



Histopathological Types of Papillary Thyroid Carcinoma: Clinicopathologic Study

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Abstract

BACKGROUND: Papillary thyroid carcinoma (PTC) is the most common type of thyroid carcinoma that represents a set of characteristic of nuclear features in which the diagnosis is depend.

AIM: The study aimed to review different variants of PTC which has different malignant potential in correlation with many prognostic and clinical factors in Iraq.

PATIENTS AND METHODS: Paraffin blocks of 227 cases of PTC were selected, subtyped, and grouped according to the malignant potential. The prognostic and clinical factors were studied.

RESULTS: The mean age was (39.29 ± 12.17) years, with female predominance (86.3%), where (55.5%) of them below 40 years, conventional variant was most common (40.1%), followed by papillary microcarcinoma variant, 197 cases (86.8%) were classified as low to intermediate malignant potential, and 30 cases (13.2%) were classified as high malignant potential. On comparison, among the tumor stages, tumor focality, native capsular invasion, lymph nodes involvement, presence or absence of vascular invasion, extrathyroid extension, and distant metastasis, there is no significant correlation between them, whereas with the tumor size, there is significant correlation between them ($p < 0.05$).

CONCLUSION: Conventional type followed by micropapillary type is most common. The mean age in Iraqi patients is lower than other countries for PTC. There is no significant association regarding prognostic factors between low to intermediate malignant potential variants and high malignant potential variants with exception of tumor diameter.

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Introduction

Papillary thyroid carcinoma (PTC) is the most common type of thyroid carcinoma which represents more than 70–90%. Papillary carcinoma is a set of characteristic of nuclear features in which the diagnosis is depend, as alteration in nuclear shape and size (overlapping and enlargement of nuclei), margination and clearing of chromatin, glassy appearance of nuclei, irregularity in nuclear contour, grooving nuclei, and presence of nuclear pseudoinclusions [1]. In Iraq, thyroid carcinoma (accounting for 1.7% of newly diagnosed malignancies, 2.75% of female cancers, it ranked tenth among the ten most common tumors, according to the latest Iraqi Cancer Registry [2]. There are many subtypes of PTC according to the 2017 WHO classification [3]. Subtyping is depend on a combination of architectural features, cytologic characteristic presence or absence of capsule, and size of growth [4]. BRAFV600E is the most frequent mutation, especially in classic and tall cell subtypes [3]. There is an increasing number of PTC in the past 15–20 years due to increasing identification of thyroid lesions on imaging [5], Hashimoto thyroiditis, and ionizing radiation early in life possible most common

causes [6]. Clinically, its presentation is painless thyroid nodule or lump or as a mass in neck or as cervical node and on scanning, it is cold [7], with general excellent prognosis [8]. Surgery alone or in combination with post-operative radiotherapy is the main stay of the management [9]. The aim of this study is to review different variants of PTC in correlation with many prognostic and clinical factors in Iraq.

Methods

Study design and setting

This is a retrospective study conducted in Pathology Department, College of Medicine, University of Baghdad. About 227 cases of PTC were collected from teaching laboratories of Baghdad Medical City, at the period from January 2019 to January 2021.

Data collection and sources

Cases distributed as lobectomy, near total or total thyroidectomy, and total thyroidectomy with nodal

neck dissection. Final histopathological detection of PTC including various variants was distinguished, using several parameters including: Gender, age, histopathologic type, size of tumor (maximum diameter), focality, side of involvement, associated conditions, encapsulation, vascular invasions, status of lymph nodes, presence of dedifferentiation, extrathyroid extension, and staging. In term of descriptive purposes, the aggressive variants were found in this study including Hobnail, columnar cell variant, and diffuse follicular variant PTC. They classified as high malignant potential and other variants were low to intermediate malignant potential. Preoperatively, all patients underwent clinical and ultrasound evaluation. Paraffin blocks were obtained for all cases and sections were stained with hematoxylin and eosin (H and E). Then, all slides were re-examined and findings were documented. The dependence on histopathologic and sonographic records in interpretation involvement lymph node or not, any case with loss of any of the above mentioned variables was excluded from the study.

Ethics committee

Approval was obtained from the Institutional Review Board of Teaching Laboratories of Baghdad Medical City, which relinquishes the requirement for informed consent due to the retrospective nature of the study.

Statistical analysis

It was performed with the Statistical Package for the Social Sciences 26 statistical software program. Univariate data were summarized using standard descriptive statistics and tabulation of categorical variables. Associations between categorical variables were assessed through cross tabulation and Chi-square. Exact tests were used to calculate the p value. T-test with bootstrapping was used to compare means of continuous variables. In all statistical analyses, $p < 0.05$ was considered significant.

