Annals of Thyroid Research

Open Access

Austin Publishing Group

Research Article

The Clinicopathological Aspects and Changing Trend of Papillary Thyroid Carcinoma in Gaza Strip: A Retrospective Study of 122 Cases Diagnosed Between 2010 and 2018

Hamada HAA[1]* and Abuharbeid S[2]

[1]Department of Pathology, Shefa Hospital, Palestine

[2]Department of Biology, Al-Aqsa University, Palestine

***Corresponding author:** Hamada HAA, Department of Pathology, Shefa Hospital, Gaza, Gaza Strip Palestine

Received: November 23, 2020; **Accepted:** December 12, 2020; **Published:** December 19, 2020

Abstract

Introduction: To investigate the clinicopathological aspects of papillary thyroid carcinoma in Gaza Strip and any changing of these aspects over the years.

Methods and Materials: 122 consecutive cases of papillary thyroid carcinoma were retrieved from the archives of pathology department-Shefa hospital, Gaza Strip and from the corresponding author's private center in Gaza diagnosed between 2010 and 2018.

Results: Male:female ratio was 1:4.8. The mean of age was 38.7. The mean of tumor diameter was 2.1. The tumor localization in the thyroid gland was 28(23%), 41(33.6%), 3(2.5%), 34(27.9%), and 6(4.9%) in the left lobe, right lobe, isthmus, multicentric and extrathyroid respectively. In 12(9.8%) of the cases the localization was unknown. 27(30%) of the valid cases revealed multifocality, 34(40%) multicentricity, 69(58.5%) thyroid capsule invasion, 46(41.1%) extracapsular extension and 21(20.4%) positive surgical margins. Male:Female ratio revealed statistically no significant changes among various age groups. Statistically significant differences in the annual means of age across the years 2010-2018 were evident. There were no significant differences among the annual means of tumor diameter across the years 2010-2018. We found a transient increase of the parameters reflecting aggressiveness in the cases diagnosed in 2014, 2015, and 2016. Then this increase returned to the previous levels in the years 2017 and 2018.

Conclusion: Gaining the clinicaopathological data; will contribute to better understanding and monitoring of the papillary thyroid carcinoma in Gaza Strip. Additional studies should be carried out to confirm the changing aspects of papillary thyroid carcinoma observed in our study and to investigate the possible causes.

Keywords: Clinicopathological; Papillary thyroid carcinoma; Gaza

Abreviations

PTC: Papillary Thyroid Carcinoma; SPSS: Statistical Package of Social Science; FFPE: Formalin Fixed Paraffin Embedded; SEER: Surveillance Epidemiology and End Results

Introduction

The global overview of Papillary Thyroid Carcinoma (PTC) performed by La Vecchia C. revealed increased incidence of thyroid cancer in both sexes in most countries, with PTC being the most common type of thyroid carcinoma and the most common endocrine malignancy [1]. PTC was also the most frequent thyroid cancer in the earlier large cohort study by Hundahl SA and constituted 71% of the malignant thyroid lesion in Rao R study [2,3]. Also 93.6% of 18047 cases in SEER (Surveillance, Epidemiology and End Results) 17 data base were PTC [4].

In this study we aim to investigate the clinicopathological aspects of PTC in Gaza Strip across the period from 2010 to 2018. The identification of the clinicopathological features of PTC will constitute a baseline for further studies in the future and will contribute to better understanding and monitoring of the PTC. This will improve the management of these patients. Also finding out any changing trends in the clinicopathological aspects of PTC will trigger the efforts to investigate and avoid the possible adverse factors causing these changes. To the best of our knowledge this has not been investigated before in Gaza Strip.

Methods and Materials

Research objectives

In this study we aim to investigate the clinico-pathological aspects of PTC in Gaza Strip and the possible changing trend across the period from 2010 to 2018.

