CLINICOPATHOLOGIC FEATURES OF THYROID CANCER IN SULAIMANI, 2004-2018

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ABSTRACT

Background

Thyroid Cancer (TC) is the most common type of endocrine malignancy.

Objectives

To evaluate some of clinicopathologic features of thyroid carcinoma according to histopathology subtype, tumor size, age, sex and stage.

Patients and Methods

We conducted a retrospective study that included the patients with histologically proven thyroid cancer at Hiwa hematology /oncology cancer hospital of Sulaymaniyah from 2000 to June 2018. Retrospective evaluation of 225 cases of thyroid cancer during the study period carried out. Incidence of thyroid cancer with variations based on tumor histopathology, size(≤1 cm, 1.1-2 cm, 2.1-5 cm, ≥5 cm), and stage (local, regional, metastatic), age, and sex were analyzed among the different time periods of 2004-2008, 2009-2013 and 2014-2018.

Results

Thyroid cancer constituted (1.2%) of total solid cancers registered. A total number of 195 cases, 80 %(155) female 20 %(40) male of Thyroid Cancer (TC) identified from 2004-2018, only 8(4.1%) of the cases diagnosed in 2004-2008, while (142) 72.8% of the cases diagnosed in 2014-2018. Female/male ratio was 3.87. Mean age was 41.52 years, 67% of them were below age 45. Proportion of patients with tumor localized to thyroid gland (local stage) was 63%. The mean size of tumors at diagnosis was 21.71 mm at their longest diameter. Most common histologic feature was papillary thyroid cancer constituting 82% of all cases of thyroid cancer

Conclusion

Papillary thyroid cancer (PTC) was the most common type of registered thyroid cancer. Thyroid cancer was more common among females. The current study showed that the disease tends to occur at a younger age, small size and more localized to thyroid gland.

Keywords: *Thyroid cancer, incidence, Overdiagnosis, Clinicopathologic feature.*

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INTRODUCTION

Thyroid cancer is uncommon and potentially curable cancer, it is the most common type of endocrine cancer[1], constitutes around 1% of malignant diseases and responsible for 0,5% of cancer death [2]. Thyroid gland composed of the follicular cells which give rise to well-differentiated cancers and anaplastic thyroid cancer (ATC), C-cell or parafollicular cell that gives rise to medullary thyroid carcinoma while immune cells and stromal cells of the thyroid are responsible for lymphoma and sarcoma, respectively. well-differentiated cancers accounts for 90% of TC, while 5% to 9% are medullary, 1% to 2% are anaplastic, 1% to 3% are lymphoma, and <1% are sarcomas or other rare tumors [3].

TC usually affects young people and for reasons that are unclear. It is 2-3 fold more common in females than males [4,5] and the peak incidence of thyroid cancer diagnosis is 45 to 49 years in women and 65 to 69 years in men [6].

The etiology of TC is not completely understood, however, there are many risk factors, but ionizing radiation is considered to have a strong relationship with TC especially during early childhood exposure and in young women [7,8].

TC is a rapidly rising cancer, in the last 3 decades its incidence has been doubled and in some country risen up to five folds and the rising is mainly in the papillary thyroid cancer (PTC) subtype [9-12] with the majority of the increase attributable to cancers measuring 1 cm or less in size [13]. Many countries from East and West have reported increase in incidence of TC with geographical variation [14-17]. Laurence et al reported that the reason behind the epidemic of thyroid cancer is still unclear[18]. In USA the TC incidence rates increased by 6.7% for females and 4.4% for males per year between 1982–1997 [9]. Dal Maso L et al reported that incidence rate of TC in Italy was two folds higher in 2001–2005 than in 1991–1995, increases were similar in both male and female and nearly exclusively due to papillary TC[19] . Another study in Emory University in USA revealed increasing incidence of differentiated thyroid cancer in the United States between 1988–2005 for all sizes of tumors among men and women of all ages [15].

