

# An 18-year study of thyroid carcinoma in the western region of Saudi Arabia: a retrospective single-center study in a community hospital

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**BACKGROUND:** Thyroid carcinoma (TC) is the ninth most common site of all cancers in women in the world and the second most common malignancy in Saudi Arabia. This reports updates data on the epidemiology of the disease in Saudi Arabia.

**OBJECTIVE:** Describe and interpret changes in the frequency of TC to compare with other populations and determine proportions of certain histological types of TC.

**DESIGN:** Medical record review.

**SETTING:** Military hospital in Jeddah, Saudi Arabia.

**PATIENTS AND METHODS:** We reviewed the pathological and clinical records from January 2000 to December 2017 of patients with TC.

**MAIN OUTCOME MEASURES:** Frequency and types of TC.

**SAMPLE SIZE:** 347 patients.

**RESULTS:** Over the 18-year period, out of 456 patients with TC, 347 patients had sufficiently complete records: 275 (79.3%) were female and 72 (20.7%) were male for a female to male ratio of 3.8:1. The mean (SD) age at surgery of all patients was 45.2 (16.0) years. There were 287 (82.7%) cases of papillary TC. The next common malignancy was follicular TC with 32 (9.2%) cases followed by Hurthle cell cancer with 11 (3.2%) cases. Lymphoma was found in only 7 (2%) cases. All TC types occurred at a younger age in females than males except for lymphoma. All TC types occurred with the greatest frequency in the fourth and fifth decades. There was a 2.3-fold increase in the number of TCs from 8 (2.3%) in 2000 to 26 (7.5%) in 2017. The rate per 100000 residents of Jeddah increased for the period from 2000 to 2002 from 1.6 to 3.4 for 2015-2017. Papillary TC cases in females accounted for most of the increase.

**CONCLUSION:** Our findings are consistent with similar studies worldwide. Etiological factors promoting the rise in TC must be investigated and may provide insight in developing suitable management strategies for the Saudi population.

**LIMITATION:** Small sample size and retrospective over a long period.

**CONFLICT OF INTEREST:** None.

Among all malignancies, thyroid carcinoma (TC) has been reported in 1% of certain areas of the Middle East and 5-10% across Saudi Arabia.<sup>1,2</sup> TC is the ninth most common site of all cancers in women in the world and the second malignancy after breast cancer in Saudi Arabia.<sup>1-5</sup> Since the late 1980s, the incidence has been increasing worldwide in both sexes.<sup>1,6,7,44</sup> This trend is consistent with temporal changes in the prevalence of some risk factors, including obesity, genetic, environmental factors and introduction of iodine supplementation in regions previously iodine deficient.<sup>43,45-49</sup> Increases could be due to awareness and improved diagnostic methods; in particular, the widespread use of neck ultrasonography and an increased ability to detect and diagnose small indolent tumors.<sup>50,51</sup> Studies of the geographical distribution of the cancer have been of value for making global comparisons and for generating epidemiological hypotheses. The aim of this study was to describe and interpret trends in the frequency of TC in Saudi men and women during the 2000-2017 period, and to compare them with other Saudi studies. We also planned to determine the proportions and changes in frequency of certain histological subtypes in the Saudi population.

## PATIENTS AND METHODS

This is a retrospective study of TC reported at the Department of Pathology, King Fahad Armed Forces Hospital, Jeddah, Saudi Arabia from January 2000 to December 2017. Pathological and clinical records of patients seen at the endocrinology clinic or other services were analyzed. The demographic data included age at the time of diagnosis and gender while the histopathological features included TC subtype according to the recommended classification by the International Classification of Diseases for Oncology, Third Edition.<sup>52</sup> The type of tumor was assessed from the pathology reports and classified mainly as papillary, follicular, anaplastic, medullary, Hurthle cell and lymphoma. Patients older than 12 years with a proven histopathological diagnosis of TC were included in this analysis.

