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Original Article

**Trends in Thyroid Cancer Incidence in the Gulf Cooperation Council States: a 15-Year Analysis**

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**Abstract**

**Introduction:** Thyroid cancer is a predominant malignancy in the Gulf Cooperation Council (GCC) states. Explicit regional assessments of incidence are crucial among countries that share similar demographic, cultural, and economic characteristics. This study provides an assessment of trends in thyroid cancer in the GCC over fifteen years.

**Methods:** Data included cases in the GCC, reported to the Gulf Center for Cancer Registration during 1998–2012 (N=10,417). Age-specific rates, age-standardized rates (ASR), and stage at diagnosis are compared between the GCC states during 1998–2002, 2003–2007, and 2008–2012. Standardization of rates was performed using the World Standard Population.

**Results:** Between 1998–2002 and 2008–2012, the frequency of thyroid cancer in the GCC was approximately fourfold higher in females than males. The average ASR increased from 1.8 to 2.4/100,000 for males and 5.7 to 8.4/100,000 for females. Age-specific incidence showed a shift towards a younger age for women and an older age for males. During 1998–2012, the proportion of localized stage at diagnosis ranged from 18% in Oman to 57% in the UAE. The proportion of unknown stage varied considerably among states, ranging from 13% to 64%. Over the study period, the proportion of unknown stage increased in all but two states (Bahrain and Saudi Arabia).

**Conclusion:** The incidence of thyroid cancer in the GCC has generally increased. This could reflect improved testing, leading to enhanced detection and diagnosis of thyroid cancers, as well as a possible increase in exposure to risk factors. Improved ascertainment of stage data is essential to reflect changes in early diagnosis activities.

**Keywords:** Thyroid cancer, Gulf Cooperation Council, Bahrain, Saudi Arabia, Kuwait, Qatar, Oman, United Arab Emirates, incidence, stage

**Introduction**

Thyroid cancer is the most common endocrine cancer. There is a widespread and persistent increase in its incidence, and it is projected to become the fourth-leading type of cancer globally. Information on risk factors are sparse and appear to be complicated and multifactorial. Several factors have been attributed to the increase in occurrence, including ionizing radiation, iodine deficiency and supplementation, as well as increased intake of nitrates, smoking, excessive alcohol, and poor diet. Comorbidities, such as chronic lymphocytic thyroiditis, diabetes, cardiovascular diseases, and viral infections have also been implicated. However, it remains unclear whether this increase in incidence is due to a true increase in the thyroid cancer cases, or merely due to overdiagnosis of small thyroid cancers through improved tests, such as biopsies and imaging.

Thyroid cancer is also predominant in the Gulf Cooperation Council (GCC) states; the Kingdom of Bahrain, the Kingdom of Saudi Arabia (KSA), the State of Kuwait, the State of Qatar, the Sultanate of Oman, and the United Arab Emirates (UAE). During 1998–2002, incidence rates of thyroid cancer were reported to be comparable, or even higher, than those of some developed countries. In 2018, thyroid cancer was the second most prevalent cancer in Saudi Arabia and Kuwait, the third in the UAE and the sixth, seventh and tenth in Oman, Qatar and Bahrain respectively. In addition to their geographic proximity, GCC states share similar demographic, socioeconomic,
cultural, and lifestyle characteristics, where westernization and nutrition transition have been attributed to the increased occurrence of adenocarcinomas, including thyroid cancer.

Regional cancer control and prevention strategies, and ensuing action plans have been developed in the GCC states to provide a comprehensive and coordinated national approach to cancer activities and services. In 1998, the Gulf Centre for Cancer Registration (GCCR) was established in Saudi Arabia, with the goal of maintaining a consistent and reliable database for cancer incidence in the GCC States. Monitoring cancer incidence in the region is crucial for evaluating the impact of primary prevention interventions, such as early detection and screening programs, and aiding the planning and prioritization of resources for cancer control. It can also provide frameworks for updating strategies for cancer prevention and control in the GCC states. Therefore, this study aims to provide an updated assessment of the trends in thyroid cancer incidence in the region, over a 15-year period, using the GCCR database.