Results

The mean age was 39.29 ± 12.172 years (range 11–86 years) and the most were women (86.3%). Cases were divided into below 40 years 126 (55.5%) and above and equal to 40 years 101 (44.5%). Right lobe was the most frequent lobe that involved by cancer in 44.1%. The mean tumor size was larger in high malignant potential group (Mean = 2.16 ± 1.24 cm) than low malignant potential group (Mean = 1.64 ± 1.22 cm), and this difference was significant (-0.52041 , 95% CI $[-1.02215, -0.05388]$, $t = -2.171$, $p = 0.03$). Regarding histopathologic types, 91 cases were conventional type (40.1%) which is the most common variant followed by papillary microcarcinoma variant in 67 cases (11.9%)

Table 1: Distribution of variables

Characteristic	Frequency (%)
Histopathologic types	
Papillary carcinoma, conventional type	91 (40.1)
Papillary microcarcinoma	67 (29.5)
Encapsulated variant	27 (11.9)
Diffuse follicular variant	25 (11.0)
Encapsulated follicular variant	3 (1.3)
Columnar cell variant	2 (0.9)
Invasive encapsulated follicular variant	5 (2.2)
Hobnail papillary thyroid carcinoma	3 (1.3)
Warthin-like variant	2 (0.9)
Mixed: Conventional and microcarcinoma	2 (0.9)
Histopathologic subtypes according to the malignant potential	
Low to intermediate malignant potential	197 (86.8)
High malignant potential	30 (13.2)
Tumor stage (AJCC/TNM Staging)	
Stage-I	214 (94.3)
Stage-II	10 (4.4)
Stage-III	1 (0.4)
Stage-IV B	2 (0.9)
Tumor focality	
Unifocal	160 (70.5)
Multifocal	67 (29.5)
Capsular invasion	
Present	38 (16.7)
Absent	189 (83.3)
Lymph nodes involvement	
Involved	55 (24.2)
Not involved	172 (75.8)
Vascular invasion	
Present	62 (27.3)
Absent	165 (72.7)
Extrathyroid extension	
Present	25 (11.0)
Absent	202 (89.0)
Distant metastasis	
Present	17 (7.5)
Absent	210 (92.5)

(which is PTC that is equal to or <1 cm) and other variants are shown in Table 1. Histopathologic subtypes according to the malignant potential were distributed as followed, 197 cases (86.8%) were low to intermediate malignant potential, while 30 cases (13.2%) were grouped as high malignant potential, which includes variants with aggressive behavior (columnar cell, hobnail, and diffuse infiltrative follicular variants). The present work has been confirmed that (65.2%) of cases were detected without need to ancillary studies like immunohistochemistry stains due to characteristic nuclear features that papillary carcinoma diagnosis is based. In our center, CK 19 positivity and occasionally with combination of CD56 negativity were used (Figure 1). Other frequencies concerning tumor stage, tumor focality, native capsular invasion, lymph nodes involvement, presence or absence of vascular invasion, extrathyroid extension, and distant metastasis are presented in Table 1, while correlation between low to intermediate malignant potential subtypes and high malignant potential subtypes regarding various prognostic factors are illustrated in Table 2.

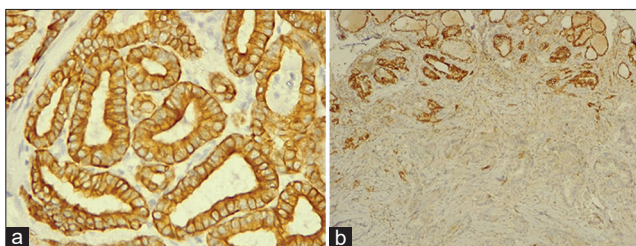


Figure 1: (a) Positive CK19 (prominent membranous and cytoplasmic staining), (b) PTC is negative for CD56 (below), while the normal follicles are positive

Discussion

The most common variant of PTC is conventional in 40.1%, followed by papillary microcarcinoma in 29.5%, which agree Singhal *et al.* [10] study. Women are the most common documented in 86.3%, which supporting with Siegel *et al.* [11] study. The mean age of patients is (39.29 ± 12.17 years), which is lower than mean age of Cho *et al.* [12] study. This is may be due to possibility that Iraqi people being exposed to radiation (which is important risk factor) due to repeated wars in Iraq in the past three decades. About 126 of the cases were aged below 40 years. Approximately 86.1% of cases belonged to the low to intermediate malignant potential variants and others classified as high malignant potential. This explained by unusual external circumstances, mean that the Iraqi people had been exposed to different external radiation during several wars, in addition to different age distribution between different variants, for example, high malignant potential variants occur usually in older patient than those of classic papillary thyroid variant and the microcarcinoma, which both are major components of first group. Multifocality figured nearly in 30%. The papillary carcinoma is the most frequent type of well-differentiated thyroid carcinoma known as multifocal. The multifocality is considered as an independent risk factor of PTC recurrence after surgical removal and the TNM stages were higher, yet, there is no significant association between low to intermediate malignant potential and high malignant potential. There are 60 cases in the first group, while seven cases in the second group of papillary thyroid microcarcinoma, this is may be due to an increment in the incidence of papillary thyroid microcarcinoma in the past decades [13]. Hashimoto's thyroiditis is the most common autoimmune lymphocytic thyroiditis. The relation of Hashimoto's disease to papillary carcinoma has been broadly correlated [14]. In this study, 25 cases (11.0%) of all cases were correlated with Hashimoto's disease, this percentage is less than parentage seen in other studies like Graceffa *et al.*, whereas 70% of cases are associated with multinodular colloid goiter, both conditions have a 1.6 times increased risk of incidence of PTC [15], the reason beyond, it is may be the effect of other carcinogens in pathogenesis of PTC in Iraq like exposure to radiation and chemical toxicants. In relation to lymph nodes spreading, 24.2% of cases showed metastasis in the lymph nodes of the neck, where (90.9%) those of low to intermediate malignant potential and (9.1%) of high-grade malignant potential, this is, in contrast to other studies stated that aggressive variants had high rate of lymph node metastasis reaching up to 70 % [16]. It is important to notify that lymph node metastases of the PTC are a sensible prognostic factor and a key for recurrence of the tumor, but not for survival as concluded by Maksimovic *et al.* [17]. Distant metastasis is the main cause of PTC mortality [18], which has been reported in (9–14%) during its clinical

