The Prevalence of Papillary Thyroid Microcarcinoma in 489 Cases of Thyroidectomy in Iraqi Patients

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ABSTRACT:

BACKGROUND:

Thyroid cancer (TC) is considered the most common malignancy of the endocrine system. Papillary Thyroid Microcarcinoma (PTMC) is defined as tumors of less than or equal to 10mm in diameter, it could be non-incidental or incidental.

OBJECTIVE:

To evaluate the prevalence rate of thyroid papillary microcarcinoma, and to correlate the prevalence rate with different parameters including: age, gender, clinical diagnosis and type of surgery.

PATIENTS AND METHODS:

The present study, which is a retrospective study, was conducted on 489 cases of thyroidectomy specimens; the study was conducted at the Teaching laboratories of Medical City over a period of one year from February 2015 to Feb. 2016. The incidence of thyroid papillary microcarcinoma was correlated with different parameters including age, sex, clinical presentation, and type of surgery.

RESULTS:

In this study , cases were divided into: 53(10.83%) cases male, and 436 (89.171%) cases females, with age range 15-68 years and age mean 41.5 years ,regarding histopathological diagnosis ,cases were analyzed as followed: Nodular hyperplasia 354(72.41%) cases. Autoimmune thyroiditis 34(7.0%) cases, thyroid adenoma 28(5.7%) cases, follicular tumors 2 (0.4%) cases, papillary microcarcinoma 28(5.7%) cases, papillary carcinoma 16(3.3%) cases, follicular carcinoma 3(0.6%) cases, medullary carcinoma 1(0.2%) cases, hyperplastic nodule 6(1.2%) cases, toxic goiter 10(2.0%) cases, infections thyroiditis 1(0.2%) case, papillary carcinoma with lymph node involvement 4(0.8%) cases, thyroglossal cyst 1(0.2%) case, parathyroid adenoma 1(0.2%) case. Eight cases of PTMC(3.3%) were below 40 years of age. 20(8.1%) cases were above 40 years. There was a statistical correlation between age and prevalence of TPMC.

CONCLUSION:

The possibility of thyroid microcarcinoma should always be kept in mind while diagnosing a benign thyroid disease. There was a significant statistical correlation between age and prevalence of thyroid papillary microcarcinoma.

KEYWORDS: thyroid carcinoma, thyroid papillary microcarcinoma, thyroid papillary carcinoma.

INTRODUCTION:

Thyroid cancer is considered the most common malignancy of the endocrine system, with an incidence that ranges from 1 to 8 per 100.000, [1] and it's incidence has continuously increased in the last three decades all over the world, this trend is present on every continent except Africa, where detection is possibly in sufficient [2] .

Based on recent data thyroid cancer is the fifth most frequent cancer in women [3] and in Italy, it is the second most frequent cancer in women between 45 years of age [4], only in few countries (Norway, Sweden) thyroid cancer is decreased [2]. The increase is nearly exclusively due to increase in the incidence of the papillary histotype, with no significant change for the follicular, medullary, or anaplastic histotypes. The increase mainly regards small tumors, although large tumors have also increased [5, 6].

Papillary thyroid cancer constitutes more than

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70% of thyroid cancer [7]. This increase in the incidence of thyroid cancer is mainly recognized as an increased detection of papillary thyroid microcarcinoma (PTMC) [8].

Microcarcinoma includes many different definitions such as incidentaloma, non-palpable carcinoma, small carcinoma, minimal carcinoma and occult carcinoma [9, 10, 11].

These terms share two meanings: the small tumor size and the non-clinical mode of tumor presentation, recently the term microcarcinoma has almost replaced all the previous definitions. Since almost all these tumors are of papillary type, the preferred definition is now micropapillary thyroid carcinoma (MPTC) [12, 13].

PTMC is defined as tumors of less than or equal to 10mm in diameter [14].