**Methods**

Data on all citizens of the GCC diagnosed with thyroid cancer during 1998–2012 were obtained from population-based national cancer registries representing the six GCC states. Data were then verified, assessed for quality control, and aggregated by the GCCR. Data included the year of diagnosis, age, and stage at diagnosis for all GCC nationals (aged 0–99 years) diagnosed with thyroid cancer between 1 January 1998 and 31 December 2012. Thyroid cancer was defined by the International Classification of Diseases for Oncology, third edition (ICD-O-3), topography code C73. Only primary invasive malignancies were included (ICD–0 behavior 3).

Patients were grouped into three consecutive calendar periods (1998–2002, 2003–2007 and 2008–2012). To enable comparisons of incidence rates over time, and between populations of varying age structures, age-standardized rates (ASR) per 100,000 population were calculated. The WHO population structure for developing countries was used for age-standardization of rates, using the direct method. The mid–point population for the three, 5–year cohorts (2000, 2005 and 2010), were obtained from each GCC state’s cancer registry.

Frequency of diagnosed cases, age–specific rates, ASR, and stage at diagnosis are presented for each calendar period and compared between the six GCC states. The average age–specific rates and average ASRs for all the GCC states combined were also estimated. Since Saudi Arabia comprises about 80% of the GCC’s total population, the total ASR for all the GCC states combined was estimated by averaging the individual ASRs for each country. This avoids the estimation of rates being heavily influenced by one country. The stage at diagnosis was based on the Surveillance Epidemiology and End Results (SEER) Summary Stage 2000, which categorizes the extent of the disease as localized, regional (with lymph node involvement, or direct extension, or both) or distant metastasis. Tumors for which the extent of progression was unknown were also included. The ASRs were produced using the Statistical Analysis System (SAS version 9.4, SAS Institute Inc., Cary, NC, USA), and all other analyses were performed using Stata version 15 (StataCorp LLC, College Station, TX).

**Results**

A total of 10,417 thyroid cancer cases were registered among GCC nationals during 1998–2012 (Table 1). The total number of thyroid cancer patients was approximately fourfold higher among females than males (2,180 and 8,237, respectively). Between 1998–2002 and 2008–2012, the total number of cases, and the average ASR for all the GCC states combined, increased for both males and females; the average ASR increased by 33% for males (1.8 to 2.4 per 100,000), and by 47% for females (5.7 to 8.4 per 100,000).

During 2008–2012, the ASR of thyroid cancer for males ranged from 1.4 per 100,000 in the UAE, to 3.3 per 100,000 in Qatar. For females, the ASR ranged from 4.5 per 100,000 in Bahrain to 10.9 per 100,000 in Kuwait (Table 1). The ASR for females steadily increased between 1998–2002 and 2008–2012 in Kuwait, the UAE, and Saudi Arabia, with an increase of 34%, 48%, and 67%, respectively (Figure 1). In Oman, the ASR for females during this period remained relatively stable (8% increase), but declined in Qatar and Bahrain by 29% and 45%, respectively. Among males, the ASR between 1998–2002 and 2008–2012 changed relatively less than that of females, with the highest increase observed for Bahraini males (58%), followed by Saudi males (33%). In Oman, Qatar, and the UAE, the ASR for males remained stable, with changes ranging from 0% to 13%, while rates slightly decreased for Kuwaiti males (–28%).

The GCC’s average age–specific incidence rates peaked at 60–64 years in 1998–2002 and 2003–2007 for both females and males (Figure 2). However, in 2008–2012 the incidence rate peaked at a younger age for females (45–49 years) and an older age for males (65–69 years).