Table 2: Cross tabs (Chi-square tests of independence)

Characteristic	Histopathologic subtypes according to the malignant potential		Fisher's Exact Test (p)
	Low to intermediate malignant potential n = 197 n (%)	High malignant potential n = 30 n (%)	
Age groups			
<40 years	110 (87.3)	16 (12.7)	0.845 (NS)
≥40 years	87 (86.1)	14 (13.9)	
Gender			
Female	172 (87.8)	24 (12.2)	0.26 (NS)
Male	25 (80.6)	6 (19.4)	
Tumor focality			
Unifocal	137 (85.6)	23 (14.4)	0.52 (NS)
Multifocal	60 (89.6)	7 (10.4)	
Pathologic background			
Hashimoto thyroiditis	23 (92.0)	2 (8.0)	0.54 (NS)
Other pathologies	174 (86.1)	28 (13.9)	
Tumor stage			
Stage: I–II	195 (87.1)	29 (12.9)	0.35 (NS)
Stage: III–IV B	2 (66.7)	1 (33.3)	
Tumor differentiation			
Differentiated	8 (100)	0	0.32 (NS)
Dedifferentiated	189 (86.3)	30 (13.7)	
Capsular invasion			
Present	33 (86.8)	5 (13.2)	1.0 (NS)
Absent	164 (86.8)	25 (13.2)	
Lymph nodes involvement			
Involved	50 (90.9)	5 (9.1)	0.21 (NS)
Not involved	147 (85.5)	25 (14.5)	
Vascular invasion			
Present	57 (91.9)	5 (8.1)	0.19 (NS)
Absent	140 (84.8)	25 (15.2)	
Extrathyroid extension			
Present	21 (84)	4 (16)	0.75 (NS)
Absent	176 (87.1)	26 (12.9)	
Distant metastasis			
Present	14 (82.4)	3 (17.6)	0.48 (NS)
Absent	183 (87.1)	27 (12.9)	

course and occur later on [18], supporting these data by a study done by Khan *et al.* [19]. Similarly, 7.5% of cases showed distant metastasis with 17.6% of them belonged to high malignant potential variants. Native capsular invasion of thyroid seen in 38 cases (16.7%), the results from one study suggested that existence of capsular invasion did not have adverse outcomes on biological behavior and on long-term prognosis in patients with PTC [20]. Vascular invasion seen in 62 of the cases, this percent is within the range of its incidence in other studies (5.6–33%), which concluded that a significant variability regarding the relationship between vascular invasions and outcome like recurrence as reported in prior studies [21]. Other studies failed to validate this observation [22]. Extrathyroid extension was seen in 25 of cases, most of them in low to intermediate malignant potential group (about 21 cases). All of the cases in the present study are of minimal invasion, that is, just extension to sternothyroid muscle or perithyroid soft tissues. This type of extension does not enhance T category or affect the mortality and recurrence rates in patients with PTC [23], whereas massive extrathyroid extension was reported to influence those mentioned rates [24]. In view of tumor size, there is a significant correlation between two groups. Primary tumor diameter has been reported as a predictor for outcome in PCT [25]. In the previous studies concluded that tumors which are more than 1 cm had worse prognosis [26], in which the patients with tumor diameter more than 1 cm had a higher risk of post-operative recurrence as compared with those whom <1 cm and during follow-up of these patients with consideration of other prognostic

factors [27]. However, there was no statistical difference in survival between them. Another studies retail on a single-size threshold of 2cm maximized prognostic distinct in with tumors more than 2cm associated with a 5 times higher risk of recurrence than those tumors with ≤ 2 cm [28]. Regarding the staging, almost all of the cases were in Stage I or II that is because 92% of the cases were < 50 years old considering the cutoff of this age as an essential variable for AJCC staging of differentiated thyroid cancer [29]. Finally, on notification of correlation between the two groups regarding the prognostic factors, this may be elaborate some study limitations as relative small sample size, small number of high malignant potential types of all collected cases, and short duration of the study.

Conclusion

Conventional type followed by micropapillary type is most common. The mean age in Iraqi patients is lower than other countries. There is no significant association regarding prognostic factors between low to intermediate and high malignant potential variants with exception of the tumor diameter.

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