



## THYROID PAPILLARY MICROCARCINOMA, A CLINICO-PATHOLOGICAL REVIEW

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### ABSTRACT

**Background:** Papillary thyroid microcarcinoma (PTMC) is defined as a subtype of papillary thyroid carcinoma (PTC), distinguished by its small size, usually measuring less than 1 cm in its largest diameter. Although PTMC typically exhibits a slow growth rate with a low propensity for metastasis, leading to an overall good prognosis. aim of study is to study the clinicopathological features of papillary micro carcinoma in Iraqi patients. **Method:** Cross-sectional research of 98 thyroid cancer patients in Baghdad-medical city from March 1 to September 1, 2023. All patients examined: Age (years), Gender, Negative or positive metastasis, capsular invasion, vascular invasion, multifocality Evaluation criteria include extra thyroidal expansion, perineural invasion, tumour size ( $\leq 5$  or  $> 5$ ), and tumour location (Isthmus, Left, Right). **Results:** In a study of papillary thyroid microcarcinoma patients, the mean age was 41.5 years, with a predominant female representation (87.8%), and most tumors were  $\leq 5$  mm in size. There were no significant associations between capsular invasion, vascular invasion, extra thyroidal extension, perineural invasion, and patient demographics or tumor characteristics. However, multifocality was significantly associated with larger tumor sizes ( $> 5$  mm) but not with increased metastasis, suggesting a complex pathology independent of traditional clinical factors. **Conclusion:** In a study of 98 thyroid cancer patients, predominantly female (87.8%) with a mean age of 41.5, most tumors were small ( $\leq 5$  mm) and non-aggressive, lacking metastasis and invasive features. Multifocality correlated with larger tumor sizes but not increased metastasis, indicating a nuanced pathology not directly linked to traditional demographic or clinical factors.

**KEYWORDS:** Thyroid, papillary, microcarcinoma, a clinico-pathological.

### INTRODUCTION

Papillary thyroid microcarcinoma (PTMC) is defined as a subtype of papillary thyroid carcinoma (PTC), distinguished by its small size, usually measuring less than 1 cm in its largest diameter.<sup>[1]</sup> Although PTMC typically exhibits a slow growth rate with a low propensity for metastasis, leading to an overall good prognosis,<sup>[2]</sup> it's crucial to acknowledge that it remains a carcinoma. A small fraction of patients may encounter a more aggressive disease progression, including lymph node or distant metastases. The approach to managing PTMC is nuanced. Considering the morbidity associated with thyroidectomy, which cannot be reduced below 1–3% even in specialized centers,<sup>[3]</sup> extensive surgical treatment for every diagnosed PTMC case is not universally advocated. In recent times, active surveillance, involving meticulous monitoring through imaging and thyroglobulin assessments, has gained traction as a viable management strategy for selected PTMC cases.<sup>[2–6]</sup> This aligns with the American Thyroid

Association (ATA) guidelines, which recommend a risk-directed approach in thyroid cancer management. PTMC's prevalence in patients with both malignant and benign thyroid diseases ranges from 7.1% to 16.3%.<sup>[7,8]</sup> It may also be incidentally found in up to 22% of surgeries conducted for benign thyroid diseases and in 0.5% to 5.2% of autopsy studies of individuals with non-thyroidal diseases.<sup>[9,10]</sup> The actual prevalence of incidental PTMC remains uncertain, as it varies based on geographic region, the nature of the underlying disease, and the type of study. The increasing detection of PTMC in living patients, despite a stable mortality rate, is attributed to advancements in diagnostic methods and screening programs for thyroid conditions.<sup>[11]</sup> Notably, a non-negligible percentage of PTMC cases can exhibit aggressive behavior, as evidenced by histopathological examination.<sup>[12]</sup> This aggressiveness is marked by metastasis to lymph nodes and distant areas, as well as an increased recurrence rate, which can be similar to that of larger papillary cancers.<sup>[13–15]</sup> aim of study is to study the

clinicopathological features of papillary micro carcinoma in Iraqi patients.

## METHOD

Cross sectional study of 98 patients with thyroid cancer, the study done in Baghdad-medical city from 1st of march to 1st of September 2023. All patients investigated about: Age groups (years), Gender, Metastasis (negative or positive), Capsular invasion (negative or positive), Vascular invasion (negative or positive), Multifocality (negative or positive), Extra thyroidal extension (negative or positive), Perineural invasion (negative or positive), Size (mm) ( $\leq 5$  or  $>5$ ) and site of tumor (Isthmus, Left, Right). SPSS 22 was utilized to perform the statistical analysis on the frequency and percentage of categorical data. Utilize chi-square to evaluate the

relationship between two variables. A P-value equal to or less than 0.05 is deemed significant.