Age-standardized, annual thyroid cancer incidence rates were calculated for the entire cohort and for each year between 2000 and 2017. Incidence rates were age adjusted using the direct method based on age distribution for the mid-average for the year 2000 (1.8 million) and 2017 (2.8 million) for the Jeddah population. With the direct method of standardization, age-specific rates from the study population were applied to the age distribution of the standard Jeddah population to yield the number of events that would have

been expected if the study population had the same age distribution as the standard population. Incidence rates were shown as the number of cases per 100000 individuals (for the population at risk). Incident thyroid cancer cases were calculated as a percentage of the total number of new patients per year. Ethical approval was obtained from Research and Ethics committee of King Fahad Armed Forces Hospital.

ANOVA was used for analysis of age at surgery by cancer type. The statistical analysis was conducted with IBM SPSS, version 22 (IBM Corp, Armonk, New York, United States). *P* value <.05 indicates statistical significance.

## RESULTS

Of the initial 456 cases, 109 subjects were excluded from the study as they were either thyroid specimens repeated for the same patients or incomplete clinical records. Of the remaining 347 patients, 275 (79.3%) were female and 72 (20.7%) were male. The ages at surgery ranged from 12 to 89 years with a mean and median age of 45.2 (16.0) and 44.5 years, respectively (**Table 1**).

There were 287 (82.7%) cases of papillary TC. The next common malignancy was follicular TC with 32 (9.2%) cases followed by Hurthle cell cancer, lymphoma, anaplastic, and medullary (**Table 1**). The mean age at diagnosis for females was 42.8 (15.4) vs. 54.4 (15.0) years for males (*P*<.0001), 12 years younger than their male counterparts. All TC types occurred at a younger age in females except for lymphoma (**Figure 1**). All TC types occurred with the greatest frequency during the fourth and fifth decades (**Table 2, Figure 2**). The most common TC was papillary with most cases in the fifth decade (69 cases; 90.1%).

TC occurred more frequently in females than males across age groups (**Figure 3**). All thyroid cancer types occurred more frequently in females than males except for lymphoma (**Figure 4**) with a sex ratio of 3.8:1. The sex distribution of patients with papillary TC was 4:1 and for Hurthle cell carcinoma the ratio was 1.7:0. Patients with medullary TC had an equal sex ratio of 1:1. The female predominance was especially pronounced for follicular TC (7:1). Lymphoma was seen more commonly in males at a 2.5:1 ratio. **Figure 5** shows the increasing incidence of TC cases in our hospital in between 2000 to 2017.

There was a 2.3-fold increase in the number of TC from 8 (2.3%) in 2000 to 26 (7.5%) in 2017. Whereas the rate per 100000 residents for the period from 2000 to 2002 was only 1.6 for 100000 per year, for the period from 2014 to 2017 the rate was 3.4 for 100000 per

**Table 1.** Age at surgery by thyroid cancer type.

Thyroid cancer type	Number of cases (%)	Age (Mean[SD])
Papillary	287 (82.7)	44.3 (15.3)
Follicular	32 (9.2)	46.2 (17.7)
Hurthle cell	11 (3.2)	47.5 (18.9)
Lymphoma	7 (2)	58.9 (6.4)
Anaplastic	6 (1.7)	65.0 (24.4)
Medullary	4 (1.2)	39.5 (17.9)
<b>Total</b>	<b>347</b>	<b>45.2 (16.0)</b>

One-way ANOVA,  $F=3.315$ ,  $P=.006$  for age at surgery.

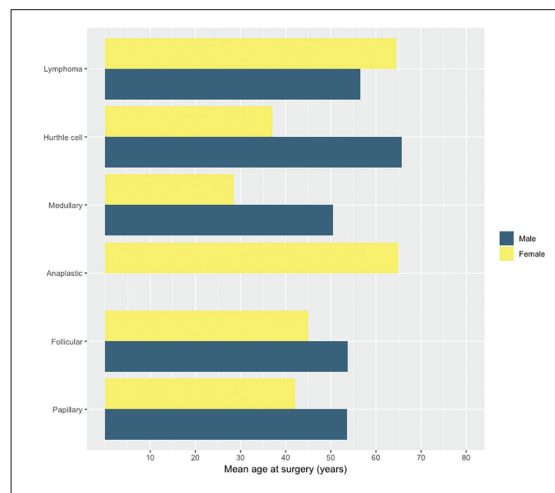
**Table 2.** Age distribution.

