RESEARCH ARTICLE

Descriptive Epidemiological Analysis of Thyroid Cancer in the Saudi Population (2001-2013)

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Abstract

Objective: Thyroid cancer has one of the highest frequency rates among thyroid diseases, and ranks second for neoplasia in the Saudi female population. This paper concerns a comprehensive evaluation of increasing incidence trends and geographical distribution of different patterns of thyroid cancer among the Saudi Arabian population using the latest Saudi Cancer Registry (SCR) reports. **Methods:** The analysis included a total of 7,670 thyroid cancer cases (1604 male and 6066 female) which were recorded in the SCR files for the period between January 2001 and December 2013. **Results:** The overall incidence of thyroid cancer increased during the period from 2001 to 2013. The most common age group affected was 35–39 years in both sexes. Najran recorded the highest differences in thyroid cancer rates with increase between 2001 and 2013. Controversially, other regions like Tabuk and the Northern provinces recorded obvious decreases in rates of thyroid cancer among females. **Conclusion:** Thyroid cancer is the second most common cancer among females in Saudi Arabia with incidence peaks in both genders aged 35–39 years and increase overtall in the country from 2001 to 2013. The specific causes of this upward trend are unknown. Further clinical and epidemiological research must be conducted for clarification, with an emphasis of causes of the variation in thyroid cancer prevalence between regions in Saudi Arabia.

Keywords: Thyroid cancer epidemiology- Saudi cancer registry- Thyroid cancer

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Introduction

Cancer is a major public health problem that threatens global health; it is considered to be the leading cause of death in the developed world and the second leading in the developing world. In 2012, the most recent published report from the International Agency for Research on Cancer (IARC), around 14.1 million new cancer cases were diagnosed, 8.2 million people died from cancer and 32.6 million people were five-year cancer survivors (Ferlay et al., 2012).

Thyroid cancer has one of the highest frequency rates among thyroid diseases, which have noticeably increased Over the last decades (Vergamini et al., 2014). Despite the fact that thyroid cancer accounts for only approximately 1% of all malignancies, it is the most common type of endocrine system malignancy (about 90%) and one of the rare cancers that is more frequent in women than in men (Nagataki and Nystrom, 2002). According to the American Cancer Society, an estimated 56,870 new thyroid cancer cases will be diagnosed in the United States in 2017, with around 2010 expected deaths in that year (ACS., 2017).

In Saudi Arabia, the IARC estimated that the age-standardised incidence rate (ASIR) for thyroid cancer was 7.5 per 100,000 females in 2012, and the age-standardised mortality rate (ASR) was 2.5 per 100,000 (Ferlay et al., 2012). In 2013, the Saudi Cancer Registry (SCR) reported that thyroid cancer ranked second in cancer incidence in the female population, and twelfth in the male population (SCR, 2013). Moreover, the same report showed that the ASIR of thyroid cancer in Saudi Arabia, which was 5.2, is somewhat high in comparison with other Arabian Gulf countries. For example, in 2013, the reported ASIRs for Oman and Bahrain were lower than for Saudi Arabia, at 4.85 and 4.6 respectively (SCR, 2013).

Only two papers have discussed the incidence of thyroid cancer in Saudi Arabia. The first one, published in 2013, used retrospective data compiled from 2000 to 2010, using a tertiary hospital tumour registry program (Hussain et al., 2013). The other paper, which was published recently (2015), analysed the data regarding female thyroid cancer incidence in Saudi Arabia carried out from 2001 to 2008, using the Saudi Cancer Registry (Alghamdi et al., 2015). At that point, the idea emerged of writing an updated overview of thyroid cancer trends in the Saudi population by using recently updated available data. Thus, this paper will describe the burden of thyroid cancer among the Saudi population during a 13-year period from 2001 to 2013, and provide a summary of the regional patterns and trends, related to the crude incidence rate (CIR) and the ASIR, of thyroid cancer cases among the Saudi population.