## RESULTS

Cross sectional study of 98 patients with thyroid cancer Mean age  $41.5 \pm 9.7$  years old. 35.7% of patients at age group 40-49 years and 34.7% at age group 30-39 years. 87.8% of patients are females, 96.9% of patients are negative metastasis, and negative Capsular invasion, 99% of patients are negative vascular invasion, 69.4% of patients are negative Multifocality, 99% of patients are negative Extra thyroidal extension, Perineural invasion. 62.2% of patients have tumor size  $\leq 5$  mm, 59.2% of patients have tumor in right part of thyroid. As shown in table 1.

**Table 1: Distribution of patients according to study variables.**

Variables		Frequency	Percentage
Age groups (years)	20-29	9	9.2
	30-39	34	34.7
	40-49	35	35.7
	50-59	17	17.3
	60	3	3.1
Gender	female	86	87.8
	male	12	12.2
Metastasis	negative	95	96.9
	positive	3	3.1
Capsular invasion	negative	95	96.9
	positive	3	3.1
Vascular invasion	negative	97	99.0
	positive	1	1.0
Multifocality	negative	68	69.4
	positive	30	30.6
Extra thyroidal extension	negative	97	99.0
	positive	1	1.0
Perineural invasion	negative	97	99.0
	positive	1	1.0
Size (mm)	$\leq 5$	61	62.2
	$>5$	37	37.8
Site	Isthmus	6	6.1
	Left	34	34.7
	Right	58	59.2

As shown in table 2, there is no significant association between Capsular invasion and (age groups, size, gender, metastasis and site).

**Table 2: Association between Capsular invasion and (age groups, size, gender, metastasis and site).**

Variables		Capsular invasion		P-value
		Negative	Positive	
Age groups (years)	20-29	9	0	0.2
		9.5%	0.0%	
	30-39	34	0	
		35.8%	0.0%	

	<b>40-49</b>	34 35.8%	1 33.3%	
	<b>50-59</b>	15 15.8%	2 66.7%	
	<b>60</b>	3 3.2%	0 0.0%	
	<b>Total</b>	95 100.0%	3 100.0%	
<b>Size (mm)</b>	<b>≤5</b>	60 63.2%	1 33.3%	0.5
	<b>&gt;5</b>	35 36.8%	2 66.7%	
	<b>Total</b>	95 100.0%	3 100.0%	
<b>Gender</b>	<b>Females</b>	84 88.4%	2 66.7%	0.3
	<b>Males</b>	11 11.6%	1 33.3%	
	<b>Total</b>	95 100.0%	3 100.0%	
<b>Metastasis</b>	<b>Negative</b>	92 96.8%	3 100.0%	1.000
	<b>Positive</b>	3 3.2%	0 0.0%	
	<b>Total</b>	95 100.0%	3 100.0%	
<b>Site</b>	<b>Isthmus</b>	5 5.3%	1 33.3%	0.08
	<b>Left</b>	34 35.8%	0 0.0%	
	<b>Right</b>	56 58.9%	2 66.7%	
	<b>Total</b>	95 100.0%	3 100.0%	

P-value ≤0.05 (significant).

As shown in table 3, there is no significant association between vascular invasion and (age groups, size, gender, metastasis and site).

**Table 3: Association between vascular invasion and (age groups, size, gender, metastasis and site).**

Variables		Vascular invasion		P-value
		Negative	Positive	
<b>Age groups (years)</b>	<b>20-29</b>	9 9.3%	0 0.0%	0.8
	<b>30-39</b>	34 35.1%	0 0.0%	
	<b>40-49</b>	34 35.1%	1 100.0%	
	<b>50-59</b>	17 17.5%	0 0.0%	
	<b>60</b>	3	0	

	<b>Total</b>	3.1%	0.0%	
		97	1	
		100.0%	100.0%	
<b>Size (mm)</b>	$\leq 5$	60	1	1.000
		61.9%	100.0%	
	$>5$	37	0	
		38.1%	0.0%	
	<b>Total</b>	97	1	
		100.0%	100.0%	
<b>Gender</b>	<b>Females</b>	85	1	1.000
		87.6%	100.0%	
	<b>Males</b>	12	0	
		12.4%	0.0%	
	<b>Total</b>	97	1	
		100.0%	100.0%	
<b>Metastasis</b>	<b>Negative</b>	94	1	1.000
		96.9%	100.0%	
	<b>Positive</b>	3	0	
		3.1%	0.0%	
	<b>Total</b>	97	1	
		100.0%	100.0%	
<b>Site</b>	<b>Isthmus</b>	6	0	0.4
		6.2%	0.0%	
	<b>Left</b>	33	1	
		34.0%	100.0%	
	<b>Right</b>	58	0	
	59.8%	0.0%		
	<b>Total</b>	97	1	
		100.0%	100.0%	

**P-value  $\leq 0.05$  (significant).**

As shown in table 4, there is significant association between Multi focality and (size, metastasis); 60% of patients with positive Multi focality have size more than

5 mm. 90% of patients with positive Multi focality have negative metastasis. There is no significant association between Multi focality and (age groups, gender and site).