Age groups (years)	Numbers of patients (%)
10-19	13 (3.8)
20-29	52 (15.4)
30-39	68 (20.1)
40-49	76 (22.5)
50-59	61 (18)
60-69	44 (13)
70-79	19 (5.6)
80-89	5 (1.5)
Data unavailable	9 (2.6)
<b>Total</b>	<b>347</b>

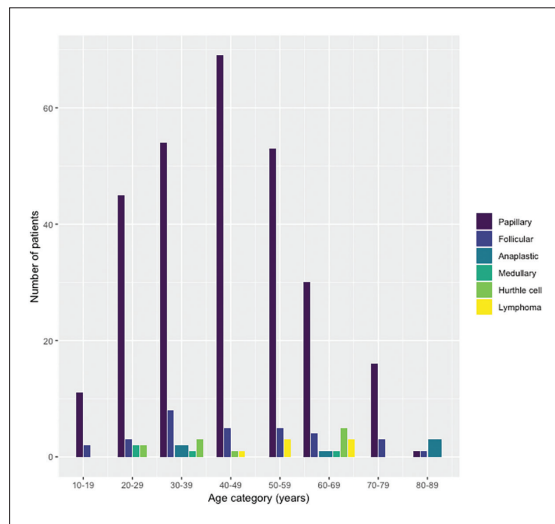
year, (Figure 6A). This change in frequency is mostly attributable to an increase in the relative occurrence of papillary TC (Figure 6B). The increase in the number of TC cases over the study period was similar in males and females (Figure 6C).

## DISCUSSION

The incidence of reported TC and study sample size have varied from one study to another from different countries. From the 1970s, incidence rates of TC increased in most European countries, although a decrease was recorded in some countries, such as Sweden and Norway.<sup>53</sup> Trends of rising incidence have also been observed the in US and Canada.<sup>7,10</sup> Saudi Arabia is not an exception. TC incidence in Jeddah city increased in both sexes between 2000 and 2017 in accordance with other national studies. Our results are consistent with the national and international data on the pattern and frequency of TC. The population of Jeddah, Saudi Arabia was reported to be 1.8 mil-



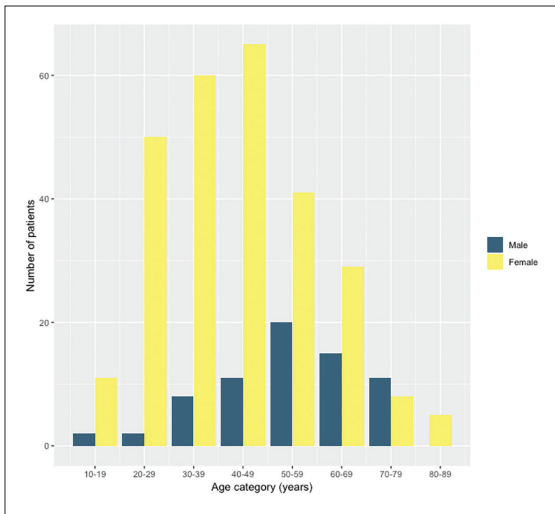
**Figure 1.** Thyroid cancer types by gender.



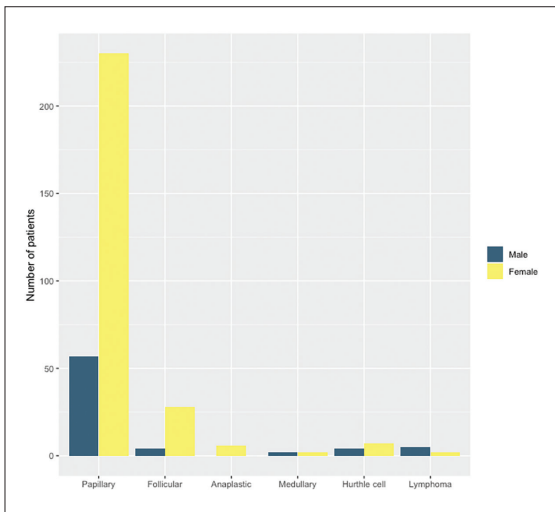
**Figure 2.** Thyroid cancer types by age category.