PTMC can be non – incidental or incidental. They are usually presented asymptomatically or in association with benign or malignant thyroid lesions. Non-incidental PTMC is usually diagnosed on the basis of fine needle aspiration biopsy (FNAB), local or distant metastasis, incidental PTMC is most commonly discovered on definitive paraffin section examination following thyroid surgery for benign thyroid diseases. [14]

The improved ability of pathologists to detect small and smaller tumors through more vigorous sectioning and studies of surgical specimens excised for benign conditions. Environmental alterations and oncogenic events have also been proposed as contributing factors for this epidemic of PTCM. [15, 16]

There is a lack of consensus in the way PTCM should be managed: this is largely due to the excellent overall prognosis for this disease. The overall survival for well differentiated thyroid carcinoma exceeds 90% and is even better for PTMC [17]. The American thyroid association and the European thyroid association recommended that: the type of the initial surgery and the postoperative care need to be determined depending on the different features of PTMC [18 19].

MATERIALS AND METHODS:

This is a retrospective study that was conducted at the teaching laboratories of medical city teaching complex , in the period: February 2015- to February 2016 (one year period), 489 cases of thyroidectomy for different causes were analyzed, regarding sex, age and type of thyroid pathology or disease, whether benign or malignant. Paraffin blocks were obtained for all cases & sections were stained with hematoxylin and eosin, slides were examined by at least two experienced pathologists.

These 489 cases were divided into: 53 males & 436 females and the age ranges between 15-68 years with median 41.5.

Cases were analyzed regarding different parameters including: clinical diagnosis, type of operation (surgery) and histopathological diagnosis.

- Statistical analysis:

All statistical analyses were performed using (SPSS version 17). A p-value of 0.05 or less was designated as significant.

RESULTS:

Age and sex :In this study 489 cases of thyroidectomy were included, cases were divided into: 436 (89.17%) cases females, and 53 (10.85%)cases male, with age range between 15-68 years and median of 41.5 years .Cases were divided into two groups regarding their age category; above 40 years 246(50.3%)cases and below 40 years 243(49.7%).

Clinical diagnosis: (pre-operative diagnosis):- Data collected from files of the cases showed the following clinical presentation or diagnosis (pre-operatively): 362 (74%) cases presented as goiter (multinoduler enlargement of the thyroid gland), 28 (5.7%) cases as toxic goiter, 63(12.9%) cases as solitary nodule 9 (1.8%) cases as tumor 21(4.3%) cases as recurrent goiter, and 6(1.2%) cases presented as cystic lesions, as shown in table (1).

Table 1: The frequency and percentage of clinical presentation of the cases.

Clinical presentation	Frequency	Percentage
Goiter	362	74.0%
Toxic goiter	28	5.7%
Solitary nodule	63	12.9%
Tumor	9	1.8%
Recurrent goiter	21	4.3%
Cyst	6	1.2%
Total	489	100%

Surgical procedure (type of operation):
The 489 cases of thyroidectomy were divided into: lobectomy 81(16.6%) cases, sub-total thyroidectomy 71 (14.5%) cases, near total thyroidectomy 51(10.4%)cases, total thyroidectomy 279 (57.1%) cases, total thyroidectomy and lymph node excision 7 (1.4%) cases, as shown in table 2.

Table 2: The frequency and percentage of type of surgical procedure.

Type of operation	Frequency	Percentage
Lobectomy	81	16.6
Sub-total thyroidectomy	71	14.5
Near – total thyroidectomy	51	10.4
Total thyroidectomy	279	57.1
Total thyroidectomy + LN	7	1.4
Total	489	100%

Histopathological diagnosis**:**
In this study 489 cases of thyroidectomy were submitted for histopathological examination, and the results were as follows:
Nodular hyperplasia 354 (72-4%) cases, autoimmune thyroiditis (lymphocytic thyroiditis) 34 (7.0%) cases, thyroid adenoma 28 (5.7%) cases, follicular tumor (of undifferentiated malignant potential) 2(0.4%) cases, papillary microcarcinoma 28 (5.7%) cases, papillary carcinoma 16(3.3%) cases, follicular carcinoma 3 (0.6%) cases, medullary carcinoma 1 (0.2%) case, hyperplastic nodule 6(1.2%) cases, toxic goiter 10(2.0%) cases, infectious thyroiditis (tuberculous thyroiditis(TB))1 (0.2%) case, papillary carcinoma with lymph node involvement 4 (0.8%) cases, thyroglossal cyst 1(0.2%) case, parathyroid adenoma 1 (0.2%) case, as shown in table 3.

Table 3: The frequency and percentage of the histopathological diagnosis.