During the 15–year period between 1998 and 2012, the distribution of stage at diagnosis between males and
females within each GCC state appeared relatively similar, with absolute differences ranging from 0% to 15% (Figure 3). The proportion of localized stage at diagnosis varied between states, ranging from 18.2% in Oman to 57.2% in the UAE. Bahrain and Oman had the highest proportion of unknown stage at diagnosis (52% and 64% respectively). Most patients were diagnosed at localized stage, with the highest proportions in the UAE (57%), Qatar (56%), and Saudi Arabia (50%), followed by Kuwait (36%) and Bahrain (30%). The proportions of distant stage at diagnosis were similar among the GCC states, ranging from 4% in Qatar to 7% in Saudi Arabia.

Between 1998–2002 and 2008–2012, the proportion of unknown stage at diagnosis increased in all GCC states, with the exception of Bahrain and Saudi Arabia. The most drastic increase was for Kuwait, where the proportion of unknown stage increased from 4% to 50%. In Saudi Arabia, the proportion of unknown stage declined steadily between 1998–2002 (17%) and 2008–2012 (12%), while there was a more substantial decline in Bahrain, specifically between 2003–2007 and 2008–2012, where the proportion of unknown stage fell from 78% to 9%.

Table 1. Number of cases and age standardized incidence rates (ASR) by country, gender, and calendar period 1998–2012.

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<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
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<td></td>
<td>(n)</td>
<td>ASR</td>
<td>(n)</td>
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<tr>
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<tr>
<td>Qatar</td>
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<td>3.8</td>
<td>43</td>
<td>13.1</td>
</tr>
<tr>
<td>UAE</td>
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<td>1.6</td>
<td>78</td>
<td>6.3</td>
</tr>
<tr>
<td>All GCC States</td>
<td>538</td>
<td>1.8</td>
<td>1,833</td>
<td>5.7</td>
</tr>
</tbody>
</table>

Figure 1. Age-standardized rates (ASR) for thyroid cancer by country, gender, and calendar periods.

Figure 2. The GCC average age-specific incidence rate, by gender and calendar periods.
Between 1998–2002 and 2008–2012, the proportion of localized stage increased from 43% to 54% in Saudi Arabia, 48% to 62% in the UAE, and 12% to 65% in Bahrain. For these states, the proportion of regional and distant stages also decreased accordingly. On the contrary, the proportion of localized stage decreased to varying degrees in Kuwait, Oman, and Qatar. However, between 1998-2002 and 2003-2007 in Oman and Qatar, where the proportion of unknown stage was similar, the proportions of localized stage increased, accompanied by a decrease in regional and distant stages.

**Discussion**

This study presents an updated assessment of trends in thyroid cancer incidence in the Arabian Gulf region, using comprehensive and robust data obtained from national registries over a 15-year period. Explicit regional assessments of incidence are crucial among countries that share similar demographic, cultural, and economic characteristics, and operate under coordinated cancer control and prevention strategies. The results of this study can aid the assessment and application of early detection, as well as facilitate frameworks to control the impacts of cancer in the region.

In the GCC, thyroid cancer was about four times more prevalent in women than men. This gender disparity has been observed in many studies\(^1\), \(^{13-16}\), and could be attributed to estrogen receptor polymorphisms in women\(^17\)-\(^19\). However, the total number of cases, and the average ASR for all the GCC states combined, increased during the 15-year study period (1998 to 2012); albeit slightly more for females than males (47% versus 33%, respectively).

During 1998–2012, the age–specific incidence rates in the GCC also seemed to be shifting towards a younger age for women and an older age for men. In our study, the incidence during 2008–2012 peaked at 45–49 years for females, and 65–69 years for males; a change from a peak at 60–64 years for both sexes during 1998–2007. In the UK between 2006 and 2010, the incidence rate was highest for females aged 40–44 years, while for males it increased steadily with age\(^16\). Our findings also coincide with the USA, where the incidence of thyroid cancer peaks earlier in females, often in their 40s or 50s, than in males who are usually in their 60s or 70s\(^20\).

