

# A Four-Year Study of Thyroid Carcinoma in Hail Region: Increased Incidence

Laila Seada, Hanan Oreiby, Fawaz Al Rashid, Ashraf Negr

**Abstract**—Background and Objective: In most areas of the world, the incidence of thyroid cancer has been increasing over the last decade, mostly due to a combination of early detection of the neoplasm resulting from sensitive procedures and increased population exposure to radiation and unrecognized carcinogens. Methods: Cases of thyroid cancer have been retrieved from the cancer registry at King Khalid Hospital during the period from August 2012 to April 2016. Age, gender and histopathologic types have been recorded. Results: Thyroid carcinoma ranked as the second most common malignancy in females (25%) after breast cancer (31%). It constituted 20.8% of all newly diagnosed cancer cases. As for males, it ranked the 4<sup>th</sup> type of malignancy after gastrointestinal cancer, lymphomas and soft tissue sarcomas. Mean age for females and males was 38.7 +/- 13.2 and 60.25 +/- 11.5 years, respectively, and the difference between the two groups was statistically significant ( $p$  value = 0.0001). Fifty-five (82%) were papillary carcinomas including 10 follicular variant of papillary (FVPC), and eight papillary micro carcinomas (PMC) and two tall cell/oncocytic variants. Follicular carcinomas constituted two (3.1%), while two (3.1%) were anaplastic, and two (3.1%) were medullary. Conclusion: Thyroid cancer incidence in Hail is ranking as the 2<sup>nd</sup> most common female malignancy similar to other regions in the Kingdom. However, this high incidence contrasts with much lower rates worldwide.

**Keywords**—Thyroid, Hail, papillary, micro carcinoma.

## I. INTRODUCTION

THYROID cancer is the most common malignant disease of the endocrine system and is rapidly increasing in incidence. This increase in variable tumor types and stages, is due to early detection of small asymptomatic cancers (papillary microcarcinomas) due to prevalence of screening [1]. Thyroid cancers mostly show biologically indolent phenotype and have both an excellent prognosis and survival rates more than 95% at 20 years. Occurring at any age, but rare in childhood, thyroid cancer affects females three to four times more than males and is usually diagnosed in the 3<sup>rd</sup> to 6<sup>th</sup> decade of life [2]. Epithelial tumors originating from thyroid follicular cells constitute most primary thyroid carcinomas. Papillary, follicular and anaplastic thyroid carcinomas are the main subtypes, while medullary carcinomas arise from parafollicular (c) cells [3].

The etiology of thyroid cancer is largely unknown, but some risk factors for the disease have been identified. Exposure to ionizing radiation (e.g. in medical procedures, including radiotherapy given in order to treat a previous cancer, fallout from power plant accidents or nuclear weapons,

exposure in occupational settings) is an established risk factor for thyroid cancer. Other risk factors include gender (thyroid cancer occurs about three times more often in women compared to men), age (the incidence peaks at ages 60–70 in men and 40–50 in women), benign and autoimmune thyroid diseases, genetic factors, and a family history of thyroid cancer or of other cancers. Potential risk factors are taller height and higher BMI (especially in women), certain dietary exposures, and reproductive factors [4]. Conventional thyroidectomy with adjuvant radioiodine ablation is the classic treatment for thyroid carcinoma, and most patients can be cured by this treatment. Surgically inoperative recurrences, refractoriness to radioiodine, poorly differentiated and anaplastic thyroid carcinomas are still lethal diseases. Nevertheless, recent developments in molecular genetics and better understanding of the pathogenesis of thyroid cancer have shown promising treatment strategies [5].

## II. METHODS

All newly diagnosed cancer cases are retrieved from the cancer registry of Histopathology Department, King Khalid Hospital, Hail, from August 2012 to April 2016. For each patient age, gender and histopathologic diagnosis was recorded. For histopathologic types, all H&E slides were retrieved and revised by two pathologists. The WHO classification (2004) has been used.

## III. RESULTS

In our series, the total number of thyroid cancer cases retrieved from the cancer registry of pathology during the period from August 2012 to April 2016 were 65 constituting 65/312 (20.8%) of all 312 newly diagnosed cancer cases. Thyroid cancer ranked as the 2<sup>nd</sup> most common malignancy among females following breast cancer (Fig. 1). The majority was female (57/65 (87%) and 8/65 (13 %), with the male to female ratio being 1:7.1. The mean age for female patients was 38.7 +/- 13.2, while the mean age for male patients was 60.25 +/- 11.5 years. The age difference between the two groups was statistically significant ( $p$  value = 0.0001) (Table I).

The most affected female age group (73.7%) was from 20-49 years; the mostly affected male age group was from 50-69 years (75%) (Table II). The mean age for both males and females was 41.3 +/- 14.8. The youngest patient was a female aged 16 and the oldest was also a female patient aged 73 years.

