

INCIDENCE OF PAPILLARY THYROID CARCINOMA AMONG PATIENTS UNDERWENT TOTAL THYROIDECTOMY IN ALDIWANIYAH TEACHING HOSPITAL.

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ABSTRACT

Background: The papillary thyroid cancer is the most frequent cancer among thyroid malignancy, and it is rapidly increasing in incidence due to availability of diagnostic tools. It occur more often in people who live in areas with excessive exposure to radiation and excessive use of x-ray which can be considered as an important risk factors. **The Aim of study:** To evaluate the incidence of papillary thyroid carcinoma among patients underwent thyroidectomy in Al-Diwaniyah teaching hospital. **Patients and methods:** A prospective study was conducted in general surgery department ,in Al- Diwaniyah Teaching Hospital during the period from February 2016 to October 2018 on (432) patients with goiter from those 62 patients proved to be papillary thyroid carcinoma **Results:** From those 62patientsfemale were 49(79%) and male were 13(21%) with solitary thyroid nodule predominant (61.3%). the radiation exposure is highly significant in patients proved to be papillary thyroid carcinoma about (85.48%), the FNAC sensitivity was low about 37%. There were 14 patients re-explored either for remnant thyroid tissue in 11 or for neck dissection in 3 patients. Only 3 cases of occult papillary thyroid carcinoma. **Conclusion:** Papillary thyroid carcinoma being the most common thyroid malignancy with 14.35%, with X- ray the significant risk factor for papillary thyroid carcinoma during childhood, with the female patients more frequently affected and more common in solitary thyroid nodule, and it's advisable to do central neck dissection.

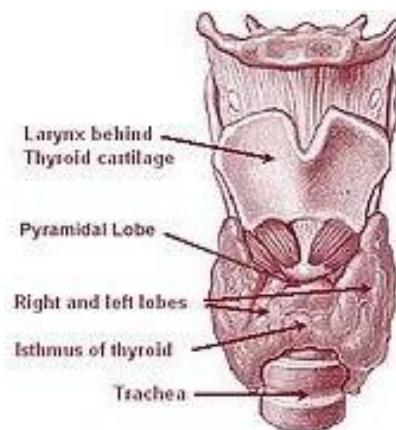
INTRODUCTION

Thyroid gland

The thyroid gland is a butterfly-shaped organ that sits at the front of the neck. It is composed of two lobes, left and right, connected by a narrow isthmus.^[1] The thyroid weighs 25 grams in adults,^[1] with each lobe being about 5 cm long, 3 cm wide and 2 cm thick, and the isthmus about 1.25 cm in height and width.^[4] The gland is usually larger in women, and increases in size in pregnancy.^[1,2]

Aim of the study

To evaluate the incidence of papillary thyroid carcinoma among patient underwent thyroidectomy in Al-Diwaniyah Teaching Hospital.



Classification

Thyroid cancers can be classified according to their histopathological characteristics.^[3]

- Papillary thyroid cancer (75% to 85% of cases^[4]) – often in young females – excellent prognosis. May occur in women with familial adenomatous polyposis and in patients with Cowden syndrome.
- Newly reclassified variant: noninvasive follicular

thyroid neoplasm with papillary-like nuclear features is considered an indolent tumor of limited biologic potential.

- Follicular thyroid cancer (10% to 20% of cases^[4]) – occasionally seen in people with Cowden syndrome. Some include Hürthle cell carcinoma as a variant and others list it as a separate type.^[5]
- Medullary thyroid cancer (5%,^[4] to 8% of cases) – cancer of the parafollicular cells, often part of multiple endocrine neoplasia type 2.^[4]
- Poorly differentiated thyroid cancer
- Anaplastic thyroid cancer (less than 5% of cases^[4]) is not responsive to treatment and can cause pressure symptoms.
- Others
- Thyroid lymphoma, squamous cell thyroid carcinoma, Sarcoma of thyroid.

Papillary thyroid carcinoma

Is the most common type of thyroid cancer.^[4] representing 75 percent to 85 percent of all thyroid cancer cases.^[5] It occurs more frequently in women and presents in the 20–55 year age group. It is also the predominant cancer type in children with thyroid cancer, and in patients with thyroid cancer who have had previous radiation to the head and neck.^[6] It is often well-differentiated, slow-growing, and localized, although it can metastasize Aiteology.