In comparison to global thyroid cancer rates, the average ASR for the GCC countries combined, during the most recent calendar period in our study (2008–2012), was generally lower than in most westernized countries. For the GCC, the ASR for females was 8.4 per 100,000, which was much lower than that reported for females in 2012 for countries with high thyroid cancer incidence.
Rates, such as Korea (108.1), Cyprus (34.0), Italy (22.6), Canada (20.3), Turkey (22.4), and the USA (18.0); all per 100,000 population. For males, the thyroid ASR in the GCC (2.4 per 100,000) was also lower than reported in those countries, which range from 25.0 per 100,000 in Korea to 6.2 per 100,000 in the USA. The ASR in the GCC was also lower than European countries such as the Netherlands, Denmark, the UK, and Germany, where the ASR ranged from 3.9–5.4 per 100,000 for females, and 1.4–2.1 per 100,000 for males.

Increases in thyroid cancer incidence rates have been reported globally, especially among countries with a high Human Development Index (HDI) such as the GCC states. Among the GCC states, the ASR for females increased between 1998 and 2012 for all countries, with the exception of Oman where the rates were stable, and Bahrain and Qatar where the incidence rates declined. For Oman, a recent study reported an increase in incidence rates for females between 2008 and 2015. For Qatar, a substantial decrease in ASR for females was observed.
only between 1998–2002 (13.1 per 100,000) and 2003–2007 (9.2 per 100,000), while it remained stable between 2003–2007 and 2008–2012 (9.2 and 9.3 per 100,000, respectively). Further monitoring is therefore required to observe whether the rates in Qatar change in the subsequent years. For Bahraini females, the ASR declined substantially between 2003–2007 and 2008–2012, where the ASR was almost halved (7.6 and 4.5 per 100,000, respectively). This decline could be attributed to possible changes in the process of registration and abstraction of cancer data in Bahrain, that is evidenced by a drastic decrease in the total proportion of unknown stage at diagnosis that fell from 78% in 2003–2007, to as low as 9% in 2008–2012.

Decreases in the ASR could also be attributed to changes in clinical practice guidelines. Between 2009 and 2016 in the USA, thyroid cancer incidence rates reached a plateau, and a possible decline was also indicated\textsuperscript{39}. The most plausible cause for this decline could be the implementation of the 2009 American Thyroid Association guidelines limiting the indications for fine-needle aspiration (FNA) of thyroid nodules\textsuperscript{36}. Subsequently, stricter guidelines were introduced in 2015\textsuperscript{27}, as well as recommendations against screening for thyroid cancer by the US Preventive Services Task Force in 2017\textsuperscript{28}. In South Korea, the incidence of thyroid cancer has increased 15-fold between 1993 and 2011, due to the widespread practice of screening asymptomatic people using thyroid ultrasound\textsuperscript{29}. However, the incidence of thyroid cancer in South Korea started to decline in 2014 due to curtailed screening practices and increased awareness among physicians and the public of the “over–diagnosis” phenomena. This refers to the diagnosis of cancers that are either non-growing, or so slow-growing that they would never lead to symptoms or death in the patient’s lifetime\textsuperscript{29}. Therefore, since incidence rates in the GCC are generally increasing, adapting such conservative guidelines, with the emphasis on avoiding “over–diagnosis” that does not ultimately coincide with decreased metastatic cancer incidence or mortality rates, could aid in driving these rising incidence rates down.

While the global rise in incidence is still controversial, it has been primarily attributed to the over–diagnosis of early tumors\textsuperscript{1, 30, 31}. Recent epidemiological reviews also emphasize the role of modifiable individual risk factors, such as obesity and increased exposure to environmental risk factors such as iodine levels and radiation\textsuperscript{2–25}. In the USA, more than 40% of the thyroid cancers diagnosed between 1992 and 2016 were attributed to factors such as obesity and cigarette smoking\textsuperscript{25}. Obesity in the GCC is a significant epidemic\textsuperscript{32}, and cigarette smoking is also a public health concern\textsuperscript{33} that is associated with an individual’s personal and social context, including their family, peers, and community. Thus, interventions targeting these risk factors are critical and could assist in slowing these escalating rates. Further studies should also assess the exposure of radiation in the GCC, a crucial factor in the etiology of thyroid cancer\textsuperscript{2, 3, 20}.