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Materials and Methods

Data

A retrospective descriptive epidemiological study was conducted of thyroid cancer cases in the Saudi population diagnosed between January 2001 and December 2013. The analysis included data for males and females. Therefore, this paper focuses on describing the pattern of the disease across the entire Saudi population. Data for this study was provided by the SCR, which is a population-based registry established in 1994 through the Ministry of Health of Saudi Arabia. Apart from published reports, data cannot be obtained directly from the SCR. There was no available data for the period 1994-1998, and the latest published report of the SCR appeared in 2013.

Since 1999, the SCR has been releasing reports on cancer patterns in Saudi Arabia. The data for 1999 and 2000 was pooled together in one report as combined figures for the two years. However, the data from 2001 to 2013 was provided for each year separately with the primary objective of defining the population-based incidence of the disease. So, the data for the period 1999-2000 was excluded from this analysis, and this paper was limited to data obtained from 13 comprehensive reports for 13 administrative regions from 2001 to 2013 that discuss the frequency of cases, the CIRs and the ASIRs, broken down by the regions of Saudi Arabia. This study was conducted to provide a descriptive epidemiological analysis of thyroid cancer in Saudi Arabia by critically gathering all the information from the SCR reports and analysing them.

Data analysis

For data analysis, version 6 of GraphPad "Prism6" software was used. The descriptive analysis of the epidemiological data was performed by calculating the mean of percentages, CIR and ASIR broken down by age group, sex, region and year of diagnosis. The age-standardised incidence rates and crude incidence rate per 100,000 were calculated by the SCR

Results

Number and percentage

The analysis included a total of 7670 thyroid cancer cases (1,604 males and 6,066 females) which were recorded in the SCR files for the period between January 2001 and December 2013.

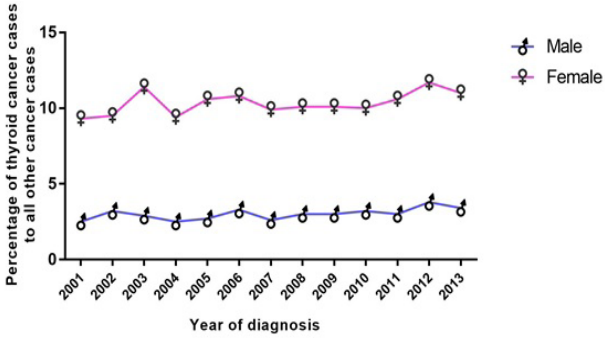

Figure 2. Trends in the Percentage of Diagnosed Thyroid Cancer Cases Compare to Other Cancer Types

In 2001, there were 325 thyroid cancer cases. About 254 cases involved female patients and 71 cases male patients (Figure1). The percentage of thyroid cancer cases out of all cancer types in that year was 9.3% for females and 2.5% for males (Figure 2). The frequency of thyroid cancer cases increased gradually from 2001 until reaching a peak in 2012 with 893 thyroid cancer cases (193 male and 700 female) (Figure 1). The percentage of thyroid cancer cases out of all cancer types in that year was 11.7% for females and 3.8% for males (Figure 2). Subsequently, the total number of thyroid cancer cases slightly decreased to 884 in 2013 (182 male and 702 female cases) (Figure 1). That decrease was reflected in the percentage of thyroid cancer cases relative to other cancer types in that year, which fell to 11% for females and 3.4% for males (Figure 2). The differences in the number of cases of thyroid cancer in the period between 2001 and 2013 increased by a factor of 2.76 for female and 2.5 for male cases (Figure 1).

Crude incidence rate

The crude incidence rate in male cases fluctuated between 0.9 and 1.3 from 2001 to 2007. The CIR steadily increased from 2008 to 2012, reaching its peak (1.9) in 2012, before dropping to 1.8 in 2013 (Figure 3). Despite the drop in 2013, the CIR value showed increase when compared to the 2001 value.

The CIR in female cases gradually increased from 3.2 in 2001 to a peak of 7 in the last two years (2012 and 2013) available in the SCR data. Finally, merging both sexes graph showed an overall increasing trend from 2 in 2001 to 4.4 in 2013 (Figure 3).