Citation: Hamada HAA and Abuharbeid S. The Clinicopathological Aspects and Changing Trend of Papillary Thyroid Carcinoma in Gaza Strip: A Retrospective Study of 122 Cases Diagnosed Between 2010 and 2018. Annals Thyroid Res. 2020; 6(3): 282-286.

Operational definition: Cases of PTC: The cases were histopathologically diagnosed as PTC after thyroid open surgery.

Age: Age of the patient at the time of diagnosis as recorded in the histopathology request form confirmed by the official records.

Place of residency: The place of residency in the histopathology request form, will be reported as one of 4 regions of Gaza strip (North, Gaza, Middle and south).

Localization of the tumor

Localization of the tumor will be reported as in the left lobe, right lobe, isthmus, multicentric (if more than one mass located in more than one of the former three locations) or extra-thyroid as documented in the histopathology report. The extra-thyroid localization will include patients with first presentation as metastatic lymph node or any other PTC mass outside the anatomic position of the thyroid gland.

Diameter of tumor

The largest diameter of the tumor (or the largest diameter of the largest mass if multicentric or multifocal) recorded in the histopathology report; reported in centimeters.

Multicentricity

The evidence of at least one tumoral focus in more than one of the following locations; left lobe, right lobe, or isthmus as documented in the histopathology report. This parameter was designated as "unknown" in cases underwent lobectomy or hemithythyroidectomy with no available data regarding the rest of the thyroid gland.

Multifocality: The evidence of more than one tumoral focus in one of the following locations; left lobe, right lobe, or isthmus as documented in the histopathology report.

Capsule invasion: The microscopic detection of tumor cells inside the thyroid capsule with or without extracapsular extension.

Extra-capsular extension: The microscopic detection of tumor cells outside the thyroid capsule; the tumor is seen inside the peri-thyroid soft tissue.

The surgical margin: The inked border

Study design

The design of this study is observational quantitative descriptive one. It will be used to describe the clinicopathological aspects of PTC. Descriptive studies generate new knowledge about concepts and identifies relationships between variables. In this study, methodology will enhance understanding of the facts on this regard.

Study population

The population in this study is the population of Gaza Strip. From this population we defined the cases pathologically diagnosed as PTC between 2010 and 2018 in the pathology department of shifa hospital and in the corresponding author's private center as the "study population". From these we selected the "sample population" which is defined as the cases diagnosed histopathologically as PTC after surgical removal only (lobectomy, hemithyroidectomy, near total, subtotal or total thyroidectomy) by one experienced pathologist. Cases diagnosed by FNAB were excluded.

Data collection, management, and quality control

The data and tissues of the PTC cases were collected from the archives of Shifa Hospital Pathology Department and the archives of the corresponding author's private pathology center. 122 Formalin Fixed Paraffin Embedded (FFPE) tumor tissues obtained from PTC patients whom were diagnosed between 2010 and 2018 during open surgery were collected. FFPE blocks were sectioned to 3 μm thickness by microtome and then routinely stained by Hematoxylin and eosin for light microscopic revision.

The results were represented as the frequency and percentage for categorical variables or mean, median, maximum and minimum for numerical data.

The following procedures were used to control the factors that may undermine the validity of the results. Only the cases diagnosed by one experienced pathologist (Hamada HAA) were considered to guarantee the accuracy of diagnosis and the standardization of the pathological data. All the cases meeting the selection criteria were included in the study. Clinicopathological feature were collected and managed by the same experienced pathologist. The paraffin sectioning and staining procedures were performed by expert technicians.

Data analysis

The researchers used Statistical Package of Social Science (SPSS) program for data entry and analysis. Frequency tables that show sample characteristics of various clinico-pathological aspects were done. Moreover, cross tabulation for main findings and advanced statistical tests such as Chi square test to compare categorical variables, One Way ANOVA test and LSD to compare means of numeric variables were used when required to analyze data.