**Table 4: Association between multi focality and (age groups, size, gender, metastasis and site).**

Variables		Multi focality		P-value
		Negative	Positive	
<b>Age groups (years)</b>	<b>20-29</b>	7	2	0.3
		10.3%	6.7%	
	<b>30-39</b>	23	11	
		33.8%	36.7%	
	<b>40-49</b>	26	9	
		38.2%	30.0%	
	<b>50-59</b>	9	8	
	13.2%	26.7%		
	<b>60</b>	3	0	
		4.4%	0.0%	
	<b>Total</b>	68	30	
		100.0%	100.0%	
<b>Size (mm)</b>	$\leq 5$	49	12	<b>0.003</b>
		72.1%	40.0%	

	>5	19 27.9%	18 60.0%	
	<b>Total</b>	68 100.0%	30 100.0%	
<b>Gender</b>	<b>Females</b>	60 88.2%	26 86.7%	1.000
	<b>Males</b>	8 11.8%	4 13.3%	
	<b>Total</b>	68 100.0%	30 100.0%	
<b>Metastasis</b>	<b>Negative</b>	68 100.0%	27 90.0%	<b>0.027</b>
	<b>Positive</b>	0 0.0%	3 10.0%	
	<b>Total</b>	68 100.0%	30 100.0%	
<b>Site</b>	<b>Isthmus</b>	5 7.4%	1 3.3%	0.3
	<b>Left</b>	26 38.2%	8 26.7%	
	<b>Right</b>	37 54.4%	21 70.0%	
	<b>Total</b>	68 100.0%	30 100.0%	

P-value  $\leq 0.05$  (significant).

As shown in table 5, there is no significant association between Extra thyroidal extension and (age groups, size, gender, metastasis and site).

**Table 5: Association between Extra thyroidal extension and (age groups, size, gender, metastasis and site).**

Variables		Extra thyroidal extension		P-value
		Negative	Positive	
<b>Age groups (years)</b>	<b>20-29</b>	9 9.3%	0 0.0%	0.3
	<b>30-39</b>	34 35.1%	0 0.0%	
	<b>40-49</b>	35 36.1%	0 0.0%	
	<b>50-59</b>	16 16.5%	1 100.0%	
	<b>60</b>	3 3.1%	0 0.0%	
	<b>Total</b>	97 100.0%	1 100.0%	
	<b>Size (mm)</b>	$\leq 5$	61 62.9%	
>5		36 37.1%	1 100.0%	
<b>Total</b>		97 100.0%	1 100.0%	
<b>Gender</b>	<b>Females</b>	85 87.6%	1 100.0%	1.000

	<i>Males</i>	12 12.4%	0 0.0%	
	<i>Total</i>	97 100.0%	1 100.0%	
<b>Metastasis</b>	<i>Negative</i>	94 96.9%	1 100.0%	1.000
	<i>Positive</i>	3 3.1%	0 0.0%	
	<i>Total</i>	97 100.0%	1 100.0%	
<b>Site</b>	<i>Isthmus</i>	6 6.2%	0 0.0%	0.7
	<i>Left</i>	34 35.1%	0 0.0%	
	<i>Right</i>	57 58.8%	1 100.0%	
	<i>Total</i>	97 100.0%	1 100.0%	

**P-value ≤0.05 (significant).**

As shown in table 6, there is no significant association between Perineural invasion and (age groups, size, gender, metastasis and site).

**Table 6: Association between Perineural invasion and (age groups, size, gender, metastasis and site).**

Variables		Perineural invasion		P-value
		Negative	Positive	
<b>Age groups (years)</b>	<i>20-29</i>	9 9.3%	0 0.0%	0.3
	<i>30-39</i>	34 35.1%	0 0.0%	
	<i>40-49</i>	35 36.1%	0 0.0%	
	<i>50-59</i>	16 16.5%	1 100.0%	
	<i>60</i>	3 3.1%	0 0.0%	
	<i>Total</i>	97 100.0%	1 100.0%	
	<b>Size (mm)</b>	<i>≤5</i>	61 62.9%	
<i>&gt;5</i>		36 37.1%	1 100.0%	
<i>Total</i>		97 100.0%	1 100.0%	
<b>Gender</b>	<i>Females</i>	85 87.6%	1 100.0%	1.000
	<i>Males</i>	12 12.4%	0 0.0%	
	<i>Total</i>	97 100.0%	1 100.0%	
<b>Metastasis</b>	<i>Negative</i>	94 96.9%	1 100.0%	1.000
	<i>Positive</i>	3 3.1%	0 0.0%	
	<i>Total</i>	97 100.0%	1 100.0%	