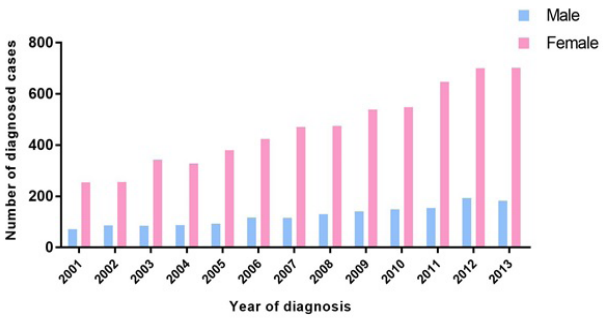

Figure1. Number of Diagnosed Cases Per Year and by Sex

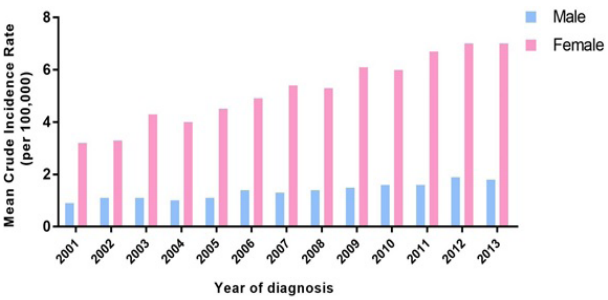

Figure 3. The Crude Incidence Rate of Diagnosed Thyroid Cancer Cases per Year by Sex

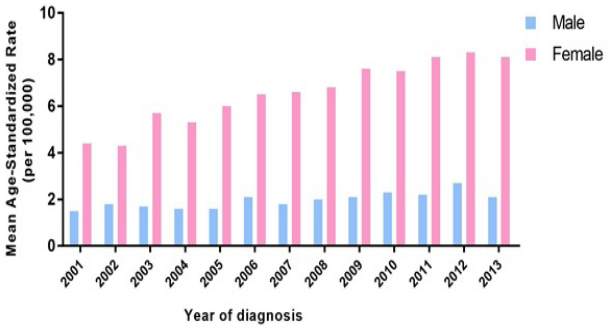

Figure 4. The Age-Standardized Rate of Diagnosed Thyroid Cancer Cases per Year by Sex

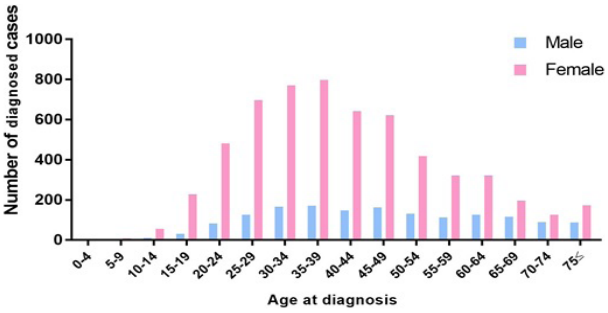

Figure 5. Number of Diagnosed Thyroid Cancer Cases by Age and Sex

Table 1. The Differences in the Percentage, CIR and ASIR of Thyroid Cancer Cases among Women in Different Regions of Saudi Arabia between 2001 and 2013

Regions	% of thyroid	cancer cases		CIR per	100,000 women		ASIR per	100,000 women	
	2013	2001	Diff.	2013	2001	Diff.	2013	2001	Diff.
Asir	11.4	14.0	-2.6	5.9	4.3	1.6	6.9	3.5	3.4
Baha	9.2	10.0	-0.8	5.2	1.9	3.3	6.0	1.7	4.3
Jazan	4.3	2.5	1.8	1.3	1.5	-0.2	1.8	0.9	0.9
Madinah	6.9	5.8	1.1	3.6	1.8	1.8	4.4	3.5	0.9
Hail	12.4	6.8	5.6	6.7	2.0	4.7	7.5	1.7	5.8
Qassim	7.7	9.5	-1.8	3.8	2.5	1.3	4.1	3.1	1.0
Najran	29.4	4.5	24.9*	11.5	1.0	10.5*	16.2	1.2	15.0*
Jouf	12.8	4.5	8.3	6.4	0.9	5.5	6.8	0.7	6.1
Tabuk	6.3	23.8	-17.5**	3.1	9.0	-5.9**	4.2	7.6	-3.4**
Northern	4.3	22.0	-17.7**	2.0	5.0	-3.0**	2.6	6.9	-4.3**
Riyadh	13.9	12.2	1.7	10.8	9.9	0.9	12.4	6.2	6.2
Makkah	11.2	4.8	6.4	7.1	2.4	4.7	8.1	1.5	6.6
Eastern Province	9.4	8.3	1.1	7.3	3.3	4.0	8.8	5.5	3.3

*Noticeable increase compare to other cities value; **Noticeable decrease compare to other cities value.