Histopathological diagnosis	Frequency	Percentage
Nodular hyperplasia	354	72.4
Autoimmune thyroiditis	34	7.0
Follicular tumor	2	0.4
Papillarymicrocarcinoma	28	5.7
Adenoma	28	5.7
Papillary carcinoma	16	3.3
Follicular carcinoma	3	0.6
Medullary carcinoma	1	0.2
Hyperplastic nodule	6	1.2
Toxic goiter	10	2.0
Infectious thyroiditis	1	0.2
Papillary Ca + LN	4	0.8
Thyroglossal cyst	1	0.2
Para thyroid adenoma	1	0.2
Total	489	100%

Analyzing these data and correlating the incidence of papillary thyroid microcarcinoma with different parameters show the following results:-
Twenty eight (5.7%) cases of incidental MPTC were detected in 489 cases of thyroidectomy for different causes. Five cases (5/28) (9.3%) were male 23/28 (5.3%) cases were female, with p value 0.220, which was statistically non-significant. There was no significant statistical correlation between the incidence of micropapillary thyroid ca MPTC and sex (gender).

- Eight (8/28) (3.3%) cases of the MPTC were below 40 years age, 20/28 (8.1%) cases were above 40 years, with p value 0.031, there was a significant statistical correlation between incidence of MPTC and age of the patient.
- Regarding clinical diagnosis 23/28 (6.4%) cases of TPMC presented as goiter, 3/28 (10.7%) cases presented with toxic goiter, 1/28 (4.8%) case presented as each solitary nodule and recurrent goiter. P value 0.497, NS there was no significant statistical correlation between incidence of MPTC and clinical presentation.

- Regarding type of surgery: 16/28 (5.8%) cases presented as total thyroidectomy, 7/28 (9.9%) cases as subtotal thyroidectomy, 4/28 (7.8%) cases as near total thyroidectomy, and 1/28 (1.2%) case as lobectomy, (p value 0.29 NS), there was no significant statistical correlation between type of operation and incidence of MPTC, as shown in table 4.

Table 4: The correlation between the incidence of micropapillary thyroid carcinoma and different parameters.

Parameter	Distribution	Microcarcinoma				P value
		Papillary MC		Others		
		Count	%	Count	%	
Gender	Male	5	9.3%	48	90.7%	0.22
	Female	23	5.3%	412	94.7%	NS
Age	< 40	8	3.3%	234	96.7%	0.03*
	>40	20	8.1%	277	91.9%	SS
Clinical diagnosis	Goiter	23	6.4%	338	93.6%	
	Toxic goiter	3	10.7%	25	89.3%	0.497
	Solitary nodule	1	1.6%	62	98.4%	NS
	Tumor	0	0	9	100%	
	Recurrent goiter	1	4.8%	20	95.2%	
	Cyst	0	0%	6	100%	
Type of operation	lobectomy	1	1.2%	80	98.8%	0.296
	Subtotal thyrodiectomy	7	9.9%	64	90.1%	NS
	Near – total thyroidectomy	4	7.8%	47	92.2%	
	Total thyroidectomy	16	5.8%	262	94.2%	
	Total thyroidectomy + LN	0	0%	7	100%	

NS= not significant

- Significant

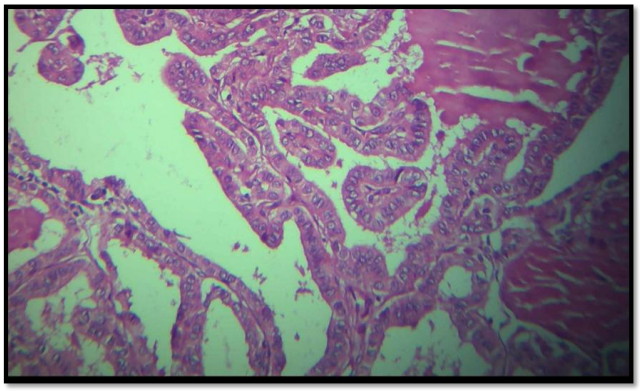

Figure 1: Showing thyroid papillary microcarcinoma (medium power X10).