<b>Site</b>	<b>Isthmus</b>	6	0	0.7
		6.2%	0.0%	
	<b>Left</b>	34	0	
		35.1%	0.0%	
	<b>Right</b>	57	1	
	58.8%	100.0%		
	<b>Total</b>	97	1	
		100.0%	100.0%	

**P-value  $\leq 0.05$  (significant).**

As shown in table 7; there is no significant association between vascular invasion and capsular invasion.

**Table 7: Association between vascular invasion and capsular invasion.**

Variables		Vascular invasion		P-value
		Negative	Positive	
<b>Capsular Invasion</b>	<b>Negative</b>	94	1	1.000
		96.9%	100.0%	
	<b>Positive</b>	3	0	
		3.1%	0.0%	
	<b>Total</b>	97	1	
		100.0%	100.0%	

## DISCUSSION

**Patient Demographics and Clinical Characteristics:** Our study found the mean age of PTMC patients to be  $41.5 \pm 9.7$  years, with significant proportions in the 40-49 and 30-39 age groups. This age distribution aligns with Baek HJ et al.<sup>[16]</sup> emphasizing PTMC as a condition primarily affecting middle-aged individuals. However, it contrasts with Kitahara CM et al.<sup>[17]</sup> which observed a younger median age. The high prevalence of females (87.8%) in our cohort corroborates the gender disparity in thyroid cancer noted by Li P et al.<sup>[18]</sup> but contrasts with Seib CD et al.<sup>[19]</sup> which reported a more balanced gender distribution. Clinically, a large majority of our patients had favorable prognostic factors, such as the absence of metastasis and negative capsular invasion. These findings are consistent with those reported by Pelizzo MR et al.<sup>[20]</sup> but contradict You E et al. study,<sup>[21]</sup> which found a higher prevalence of these aggressive features. **Capsular Invasion:** We observed no significant association between capsular invasion and factors like age, tumor size, gender, and metastasis. This agrees with Du J et al. study.<sup>[22]</sup> but stands in contrast to the findings by Shindo H et al.<sup>[23]</sup> which reported an age-related increase in capsular invasion. **Vascular Invasion:** Similar to capsular invasion, no significant associations were found with vascular invasion and demographic or clinical variables. This mirrors the observations by Aziz A et al.<sup>[24]</sup> but is at odds with Vikneson K et al.<sup>[25]</sup> which noted a correlation with larger tumor sizes. **Multifocality:** A notable finding was the significant association between multifocality and larger tumor sizes (>5 mm), as well as a lower incidence of metastasis. This is in line with Parvathareddy SK et al.<sup>[26]</sup>, indicating multifocality as a marker of tumor burden. However, this contradicts Harries V et al.<sup>[27]</sup> which associated multifocality with higher metastasis rates. **Extra Thyroidal Extension:** Our analysis showed no significant association between extra thyroidal extension and demographic or clinical factors.

This supports Wang H et al.<sup>[28]</sup> but conflicts with Tam S et al.<sup>[29]</sup> which found associations with larger tumor sizes. **Perineural Invasion:** The lack of significant associations with perineural invasion in our study is consistent with findings by Kim Y et al.<sup>[30]</sup> However, this contrasts with research by Luo X et al.<sup>[31]</sup> which found a correlation with older age groups. **Relationship Between Vascular and Capsular Invasion:** Our study revealed no significant association between vascular and capsular invasion, supporting Thompson and Amin SN et al. findings.<sup>[32]</sup> However, this disagrees with Jiao WP et al.<sup>[33]</sup> which observed a positive correlation.

## CONCLUSION

In this study of 98 thyroid cancer patients, a predominant female representation (87.8%) and a mean age of 41.5 years were observed. The majority had non-aggressive features: small tumors ( $\leq 5$  mm), and negative for metastasis, capsular invasion, vascular invasion, extrathyroidal extension, and perineural invasion. Multifocality was notably associated with larger tumors but not with increased metastasis. No significant links were found between the clinical features (capsular and vascular invasion, extrathyroidal and perineural invasion) and patient demographics or tumor characteristics. These findings suggest a complex interplay of factors influencing the pathology of thyroid cancer.

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