

# Indiscriminate Nodule Sampling in Goitre: A Series of 5 Cases of Thyroid Microcarcinoma

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## ABSTRACT

Papillary Thyroid Carcinoma (PTC), which is a form of thyroid cancer, originates from follicular epithelial cells and can be identified histopathologically by distinct nuclear characteristics and architecture. It is the most common thyroid neoplasm and is typically found in young females, with a good prognosis. Within the subset of PTC, exists incidentally detected lesions called papillary microcarcinomas (IPMC), having a size  $\leq 1$  cm which are usually clinically not suspected, radiologically undetected, and often missed in gross pathological examinations. The present case series highlights five cases (2 males and 3 females) of papillary microcarcinomas that were detected over the course of one year. The patients' ages ranged from 31 to 60 years, with a mean age of  $48.8 \pm 10.1$  years. The male-to-female ratio was 1:1.5. These patients presented with complaints of neck swelling and were initially diagnosed with benign nodular goitre in 47 cases based on clinical and radiological evaluations. The detection rate of papillary microcarcinomas was 10.6%, with one case showing bilaterality (20%). The authors of the present case series adopted a novel approach of indiscriminate nodule sampling of thyroidectomy specimens to observe changes in detection rates. This approach facilitated a higher yield of papillary microcarcinomas. The authors also considered the dilemma of surgical measures and prognostic outcomes in such cases.

**Keywords:** Incidental papillary thyroid microcarcinoma, Multinodular goitre, Occult thyroid cancer, Papillary thyroid carcinoma, Papillary thyroid microcarcinoma

## INTRODUCTION

Papillary Thyroid Carcinoma (PTC) is the most commonly encountered thyroid neoplasm, exhibiting follicular cell differentiation and a set of distinctive nuclear features, and it carries the best overall prognosis. The tumour usually appears as an irregular solid mass, but in rare cases, it may have cystic features [1]. Most occult thyroid carcinomas, also called incidental or microcarcinomas, are small thyroid carcinomas that are  $\leq 1$  cm, and the prognosis is poor when metastatic lesions are evident. Occult PTCs have been reported not to be detected as primary tumours on preoperative Ultrasonography (USG) or postoperative gross pathological examination [2]. The mean age at diagnosis for PTC is 45 years, and it is also the most common thyroid malignancy occurring in children. Papillary Thyroid Microcarcinoma (PMC) is a specific subgroup of PTC and is defined by the World Health Organisation (WHO) 2017 classification of thyroid carcinomas, based on the largest dimension of 1.0 cm or less. Most PMCs are not detectable during clinical examination and are diagnosed incidentally during the pathological examination of thyroid specimens after surgery for benign thyroid diseases or in autopsies [1]. Some studies have suggested that missing a PMC could pose a future risk of distant

metastasis or adverse clinical outcomes, and hence the preoperative detection of these lesions would be desirable [3].

Unfortunately, studies have reiterated the difficulty of detecting PMC in the setting of multinodular goitre [4].

This series presents 5 cases of PMC, which were found incidentally from 47 thyroidectomy specimens removed for benign conditions solitary nodular goiter, multinodular goiter, Hashimoto's thyroiditis etc., over a period of one year. This was achieved by adopting an indiscriminate sampling approach from every nodule of otherwise benign-appearing multinodular goitre, considering possible future surgical measures and prognostic outcomes in such cases.

## CASE SERIES

In the present case series, the authors encountered five cases of incidentally discovered PMC during a postoperative detailed pathological examination, using a modified grossing protocol. All of these lesions were missed during the preoperative diagnostic work-up, including radiology and Fine Needle Aspiration Cytology (FNAC) [Table/Fig-1].

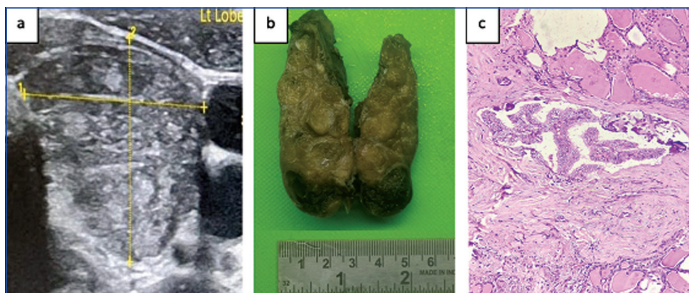
Case No.	Sex	Age	Complaints, duration	Clinic radiological diagnosis	Specimen type	Final diagnosis	Location	Follow-up
Case 1	Male	53	NS, DS 3 months	MNG	Left hemithyroidectomy	IPMC	Left lobe	4 months, uneventful
Case 2	Female	55	NS 6 months	SNG	Left hemi thyroidectomy	IPMC	Left lobe	5 months, uneventful
Case 3	Female	31	NS 7 months	Right lobe CG	Right hemi thyroidectomy with isthmectomy	IPMC	Isthmus	4 months, uneventful
Case 4	Male	60	NS 4 months	MNG	Total thyroidectomy	IPMC	Right lobe	3 months, uneventful, LTF
Case 5	Female	45	NS- 2 years DS- 3 months	MNG	Total thyroidectomy	Bilateral IPMC	Both right and left lobes	RAI 6 months, uneventful, LTF