Results

Of the 122 cases 101 (82.8%) were females and 21 (17.2%) were males with male:female (M:F) ratio being 1:4.8. The mean of age was 38.7, median 39, minimum 10, and maximum 78 with standard deviation 13.085. The main age of females was 39, minimum 16, maximum 78, and median 40. The main age of males was 37 minimum 10, maximum 60, and median 39. The distribution of the cases according to the Gaza Strip regions was 72 (59%), 26 (21.3%), 15 (12.3%) and 9 (7.4%) from Gaza, middle, north and south governorates respectively. The mean of largest diameter of the tumor was 2.1 cm, median 1.8 cm, minimum 0.1 cm, maximum 6 cm and the standard deviation 1.3731. 28 (23%) of the cases were located in the left lobe, 41 (33.6%) were located in the right lobe, 3 (2.5%) were located in the isthmus, 34 (27.9%) were multicentric (more than one mass in more than one localization of the followings; the left lobe, right lobe or isthmus). 6 (4.9%) cases were presented as extrathyroid mass (metastatic lymph node or probably originated from ectopic thyroid tissue). In 12 (9.8%) of the cases the localization was unknown.

Regarding the parameters of aggressiveness 27 (30%) of the valid cases revealed multifocality, 34 (40%) revealed multicentricity, 69 (58.5%) revealed thyroid capsule invasion, 46 (41.1%) revealed extracapsular extension and the surgical margins were positive in 21 (20.4%) of the valid cases (Table 1).

We divided age of the patients into 7 groups as depicted in Table 2. Considering M:F ratio 1:5 (which is almost equal to that of the

Table 1: Frequency, Percent and Valid Percent of Variables.

Variable	Category	Frequency	Percent	Valid Percent
Gender	Female	101	82.8	82.8
	Male	21	17.2	17.2
Governorate	Gaza	72	59.0	59.0
	Middle	26	21.3	21.3
	North	15	12.3	12.3
	South	9	7.4	7.4
Localization	Extrathyroid	6	4.9	5.5
	Isthmus	3	2.5	2.7
	Left	27	22.1	24.5
	Multicentric	34	27.9	30.9
	Right	40	32.8	36.4
	Unknown	12	9.8	-----
Multifocality	Multifocal	27	22.1	30.0
	Non	63	51.6	70.0
	Not-applicable	5	4.2	-----
	Unknown	27	22.1	-----
Multicentricity	Multicentric	34	27.9	40.0
	Non	51	41.8	60.0
	Not-applicable	6	4.9	-----
	Unknown	31	25.4	-----
Capsule	Free	49	40.2	41.5
	Invaded	69	56.5	58.5
-	Unknown	4	3.3	------
Extra capsular extension	Free	66	54.1	58.9
	Invaded	46	37.7	41.1
	Unknown	10	8.2	------
Margin	Free	82	67.2	79.6
	Invaded	21	17.2	20.4
	Unknown	16	13.1	-----
	Not-Applicable	3	2.5	-----
Total	------	122	100%	100%

entire cases) as a reference value, we compared the M:F ratio of each of the 7 age groups with this value. We found that the M:F ratio of each age group revealed no statistically significant difference from the 1:5 value (Table 2).

Also, we investigated some parameters across the years from 2010 to 2018. One Way Anova test revealed statistically significant differences among the annual means of age across the period from 2010 to 2018. p. value was less than 0.05. On the other hand, there was no significant differences among the annual means of tumor diameter across the years from 2010 to 2018 (Table 3&4).

We used the LSD (Least Significant Difference) method to find the differences in means of age between the years. The significant differences in means of age between different years are shown in (Table 5).

Table 2: Male/female ratio in the age groups and the Chi-square results comparing these ratios with the reference value 1:5. There is no statistically significant differences. P value >0.05.