Researchers believe that changes in certain genes cause thyroid cells to abnormally develop and divide, and this may cause the development of papillary thyroid cancer. There are several genes that have been connected to this form of thyroid cancer.^[7]

- RET/PTC gene: Mutations of the RET/PTC gene are apparent in 10% to 30% of papillary thyroid cancer patients.^[7]
- BRAF gene: Mutations of the BRAF gene are found in 30% to 70% of patients.
- A family history of thyroid cancer
- A personal or family history of goiters
- Whole-body radiation for bone marrow treatment
- Exposure to high levels of radiation caused by nuclear accidents or weapons testing
- Having a personal or family history of certain genetic syndromes, such as Cowden syndrome. Woman is considered a risk factor.^[8]

Diagnosis

FNA accuracy is very high and it is a process widely used in these cases. Other investigation methods include ultrasound imaging and nuclear scan. The ultrasound is a useful test to distinguish solid from cystic lesions and to identify calcifications.^[9] The thyroid ultrasound is also very effective to discover micro carcinomas, which refer to very small carcinomas (<1 cm).^[10]

A thyroid nodule is a discrete lesion within the thyroid gland that is radiologically distinct from the surrounding

thyroid parenchyma. Some palpable lesions may not correspond to distinct radiologic abnormalities.^[11] In very rare cases, some nodules.

<1 cm lack these sonographic and clinical warning signs yet may nonetheless cause future morbidity and mortality. This remains highly unlikely, and given the unfavorable cost/benefit considerations.^[12]

Markers

Thyroglobulin can be used as a tumor marker for well-differentiated papillary thyroid cancer.^[12,13] HBME-1 staining may be useful for differentiating papillary carcinomas from follicular carcinomas; in papillary lesions it tends to be positive.^[11]

Pathology

Papillary thyroid cancer gets its name from the papillae among its cells, visible on microscopy. Features include:

Characteristic Orphan Annie eye nuclear inclusions (nuclei with uniform staining, which appear empty due to powdery chromatin and marginal micronucleoli)^[13] and psammoma bodies on light microscopy. The former is useful in identifying the follicular variant of papillary thyroid carcinomas.^[14]

Lymphatic spread is more common than hematogenous spread Multifocality is common The so-called Lateral Aberrant Thyroid is actually a lymph node metastasis from papillary thyroid carcinoma.^[15]

Papillary microcarcinoma is a subset of papillary thyroid cancer defined as measuring less as or equal to 1 cm.^[16] The highest incidence of papillary thyroid microcarcinoma in an autopsy series was reported by Harach et al. in 1985, who found 36 of 101 consecutive autopsies to have an incidental microcarcinoma.^[17] Michael Pakdaman et al. report the highest incidence in a retrospective surgical series at 49.9 percent of 860 cases.^[18] It was Woolner et al. who first arbitrarily coined the term "occult papillary carcinoma" in 1960, to describe papillary carcinomas ≤ 1.5 cm in diameter.^[19]

The encapsulated follicular variant, specifically when noninvasive, has been newly reclassified as the noninvasive follicular thyroid neoplasm with papillary-like nuclear features.^[20] Although papillary carcinoma has a propensity to invade lymphatics, it is less likely to invade blood vessels.^[21,22]

Prognosis

Depending on source, the overall 5-year survival rate for papillary thyroid cancer is 96 percent,^[24] or 97 percent,^[25] with a 10-year survival rate of 93 percent.^[24]

- AGES - Age, Grade, Extent of disease, Size
- AMES - Age, Metastasis, Extent of disease, Size
- MACIS - Metastasis, Age at presentation, Completeness of surgical resection, Invasion (extrathyroidal), Size [26,27, 28] (this is a

modification of the AGES system). It is probably the most reliable staging method available. Also known as the MAICS system.