**[Table/Fig-1]:** Case details.

NS: Neck swelling; DS: Difficulty swallowing; MNG: Multinodular goiter; SNG: Solitary nodular goiter; CG: Colloid goiter; IPMC: Incidental papillary thyroid microcarcinoma; LTF: Lost to further follow-up; RAI: Radioactive iodine therapy

### Case 1

A 53-year-old male presented to the Surgery Outpatient Department (OPD) with complaints of swelling in the front of his neck and difficulty swallowing for three months. On clinical examination, a 6×3 cm swelling was observed to the left of the trachea, which moved on deglutition. There was no hoarseness of voice or any associated pain with the swelling. The clinical diagnosis was multinodular goiter. Ultrasound examination showed multiple scattered iso to hyperechoic nodules varying in size from 2.5 cm to subcentimetric in the left lobe of the thyroid, some with degeneration, suggesting multinodular goiter. FNAC showed clusters and singly scattered thyroid follicular epithelial cells against a background of cyst macrophages and blood-mixed colloid, leading to a diagnosis of colloid goiter. The thyroid profile was within normal limits. The patient underwent left hemithyroidectomy. Gross examination of the left hemithyroidectomy specimen revealed nodularity on the external surface, with the cut surface showing multiple nodules, the largest measuring 2.5×2.5×2 cm, some with haemorrhage and degeneration. After extensive sampling, microscopic examination revealed mainly follicles of varying sizes and areas of fibrosis. Within this, an unencapsulated focus of Incidental Papillary Microcarcinoma (IPMC) measuring 5.0 mm across was observed. The IPMC had well-formed papillae with fibrovascular cores, lined by a layer of neoplastic epithelial cells with optically clear nuclei. Areas of dystrophic calcification were also noted along the rims of the focus. The patient subsequently underwent a completion thyroidectomy, which revealed no other lesions, and subsequent follow-up over four months has been uneventful [Table/Fig-2a-c].

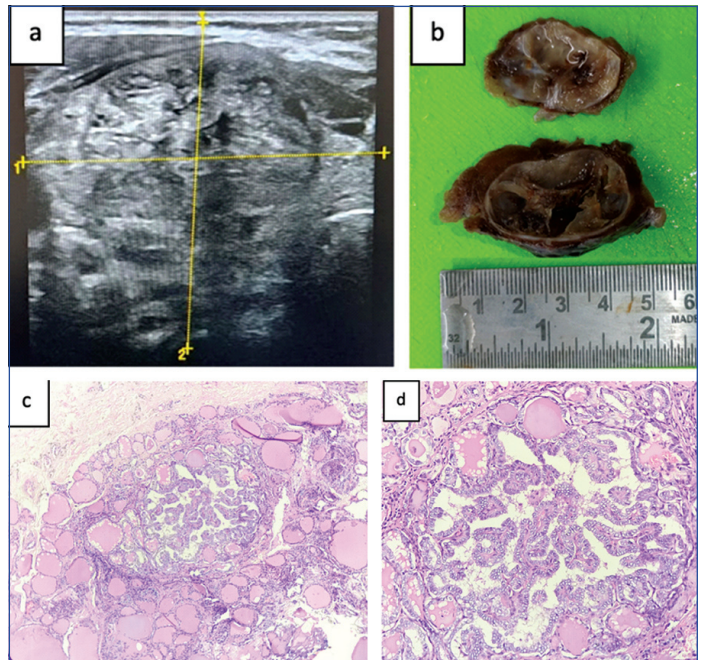


**[Table/Fig-2]:** Case 1: a) Ultrasound- Left lobe shows multiple scattered iso to hyperechoic nodules some with degeneration; b) Gross description- Left lobe of thyroid with multiple nodules with focal areas of haemorrhage and degeneration; c) Microscopy- H&E (200X magnification) section shows a focus of IPMC in MNG with areas of fibrosis. Some areas of calcification are noted along the rim of the lesion. Clinico-radiological diagnosis- Multinodular goitre; Specimen- Left hemithyroidectomy; Diagnosis- Papillary microcarcinoma; Involvement- Left lobe.

### Case 2

A 55-year-old female presented to the OPD with complaints of a left-sided swelling in the front of her neck that had gradually increased in size over six months. On clinical examination, a roughly 3×2 cm swelling was observed to the left of the trachea, which moved on deglutition. There was no hoarseness of voice or any associated pain with the swelling. A provisional diagnosis of solitary thyroid nodule was made. Ultrasound revealed a well-defined, large isoechoic nodule measuring 3.5×2 cm in the left lobe, with multiple cystic areas. The right lobe showed a few scattered iso to hyperechoic subcentimetric nodules. Based on these findings, it was clinically and radiologically diagnosed as solitary nodular goiter, with a possible differential diagnosis of multinodular goiter. FNAC showed benign thyroid follicular epithelial cells arranged in clusters and singly against a background of cyst macrophages and blood-mixed colloid. A cytological diagnosis of colloid nodule with degeneration was given. The thyroid profile was within normal limits. The patient underwent a left hemithyroidectomy, and the specimen was sent for histopathological evaluation. Gross examination revealed a solitary nodule measuring 3.5×2.5×2.5 cm, with areas of cystic degeneration on the cut surface. Microscopic examination showed mainly follicles of varying sizes and areas of fibrosis. Within this, a focus of unencapsulated incidental PMC measuring 3 mm across

was observed. The IPMC had well-formed papillae with fibrovascular cores, lined by a layer of neoplastic epithelial cells with optically clear nuclei. The patient subsequently underwent a completion thyroidectomy, which revealed no other lesions, and subsequent follow-up over five months has been uneventful [Table/Fig-3a-d].