Age-Standardised Rate (ASR)

Between 2001 and 2007, the ASR of male cases fluctuated between 1.5 and 1.8. In 2008, the trend accelerated, with ASR reaching a peak (2.7) in 2012, then dropping to 2.2 in 2013 (Figure4).

There was a dramatic increase in the ASR of female cases from 4.4 in 2001 to a peak of 8.3 in 2012, then declined somewhat to 8.1 in 2013. Thus, the overall ASR for both sexes increased from 3 in 2001 to 5.5 in 2012, then declined to 5.1 in 2013 (Figure 4).

Age

The distribution of thyroid cases by age groups from 2001 to 2013 was calculated in the SCR reports. The groups reported on correspond to ages 0-4, 5-9, 10-14, 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74 and older than 75 years. Based on the overall numbers and percentages from 2001 to 2013, female patients aged 0-4 were the least affected age group, with less than (0.05%) of the total number of cases (Figure 5). (The same phenomenon was observed among males with the age group of 0-4 being the least affected age group.)

The highest number of female cases was in the age group 35–39 years (798 cases, 13.6%), followed by 30-34 yeras (771 cases, 13.1%) and 25-29 years (696 cases, 11.8%) (Figure 5).

In the male group, the highest number of cases was in the age group 35–39 years (171 cases, 11%), followed by 30-34 years (165 cases, 10.6%) and 45-49 years (163 cases, 10.44%) (Figure 5).

Regionally

The ASIR and CIR mean data for the period between

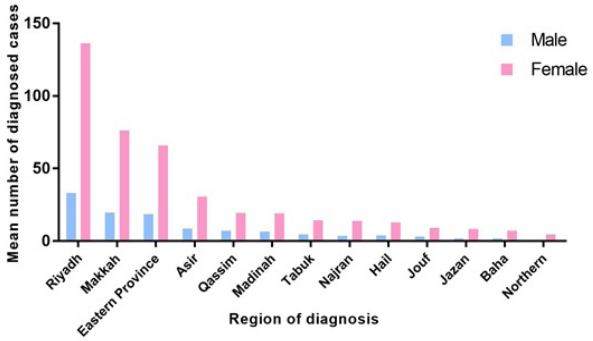

Figure 6. The Mean Number of Diagnosed Thyroid Cancer Cases by Regions

Table 2. The Differences in the Percentage, CIR and ASIR of Thyroid Cancer Cases Among Men in Different Regions of Saudi Arabia between 2001 and 2013

Regions	% of thyroid cancer cases			CIR per 100,000 men			ASIR per 100,000 men		
	2013	2001	Diff.	2013	2001	Diff.	2013	2001	Diff.
Asir	4.3	1.0	3.3	2.2	0.5	1.7	2.5	0.3	2.2
Baha	2.7	0.0	2.7	1.1	0.0	1.1	0.9	0.0	0.9
Jazan	0.0	2.9	-2.9	0.0	*	0.0	0.0	0.8	-0.8
Madinah	4.0	2.7	1.3	2.1	0.7	1.4	2.7	0.7	2.0
Hail	4.3	6.7	-2.4	1.5	2.4	-0.9	2.0	1.8	0.2
Qassim	1.9	1.1	0.8	0.8	*	0.8	1.0	0.8	0.2
Najran	3.9	1.8	2.1	1.4	1.8	-0.4	1.1	0.6	0.5
Jouf	3.8	2.8	1.0	1.6	0.9	0.7	1.7	0.7	1.0
Tabuk	3.9	1.2	2.7	1.6	0.5	1.1	2.1	0.4	1.7
Northern	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Riyadh	4.4	2.6	1.8	2.8	2.5	0.3	3.8	1.4	2.4
Makkah	3.3	3.0	0.3	1.6	1.9	-0.3	1.9	1.0	0.9
Eastern Province	2.1	2.1	0.0	1.3	*	1.3	2.0	1.7	0.3