Age groups	Male	Female	Total	Male: Female ratio	p.value (Chi-square)
Less than 20	2 (28.6%)	5 (71.4%)	7	1:2.5	0.398
20-29	5 (17.9%)	23 (82.1%)	28	1:4.6	0.866
30-39	4 (13.3%)	26 (86.7%)	30	1:6.5	0.624
40-49	7 (22.6%)	24 (77.4%)	31	1:3.43	0.377
50-59	2 (12.5%)	14 (87.5%)	16	1:7	0.654
60-69	1 (14.3%)	6 (85.7%)	7	1:6	0.866
70-79	0 (0.0%)	2 (100.0%)	2	0:2	------
All	21 (17.4%)	100 (82.6%)	121*	1:4.76	0.872

*One case with unknown age was ignored

Table 3: Number of cases, means of age, and means of tumor diameter for each year.

Year	Number of cases	Means of age	Means of tumor diameter
2010	5	40.60	2.48
2011	3	23	1.9
2012	11	35.73	2.04
2013	16	42.63	1.944
2014	26	37.42	2.315
2015	30	40.40	2.087
2016	20	35.79	1.863
2017	5	27.60	2.2
2018	6	54.50	1.42

Table 4: One Way Anova results of age and largest diameter across the years. There is a statistically significant difference in the means of age across the years 2010-2018. p. value is less than 0.05. There is statistically no significant difference in the means of tumor largest diameter across the years 2010-2018. P value is larger than 0.05.

Variable	Source of Variation	Sum of Squares	df	Mean Square	F	P
Age	Between Groups	3504.886	8	438.111	2.879	*0.006
	Within Groups	17042.536	112	152.165		
	Total	20547.421	120			
Largest diameter	Between Groups	5.773	8	0.722	0.366	0.936
	Within Groups	216.712	110	1.970		
	Total	222.486	118			

df = Degrees of freedom; *p value < 0.05

The parameters considered as signs of more aggressive behavior (such as multifocality, multicentricity capsular invasion and extra capsular extension) revealed considerable changes across the years from 2010 to 2018; i.e. these parameters increased significantly in the cases diagnosed in the years (2014, 2015, 2016), then returned to the previous levels in the years 2017 and 2018 (Table 6, and Figure 1).

Discussion

The Shifa Hospital is the main tertiary healthcare center in Gaza strip. Gaza Strip (365 Km2 and population more than 2 million) is composed of 5 governorates; North, Gaza, middle and 2 south governorates. The Shifa Hospital is located in the center of Gaza Governorate. The author's private center is also located in the same

Table 5: LSD (Least Significant Difference) method shows the significant difference in means of age between years.

Year	Year	Mean Difference	P
2011	2013	-19.625	*0.013
	2015	-17.4	*0.022
	2018	-31.5	*0.000
2012	2018	-18.773	*0.000
2013	2017	15.025	*0.019
	2018	-11.875	*0.047
2014	2018	-17.077	*0.003
2015	2017	12.8	*0.034
	2018	-14.1	*0.012
2016	2018	-18.711	*0.002
2017	2018	-26.9	*0.000

*p value < 0.05

region. Most of the cases; 72 (59%) had been received from Gaza governorate, the rest of the cases had been received from middle, north and south governorates {26 (21.3%), 15 (12.3%) and 9 (7.4%) respectively} (Table 1). PTC is increasing in incidence with downward trend in mortality for most areas of the world [1].

Our 122 cases revealed M:F ratio 1:4.8 (Table 1). This was lower than the 1:3.3 in the cohort of Hundahl SA and closer to the ratio of Rao R cases which was 1:5.5, and much lower than the ratio 1:2.1 of the pediatric group reported by Poyrazoğlu Ş [2,3,5]. The M:F ratio of the 291 thyroid cancer cases (of which 85% were PTC) reported by Moo-Young TA was 1:4.6 [4]. Within SEER 17 data base 93% of the cases were PTC and the M:F ratio of thyroid cancer cases was 1:3.5 [4].