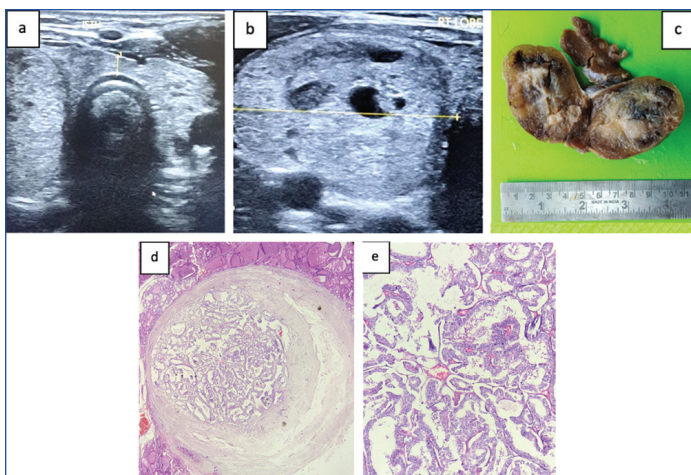
**[Table/Fig-3]:** Case 2: a) Ultrasound- Left lobe shows a well-defined large isoechoic nodule with multiple cystic areas and the right lobe shows a few scattered iso to hyperechoic subcentimetric nodules; b) Gross description- Left lobe of thyroid with a large colloid nodule with cystic change; c and d) Microscopy- H&E section (200X and 400X magnification) focuses on IPMC showing characteristic optically clear nuclei, and papillary architecture with fibrovascular cores in a colloid goitre with degeneration. Clinico-radiological diagnosis- Nodular goitre of the left lobe; Specimen- Left hemithyroidectomy; Diagnosis- Papillary microcarcinoma; Involvement- Left lobe.

### Case 3

A 31-year-old female presented to the Surgery OPD with complaints of a right-sided swelling in the front of her neck for seven months. On clinical examination, a diffuse swelling measuring approximately 3×3 cm was felt in front of the neck, more towards the right-side of the trachea, which moved on deglutition. There was no hoarseness of voice or pain associated with the swelling. Ultrasound examination showed multiple hyperechoic nodules with a hypoechoic halo in the right lobe, ranging from 2 cm to a few subcentimetric ones. The isthmus also showed a few subcentimetric nodules. Peripheral vascularity was noted in both lobes, leading to a radiological diagnosis of right lobe colloid goiter with a possibility of lymphocytic thyroiditis. FNAC showed clusters and singly scattered thyroid epithelial cells, some admixed with lymphocytes, against a background of thick and thin blood-mixed colloid. A diagnosis of colloid goiter with lymphocytic thyroiditis was given. The thyroid profile was within normal limits. Right hemithyroidectomy with isthmectomy was performed. Gross examination of the specimen, measuring 4×4×2.5 cm, showed slightly nodular right lobe and isthmus on the external surface, with the cut surface revealing grey-white to grey-brown areas and areas of degeneration. A few nodules were also seen in the isthmus. Thorough sampling was done for all the nodules and other areas of interest, which were submitted for processing. Microscopic examination revealed a focus of encapsulated IPMC measuring 5.5 mm across, located in the periphery of the isthmus, amidst thyroid follicles of varying sizes. The patient subsequently underwent a completion thyroidectomy, during which no additional lesions were identified. Subsequent follow-up over four months has been uneventful [Table/Fig-4a-e].

### Case 4

A 60-year-old male presented to the OPD with complaints of swelling in the front of his neck that had been noticed for four months. On