Why this increase in TC incidence? Is it a true increase in its occurrence or its just due to over diagnosis. There are many hypotheses behind raising the incidence of TC; Morris et al attributed the reason behind the over diagnosis of TC to a large reservoir of occult disease and escalating levels of diagnostic scrutiny, with wide spread use of neck ultrasound , fine needle aspiration and incidental finding of small nodules "incidentalomas" during imaging for non-thyroid problems leading to detection of the disease reservoir [2, 10, 12]. Environmental radiation considered to be another factor to the increase of TC incidence rate [20], or fallout from nuclear weapon testing [21]. Other possible explanations that have been suggested include the increase utilization of total thyroidectomy for benign multi nodular goiter or due to a change in diagnostic threshold used by pathologist which has led to minimally atypical lesions that previously have been considered benign now been classified as carcinoma [2].

The aim of our study is to investigate the clinicopathologic feature of TC in Sulaymani from 2004 -2018 using variables of tumor histopathology, size, stage, age and sex.

PATIENTS AND METHODS

After granting approval from the research and ethics committee of the Hiwa Hematology/Oncology Cancer Teaching Hospital and University for the collection and use of these data, we evaluated a retrospective cohort of patients from 2004 to July 2018 in database of Hiwa Hospital which is the only referral center for cancer registry for the whole Sulaymani governorate, yielding 225 thyroid cancer cases for these 15-years period that have been diagnosed by histopathology and laboratory investigation including thyroid function test, tumor markers and radiology. Out of the 225 cases 35 cases were deleted by manual and computerized linkage due to missing data, duplicated names and refugees from other governorate of Iraq. The remaining 195 cases are those from the Sulaymani governorate. Information obtained via direct interview with patients, phone calls and patient's database provided in their files in the registry unit at the hospital.

Thyroid cancer cases were categorized in to four histopathology categories: papillary TC, follicular TC, medullary TC, and anaplastic TC thyroid carcinoma. Tumor size was split into the following: (≤1 cm) microcarcinoma, (1.1-2 cm), (2.1-5 cm), and (>5, 1 cm). Stages included local disease: (tumor confined to the thyroid), regional disease (extra thyroid/lymph node involvement), or distant disease (metastatic spread to distant organs), gender (men, women) and age (≤45,>45).variables were analyzed among 3 different time periods of 2004-2008, 2009-2013 and 2014-2018.

Data were recorded in a data sheet excel program. SPSS 21-version used for statistical evaluation and excel version 10, the level of P-value < 0.05 considered as significant value.

RESULTS

A total of 225 cases of TC, 171 (76%) female and 54(24%) male were reported by Hiwa cancer Hospital registry unit in 2004-2018.). 30 cases were excluded due to missing data. TC constituted (1.2%) of total solid cancers registered throughout the study period, Table1

Histopathology and gender

The frequencies of tumor types were as follows: Papillary TC constituted 158 (82.0%) of the cases; follicular TC 21(8.8%); anaplastic TC 6(3%); and medullary TC 9(5%). Papillary TC was by far the most frequent histological type in both gender (73% of all TC in women and 66% in men) and the only type that showed large increases in frequency between 2009-2013 and 2014-2018 (21% to 77% in women; 27% to 63% in men), (Table2).

The incidence of TC was higher among women 155 (79.5%) than men 40 (20.5%). Among both gender the higher incidence frequency was observed between 2014-2018, female (76.1%), male (60%) (P value 0.04) (Table3). The F/M ratio in the entire study period was 3.87, with higher female: male ratios for papillary and follicular TC (4.24 and 4.25, respectively) than for medullary (1.25) and anaplastic (2.5) TC (Table 2).

Age

The mean age of TC in both genders was 41.5 years. Among females, mean age decreased from 50 years in 2004-2008 to 40 years in 2014-2018 (p value 0.1) while for male there was no change, (Fig. 2). As illustrated in (Table4) 105 (67.7%) of females and 25 (62.5%) of males were below the age 45 years.

Size

With regard to tumor size, the mean size of tumors was (21.71 mm). Tumors ≤ 10 mm (microcarcinoma) constituting 67 (34.4%) of all tumor size although was not significant statically. The mean size of PTC was smallest (18 mm), while mean size of anaplastic TC was largest (58 mm). Mean tumor size of TC in relation to the histologic type is shown in, (Fig. 3).