lion in 2000 and 2.8 million in 2017.<sup>54</sup> The rate of TC showed an increase from 1.6 cases per 100 000 in 2000 to 3.4 cases per 100 000 in 2017. This rapid increase in recent decades has also been observed in many other countries.<sup>7,10</sup>

After the release of the American Thyroid Association (ATA) guideline in 2009, TC incidence increased, and our report may reflect this increase.<sup>55</sup> The rates of TC in Saudi Arabia are lower than those of industrialized nations, but are expected to rise due to growth of the population, rapidly changing lifestyles including dietary habits, an aging population, obesity, iodine deficiency, lack of exercise, and urbanization.<sup>56</sup> This trend is partially attributable to more intensive diagnostics. Advanced medical procedures such as ultrasound and fine-needle aspiration biopsy have contributed to detection of

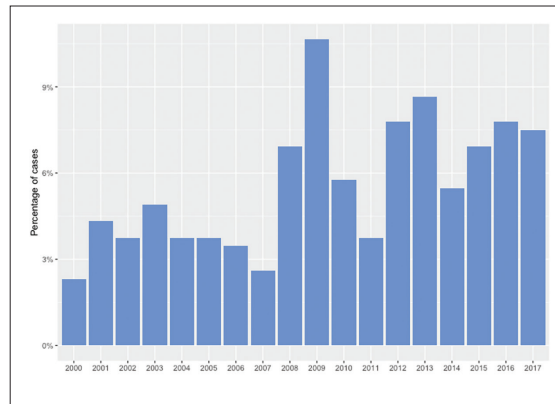


**Figure 3.** Age category by gender.

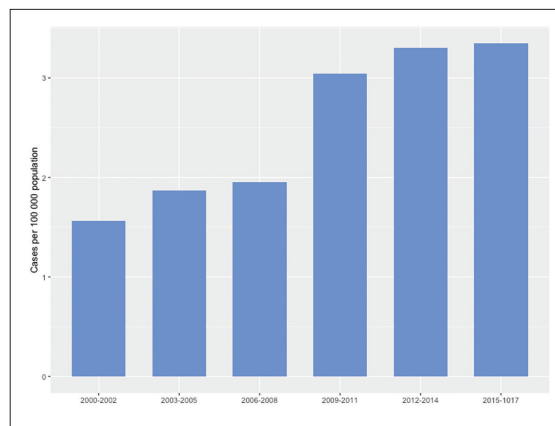


**Figure 4.** Thyroid cancer types by gender.

TC, especially smaller tumors,<sup>15,57</sup> but there have also been more TCs larger than 4 cm.<sup>13,40</sup> There is growing evidence suggesting that changes in obesity, diabetes, autoimmune thyroiditis and smoking prevalence have contributed to increasing TC rates.<sup>58-60</sup> Excessive leptin, one of the molecules causing obesity, could be caused by excessive food intake. The amount that leptin plays a role in an increased frequency of TC needs further study.<sup>61</sup> Paralleling trends in TC incidence, obesity prevalence has increased among Saudi adults (70%).<sup>62</sup> Epidemiological studies have consistently found positive associations between excess adiposity in childhood and adulthood and subsequent risk of TC, including papillary TC, whereas current smoking consistently has been associated with a 30% to 40% reduction in TC



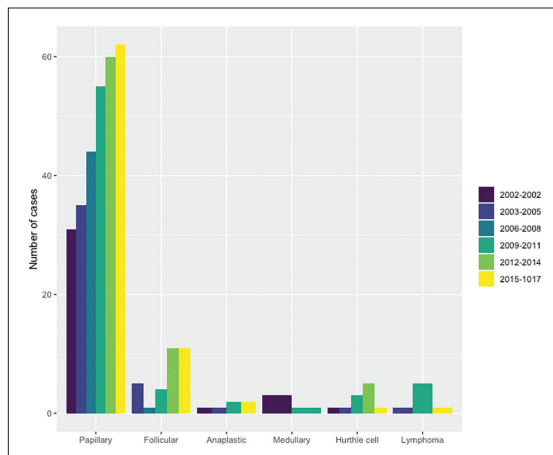
**Figure 5.** Percentage of thyroid cancer cases per year during the period 2000 to 2017 at King Fahad Armed Forces Hospital, Jeddah.