Our median of age (39) was lower than the median (44) in the cohort of Hundahl SA [2]. The range of age of our cases was 10-78 which is almost identical to that found by Rao R (8-78) [3]. The median age of Moo-Young TA cases of thyroid cancer was 44 and the range was 13-88 [4]. The median age of the 18047 cases reported by SEER 17 data base was 48 (range 14–85) [4]. In our cases the median age of females was 40. The median age of males was 39.

The median largest diameter of the tumor was 1.8 cm in our study, almost similar to the 1.7 cm in Hundahl SA cohort [2]. The main of largest tumor dimension of the pediatric patients reported by Poyrazoğlu Ş was 2.2 [5]. The median tumor dimension of the cases of SEER 17 data base was 1.4 (range 0.1-9.5) [4]. About 28% of our cases corresponds to the designation "micropapillary carcinoma" (largest tumor dimension 1 cm or less) this was prominently higher than the Indian rate reported by Rao R which was less than 3% and

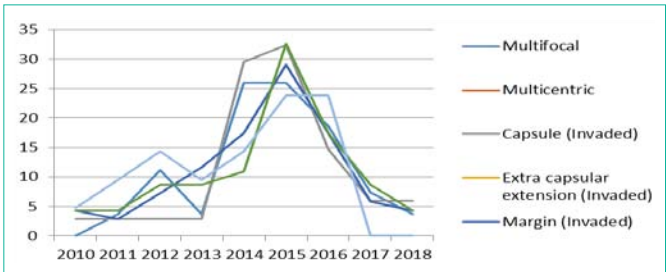

Figure 1: Percent of the "parameters of aggressiveness" across the years from 2010 to 2018. The percent of these parameters revealed statistically significant increase in the years 2014, 2015, and 2016, then returned to the previous levels in 2017 and 2018.

considerably higher than the rate 11.5% of large autopsy series [3,6] reflecting adequate macroscopic and microscopic examination of our cases. Poyrazoğlu Ş reported 30.7% micropapillary carcinoma of the pediatric patients [5]. In the large cohort of SEER 17 data base 37% of the thyroid cancer cases were less than 1 cm (this cohort included 93.6% PTC) [4].

28 (23%) of the cases were located in the left lobe, 41(33.6%) were located in the right lobe, 3 (2.5%) were located in the isthmus, 34 (27.9%) were multicentric and 6 (4.9%) cases were presented as extrathyroid mass. In 12 (9.8%) of the cases the localization was unknown (Table 1). Apparently, the right lobe was the most frequent site of PTC in our cohort. We may suggest more careful and detailed macroscopic examination of the right lobe.

In our cases 27 (30%) of the valid cases revealed multifocality, 34 (40%) revealed multicentricity (as those two parameters were defined in our methodology) (Table 1). The parameter designated as "multifocality" in Hundahl SA cohort and Rao R study was 28.8% and 8% respectively [2,3]. The "multicentricity" reported by Poyrazoğlu Ş in the pediatric patients was 49.3% [5]. 69 (58.5%) of our cases revealed thyroid capsule invasion, 46 (41.1%) revealed extracapsular extension and the surgical margins were positive in 21 (20.4%) of the valid cases (Table 1). Capsule invasion was 40% in the pediatric patients of Poyrazoğlu Ş [5].

We divided age of the patients into 7 groups as depicted in Table 2. About 79% of our cases were in their second to fifth decade, this was slightly higher than the 75% found in Rao R study [3]. Considering M:F ratio 1:5 (the M:F ratio of all cases in our cohort is 1:4.8) as a reference value, we compared the M:F ratio of each age group with this value. We found that the M:F ratio of each age group revealed no statistically significant difference from the reference value 1:5 (Table 2). In these age groups, although not statistically significant, we noticed that the M:F ratio was higher in 2 age groups; the "less

Table 6: The results of chi-square test revealed statistically significant differences in the percent of multifocality, multicentricity, capsule invasion, and extracapsular extension across the years 2010-2018.