*Data were missing in CHS reports

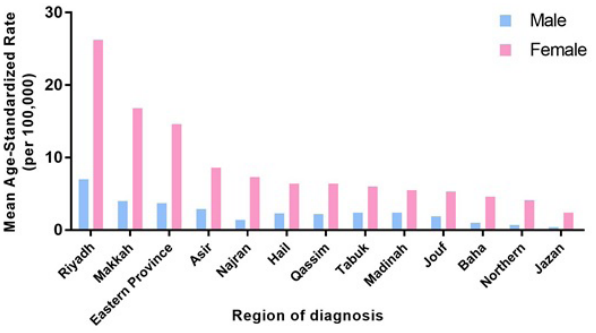

Figure 7. The Age-Standardized Rate of Diagnosed Thyroid Cancer Cases per Regions

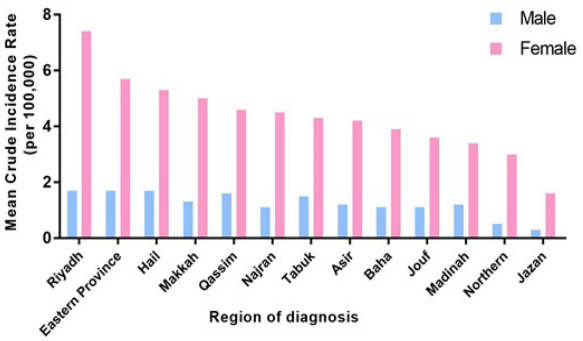

Figure 8. The Crude Incidence Rate of Diagnosed Thyroid Cancer Cases per Regions

2001 and 2013 was calculated from the data of the SCR published reports. This data has been used to investigate the pattern of thyroid cancer among the Saudi population on a region-by-region basis. The Riyadh region recorded the highest number of thyroid cancer cases in the period from 2001 to 2013 with an average of 169.4 per year (Figure 6). It was followed by the Makkah region with an average of 95.6 and the Eastern Province with 84.4 per year (Figure 6). In contrast, the Northern Province, Baha and Jazan recorded the lowest averages at 4.6, 8.7 and 10 per year respectively (Figure 6).

The ASIR data

The male data revealed a huge variation in the ASIR mean of thyroid cancer between regions. The Riyadh region had the highest overall ASIR with an average of 7, followed by the Makkah region at 4 and the Eastern Province at 3.7 (Figure 7). In contrast, Jazan, Northern Province, and Baha recorded the lowest ASIR average at 0.4, 0.7 and 1 respectively (Figure 7).

The female ASIRs were compatible with male ASIR data in terms of the ranking of regions. Therefore, the Riyadh region had the highest overall ASIR with an average of 26.2, followed by the Makkah region at 16.8 and Eastern Province at 14.6 (Figure 7). Additionally, Jazan, Northern Province, and Baha recorded the lowest ASIR averages at 2.4, 4.1 and 4.6 respectively (Figure 7).

The CIR data

The CIR data for males did not indicate large differences between regions. So, the CIR mean for thyroid cancer ranged from 1.7 (in the Riyadh region) to 1.2 (in

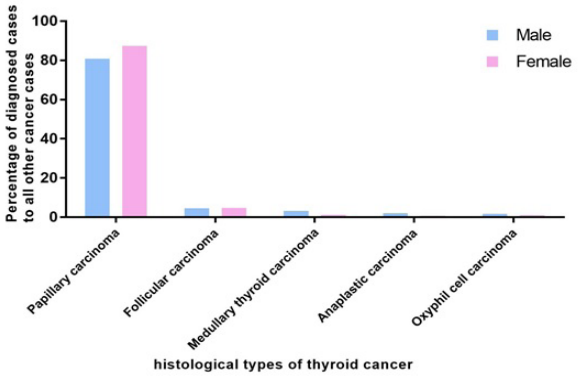

Figure 9. Percentage of Histological Sub-Type of Thyroid Cancer Cases Compare To All Other Subtypes