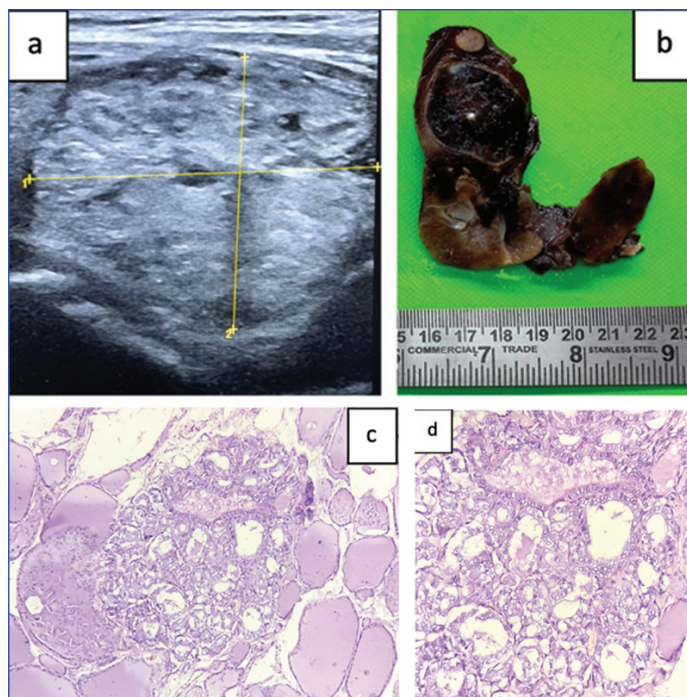


**[Table/Fig-4]:** Case 3: a and b) Ultrasound- Multiple hyperechoic nodules with hypoechoic halo and a few subcentimetric nodules, peripheral vascularity in both lobes; c) Gross description- Right hemithyroidectomy with isthmectomy showing grey white to grey brown areas with areas of degeneration; d and e) Microscopy- H&E section (200X and 400X magnification) from isthmus shows a well-encapsulated IPMC. Lymphocytic thyroiditis was observed in other areas. Clinicoradiological diagnosis- Right lobe colloid goitre; Specimen- Right hemithyroidectomy with isthmectomy; Diagnosis- Papillary microcarcinoma; Involvement- Isthmus.

clinical examination, a diffuse swelling measuring 5x2 cm was felt in front of the neck, more towards the left-side of the trachea. Ultrasound showed well-defined, multiple large isoechoic nodules with cystic degeneration and a few coarse calcifications, primarily in the left lobe. There were also a few subcentimetric nodules in the right lobe, leading to a radiological diagnosis of multinodular goiter. FNAC revealed clusters and singly scattered thyroid follicular epithelial cells against a colloid background, resulting in a cytological diagnosis of nodular colloid goiter. The thyroid profile was within normal limits. The patient underwent total thyroidectomy, and gross examination of the specimen revealed large nodules ranging from 2 cm to 1 cm in diameter in the left lobe of the thyroid, as well as subcentimetric nodules in the right lobe. Histopathological examination showed that the nodules in the left lobe were colloid goiter. However, surprisingly, the right lobe, which appeared relatively normal grossly, harbored an unencapsulated micropapillary carcinoma with follicular architecture measuring 3 mm across. Subsequent follow-ups over three months have been uneventful, but later the patient was lost to further follow-up [Table/Fig-5a-d].

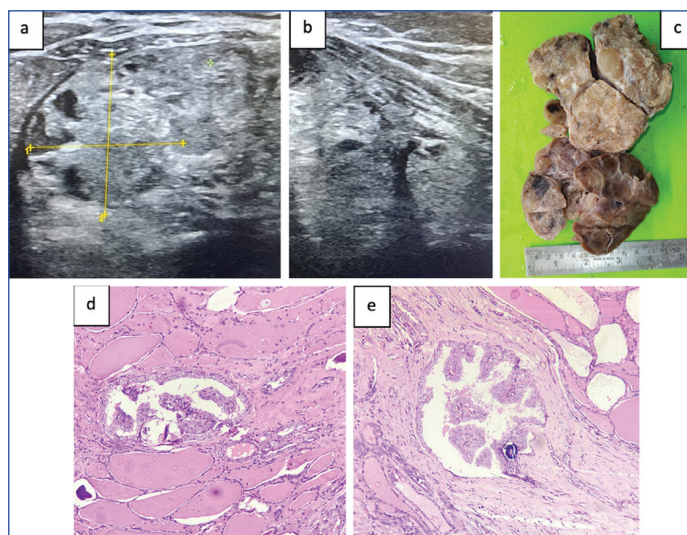
### Case 5

A 45-year-old female presented to the OPD with complaints of a large, diffuse swelling in the front of her neck that had gradually increased in size over two years. She also reported difficulty swallowing for the past three months. On clinical examination, a large nodular swelling roughly measuring 12x9 cm was observed in front of the neck, which moved on deglutition. There were no complaints of hoarseness of voice or pain associated with the swelling. Ultrasound reports revealed that the parenchyma of the thyroid gland was completely replaced by multiple heterogeneously hyperechoic nodules, ranging in size from 4 cm to subcentimetric ones. Multiple cystic areas were also noted, and no obvious calcific foci were seen. The radiological impression was multinodular goiter. FNAC yielded clusters and singly scattered thyroid follicular epithelial cells against a background of thick and thin colloid, admixed with cyst macrophages. A diagnosis of multinodular colloid goiter with degenerative changes was given. Thyroid Stimulating Hormone (TSH) was elevated in the present case. The patient underwent a total thyroidectomy, and gross examination of the specimen showed multiple nodules of varying sizes, ranging from 4x4 cm to subcentimetric ones. Some of the nodules demonstrated areas of degeneration. All the nodules were sampled and submitted for tissue processing. Microscopic examination revealed plenty of areas with varying-sized follicles, lymphocytic aggregates, and fibrosis. Within