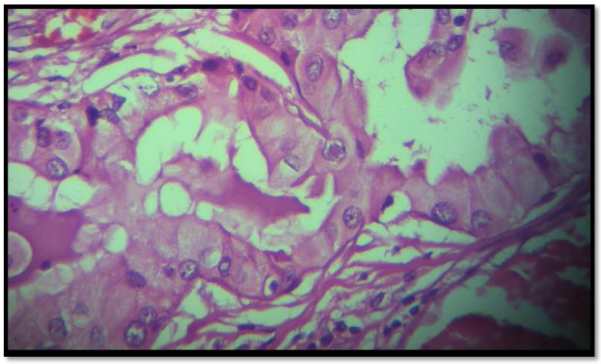

Figure 2:showing thyroid papillary microcarcinoma (oncocytic variant) nuclear pseudoinclusion and nuclear grooving (high power X40).

DISCUSSION:

In this study 28 cases of thyroid micropapillary carcinoma were diagnosed in a group of 489 cases of thyroidectomy for different causes, five cases 5/28 (9.3%) cases were male, 23/28 (5.3%) cases were female, 8/28 (3.31%) cases were below 40 years of age and 20/28 (8.1%) cases were above 40 years of age, there was a significant statistical relationship between age of the patient and the incidence of MPTC. Slijepcevic N et al 2015[20] found MPTC in 345 (16.2%) females and 58 (17.2%) males, age ranged from 14-85 years (mean 54year) they stated that sex and age were not related to the incidence of MPTC, and they found it's incidence 16.3%.

In this study the overall incidence of MPTC was 28/489 (5.7%). Harach HR et al reported the prevalence of MPTC in an autopsy study to be 36% among (101) autopsies [11], other autopsy studies reported prevalence as low as 2.3%. [21, 22, 23]. There are many autopsy series in the literature, reporting MPTC prevalence between these two figures. The wide range in the reported prevalence (2.3-36%) is probably in part due to different methodological approaches, the histopathological criteria used to diagnose MPTC and geographic differences [24].

Incidental foci of MPTC were found in a large percentage of patients after thyroidectomy for presumably benign thyroid conditions ranged 2-24 %[25].

Slijepcevic N et al [20] did not find sex to be an independant predictor for MPTC although there was a 1% higher incident among male patients 17.2% versus 16.2%. Noguchi S et al find an even higher female to male ratio of MPTC in their study (9:1) [26].

Roti et al agree that sex is not an independant predictor for MPTC, and explain the higher incidence of MPTC in women being the result of a higher incidence of benign thyroid disease in women [27].

Some authors find that age is related to MPTC as a prognostic factor, while others don't, but it is not considered an independent predictor [28]. Even though certain authors consider age as an independent predictor for MPTC for patients older than 45 years, autopsy studies do not show such pattern [29].

The mean age at diagnosis of patients with MPTC has been reported by different studies to be 41.9 - 48.5 years; it is much more common in female compared to males [30]. MPTC is typically without any symptoms, being seen either during autopsy or incidentally found in the histopathology of gland removed for benign conditions, the average size of MPTC is about 6mm, multiple foci of MPTC may be limited to one lobe or both, multifocality is found in 30-40% of cases and bilaterality in approximately 20%[31].

In this study 23/28 cases of MPTC presented as goiter, 3/28 cases as toxic goiter. 1/28 case as solitary nodule, 1/28 case as recurrent goiter, no significant statistical correlation was found between prevalence of MPTC and the clinical diagnosis. The prevalence of MPTC in multinodular goiter is generally high, and based on previous studies varies significantly ranging from 7% to 17% [20].

The prevalence of malignancy in single nodule has been estimated at 5%. As indicated in the recent guidelines for the management of thyroid nodules, patients with multiple thyroid nodules

have the same risk of malignancy as those with solitary nodules [32].

In this study 16/28 cases of MPTC found in total thyroidectomy 7/28 cases in subtotal thyroidectomy, 4/28 cases in near total thyroidectomy and 1/28 case in lobectomy, no significant statistical correlation was found between prevalence of MPTC and type of surgery.

Slijepcevic N et al [20] found that the incidence of MPTC in benign thyroid disease is statistically connected with the extend of the surgery, and found a three- fold increase in the incidence of MPTC in the total thyroidectomy groups compared to subtotal thyroidectomy. When pre-operative diagnosis was benign nodule, the prognosis was slightly better than when pre-operative diagnosis was a malignant nodule, comparing the pre-operative diagnosis regard less of tumor size and nodal metastasis, patient with Hashimoto's diseases or Grave's disease had better prognosis [33].