During the 15–year period, the proportion of unknown, or missing stage at diagnosis was similar between males and females. However, it varied considerably among the GCC countries, ranging from 13% to 30% in the UAE, Saudi Arabia, Qatar, and Kuwait, and over 50% in Bahrain and Oman. This consequently hindered comprehensive stage comparisons between these states. If we assume, however, that stage data in these GCC states were missing at random, the lowest proportion of unknown stage, reported among the GCC states during 1998–2012 in our study, was much higher than that in the USA during 1974–2013, where the same SEER Summary Stage classification system was used (13.4% in the UAE compared to 2.4% in the USA\textsuperscript{34}).

The proportion of unknown stage also increased unpredictably in all GCC states between 1998 and 2012, with the exception of Bahrain and Saudi Arabia. The proportion of unknown stage also increased in Kuwait, Oman, and the UAE for cervical cancer during the same period\textsuperscript{35} and for 18 other tumors in Kuwait between 2000 and 2013\textsuperscript{36}. This suggests that the variable increase in unknown stage could be related to the states’ overall system of staging, abstraction, and registration of cancer cases, that is not exclusive to thyroid cancer. Increased travel abroad for staging and treatment of cancer, following the patients’ initial diagnosis, was also reported as a plausible cause\textsuperscript{35, 36}. Traveling abroad for treatment is a service provided by most GCC states to their citizens, where the full cost of treatment is generally covered. For states where many cancer patients utilize this option for cancer treatment, extra efforts and regulations should be placed to ensure completeness of stage information, as monitoring the stage at diagnosis can provide a useful assessment of cancer control strategies.

Identifying changes in the localized stage at diagnosis over time can provide a useful assessment of the region’s early detection activities. Between 1998 and 2012 in Saudi Arabia, the UAE and Bahrain, the proportion of localized stage increased, while the proportion of regional and distant stages dropped. In Kuwait, Oman, and Qatar, the proportion of localized stage decreased over the 15 years, however, an increase was observed in Oman and Qatar between calendar periods where the proportions of unknown stage were similar (1998–2002 and 2003–2007). This, therefore, indicates that the decline in localized stage within the GCC states could
principally be due to the increased proportion of unknown stages, between the calendar periods. Diagnosis of more patients at localized stage in the GCC could suggest that increased detection may have played an essential role in the increasing incidence trend observed in this study. Increases in incidence rates are also primarily driven by papillary thyroid cancer\textsuperscript{1, 23}, which generally has a good prognosis\textsuperscript{37}. Thus, further studies are also required to assess changes in the tumor’s histological characteristics to assess whether there are changes in the diagnosis of more aggressive or fatal tumors over time in the GCC.

Only GCC citizens were included in this study since data on non–citizens were not available from all the GCC states. Non–citizens account for almost half of the GCC population, and while the majority are on short–term, two–year contracts and, therefore possibly exposed to different risk factors than those residing long–term in the country, their inclusion is critical for planning the provision of cancer–care services in the country.

Conclusion

The incidence of thyroid cancer in the GCC has generally increased in males and females, while the age at diagnosis seems to have shifted to a younger age for women and an older age for males. Changes in age–standardized incidence rates in the region could reflect improved testing, such as the growing use of biopsies and diagnostic imaging, which leads to enhanced detection and diagnosis of thyroid cancers, as well as a possible increase in exposure to risk factors. More assessments are required to determine the underlying causes of the changes in incidence, and further surveillance is also needed to assess whether changes in clinical practices and awareness could initiate a decline in thyroid cancer rates, as observed in some westernized countries. This can be supported by continued assessments of changes in the distribution of stage at diagnosis that reflect early diagnosis activities, thus highlighting the importance of ensuring complete ascertainment of stage information.

Acknowledgment

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