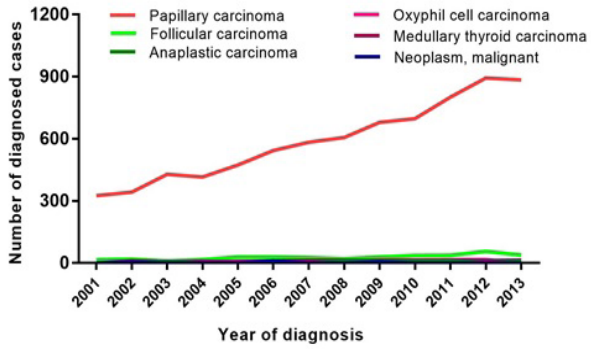

Figure 10. Trends in The Number of Thyroid Cancer Cases by Histological Subtype

the Madinah region) (Figure 8). However, the Jazan and the Northern regions recorded the lowest CIR averages at 0.3 and 0.5 respectively (Figure 8).

The female data showed that Riyadh is again at the top of the list with a CIR average of 7.4 (Figure 8). Next, the CIR mean value of other regions ranged from 5.7 in the Eastern Province to 3 in the Northern Province. The Jazan region was at the end of the list with a 1.6 CIR average (Figure 8).

Differences in the CIR and ASIR

The differences in the CIR and ASIR between 2001 and 2013 were calculated on the basis of data from published SCR reports, and the pattern of thyroid cancer in Saudi population in different regions was investigated (Table 1and 2). The greatest changes in percentages and rates of thyroid cancer among females were observed in the Najran region (24.9 %, 10.5 CIR and 15 ASIR) (Table 1). The percentage of thyroid cancer cases among Saudi women in Najran increased by 24.9% in 2013 compared to 2001. Additionally, the CIR and ASIR increased by 10.5 and 15 cases per 100,000 women respectively. In contrast, other regions such as Tabuk and the Northern provinces recorded clear decreases in thyroid cancer rates among females. The percentages of change in the incidence of thyroid cancer cases among women in those two regions were -17.7% and -17.5% respectively. Also, the rates of change in the CIR and ASIR were -5.9 and -3.4 for the Tabuk region and -3 and -4.3 for the Northern provinces region. Despite this downward trend, the overall CIR and ASIR for Tabuk and the Northern provinces are still very high in comparison with other Saudi Arabian regions (Table 1).

Finally, the male data regarding differences in the CIR and ASIR rates did not show any noticeable changes, either increases or decreases, for the period between 2001 and 2013 (Table 2).

Histopathology

The percentages of each thyroid cancer subtype were calculated from the total number of cases in the 2001-2013 period (Figure 9). The most common form of thyroid cancer among men and women was the papillary carcinoma subtype, constituting 80.8% and 87.3% respectively (Figure 9). The follicular carcinoma subtype came second at 4.5% among male cases and 4.8% among female cases. Around 3.3% of male cases and 1.3% of female cases were medullary thyroid carcinoma. Malignant neoplasm was the rarest thyroid cancer subtype, constituting less than 0.4% in both genders (Figure 9).

Between 2001 and 2013, the overall incidence rate of papillary thyroid cancer for both sexes increased by 191% (Figure 10). Also, the percentage of papillary tumours among the various subtypes increased quite significantly – from 82.7% in 2001 to 88% in 2013 of diagnosed cases (Figure 10).

Discussion

Based on CIR and ASIR data for the period between 2001 and 2013, we can clearly state that the incidence of thyroid cancer in the Saudi Arabian population doubled during that period. A variety of possible causes could be linked to the above outcome. The increase in the accessibility of health provider centres equipped with advanced imaging and diagnostic techniques is at the top of the list of causes of the apparent increase in the number of diagnostic thyroid cancer cases. In 2002, the Saudi national health system was established with the aim of providing comprehensive and integrated health care to the Saudi population. So, the number of hospitals that under the Ministry of Health umbrella increased from 189 in 2002 to 268 in 2013 (MOH.).