Stage

122 (62.6%) of the cases confined to thyroid gland at time of diagnosis. Frequency of localized tumor was higher in 2014-2018 than in 2004-2008 (p value 0.01) Table 5.

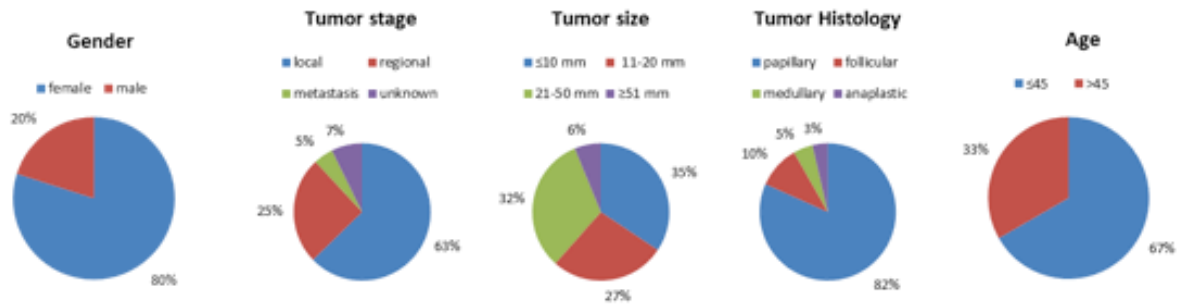

Figure 1. Characteristics of thyroid cancer with regard to histopathology, age, sex, size and stage.

Table 1. Incidence of TC in regard to total solid cancer throughout study period.

year	Number of solid cancers	Thyroid cancer	Thyroid cancer %
2004-2008	1493	18	1.2%
2009-2013	7390	55	0.7%
2014-2018	9292	152	1.6%
Total	18175	225	1.2%

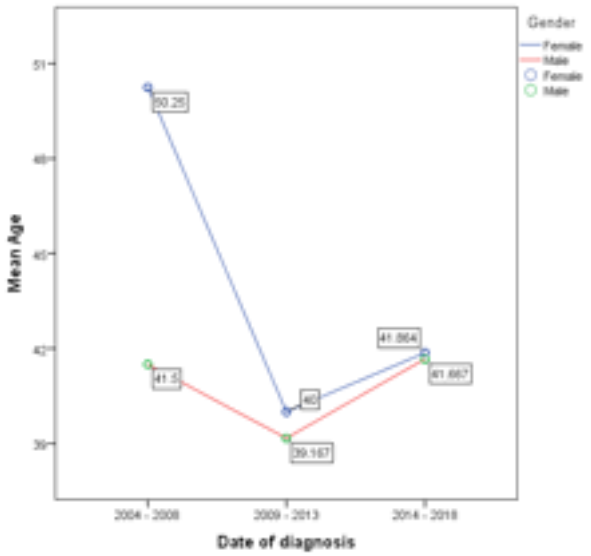

Figure 2. Illustrating mean age of female and male with regard to date of diagnosis, p value 0.1

Table2. Incidence of TC regarding histopathological subtype according to gender, (n) observed cases of TC, F/M ration of thyroid cancer, 2004-2018.

Histopathology Type	Female				Male				F/M ratio
	Date of diagnosis			Total	Date of diagnosis			Total	
	2004 - 2008 n (%)	2009 - 2013 n (%)	2014 - 2018 n (%)		2004 - 2008 n (%)	2009 - 2013 n (%)	2014 - 2018 n (%)		
Papillary	2 (1.6)	27 (21.1)	99 (77.3)	128 (100.0)	3 (10.0)	8 (26.7)	19 (63.3)	30 (100.0)	4.24
Follicular	2 (11.8)	5 (29.4)	10 (58.8)	17 (100.0)	1 (25.0)	0 (0.0)	3 (75.0)	4 (100.0)	4.25
Medullary	0 (0.0)	1 (20.0)	4 (80.0)	5 (100.0)	0 (0.0)	3 (75.0)	1 (25.0)	4 (100.0)	1.25
Anaplastic	0 (0.0)	0 (0.0)	5 (100.0)	5 (100.0)	0 (0.0)	1 (50.0)	1 (50.0)	2 (100.0)	2.5
Total	4 (2.6)	33 (21.3)	118 (76.1)	155 (100.0)	4 (10.0)	12 (30.0)	24 (60.0)	40 (100.0)	3.87

Table 3. Incidence of thyroid cancer by gender, (n) observed cases of TC, 2004-2018.