The diagnosis of MPTC is usually based on a combination of clinical examination, laboratory investigations and radiological techniques, for clinically undetectable tumors, nowadays with the help of high resolution transducers, tumors measuring even 1 and 2 mm in diameters can be detected [34].

Patients with MPTC have favorable long term prognosis, earlier conservative treatment in the form of unilateral lobectomy was advocated for patients with these tumors. However cases of local regional recurrence have been reported in 0.11% [35]. Few cases of distant metastasis have also been reported and finally death related MPTC have been reported in very few cases [35]

Page C et al published a series of 41 cases these cases were considered to be aggressive because of presence of several risk factors such as: tumor size of more than 5mm, tumor extension of metastatic lymphadenopathy. All patients had total thyroidectomy, cervical lymph node dissection and radioactive iodine ^{131},they observed no recurrent at all in this sub group over a period follow up ranging from 6 month to 8 years [36].

CONCLUSION:

The incidence of incidental thyroid papillary microcarcinoma in presumably benign thyroid disease is not very low, therefore the possibility of thyroid micro carcinoma should always be kept in mind while diagnosing a benign thyroid disease. There was a significant statistical correlation between age and prevalence of thyroid papillary microcarcinoma.

REFERENCES:

1- Curado Mp, Edwards B, shin HR, etal, cancer incidence in five contents, vol ix. Lyon: IARC scientific publications 2007, No 160. (google scholar)

2- Kifoy B.A, Zheng T, Holford T.R. etal, International patterns and trends in thyroid cancer incidence 1973-2002,Cancer causes and control, 2009 vol. 20, no.s, pp. 525-531

3- Jemal A, siegel R, Xu J, et al, cancer statistics, 2010, CA: A cancer Journal for Clinicians, 2010, vol.60 no.5, 5,pp. 277-330.

4- Dal Masol, Lise M, Zamboon P,etal, Incidence of Thyroid cancer in Italy, 1991-2005: time trends and age-period-cohort effects. Annals of oncology, 20011. Vol 22(4), app. 957-963.

5- Enewold L,Zhuk, Ron E, etal, Rising Thyroid cancer incidence in the united states by demographic and tumor characteristics 1980-2005, Cancer Epidemology Biomarkers prevention, 2009; 18(3). Pp. 784-791.

6- Kent WD, Hall SF, Isotalo PA, etal, Increased incidence differentiated Thyroid Carcinoma and Detection of Sub-clinical disease, Canadian Medical Association Journal, 2007(177), 11: 1357-1361

7- Khan A, Nose V. Differential diagnosis and molecular advances In: Lloyd RV, editor. Endocrine pathology. 2nd ed. New york: springer 2010p.181-236

8- Kent WD, Hall SF, Istalo PA et al. Increased Incidence of differentiated Thyroid carcinoma and detection of sub clinical disease. CMAJ. 2007; 177: 1357-1361.

9- Kasai N, Sakamoto A. New subgrouping small Thyroid carcinoma. Cancer, 1987; 60: 1767-1770.

10- Franssila KO, Harach HR. Occult papillary carcinoma of the thyroid in children and young adults. A systemic autopsy study in Finland. Cancer 1986; 58: 715-719

11- Harach HR. Franssila Ko, wasenius VM, occult papillary carcinoma of the thyroid, A normal finding in Finland . A systemic autopsy study. Cancer 1986; 58: 715-719.

12- De Lellis RA, Lloyd RA, Heitz, world Health Organization Classification of Tumors: pathology and genetics of tumor of the endocrine organs. Lyon, France: 1ARC press: 2004.

13- Arem R, Padayatty SJ, Saliby AH, etal. Thyroid micro carcinoma prevalence, prognoses and management. Endocr. Pract, 1999; 5: 148-156.

14- Edge SB, Compton CC, The American joint Committee on cancer: the 7th edition of the Ajcc cancer staging manual and the future of TNM. Ann surg Oncol. 2010; 177;- 1357-1361.