**[Table/Fig-5]:** Case 4: a) Ultrasound- Well-defined multiple large isoechoic nodules with cystic degeneration and a few coarse calcifications; b) Gross description- Total thyroidectomy specimen with enlarged left lobe showing a large nodule with central calcification with adjacent smaller nodules. The right lobe shows multiple subcentimetric nodules; c and d) Microscopy- H&E section (200X and 400X magnification) from the right lobe shows a follicular variant of IPMC. Clinicoradiological diagnosis - Multinodular goitre; Specimen- Total thyroidectomy; Diagnosis- Papillary microcarcinoma; Involvement- Right lobe.

these, two foci of micropapillary carcinoma were identified; one in the right lobe measuring 8 mm across, and the other in the left lobe measuring 9 mm across, with a focus of calcification. Further sampling was done to look for additional foci considering the size of the thyroid, but no other lesions were observed. Hence, a diagnosis of bilateral IPMC was rendered on histopathology. The patient was referred to a higher centre and underwent Radioactive Iodine Therapy (RAI). Subsequent follow-up over a period of six months has been uneventful, after which she was lost to further follow-up [Table/Fig-6a-e]. All cases have been summarised in [Table/Fig-1].



**[Table/Fig-6]:** Case 5: a and b) Ultrasound- Parenchyma is completely replaced by multiple heterogeneously hyperechoic nodules with multiple cystic areas. No obvious calcific foci; c) Gross description- Total thyroidectomy shows multiple large nodules in both lobes and isthmus; d and e) Microscopy- H&E (200X magnification), one from each lobe (bilateral) shows foci of IPMC with one showing calcification. Clinicoradiological diagnosis - Multinodular goitre; Specimen- Total thyroidectomy; Diagnosis- Papillary microcarcinoma; Involvement- Right and Left lobes.

## DISCUSSION

The term PMC refers to papillary carcinoma with a diameter of less than 1 cm, according to the 2017 WHO classification. However,

the recent 2022 update does not clarify the surgical and medical management of PMC cases [5]. In the present study, authors received 47 out of 51 thyroidectomy specimens for various benign conditions, and incidentally identified 5 papillary microcarcinomas (10.6%) on microscopy. Among the 51 cases, four had presurgical malignancy diagnosis, with three being classical PTC and one medullary carcinoma. Among the five IPMCs, three were found in hemithyroidectomies and two in total thyroidectomies, with one case showing bilateral IPMC (20%). These findings, along with age and gender distribution, align with other IPMC case series and studies [6,7]. Grossing protocol modifications in the present study appear to have increased IPMC detection, while low incidence rates are possibly due to under-sampling in cases of multinodular goitre, attributed to a lack of a uniform protocol for grossing benign specimens, as indicated in other studies [Table/Fig-7] [6-13]. None of the patients in the present study had vascular invasion, capsular invasion, or nodal metastasis. One case showed thyroid profile derangement. Outcomes following thyroidectomies for three hemithyroidectomies were uneventful, while three cases were followed-up, and two were lost to follow-up.

Name of authors	Place and year	Duration	Type of study	Age (in years)	Male	Female	M:F ratio	Numbers of IPMC	Rate of IPMC
Present study	Tamil Nadu	1 year	Prospective	48.8±10.1*	2 (40%)	3 (60%)	1:1.5	5/47	10.60%
Senel F et al., [6]	Turkey, 2019	4.5 years	Retrospective	48 (26-69) <sup>†</sup>	7 (11.7%)	53 (88.3%)	1:7.6	60/827	8.01%
Vasileiadis I et al., [7]	Greece, 2014	8 years	Retrospective	50.85±12.53*	42 (16.3%)	216 (83.7%)	1:5.1	258/2236	12%
Venkatesh S et al., [8]	India, 2020	1 year	Retrospective	43.9 (29-72)*	1 (10%)	9 (90%)	1:10	10/437	2.30%
Al Qaraghuli MMS and Alsaadawi [9]	Iraq, 2022	2 years	Retrospective	41.8 (17-85)*	13 (15.1%)	73 (84.9%)	1:5.6	86/885	9.71%
Mathai AM et al., [10]	India, 2019	8 years	Retrospective	39 (16-62) <sup>†</sup>	0 (0%)	34 (100%)	NA	34/163	20.85%
Peluso G et al., [11]	Italy, 2020	9 years	Retrospective	46.7 (19-75) <sup>†</sup>	18 (20.2%)	71 (79.8%)	1:3.9	89/1777	5.02%
Venu N and Hassan MB [12]	India, 2021	3 years	Retrospective	40 (25-65)*	3 (13.6%)	19 (86.4%)	1:6.3	22/299	7.35%
Sadacharan D et al., [13]	India, 2018	6 years	Retrospective	45.2 (21-61)*	6 (14.3%)	36 (85.7%)	1:6	42/1740	2.43%

**[Table/Fig-7]:** Comparison of demographic details and case rates with various studies [6-13].

\*Mean (SD); <sup>†</sup>Median (IQR)

Grossing protocols vary among institutions, but the main goal is to obtain enough tissue for an accurate diagnosis. The sampling process is influenced by visual examination findings and other clinical, cytological, and radiological details. Different textbooks in India suggest various approaches for sampling specimens.