- TNM staging - Tumor, node, metastasis. Remarkable about the TNM staging for (differentiated) thyroid carcinoma is that the scoring is different according to age Stage

Based on overall cancer staging into stages I to IV, papillary thyroid cancer has a 5- year survival rate of 100 percent for stages I and II, 93 percent for stage III and 51 percent for stage IV.^[29]

Treatment

Surgery remains the mainstay of treatment for papillary thyroid cancer.^[30] total thyroidectomy, and central compartment lymph node removal is the therapy of choice. Arguments for total thyroidectomy are,^[31] Reduced risk of recurrence.

Papillary tumors tend to be more aggressive in patients over age 45. In such cases, it might be required to perform a more extensive resection including portions of the trachea. Also, the sternocleidomastoid muscle, jugular vein, and accessory nerve after surgical thyroid removal, the patient waits around 4–6 weeks to then have radioiodine therapy. This therapy is intended to both detect and destroy any metastasis and residual tissue in the thyroid. The treatment may be repeated 6–12 months after initial treatment of metastatic disease where disease recurs or has not fully responded.^[32] Approximately 20 percent of patients will develop multiple tumors within the thyroid gland.^[33] Recent studies have examined a more conservative approach to surgery and demonstrated that hemi-thyroidectomy may be acceptable for patients with low-risk papillary thyroid with stage I and II papillary thyroid cancer size 1–4 cm receiving total thyroidectomy versus hemi-thyroidectomy.^[34]

Patient and method

A prospective study was conducted in Al- Diwanayah teaching hospital during the period from February 2016 to October 2018 on (432) patients with goiter whether multinodular or solitary thyroid nodule , who underwent total thyroidectomy Of those (432) patients there were (123) male and (309) female. The age range from 30-60 years with mean (49.6). From those (432) patients we found (62) patients proved to be papillary thyroid carcinoma.

All those patients were carefully evaluated by detailed history and thorough clinical examination were done at time of admission.

After detailed clinical assessment the following were done for all patients

1. Chest x-ray, neck x-ray.
2. Blood test (CBP, blood urea, blood sugar, viral screen, and liver function test).
3. ECG and echo study.

4. Thyroid function test.
5. Neck ultrasonography.
6. FNAC and TRUE-CUT biopsy.
7. ENT consultation for vocal cord assessment.

After full clinical assessment and selection of patient for surgery according to patient indication we admit the patient to the hospital and the following was prerequisite;

- Informed consent of all patients for surgery was taken
- Medical and anesthetics consultation for fitness for general anesthesia
- Prophylactic antibiotic (1g ceftriaxone vial) intravenously on induction of anesthesia

After full preparation of all patients for surgery we proceed for operation next day Total thyroidectomy was the procedure of choice with neck dissection preserved for only nodal metastasis.

Post operatively patients kept in the surgical ward with head elevation 30 degree with observation of breathing and oxygen saturation, stridor, hematoma formation patient received analgesia and antibiotic, drain was removed in 24-48hour depending on quantity of collection in drain. Thyroid specimen sent for private laprotory for histopathological study

Statistical analysis

The quantitative variables that had a parametric distribution are presented as mean and standard deviation the qualitative variable are presented as absolute and relative frequencies. The relationship between qualitative variables was analyzed by comparing their frequencies using the chi-square test. The statistical software SPSS® (SPSS® Inc. Illinois, USA) was used for all analyses, and the statistical significance was set at $p \leq 0.05$.

RESULT

Four hundred thirty two patients with goiter were included in this study. Ranging patients aged between 30-60 years with the mean age of patients 49.6 year and the most frequent ages were between 40-50 years.

Table 1: Gender distribution.

Gender	NO.	%
male	123	28.5%
female	309	71.5%
Total	432	100%

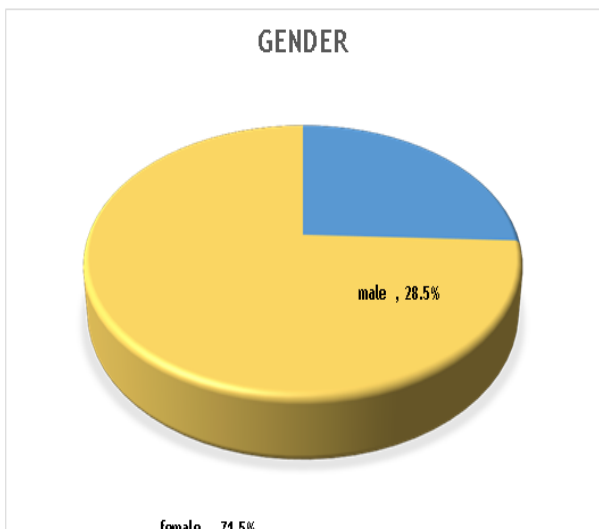


Figure 1: Gender distribution and percentage of all patients underwent thyroidectomy.

