodine sufficiency. Thyroid. 1998 Dec;8(12):1179-83.
13. Rao R, Giriyan SS, Rangappa PK. Clinicopathological profile of papillary carcinoma of thyroid: A 10-year experience in a tertiary care institute in North Karnataka, India. Indian journal of cancer. 2017 Jul 1;54(3):514-8.
14. Carcangiu ML, Zampi G, Pupi A, Castagnoli A, Rosai J. Papillary carcinoma of the thyroid. A clinicopathologic study of 241 cases treated at the University of Florence, Italy. Cancer. 1985 Feb 15;55(4):805-28.
15. Heitz P, Moser H, Staub JJ. Thyroid cancer. A study of 573 thyroid tumors and 161 autopsy cases observed over a thirty-year period. Cancer. 1976 May;37(5):2329-37.
16. Choi WJ, Kim J. Dietary factors and the risk of thyroid cancer: a review. Clinical nutrition research. 2014 Jul 1;3(2):75-88.
17. Joshi A, Yonzon P, Sharma T. Clinical profile of thyroid cancer patients attending a tertiary endocrine center in Nepal. InEndocrine Abstracts 2020 Aug 21 (Vol. 70). Bioscientifica.
18. Dorairajan N, Pandiarajan R, Yuvaraja S. A descriptive study of papillary thyroid carcinoma in a teaching hospital in Chennai, India. Asian Journal of Surgery. 2002 Oct 1;25(4):300-3.
19. Rossing MA, Voigt LF, Wicklund KG, Daling JR. Reproductive factors and risk of papillary thyroid cancer in women. American journal of epidemiology. 2000 Apr 15;151(8):765-72.
20. Sakoda LC, Horn-Ross PL. Reproductive and menstrual history and papillary thyroid cancer risk: the San Francisco Bay Area thyroid cancer study. Cancer Epidemiology Biomarkers & Prevention. 2002 Jan 1;11(1):51-7.
21. Mack WJ, Preston-Martin S, Bernstein L, Qian D, Xiang M. Reproductive and hormonal risk factors for thyroid cancer in Los Angeles County females. Cancer Epidemiology Biomarkers & Prevention. 1999 Nov 1;8(11):991-7.
22. Cătană RA, Boilă AD, Borda A. Thyroid cancer profile in Mures County (Romania): a 20 years study. Rom J Morphol Embryol. 2012 Jan 1;53(4):1007-12.
23. Sarita KC, Dutta VB, Mahaseth RK, Bhattarai S. Clinico-histopathological Profile of Papillary Thyroid Cancer in a Tertiary Care Hospital. JMEC. 2021 Jan.
24. Karkuzhali P, Yogambal M, Kumar M. An Indian tertiary care hospital scenario of papillary carcinoma of thyroid. Journal of clinical and diagnostic research: JCDR. 2017 Jun;11(6):EC26.
25. Plauche V, Dewenter T, Walvekar RR. Follicular and papillary carcinoma: a thyroid collision tumor. Indian Journal of Otolaryngology and Head & Neck Surgery. 2013 Jul;65:182-4.
26. Roti E, degli Uberti EC, Bondanelli M, Braverman LE. Thyroid papillary microcarcinoma: a descriptive and meta-analysis study. European Journal of Endocrinology. 2008 Dec;159(6):659-73.
27. Feng JW, Qu Z, Qin AC, Pan H, Ye J, Jiang Y. Significance of multifocality in papillary thyroid carcinoma. European Journal of Surgical Oncology. 2020 Oct 1;46(10):1820-8.
28. Kawaura M, Pathak I, Gullane PJ, Mancer K. Multicentricity in papillary thyroid carcinoma: analysis of predictive factors. Journal of Otolaryngology-Head & Neck Surgery. 2001 Apr 1;30(2):102.
29. Al Afif A, Williams BA, Rigby MH, Bullock MJ, Taylor SM, Trites J, Hart RD. Multifocal papillary

thyroid cancer increases the risk of central lymph node metastasis. Thyroid. 2015 Sep 1;25(9):1008-12.

30. Agarwal S, Chand G, Jaiswal S, Mishra A, Agarwal G, Agarwal A, Verma AK, Mishra SK. Pattern and risk factors of central compartment lymph node metastasis in papillary thyroid cancer: a prospective study from an endocrine surgery centre. Journal of Thyroid Research. 2012 Jan 1;2012.
31. So YK, Son YI, Hong SD, Seo MY, Baek CH, Jeong HS, Chung MK. Subclinical lymph node metastasis in papillary thyroid microcarcinoma: a study of 551 resections. Surgery. 2010 Sep 1;148(3):526-31.
32. Shrikhande SS, Phadke AA. Papillary carcinoma of the thyroid gland: A clinicopathological study of 123 cases. Indian journal of cancer. 1982;19(2):87-92.
33. Chung YS, Kim JY, Bae JS, Song BJ, Kim JS, Jeon HM, Jeong SS, Kim EK, Park WC. Lateral lymph node metastasis in papillary thyroid carcinoma: results of therapeutic lymph node dissection. Thyroid. 2009 Mar 1;19(3):241-6.