For multinodular thyroid glands, Rosai's Surgical Pathology manual; recommends taking one section of each nodule (up to five nodules) including rim and adjacent normal gland. Larger nodules may require multiple sections [1]. Zhai's manual suggests documenting and marking unsampled areas in larger goiter specimens for potential further sampling if malignancy is detected [14].

Lester's Manual does not provide specific guidelines for sampling clinically diagnosed and radiologically evaluated MNG [15]. In the present study, the authors adopted a novel approach, where thyroidectomy specimens were subjected to indiscriminate nodule sampling by trained pathologists, ensuring that every nodule was sampled after an initial thorough visual inspection. Serial sectioning along the long axis of the specimen at 0.5 cm intervals and inking of surgical margins were performed. The processed tissue sections were then stained and evaluated microscopically.

Sugitani I et al., classified PTCs ≤1 cm into asymptomatic and symptomatic PMCs based on metastatic lesions and symptoms. Asymptomatic PMCs (148 cases, 83%) without apparent lymph node metastasis or nerve palsy showed no distant metastasis or cancer-related deaths postsurgery [3].

Three biologically different PMC types emerged:

Type I: Incidentally detected asymptomatic PMCs with low risk. Ultrasonography follow-up every 6 or 12 months is suitable.

Type II: Early-stage low-risk papillary carcinoma. Lobectomy is sufficient if the size increases during follow-up.

Type III: Clinically symptomatic PMC with high-risk. Wider resection, radioiodine treatment, and TSH suppression are recommended [3].

In a one-year retrospective study of IPMC, Venkatesh S et al., found 10 cases out of 437 thyroidectomy specimens, representing a 2.3% incidence rate. This rate is slightly lower than the 3-17% published rates in the literature for patients previously diagnosed with benign thyroid disease [8,16]. Al Qaraghuli MMS and Alsaadawi conducted a 2-year study and discovered 86 IPMC cases out of 885 thyroidectomy specimens, resulting in an incidence rate of 9.71%, which is comparable to the 10.60% in our study [9].

The incidence of IPMC is increasing in certain populations, notably in South India [10], with the highest incidence globally observed in Finland (35.6%) and Japanese populations (18-24%), while Switzerland exhibits the lowest overall incidence at 1.2% [3,8,17]. The mean age of presentation in the present study is 48.8 years, which is comparable to other studies [6,9,11,18]. However, some studies have reported both lower and higher mean ages of presentation [7,10,12,19,20]. Age over 55 years is considered a risk factor for aggressive PMCs [10,11,18-20] and impacts clinical staging according to American

Joint Committee on Cancer (AJCC) staging guidelines [8]. In the present study, five cases were analysed, with three females and two males, indicating a slight female predominance (female-to-male ratio of 1.5:1). This trend aligns with other research [8,11,13,17]. Some studies found IPMC exclusively in females [10], while a few reported higher detection rates in males [1]. Gender as a risk factor showed varying outcomes in some studies [18]. Notably, some authors reported male sex as an independent risk factor for recurrence [19]. The mean tumour size in the five cases of IPMC detected in the institution was 5 mm±2.3 mm, which corresponds to the mean tumour size reported in similar studies [6,8,11]. Of the five cases, two foci had tumour sizes >6 mm in the present study. Other studies reported mean tumour sizes that were much larger at the time of detection [13,18,20], with Noguchi S et al., reporting that over 40% of their cases had tumour sizes >6 mm [17]. As highlighted in these studies, a mean tumour size of >6 mm remains an independent risk factor for recurrence. Multifocality of PMC, linked to higher recurrence and distant metastasis, is defined as more than one focus in one lobe or one or more foci in one or both lobes. Bilaterality refers to foci in both lobes [10-13,21]. IPMC's reported multifocality rate is 13-14% [12]. Multifocal IPMCs show aggressive behaviour, with recurrence and metastasis even after therapy [8,17]. Bilaterality is considered a risk factor, possibly more important for patient outcomes than multifocality [18,22]. Peluso G et al., reported 11 multifocal cases (12.3%), seven of them being bilateral IPMCs (7.8%) [11]. In contrast, the present study had one case of bilateral IPMC (20%) with a focus in each lobe. This difference may be due to the larger sample size in the former study.

When considering IPMC with aggressive clinical behaviour, important risk factors include extrathyroidal extension and lymph

node metastasis. Sadacharan D et al., reported one case of extrathyroidal extension (2.4%) where, on a 6-month follow-up, the patient developed cervical lymph node metastasis, leading to neck dissection [13]. Venkatesh S et al., described one case with histological extrathyroidal extension and lymph nodal metastasis (9.09%), while Baudin E et al., reported higher rates (15%) [8,20]. Both were significantly higher than the rates in studies by Hay ID et al., (2.0%) and Noguchi S et al., (2.4%) [17,18]. However, Baudin E et al., and Hay ID et al., had higher rates of lymph node metastasis, likely due to their decades-long follow-up periods. In this case series, no extrathyroidal extension or lymph node metastasis was histologically detected, and the three cases with regular follow-up showed no lymph node metastasis to date. In most studies, distant metastasis was uncommon. Some studies showed lung metastasis 20 months postsurgery [13]. Noguchi S et al., found five lung, four bone, and one mediastinal metastasis after 10.29 years [17]. The present study, a case series, might need a longer follow-up period of 10 years or more to establish this parameter in the present patients without distant metastasis to date.