Date of diagnosis	Gender		F/M ratio	P- value
	Female n (%)	Male n (%)		
2004 - 2008	4(2.6)	4 (10.0)	1	
2009 - 2013	33 (21.3)	12 (30.0)	2.75	
2014 - 2018	118 (76.1)	24 (60.0)	4.9	0.04
Total	155 (100.0)	40 (100.0)	3.87	

Table 4. Incidence of thyroid cancer with regard to age in male and female. 2004-2018 demonstrating increase in TC frequency among male and female younger than 45 year.

Gender	Date of diagnosis	Age		Total	P-value
		≤ 45	< 45		
Female	**2004 - 2008**	3 (75.0)	1 (25.0)	4 (100.0)	0.91
	2009 - 2013	23 (69.7)	10 (30.3)	33 (100.0)	
	2014 - 2018	79 (66.9)	39 (33.1)	118 (100.0)	
	Total	105 (67.7)	50 (32.3)	155 (100.0)	
Male	**2004 - 2008**	3 (75.0)	1 (25.0)	4 (100.0)	0.20
	2009 - 2013	5 (41.7)	7 (58.3)	12 (100.0)	
	2014 - 2018	17 (70.8)	7 (29.2)	24 (100.0)	
	Total	25 (62.5)	15 (37.5)	40 (100.0)	

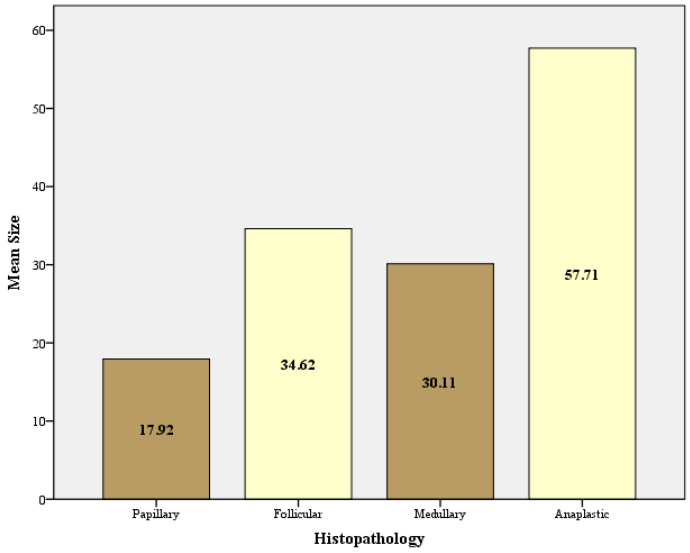

Figure 3. Mean tumor size in relation with histopathology. Anaplastic carcinoma had largest size at time of presentation.

Table 5. Incidence of thyroid cancer by stage, (n) observed number of TC in 2004-2018.

Date of diagnosis	Stage of tumor				Total	P-value
	Local	Region	Metastasis	Unknown		
2004 - 2008	4 (50.0)	2 (25.0)	0 (0.0)	2 (25.0)	8 (100.0)	0.01
2009 - 2013	27 (60.0)	9 (20.0)	1 (2.2)	8 (17.8)	45 (100.0)	
2014 - 2018	91 (64.1)	39 (27.5)	8 (5.6)	4 (2.8)	142 (100.0)	
Total	122 (62.6)	50 (25.6)	9 (4.6)	14 (7.2)	195 (100.0)	

DISCUSSION

In our study papillary and follicular cancers comprised the vast majority of all thyroid cancers, that was comparable to international literatures as well as to Middle Wast Arabic country literatures like Libya, Saudi Arabia , Turkey, Jordan, Iran and Israel [22 ,17,23,4 ,5 ,16].