As regards to histological types, papillary thyroid carcinoma (PTC) of the conventional classic type was

diagnosed in 55/65 (82%) of cases and FVPC was found in 10/55 (19.2%) of all cases (Figs. 2 and 3). Multi-focal neoplasm was present in two cases, while PMC, tumor size  $\leq 1$  cm, was seen in 8/55 (14.5%) of total papillary carcinomas diagnosed. Tall cell variant was present in two cases. Follicular carcinoma was only seen in only two cases, one of which was diagnosed as minimally invasive, with Hurthle cell neoplasm in both cases. Two cases of medullary carcinoma were also diagnosed. Anaplastic/poorly differentiated carcinoma was reported in another two cases. Mucosa associated lymphatic tissue lymphoma (MALT) were diagnosed in two cases (Fig. 4).

The majority of cases 63/65 (96.9%) presented as primary malignancy and only 2/65 (3.1%) of cases presented as lymph node metastases. One 69 year old male patient presented with a recurrent papillary carcinoma.

TABLE I  
 MEAN AGE FOR MALES AND FEMALES IN 65 THYROID CARCINOMAS

	Males	Females	P value
No.	8/65	57/65	
(%)	13 %	87%	
Mean age	60.25	38.7	0.0001**
Standard Deviation	+/- 11.5	+/- 13.2	

p value <0.05, \*\*highly significant

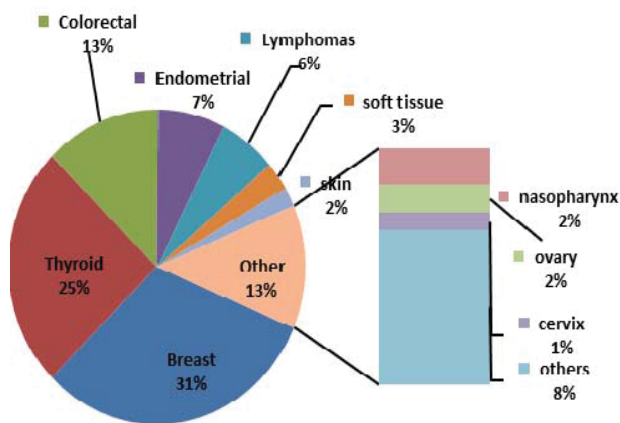


Fig. 1 Cancer Types among females in Hail Region

TABLE II  
 AGE GROUPS AND FREQUENCY OF THYROID CARCINOMA AMONG MALES AND FEMALES

Age Group	Females no.	Females %	Males no.	Males %
10-19	3	5.3%	0	0%
20-29	12	21.1%	0	0%
30-39	17	29.8%	1	12.5%
40-49	13	22.8%	0	0%
50-59	7	12.3%	2	25%
60-69	4	7%	4	50%
70-79	1	1.7%	1	12.5%

Preoperative primary evaluation by fine needle aspiration (FNA) was obtained in 49/65 (75.4 %) of the cases. Only in 6/49 (12.2%) of cases the aspiration diagnosis was false-negative. In one case, a colloid nodule was diagnosed (in a multifocal neoplasm), one diagnosed as Hurthle cell neoplasm

came out to be micro papillary carcinoma, and in four cases the carcinoma masqueraded behind a cystic lesion, where cyst fluid only was obtained during aspiration. In the remaining cases, FNA diagnosis was either malignant or suspicious for malignancy.

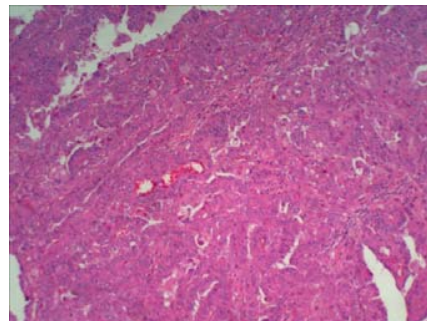


Fig. 2 Classic papillary carcinoma (H&E x 400)

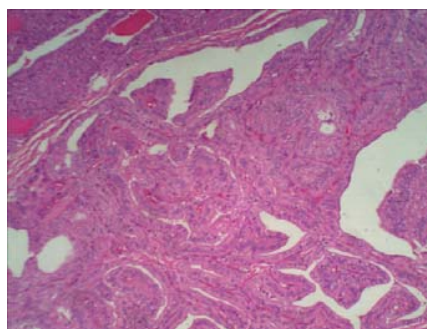


Fig. 3 FVPC (H&E x 400)