Year	2010	2011	2012	2013	2014	2015	2016	2017	2018	P.value (Chi-square)
Percent of multifocality	0.0	3.7	11.1	3.7	25.9	25.9	18.6	7.4	3.7	0.048*
Percent of multicentricity	2.9	2.9	2.9	2.9	29.5	32.4	14.7	5.9	5.9	0.000*
Percent of capsule invasion	4.3	2.9	7.2	11.6	17.4	29.0	17.4	5.8	4.3	0.000*
Percent of extracapsular extension	4.3	4.3	8.7	8.7	10.9	32.6	17.4	8.7	4.3	0.001*
Persent of Invaded margin	4.8	9.5	14.3	9.5	14.3	23.8	23.8	0.0	0.0	0.587

*p.value < 0.05.

than 20" and "40-49" groups. In our cohort the age group "less than 20" M:F ratio was 1:2.5 similar to that reported in the pediatric patients (1:2.1) by Poyrazoğlu Ş [5], suggesting a hypothesis that PTC may tend to affect males more frequently in adolescent/pediatric population in comparison with adult population. Additional studies with larger number of patients may be required to clarify this point.

We found statistically significant differences in the annual means of age among the years from 2010 to 2018 (Table 3&4). We used the LSD method to find the differences in means of age between the years. The significant differences in means of age between various years are shown in Table 5. Larger cohorts are required to confirm this finding and to explain the heterogenity of age means among the years. On the other hand, there was no significant differences between the annual means of tumor diameter across the years from 2010 to 2018 (Table 3&4).

The aspects reflecting aggressiveness; multifocality, multicentricity capsular invasion and extra capsular extension revealed considerable changes across the years from 2010 to 2018 i.e these parameters increased significantly in the cases diagnosed in the years 2014, 2015, and 2016, then returned to the previous levels in the years 2017 and 2018 (Table 6, and Figure 1). This finding suggests some environmental factor/s or "event/s" during or before this period. Also, molecular studies; such as BRAF mutation may be required.

Conclusion

In addition to offering information concerning the clinicopathological aspects of PTC, gaining the clinical and pathological data of PTC will trigger further studies in the future and will contribute to better understanding and monitoring of the PTC in this region and worldwide. This will inevitably improve the management of these patients.

References

1. La Vecchia C, Malvezzi M, Bosetti C, Garavello W, Bertuccio P, Levi F, et al. Thyroid cancer mortality and incidence: a global overview. Int J Cancer. 2015; 136: 2187-2195.
2. Hundahl SA, Cady B, Cunningham MP, Mazzaferri E, McKee RF, Rosai J, et al. Initial results from a prospective cohort study of 5583 cases of thyroid carcinoma treated in the united states during 1996. U.S. and German Thyroid Cancer Study Group. An American College of Surgeons Commission on Cancer Patient Care Evaluation study. Cancer. 2000 Jul; 89: 202-217.
3. 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 J Cancer. 2017; 54: 514-518.
4. Moo-Young TA, Panergo J, Wang CE, Patel S, Duh HY, Winchester DJ, et al. Variations in clinicopathologic characteristics of thyroid cancer among racial ethnic groups: analysis of a large public city hospital and the SEER database. Am J Surg. 2013 Nov; 206: 632-640.
5. Poyrazoğlu Ş, Bundak R, Baş F, Yeğen G, Şanlı Y, Darendeliler F, et al. Clinicopathological Characteristics of Papillary Thyroid Cancer in Children with Emphasis on Pubertal Status and Association with BRAFV600E Mutation. J Clin Res Pediatr Endocrinol. 2017; 9: 185-193.
6. Lee YS, Lim H, Chang HS, Park CS. Papillary thyroid microcarcinomas are different from latent papillary thyroid carcinomas at autopsy. J Korean Med Sci. 2014; 29: 676-679.