In various studies, the most common histopathological variant of IPMC is the classical type, which can be encapsulated or unencapsulated [9,11,17,19], followed by the follicular variant. Rare aggressive types include diffuse sclerosing, tall cell, columnar cell variants, and papillary microcarcinoma with focal insular component [10]. The present study observed the most common subtype as classical unencapsulated (3 cases), one classical encapsulated, and one follicular variant. Kaliszewski K et al., suggested that the BRAF V600E mutation may explain clinically aggressive IPMCs in the classical variant [21]. PMCs associated with Graves' disease, Hashimoto's thyroiditis, and lymphocytic thyroiditis may have reduced recurrence rates [17,18]. In the present study, one IPMC case was linked to lymphocytic thyroiditis with uneventful follow-up.

The PTCs and PMCs are increasingly detected via ultrasonographic diagnosis, even as small as 3 mm [21,22]. However, authors note that some IPMCs remain undetectable presurgery, often due to co-existing with large multinodular goitre. The small focus and deep location within nodules, especially when obscured by cystic degeneration, necessitate multiple passes during USG for multinodular goitre. Thus, these authors stress the fact that in every multinodular goitre, each and every nodule should be thoroughly examined, both by USG and postoperatively during grossing, as microscopic evaluation of the surgical specimen still remains the gold standard for detecting neoplasms in thyroid nodules [10,21,23].

The IPMCs are generally asymptomatic, but aggressive variants carry risks, leading to different management protocols worldwide. For example, Japanese centres opt for surveillance in low-risk IPMCs using repeat USG scans or biopsies [3,17], while elsewhere others perform total or near-total thyroidectomies upon discovery [11,23]. South Indian studies report a combination of total or near-total thyroidectomies, most without central neck node dissection, and some with radioiodine ablation for multifocal, bilateral, or large tumours (>6 mm) [8,10,12,13,19]. In the institution, three cases of hemithyroidectomies underwent completion thyroidectomies to treat IPMC after diagnosis, and the two total thyroidectomies were followed-up, with one undergoing RAI for bilaterality and larger tumour size. Since reports of postsurgical recurrence are variable, the definitive treatment and follow-up for these patients still remain controversial.

## CONCLUSION(S)

It is observed that cases of PMC are being missed due to under-sampling, often due to practical considerations such as cost and

time constraints in most institutions. Additionally, the lack of a unified grossing protocol adopted in India contributes to this issue. Since studies show that IPMCs can exhibit clinical behaviour ranging from low risk to high-risk for metastasis and adverse clinical outcomes, the authors advocate for an indiscriminate sampling approach of thyroid specimens, regardless of the clinicoradiological conclusion. This approach is necessary to avoid missing these potentially troublesome lesions and to assist the clinical team in making timely and appropriate medical and/or surgical interventions.