Iodine deficiency could be another cause of the increase in thyroid cancer incidence. Various studies have found a link between iodine deficit and increases in the number of diagnostic thyroid cancer cases (Zimmermann and Galetti, 2015; Kim et al., 2017). Despite the lack of substantial historical data on iodine deficiency in the Saudi Arabia, several studies have shown that the Saudi population, especially in the southern regions, has a degree of deficit in iodine (Al-Nuaim et al., 1997; Alsanosy et al., 2012; Abbag et al., 2015; Al-Dakheel et al., 2016).

Another possible cause for the increase in thyroid cancer incidence in the last decade is the rapid urbanisation and modernisation due to fast-paced economic development reflected in the lifestyles of Saudi citizens. Rapid urbanisation is usually accompanied by unhealthy dietary practices, consumption of junk food, sedentary lifestyles and obesity (Contaldo et al., 2015), all of which are risk factors for thyroid cancer (Mijovic et al., 2011; Marcello et al., 2014; Ma et al., 2015).

The gender data shows that the rate of thyroid cancer among women is more than three times higher than among men. In females, the age-specific incidence rate rises sharply at the beginning of the reproductive years (15-19) and peaks at 35–39 years (the starting age of the pre-menopausal period). These findings are consistent with various other studies that have focused on gender differences in thyroid cancer (Machens et al., 2006; Rahbari et al., 2010; Hsieh et al., 2012). The female prevalence of thyroid malignancy and the occurrence of its peak rates among pre-menopausal women suggest that female sex hormones may play a role in the enhancement of thyroid tumours. Moreover, there is a well-established connection between thyroid tumours and breast cancer.

Many studies have found that an individual with a history of breast cancer has a higher risk of developing thyroid cancer (Ron et al., 1984; Teppo et al., 1985) and, equally, an increased risk of breast cancer in individuals with a history of thyroid cancer has also been noticed (Teppo et al., 1985; Chen et al., 2001). It has consequently been suggested that breast cancer, which is usually an estrogen-responsive malignancy, and thyroid cancer may share some common etiological factors.

There is a difference in the incidence of thyroid cancer among Saudi females compared to the international ratio.. In 2012, the most recent published report from the International Agency for Research on Cancer, thyroid cancer was the eighth most common cancer among women worldwide, with an ASR of 6.1 (Ferlay et al., 2012), while in Saudi Arabia, it is the second most common cancer among women, with an ASR of 7.5. This indicates that there is an etiological local factor behind this variation. Many studies have linked the deficiency of Vitamin D with cancers (Garland et al., 2006; Holick, 2006; Holick, 2007), especially with thyroid carcinoma (Kim et al., 2014). So, the role of vitamin D deficiency cannot be excluded as a local risk factor behind this increase in the incidence of thyroid carcinoma among Saudi females compared to the global ratio. A recent study has suggested that Saudi females are suffering from a severe deficiency in vitamin D compared to men. That deficiency is due to the lack of exposure to sunlight (Fonseca et al., 1984).

The geographic distribution and changes in the CIRs and ASIRs of thyroid cancer among women in different regions from 2001 to 2013 were observed in this study. The data showed that the Najran region is the only region that saw a noticeable increase in rates of thyroid cancer among females. In contrast, regions like Tabuk and the Northern provinces recorded obvious decreases in rates of thyroid cancer among females. Despite the shortage of published articles discussing the pattern of geographic distribution of thyroid cancer in the Saudi population, this data should form a cornerstone for generating hypotheses about the potential risk factors for thyroid cancer in Saudi Arabia's regions.

In conclusion, thyroid cancer is the second most common cancer among females in Saudi Arabia. The most common age group affected were male and female aged 35–39 years. The incidence of thyroid cancer for both sexes increased during the period from 2001 to 2013. The specific causes of this upward trend are unknown. Nevertheless, several etiological factors have been suggested for that increase. Further clinical and epidemiological research needs to be conducted to illuminate the causes of the large increases and decreases in the incidence of female thyroid cancer in various regions in 2013 compared to 2001.

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