Table 2: Age groups of patients with goiter.

Age groups	No.	%
30-40 y	160	37
40-50 y	220	50.9
50- 60 years	34	7.9
Above 60 y	18	4.2
Total	432	100

About 50% of patients with goiter were among age group (40-50 y) with percentage of (50.9%).

From those patients (432) that were underwent thyroidectomy, the number of patients were proved to be papillary thyroid carcinoma found to be.^[62] With the percentage of papillary thyroid carcinoma from the total number of patients were (14.35%).

Table 3: Gender distribution of patients proved to be papillary thyroid carcinoma.

Gender	No.	%
male	13	21 %
Female	49	79 %
Total	62	100 %

From those (62) papillary thyroid carcinoma patients, male patients (13) and their percentage were about 21%, and female patients (49) with a percentage about 79% this table significant with p value < 0.05.

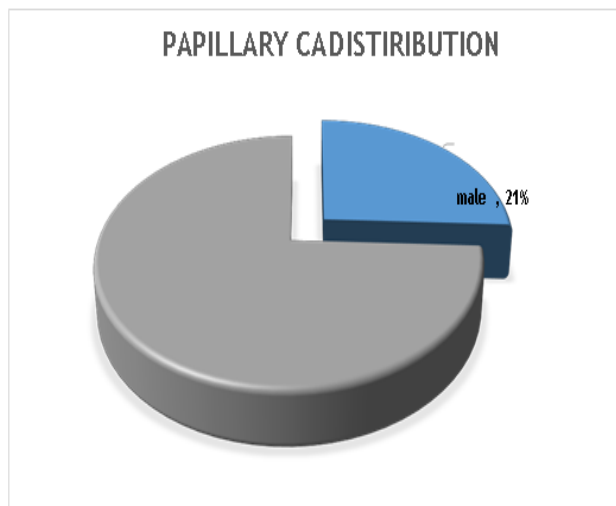


Figure 2 Gender distribution of papillary thyroid carcinoma.

Table 4: Number and percentage of solitary and multinodular among papillary thyroid carcinoma proved cases.

Texture of thyroid gland	No.	%
solitary	38	61.3%
mulinodular	24	38.7%
Total	62	100

The number and percentage of solitary nodule that proved to be papillary thyroid carcinoma is greater than that with multinodular goiter, which is significant.

Table 5: Numbers and percentages of solitary and MNG according to the gender.

Gender	Solitary	MNG	Total
male	10(16.1%)	3(4.8%)	13
female	28(45.2%)	21(33.9%)	49
Total	38	24	62

The percentage of papillary thyroid carcinoma in solitary thyroid nodule is greater than that with multinodular with the solitary thyroid nodule higher in female patients about (45.2%) while in male patients (16.1%), Also the percentage of papillary thyroid carcinoma among patients with multinodular goiter in female were (33.9%) while was about (4.8%) in male patients. It was not significant statistically based on p value set at <0.05.

Table 6: Number of patients with history of low dose radiation exposure (repeated CXR or CT SCAN) during childhood period.

Radiation exposure	Patients with papillary CA
positive	53(85.48%)
negative	9(14.51%)
Patients NO.	62

We found significant to those with papillary thyroid carcinoma patients with p value 0.001.

Table 7: Number and percentage of patient with low dose radiation exposure who proved to be papillary thyroid carcinoma whether solitary or multinodular goiter.

x-ray exposure	solitary	multinodular	p-value
Positive	38	15(62.5%)	0.05
Negative	0	9(37.5%)	
total	38	24	62

The X-RAY exposure was about 62.5% of multinodular goiter in cases proved to be papillary thyroid carcinoma while it was 100% in solitary thyroid nodule we found statistically significant at p value set < 0.05.