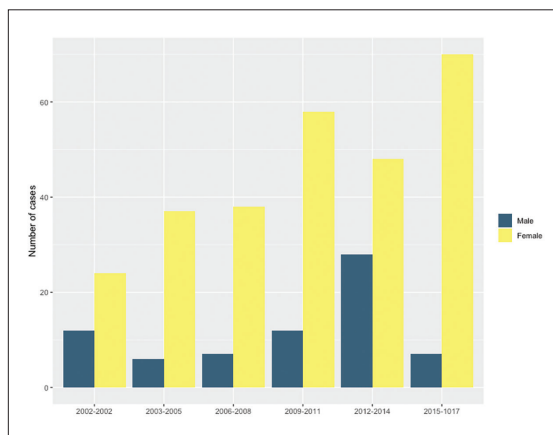
**Figure 6A.** Frequency of thyroid cancer by 3-year study intervals (cases per 100,000 population).

risk, independent of obesity and other risk factors.<sup>45-49</sup> Obesity and smoking could influence TC development via insulin resistance, thyroid hormone, and estrogen-related pathways.<sup>47,48</sup> Estimates are that these factors are related to more than 40% of all new cases of TC annually in the United States.<sup>47</sup>

The mean age at surgery for the current study are within the 45-48 years quoted in various local and Western studies (**Table 3**). The mean age at the diagnosis for females was significantly younger than for males. The mean age for females was 12 years younger than that for males.<sup>2</sup> TC occurred almost equally during the fourth and fifth decades of life, but there were differences when gender was considered with more cases in females than males occurring mostly in the fifth decade (40-49 years) and more cases of TC in males than females occurring in the eighth decade (70-79 years) in accordance with a similar report.<sup>2</sup> The younger mean age at presentation may reflect the changing epi-



**Figure 6B.** Number of cases of thyroid cancer types by 3-year study intervals.



**Figure 6C.** Number of cases of thyroid cancer for 3-year study intervals by gender.

miological behavior of the disease, a late detection of cases or a true change in the pattern of the disease—with a younger age of onset compared to the past, an assumption that needs further evaluation. The marked female preponderance in this study is similar to various local and international reports. Studies by several authors also show a female predominance in TC with a varying female to male ratio of 2.4:1 to 10.6:1 (Table 3). There are possible explanations as to why TC is significantly more frequent among women in Saudi Arabia compared to other countries. One possibility is iodine deficiency. TC is more frequently observed in countries where iodine is not part of the diet and, for that reason, is less frequently diagnosed in the US. The increased risk of follicular TC was associated with endemic goiters

and iodine deficiency.<sup>63</sup> This observation suggests that a specific susceptibility gene with sex hormone receptor elements such as an expression of estrogen receptors on TC epithelium may be involved in the pathogenesis of TC.<sup>64</sup>

Papillary TC was the most frequently differentiated TC, followed by follicular. The incidence of papillary and follicular TC are within the reported Saudi and Western experience. The same is true for the low incidence of anaplastic TC, medullary TC, Hurthle cancer and thyroid lymphoma (1.7%, 1.2%, 3.2 and 2%, respectively). These percentages contrast with significantly different percentages in the current study reflecting a possible change in thyroid histopathological pattern and/or improvement and change in thyroid histopathological classification.

Epidemiologic studies are limited by their dependence on population-specific registries, which subject them to bias from regional influences such as case definitions, diagnostic practices, and the reporting pattern. Poorly differentiated carcinoma remains a controversial entity, and it is therefore difficult to evaluate whether the different prevalence rates among different geographic regions reflect true etiological differences or mere variations in diagnostic criteria. The limitations of our study include its retrospective nature over a long period, the small sample size, the fact that cases were from a single hospital but managed by different teams and not all patients had follow up. Thus, the findings might not be reflective of the overall general population. It is only possible to speculate about potential explanations for the observed thyroid cancer trends due to the descriptive nature of this study. Lifestyle-related factors and individual-level environmental exposures were not captured by registries. The current study did not evaluate the influence of treatment on these trends.