## REFERENCES

- [1] Tallini G, Giordano TJ. Thyroid gland. In: Goldblum JR, Lamps LW, McKenney JK, Myers JL, editors. *Rosai and Ackerman's Surgical Pathology*, vol 1, 11<sup>th</sup> ed. Philadelphia: Elsevier; 2018, pp. 278-354.
- [2] Yamashita G, Kondo T, Okimura A, Nakatsugawa M, Hirano H, Takeda A, et al. Occult papillary thyroid carcinoma without detection of the primary tumour on preoperative ultrasonography or postoperative pathological examination: A case report. *Case Rep Oncol*. 2020;13(1):105-12.
- [3] Sugitani I, Toda K, Yamada K, Yamamoto N, Ikenaga M, Fujimoto Y. Three distinctly different kinds of papillary thyroid microcarcinoma should be recognized: Our treatment strategies and outcomes. *World J Surg*. 2010;34(6):1222-31.
- [4] Thomas A, Mittal N, Rane SU, Bal M, Patil A, Ankathi SK, et al. Papillary and medullary thyroid carcinomas presenting as collision tumours: A case series of 21 cases at a tertiary care cancer center. *Head and Neck Pathol*. 2021;15(4):1137-46.
- [5] Jung CK, Bychkov A, Kakudo K. Update from the 2022 World Health Organization Classification of thyroid tumours: A standardized diagnostic approach. *Endocrinol Metab*. 2022;37(5):703-18.
- [6] Senel F, Karaman H, Aytekin A, Silov G, Bayram A. Incidental papillary thyroid microcarcinomas in thyroidectomy specimens: A single-center experience from Turkey. *Indian J Pathol Microbiol*. 2019;62(2):211-15.
- [7] Vasileiadis I, Karatzas T, Vasileiadis D, Kapetanakis S, Charitoudis G, Karakostas E, et al. Clinical and pathological characteristics of incidental and nonincidental papillary thyroid microcarcinoma in 339 patients. *Head Neck*. 2014;36(4):564-70.
- [8] Venkatesh S, Krishnan D, Kumar SP. Papillary microcarcinoma of thyroid-A clinicopathological study in a tertiary care hospital in South India. *J Evolution Med Dent Sci*. 2020;9(21):1627-32. Doi: 10.14260/jemds/2020/357.
- [9] AlQaraghuli MMS, Alsaadawi AR. The prevalence of micro papillary thyroid carcinoma and its correlation with age, gender and the histological background. *WJAH*. 2022;6(11):01-04.
- [10] Mathai AM, Preetha K, Valsala Devi S, Viclip S, Pradeep R, Shaick A. Analysis of malignant thyroid neoplasms with a striking rise of papillary microcarcinoma in an endemic goiter region. *Indian J Otolaryngol Head Neck Surg*. 2019;71(Suppl 1):121-30. Doi: 10.1007/s12070-017-1156-8. Epub 2017 Jul 20. PMID: 31741946; PMCID: PMC6848467.
- [11] Peluso G, Masone S, Campanile S, Criscitello C, Dodaro C, Calogero A, et al. Incidental thyroid papillary microcarcinoma on 1777 surgically treated patients for benign thyroid disease. *memo - Magazine of European Medical Oncology*. 2020;13:126-33. <https://doi.org/10.1007/s12254-019-00567-y>.
- [12] Venu N, Hassan MB. Incidental micropapillary carcinoma in thyroidectomy specimens and criteria employed for diagnosis - A retrospective study. *Int J Clin Diagn Pathol*. 2021;4(2):84-86. Doi: 10.33545/pathol.2021.v4.i2b.363.
- [13] Sadacharan D, Chandru RK, Ayub MF, Ferdinand J. Incidental papillary thyroid microcarcinoma: Experience from a tertiary care center in south India. *International Journal of Contemporary Medical Research*. 2018;5(10):J5-J7.
- [14] Asa SL. Thyroid. In: Zhai Q, editor. *Grossing, staging, and reporting - An Integrated Manual of Modern Surgical Pathology*, 1<sup>st</sup> ed. Illinois: College of American Pathologists; 2021, Pp. 28-36.
- [15] Lester SC. Thyroid and Parathyroid Glands. In: Lester SC, editor. *Manual of Surgical Pathology*, 3<sup>rd</sup> ed. Philadelphia: Elsevier Saunders; 2010, Pp. 555-63.
- [16] Miccoli P, Minuto MN, Galleri D, D'Agostino J, Basolo F, Antonangeli L, et al. Incidental thyroid carcinoma in a large series of consecutive patients operated on for benign thyroid disease. *ANZ J Surg*. 2006;76(3):123-26. Doi: 10.1111/j.1445-2197.2006.03667.x. PMID: 16626346.
- [17] Noguchi S, Yamashita H, Uchino S, Watanabe S. Papillary microcarcinoma. *World J Surg*. 2008;32(5):747-53. Doi: 10.1007/s00268-007-9453-0. PMID: 18264828; PMCID: PMC2323028.
- [18] Hay ID, Hutchinson ME, Gonzalez-Losada T, McIver B, Reinalda ME, Grant CS, et al. Papillary thyroid microcarcinoma: A study of 900 cases observed in a 60-year period. *Surgery*. 2008;144(6):980-87.
- [19] John AM, Jacob PM, Oommen R, Nair S, Nair A, Rajaratnam S. Our experience with papillary thyroid microcancer. *Indian J Endocrinol Metab*. 2014;18(3):410-13. Doi: 10.4103/2230-8210.131211. PMID: 24944940; PMCID: PMC4056144.
- [20] Baudin E, Travagli JP, Ropers J, Mancusi F, Bruno-Bossio G, Caillou B, et al. Microcarcinoma of the thyroid gland. *Cancer*. 1998;83(3):553-59.
- [21] Kaliszewski K, Zubkiewicz-Kucharska A, Kielb P, Maksymowicz J, Krawczyk A, Krawiec O. Comparison of the prevalence of incidental and non-incidental papillary thyroid microcarcinoma during 2008-2016: A single-center experience. *World J Surg Oncol*. 2018;16(1):202. Doi: 10.1186/s12957-018-1501-8. PMID: 30305094; PMCID: PMC6180613.

[22] Rodriguez Schaap PM, Lin JF, Metman MJH, Dreijerink KMA, Links TP, Bonjer HJ, et al. Bilaterality, not multifocality, is an independent risk factor for recurrence in low risk papillary thyroid cancer. *J Natl Cancer Inst.* 2023:djad105. Doi: 10.1093/jnci/djad105. PMID: 37267155.

[23] Abdul Jabbar MQ, Mutlak NS, Abdul Hussein W, Sulaiman TI. Incidental thyroid carcinoma. *J Fac Med Bagdad.* 2016;58(3):245-49.

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**PLAGIARISM CHECKING METHODS:** [Jain H et al.]

- Plagiarism X-checker: Apr 21, 2023
- Manual Googling: Jun 17, 2023
- iThenticate Software: Jul 21, 2023 (9%)

**ETYMOLOGY:** Author Origin**EMENDATIONS:** 6**AUTHOR DECLARATION:**

- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Apr 19, 2023**Date of Peer Review: **Jun 04, 2023**Date of Acceptance: **Jul 26, 2023**Date of Publishing: **Oct 01, 2023**