There are many explanations for this phenomenon like correction of iodine deficiency; Iodine deficient areas (IDA) have different distribution of histologic types of TC from iodine sufficient areas (ISA). In IDA follicular TC is more common, while in ISA papillary TC is more common[24]. Correction of the iodine deficiency with the iodized salt prophylaxis and increase consumption of food containing iodine as well as increased awareness of risks associated with red meat consumption led to increase in the relative proportion of PTC with concurrent drop in frequency of the follicular and anaplastic TC[22, 25].

PTC is the most common type of TC, with a low degree of malignancy, majority diagnosis in early stages with good prognosis[17, 26]. After Iraqi operation freedom in 2004 improvement in medical surveillance, better cancer registry, health education, lifestyle changes, good family income, good access to health system, as the number of diagnostic radiology examinations have doubled in the past 10–15 years in the United States and other countries [19]. Kurdistan was not an exception. We think that all these factors have impact on overdiagnosis of papillary TC. Overdiagnosis, is the identification of a disease which if left undetected would not cause symptoms or death for that patient during his or her lifetime[12]. Radiation exposure; a major cause for TC which has decreased over the last 60 years [23]. Other sources of radiation are Radon and Thoron. Radiation exposure from medical sours like X-ray and CT scan [35], although they have much lower radiation dose than these historical sources, with a very low estimated excess attributable cancer risk of <0.01%–0.05% over a lifetime [36]. Radiation exposure resulting from airplane travel, but at a dose several orders of magnitude below a CT scan (<0.1 mSv compared to 100 mSv for a full body CT scan [12]. Other causative factors include change in the body mass index [37], change in menstrual cycle [38], and consumption of fertility drugs [39].

Similar to other studies, in our study TC was about four fold more common in women than men (p vale0.04). one possible explanation is women's oestrogen level which is proved to be one of the risk factor of TC, oestrogen level is actually higher in female than it is in male [27, 28]. Another explanation for high incidence among females in early lifetime may be due to greater detection during annual obstetrical and gynecological examinations during the reproductive years, whereas the slower rise in incidence among males might reflect more frequent medical visits later in life [29].

Chen et al who demonstrated increase in TC incidence in those aged >45 in both male and female[15, 12]. Our study showing increase in frequency in both female and male aged <45 for PTC, but our results was not statistically significant. A possible explanation is that the residents aged ≤45 years are more educated and might pay more attention to the physical examinations as they enter early old age.

Similar to other literatures majority of the TC in our study was small tumors localized to thyroid gland especially during the late period of our study. PTC had the smallest mean size at presentation which could explain the fact that PTC has a better prognosis, while anaplastic TC had the largest mean size at presentation proving its aggressive nature. Some authors [19, 30, 31] reported that high incidence in PTC was limited or disproportionately higher for small TC (papillary microcarcinoma) which is known to has a lower risk and better outcome , and attributed the reason to increase adoption of ultrasonography and fine-needle aspiration for thyroid nodules [32]. Some authors concluded that there was no increase in TC incidence when Papillary microcarcinoma were excluded [2 , 33, 34], which raise the question whether improved technique can have role in this trend.

Our study has important limitations, related to the fact that data was collected only from Hiwa Cancer Hospital in Sulaymani firstly; secondly poor histopathological reports, especially during early time period of our study. lastly; cancer registry in Kurdistan was under estimated especially before Iraqi operation freedom in 2004 and even after that for a while. Till now many cases have not been registered nor treated in our referral hospitals, and they go to other neighboring or European countries to seek medical attention, partly due to lack of trust between patients and doctors which is a common problem in developing countries as well as in Iraq and Kurdistan. For the early years under the study the collected data could suffer from underestimations. Acknowledging such limitations does not abolish the data used.

In conclusions; our study has presented an overview of the clinicopathological features of TC over the last 14 years in Sulaymani governorate in Iraq. PTC was the most common type of TC with female predominance. This pattern is consistent with the results of other studies. The disease tends to appear at a younger age, localized to thyroid gland with small size less than 2 cm at presentation. Further studies are needed to identify epidemiological features on a national level and identify trends in TC incidence and further improvement toward a good cancer registry.

Conflicts of interest

The authors declare that no competing financial interests exist.

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