In conclusion, the current study showed the incidence of TC has distinctly increased over the study period with the greatest rise occurring in papillary TC in females. Our findings are consistent with similar studies worldwide. Etiological factors promoting the rise in TC must be investigated and may provide insight in developing suitable management strategies for the Saudi population.

**Acknowledgment**

*The authors would like to thank all colleagues from the Departments of Endocrinology and pathology for helping in data collection.*

**Table 3.** Summary of studies from Saudi Arabia for the years of 1975 to 2018.

Parameters	References									
	2	25	26	23	27	28	6	31	32	
<b>Publication year</b>	1975	2001	2002	2004	2009	2010	2013	2014	2014	
<b>Study (years)</b>	Covered period	1975-1989	1993-1999	1996-2000	2000-2003	1997-2008	1998-2007	2000-2010	2006-2013	--
	Duration	14	6	4	3	11	9	10	7	6
<b>Numbers</b>	857	87	103	45	256	92	2294	74	32	
<b>Mean age (years)</b>	46	36	37	41	45	40	38	42	50	
<b>Gender</b>	Female	71	67	89	70.2	78.2	74.3	76.3	78.1	76.7
	Male	29	20	8.7	29.8	21.8	25.7	23.7	21.9	23.3
<b>Ratio (F:M)</b>	2.4:1	3.4:1	10.2:1	2.4:1	3.6:1	2.9:1	3.2:1	3.6:1	3.3:1	
<b>Papillary</b>	79	90	89	82.2	81.6	91.3	90	75.1	78.1	
<b>Follicular</b>	4.3	10	9	4.4	5.1	4.3	5.1	13.4	15.6	
<b>Anaplastic</b>	5.4	--	--	6.7	2.7	--	1.4	3	6.3	
<b>Hurthle</b>	3.6	--	--	--	2	3.3	-	1.5	--	
<b>Medullary</b>	5.3	--	2	6.7	5.1	--	2.2	3	--	
<b>Lymphoma</b>	0.9	--	--	--	2.3	1.1	-	4	--	

**Table 3 (cont.).** Summary of studies from Saudi Arabia for the years of 1975 to 2018.

Parameters	References											
	29	33	34	22	35	36	37	38	39	30	Current	
<b>Publication year</b>	2014	2015	2016	2016	2016	2016	2017	2017	2018	2018	2018	
<b>Study (years)</b>	Covered period	1982-2008	2001-2008	2001-2010	2013	2000-2012	2011-2016	2011-2016	2004-2005	2012-2016	2008-2011	2000-2017
	Duration	26	7	9	1	12	5	5	2	4	3	18
<b>Numbers</b>	143	8	114	28	370	31	48	600	65	8	347	
<b>Mean age (years)</b>	38	35	40	42	60	44	47	39	41	43	45	
<b>Gender</b>	Female	--	79.8	25	78.9	78.9	82.1	76.5	91.4	87.5	87.3	79.3
	Male	--	20.2	75	21.1	21.1	17.9	23.5	8.6	12.5	12.7	20.7
<b>Ratio (F:M)</b>	4.3:1	4:1	1:3	3.7:1	3.7:1	4.6:1	3.3:1	10.6:1	7:1	6.9:1	3.8:1	
<b>Papillary</b>	74	62.5	77	64.3	93	64.3	72.6	90.3	65.7	100	82.7	
<b>Follicular</b>	14	37.5	17	10.7	7	10.7	10.6	3.2	31.4	--	9.2	
<b>Anaplastic</b>	5	--	2	7.1	--	7.1	4.8	--	--	--	1.2	
<b>Hurthle</b>	7	--	4	--	--	--	4.8	1.3	2.9	--	1.7	
<b>Medullary</b>	0	--	--	14.3	--	14.3	2.4	--	--	--	3.2	
<b>Lymphoma</b>	--	--	4.9	--	--	--	4.8	--	--	--	2	

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