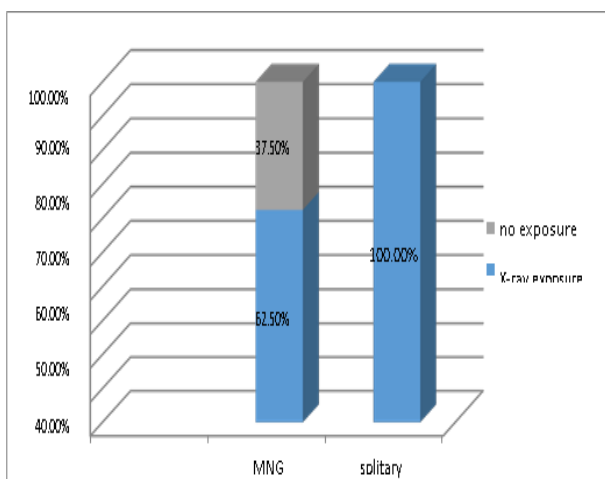


Figure 3: Percentages of patients with or without X-ray exposure in solitary and multinodular goiter.

Table 8: The number and percentage of pre-operative diagnostic procedure (FNAC) and there significance.

Diagnostic tools	NO.	%
FNAC +ve	23	37.1%
FNAC -ve	39	62.9%

Number of patients proven to be papillary thyroid carcinoma by FNAC were 23 about (37.1%) and those with negative FNAC were 39(62.9%). Statistically we found significant at p value < 0.05, with the sensitivity of the test 37%. Those patients with negative FNAC the papillary thyroid carcinoma was proven by either TRUE-CUT or histopathology.

Table 9: The number and percentage of patients with negative FNAC proven for papillary carcinoma by other modality of investigation.

Negative FNAC	NO	%
TRUE-CUT	3	7.6%
histopathology	36	92.4%
Total NO.	39	

The (39) patients with negative FNAC we use other modality for proving the papillary thyroid carcinoma the true-cut biopsy done for only 3 cases depending on

clinical suspension All patients who were underwent thyroidectomy, there thyroid gland specimens were sent for histopathological study whether it was negative or positive for FNAC.

Table 10: the type and number of patients underwent neck dissection during thyroidectomy in the same time or in another exploration revision for completion of neck dissection.

Level of neck dissection	NO. of patients
Level I and II	59
level III	3
Total NO.	62

Neck dissection Level I and II have been done for 59 while 3 patients level III dissection was the procedure.

Table 11: Number of patients who re-explored for either remnant of thyroid tissue or completion of neck dissection.

Re – exploration reason	No of patients and percentages
Remnant thyroid tissue	11(17.4%)
Completion of neck dissection	3(4.8%)

Out of 62 patients diagnosed with papillary thyroid carcinoma there were 3 patient presented with LN and no palpable thyroid nodule (occult carcinoma of the thyroid gland). Which represent (4.8%) from papillary thyroid carcinoma cases.

DISCUSSION

In our study we found that goiter presented in female predominantly, 71.5% female, 28.5% male, which goes with study by Ali Al Katib in Hilla city in which 75% female,^[35] in study in Baghdad city found Females are more affected with goiter (82.5% 132 patients) than males (17.5% 28 patients) with ratio 4.7/1 female to male.^[36]

The commonest ages at presentation in our study were (40-50 years), which resembling with study by Fazal Hussain(2013)in saudi Arabia,^[37] while other study by Al- Katib reported that mostly the patients are in the range (31-40 years), 33.3% ,in study by Seetu Palo (2016) demonstrated majority of the patients were in the 3rd and 4th decade of life.^[38]

This generally talk about all 432 patients present with goiter and underwent thyroidectomy.

Our study about the 62 patients proved to be papillary thyroid carcinoma the female were predominant 49 (79%) and male were 13(21%).

In our study papillary thyroid carcinoma rate was 14.35% from patient with goiter, the incidence of

papillary cancer has increased from 4.8 to 14.9 per 100,000 from 1975 to 2012. Females are more likely to get papillary cancer when compared to males with incidence ratio of 2.5 to 1 where most of the cancers are diagnosed between 40 and 50 years old in females,^[10] and this is compatible with our study.