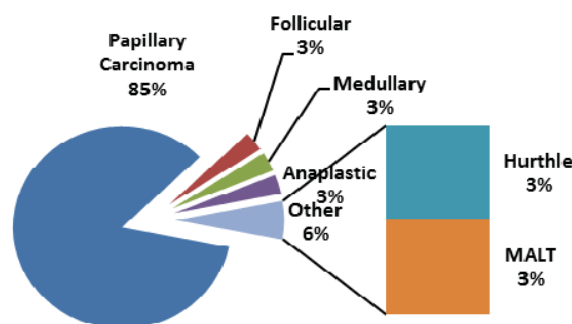


Fig. 4 Histological Types of 65 thyroid carcinomas

#### IV. DISCUSSION

Thyroid gland neoplasms occur globally with geographical variation in incidence and histopathological pattern related to age, sex, dietary and environmental factors. In the present series, taken over a four year period, the incidence of thyroid carcinoma reached 20.8% of all newly diagnosed cancer cases. Among females, it was the second most common cancer forming one fourth of all cancer cases, only preceded by breast carcinomas. Among males it ranked as the 6<sup>th</sup> most common malignancy [Fig. 1].

In other Middle East and Gulf countries, the incidence was different and variable. In Jordan, most common female cancers were breast, colorectal, leukemia, thyroid and non-

Hodgkin's Lymphomas (NHL). As for males, bronchus and lung, colorectal, bladder, leukemia and prostate cancers were the most common [6].

In an Emirates study group, 78 cancer patients (58%) were diagnosed before the age of 45 years, with an overall peak incidence in the fourth and fifth decades. The female to male ratio was 2.4:1. Eighty-four percent had PTC, while follicular thyroid carcinoma (FTC), anaplastic thyroid carcinoma and medullary carcinoma comprised 14%, 1.4% and 0.6%, respectively. The conventional classical variant of papillary carcinoma was the most common type. Minimal invasive follicular carcinoma was the most common variant of follicular carcinoma [7].

In Egypt, thyroid cancer incidence was low, representing approximately 1% of all cancers, according to Ahmed et al., 2015 [8]. Another study based upon results of the National Cancer Registry Program (NCRP), thyroid cancer in Egypt ranked as the 6<sup>th</sup> most common cancer in females with an incidence of 3.28%. It was preceded by breast, liver, brain, ovary and NHL [9].

In Africa, in a study by a Nigerian group, the female to male ratio of 4.8:1, mean age of 35.8 years and peak occurrence in the 4th decade. Papillary carcinoma predominated (53%), followed by follicular carcinoma (33.3%) and medullary carcinoma (9.1%), and with one case each (1.5%) of anaplastic carcinoma [10].

In Saudi Arabia, several studies have dealt with thyroid carcinoma incidence. In the Southwestern area, papillary carcinoma constituted 50%, while follicular carcinoma formed only 4.3% of malignant cases. Lymphoma ranked third with only 1.1% of all malignant thyroid lesions. No cases of medullary carcinoma were found [11].

Another study of cancer incidence in Al Jouf in the Northern part of Saudi Arabia, the most common cancers in the whole population irrespective of sex were carcinoma of the breast, NHL and colorectal cancer. As for females, thyroid cancer was the second after breast cancer followed by lymphomas and leukemia combined [12].

Al Madina group studied 292 thyroidectomy specimens, 230 (78.8%) females and 62 (21.2%) males giving a female: male ratio of 3.7:1. In their series, papillary type was the most common, accounting for 87.8%, followed by lymphomas, follicular and medullary carcinomas. However, they mentioned no micropapillary carcinomas [13].

In a study at King Faisal Specialized Hospital (KFSH), thyroid cancer was also the second most common malignancy among females accounting for about 11% of all newly diagnosed female cancers. It constituted about 9% of all malignancies and 12% of all female malignancies, which are significantly higher compared to the United States, where thyroid cancer represents only 2.9% of all malignancies and 4.6% of all female malignancies. They reported a median age at diagnosis of 38 years and the highest incidence was in the 30-39 year age group [14].

The most common type in our series was classical papillary carcinoma, while medullary and anaplastic thyroid carcinoma formed a small fraction, which is in accordance with other

studies worldwide [3]. Among subtypes of thyroid carcinoma, PMC is being diagnosed with increasing frequency. In our experience, the increased incidence of the PMC is due to increased awareness for thyroid cancer and more thyroidectomies performed during the past four years [15]. The application of fine needle aspiration on palpable nodules was also a helpful tool in early diagnosis. Its accuracy, in our series, reached more than 90% in diagnosing papillary carcinoma. However, cystic lesions were a challenge with a hidden neoplasm that was missed during the aspiration. This was in accordance with a few case reports in the literature dealing with a papillary carcinoma masquerading as a branchial cyst or colloid cyst [16]

In our study, the female to male ratio was 7.1:1, which is considered the highest compared to other series. The age of female patients was significantly lower than males ( $p=0.001$ ). In a study by a Lebanese group, where papillary-carcinoma constituted 26%, female/male sex ratio of the studied population was 3.7:1. The mean age of female patients was also significantly lower than that of the male patients [17].