15- Nikiforov YE. Is lonizing radiation responsible for the increasing incidence thyroid cancer? Cancer 2010; 116: 1626-1628.

16- Kondo T, Ezzat S, Asa SL, pathogenetic mechanisms in Thyroid follicular-cell neoplasm. Nat Rev Cancer 2006; 292-306.

17- Sherman ST. Thyroid Carcinoma. Lancet 2003; 361: 501-511.

18- Cooper DS, Doherty GM, Haugen BR, etal , Revised American Thyroid association management guidelines for patients with Thyroid nodules and differentiated thyroid cancer. Thyroid 2009; 19: 1167-1214.

19- Pacini F, schlumberger M, Dralle H, etal. European Thyroid Cancer taskforce. European consensus for the management of patients with differentiated Thyroid Carcinoma of the follicular epithelium. Eur J Endocrinal 2006; 154: 787-803.

20- Slijepcevic N, Zivalijevic V, Marinkovic J, etal. Retrospective evaluation of the incidental findings of 403 papillary thyroid microcarcinomas in 2466 patients undergoing thyroid surgery for presumed bengin thyroid disease. BMC cancer 2015; 15: 330

21- Bisi H, Femandes VS, de camargo RY, etal. The Prevelance of unsuspected Thyroid Pathology in 300 Sequential autopsies, with special reference to the incidental carcinoma. Cancer 1989; 64: 1888-1893.

22- Komorowski RA, Hanson GA, occult thyroid pathology in young adult. An autopsy study of 138 patients without clinical thyroid disease. Hum Pathol, 1988; 19: 689-696.

23- Bramley MD, Harrison BJ, papillary microcarcinoma of the thyroid gland. Br. J. surg 1996; 83: 1674-1683.

24- Mc Conahey WM, Hay ID, woolner LB, etal, papillary thyroid cancer treated at the Mayo clinic 1946- Through 1970. Intitial manifestation, pathological findings Therapy and outcome. Mayo clinic proc 1986; 61: 978-96.

25- Fink A, Tomlinson G, Freeman JL, etal. Occult Micropapillary Carcinoma associated with benign follicular thyroid disease and unrelated Thyroid Neoplasms, Mod pathol, 1996; a: 816-820.

26- Noguchi S, Yamashita H, Uchinos, et al. papillary microcarcinoma world J surg. 2008; 32: 747-53.

27- De Matos PS, Ferreria AP ward LS, prevalence of papillary micro carcinoma of the thyroid in Brazillian autopsy and surgical series. Endocr pathol, 2006; 17: 165-173.

28- Ito Y, Miyauchi A, Kihara M, etal. Patient age in significantly related to the prognoses of papillary microcarcinoma of the thyroid under observation. Thyroid, 2014; 24: 27-34.

29- Hughes DT, Haymart MR, Miller Bs, etal. The most commonly occurring papillary thyroid cancer in the united states is now a micro carcinoma in a patient older than 45 years. Thyroid, 2011; 21: 231-238.

30- Cramer JD, Fu P, Harth Kc, etal. Analysis of the rising incidence of thyroid cancer using the surveillance Epidemiology and End Results national cancer data registry. Surgery, 2010; 148:1147-1152.

31- Chow SM, Lawsc, chan JK, etal. Papillary microcarcinoma of the thyroid-prognostic significance of Lymph node metastasis and multifocality cancer, 2003; 98:31-40

32- Prades JM, Dumollard JM, Trimoshenko A, etal, multinodular goiter: surgical management and histopatholgical findings, Eur Arch otorihinolaryngol. 2002; 259: 217-221.

33- Noguchi Sh, Yamashita H, Uching Sh, etal. Papillary micro carcinoma. World J surgery, 2008; 32(5): 747-753.

34- Senchenkov A, Staren ED, Ultrasound in head and neck surgery thyroid, parathyroid and cervical lymph nodes. Surg clin North Am 2004,84:973-1000.

35- Mazzaferri EL. Jhiang SM, long term Impact of intial surgical and medical therapy on papillary and follicular thyroid cancer, Am JMed, 1994; 97: 418-428.

36- Page C, Biet A, Boute P, etal. Aggressive papillary thyroid micro carcinoma. Eur Arch otorhinolaryngol, 2009; 266: 1959-1963.