We found in our study that the percentage of papillary thyroid carcinoma in solitary thyroid nodule (61.3%) which is greater than that with multinodular (38.7%) with the solitary thyroid nodule higher in female patients about (45%) while in male (16.1%) This goes with study by Seetu Palo 2016 where they found the carcinoma in solitary, were 38% (38) while multinodular 15%, and female patients were more frequent thyroid malignancy than male in the same study, and consider the second most common malignancy affecting female patients in Arab Gulf.^[38]

In our findings there was a positive association between patients who have papillary thyroid carcinoma with X-ray and CT scan exposure and radiation in childhood, in our study we found that the percentage of patients that were proved to be papillary thyroid carcinoma with history of low dose exposure of X-RAY were (85.48%).

In a study by Maria L. Argentina in 2017. Papillary carcinoma (PTC) is the most frequent form of thyroid carcinoma diagnosed after radiation exposure, with a higher prevalence of the solid subtype in young children with a short latency period and of the classical subtype in cases with a longer latency period after exposure. Molecular alterations, including intra-chromosomal rearrangements, are frequently found.^[39]

In our study the patients proven of papillary thyroid carcinoma by FNAC were 23 about (37.1%) and those with negative FNAC were 39 (62.9%). The sensitivity was about 37% The FNAC done by cytologist not pathologist and not under ultrasound guidance in comparing with study by Masereka R, Okeny PK in Uganda, experience that reveals the sensitivity was 61.5% and specificity 89.5%. This study revealed high specificity and low sensitivity of fine needle aspiration cytology (FNAC) at detecting malignancy in thyroid nodules.^[40]

The negative FNAC cases proven by histopathological examination which confirm the papillary thyroid carcinoma. Our patients who included in the study those who confirm to be papillary thyroid carcinoma by FNAC or depending on clinical suspension.

During thyroidectomy central neck dissection had been done for 59 patients and only 3 patients the lateral neck dissection done for them. This concept with study by Hughes DT et al, in 2018 central neck dissection in clinically node-negative papillary thyroid cancer will detect occult lymph node metastasis in approximately half of patients. This may change their postoperative

management. With regard to adjuvant radioiodine therapy.^[41] And the lateral neck dissection were preserved for the clinically or histopathological proven papillary thyroid lymphatic metastasis.

In our study we found only 3 cases of occult papillary thyroid carcinoma, occult thyroid carcinoma is mostly discovered by autopsy or by other causes of thyroid surgery. To the best of our knowledge, there have been only a few reports concerning the situation that cervical mass was the initial manifestation of occult papillary thyroid carcinoma in comparison to a study by Yongfu Z et al, in China in 2018 they found only 3 cases of occult papillary thyroid carcinoma.^[42]

In our study we re-explored 14 patients 11 of them for remnant thyroid tissue and 3 patients for completion of neck dissection.

CONCLUSION

1. Papillary thyroid carcinoma is the most common thyroid malignancy. With the thyroid malignancy became common in our region.
2. The papillary thyroid carcinoma being the most among patients with goiter underwent thyroidectomy, with the female more frequently affected. With the solitary thyroid nodule more prone for malignancy than multinodular.
3. With the X-ray exposure in childhood was significant risk factor for thyroid malignancy.
4. The FNAC sensitivity was low and this depending on the pathologist and technique used for procedure, we depend on the histopathological examination.
5. Central neck dissection is advisable for all patients suspicious for malignancy, with the lateral neck dissection kept for only lymphatic metastasis.
6. The occult papillary thyroid carcinoma represent rare presentation for papillary thyroid carcinoma.

RECOMMENDATIONS

1. Further national research should be done to confirm our result.
2. We need for the activation of the cancer registration center because cancer is very common in our country due to environmental factor.
3. The use of x-ray especially in childhood should be limited and used only when it is indicated.
4. We need a screening program to detect any development of cancer in pre-existing goiter as Iraq is an endemic goiter area.
5. We advise the central neck dissection in all patients with papillary thyroid carcinoma.

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