## V. CONCLUSION

According to our results, Hail is considered one of the highest incidences for thyroid carcinoma. If we consider the mountainous nature and iodine deficiency, the high incidence in females is also much higher, reaching 7.1:1 in our series. The older age group of affected male patients is also high compared to other parts of the Kingdom.

Incidence of thyroid cancer is the 2<sup>nd</sup> most common malignancy among females is in accordance with other parts of the Kingdom, according to King Faisal Specialist and Research Centre statistics [14]. However the incidence is much higher than in other parts of the world. The rising incidence of thyroid cancer in Hail may be due to the increased screening, early detection and diagnosis of the thyroid cancers and not only an increase in the true occurrence of thyroid cancer.

## 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 May 1;136(9):2187-95.
- [2] Katoh H, Yamashita K, Enomoto T, Watanabe M: Classification and General Considerations of Thyroid Cancer. *Ann Clin Pathol* 2015.3(1): 1045.
- [3] Sinnott B, Ron E, Schneider AB. Exposing the thyroid to radiation: a review of its current extent, risks, and implications. *Endocr Rev*. 2010;31:756-73.
- [4] Dal Maso L, La Vecchia C, Franceschi S, et al. A pooled analysis of thyroid cancer. V. Anthropometric factors. *Cancer Causes Control*. 2000; 11:137-446.
- [5] Dal Maso L, Bosetti C, La Vecchia C, Franceschi S. Risk factors for thyroid cancer: an epidemiological review focused on nutritional factors. *Cancer Causes Control*. 2009; 20:75-86.
- [6] Ismail SI, Soubani M, Nimri JM, Al-Zeer AH. Cancer incidence in Jordan from 1996 to 2009--a comprehensive study. *Asian Pac J Cancer Prev*. 2013;14(6):3527-34.
- [7] Al-Zaher N, Al-Salam S, El Teraifi H. Thyroid carcinoma in the United Arab Emirates: perspectives and experience of a tertiary care hospital. *Hematol Oncol Stem Cell Ther*. 2008 Jan-Mar;1(1):14-21.

- [8] Ahmed RA, Aboelnaga EM. Thyroid cancer in Egypt: histopathological criteria, correlation with survival and oestrogen receptor protein expression. *Pathol Oncol Res.* 2015 Jul;21(3):793-802.
- [9] Ibrahim AS, Khaled HM, Mikhail NN, Baraka H, Kamel H. Cancer incidence in Egypt: Results of the National Population-based Cancer Registry Program. *J Cancer Epidemiol.* 2014;2014:437971.
- [10] Raphael S, Mohammed AZ, Iliyasu Y: Histological pattern of thyroid gland neoplasms in Kano, Northern Nigeria. *Niger J Med.* 2015 Jan-Mar;24(1):5-11.
- [11] Refeidi AA, Al-Shehri GY, Al-Ahmary AM, Tahtouh MI, Alsareii SA, Al-Ghamdi AG, et al.: Patterns of thyroid cancer in Southwestern Saudi Arabia. *Saudi Med J.* 2010 Nov;31(11):1238-41.
- [12] El Hag IA, Katchabeswaran R, Chiedozi LC, Kollur SM. Pattern and incidence of cancer in Northern Saudi Arabia. *Saudi Med J.* 2002 Oct;23(10):1210-3.
- [13] Albasri A, Sawaf Z, Hussainy AS, Alhujaily A.:Histopathological patterns of thyroid disease in Al-Madinah region of Saudi Arabia. *Asian Pac J Cancer Prev.* 2014;15(14):5565-70.
- [14] Hussain F, Iqbal S, Mehmood A, Bazarbashi S, ElHassan T, Chaudhri N. Incidence of thyroid cancer in the Kingdom of Saudi Arabia, 2000-2010. *Hematol Oncol Stem Cell Ther.* 2013 Jun;6(2):58-64.
- [15] Pearce EN, Braverman LE. Papillary thyroid microcarcinoma outcomes and implications for treatment. *J Clin Endocrinol Metab.* 2004 Aug;89(8):3710-2.
- [16] Muthalagan EI, Subashchandrabose PI, Sivasubramanian PB1, Venkateswaran S A case of papillary microcarcinoma of the thyroid with abundant colloid (masquerading as colloid goiter with papillar hyperplasia): Cytological evaluation with histopathological correlation. *Cytol.* 2015 Oct-Dec;32(4):278-280
- [17] Abboud B, Sader Ghorra C, Rassy M, El Naderi S, Trak-Smayra V, Abadjian G et al.: Epidemiological Study of Thyroid Pathology in a University Hospital. *Acta Chir Belg.* 2015 Nov-Dec;115(6):414-417.