
ABSTRACT

Background: No population-based data on thyroid cancer exist in Saudi Arabia. This is the first study describing thyroid cancer incidence in the Eastern Region. Methods: Population-based registrars in 1987 and 1988, was obtained from all health facilities in the eastern region. Population census available. Data on cancer death were obtained from death registries. Data on thyroid cancer was: relative frequency rate, crude incidence rate, age specific incidence rate, age standardized incidence rate, standard world population, and relative age standardized incidence rate. Results: Sixty-four cancer were registered in 1987 & 1988. Relative frequency rate of thyroid cancer among Saudi females, 7.1%, was significantly lower than that of Saudi males, 13.3%. Mean age of Saudi females in years, 49, was lower than that of Saudi males, 56.1. Age standardized incidence rate/100,000 population per year in females was significantly higher than that in Saudi males, 1.8, and occupied the 23rd highest rank on the international scale. Conclusions: Thyroid cancer in the Eastern Region of Saudi Arabia, frequency rate, age standardized incidence rate and relative age standardized incidence rate, particularly for females.

Keywords: Cancer epidemiology, thyroid cancer; tumor registry, Saudi Arabia.

Thyroid cancer accounts for 1.1% of all new malignancies diagnosed yearly in USA. Although the average annual age standardized incidence rate in USA is about 4.0 per 100,000 population, only 1000 patients die each year from all types of thyroid cancer. This means that only ten percent of thyroid cancer patients die from the disease, given that the USA population is about 250 million. Hence, the disease has a favorable prognosis, especially the papillary type and the clinical presentation is much less frequent than autopsy findings of occult papillary cancer. It has been estimated that ten million Americans have occult thyroid cancer and its prevalence rates are 28% in Japan, 24% in Hawaii and 6% in Canada. The incidence of thyroid cancer shows striking differences among different age groups, genders, ethnic backgrounds and geographical locations. It is more common among women below the age of 45 years and fewer blacks are affected than whites. The highest incidence rates have been reported from Hawaii, California, Saskatchewan (Canada), Iceland and New Zealand. In the Middle East, the incidence of thyroid cancer shows the same variation. In Saudi Arabia, the real incidence of thyroid cancer has yet to be established. The frequency rate of thyroid cancer among all malignancies reported to the Specialist Hospital and Research Center (KFSH&RC) tumor registry was 5.7% among females, occuping the 16th highest rank on the international scale. This shows that thyroid cancer morbidity is significant in Saudi Arabia. The same center has shown in a separate study that thyroid cancer morbidity is higher in females, after breast cancer, with a frequency rate of 7.5%.

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Table 1 - Comparison of the mean age (±SD) of patients with thyroid cancer among Saudis and non-Saudis in either gender Eastern Region, Kingdom of Saudi Arabia, 1987-1988. (N=67)

<table>
<thead>
<tr>
<th></th>
<th>Saudi</th>
<th>Non-Saudi</th>
<th>Total</th>
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<tbody>
<tr>
<td>Males</td>
<td>61.1±22.9*</td>
<td>39.5±8.6*</td>
<td>49.3±19.5**</td>
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<td></td>
<td>(9)</td>
<td>(11)</td>
<td>(20)</td>
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<tr>
<td>Females</td>
<td>40.1±13.9*</td>
<td>37.1±10.2</td>
<td>39.3±13.0**</td>
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<td>(34)</td>
<td>(13)</td>
<td>(47)</td>
</tr>
<tr>
<td>Both</td>
<td>44.5±18.1</td>
<td>38.2±9.4</td>
<td>42.3±15.8</td>
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<td>(43)</td>
<td>(24)</td>
<td>(67)</td>
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**(p<0.01)**, (p<0.001)**, ***(p<0.05) \( (\text{number of cases})

hospital statistics and reported as relative frequency rates. While such data provide valuable information, they cannot be used for inference on the incidence rate of this disease in the Kingdom as they are influenced by the known bias of hospital-based studies. Moreover, no population-based data on the incidence rates of this disease exist in the eastern or other regions of Saudi Arabia. It is important, therefore, to have baseline data on the true incidence of thyroid cancer from this region for future comparison with those from other regions within the Kingdom, when available, and with published information from neighboring countries and/or other regions of the world.

In this article, we provide an analysis of population-based tumor registry data on thyroid cancer obtained from the tumor registry of the Eastern Region of Saudi Arabia between January 1st, 1987 and December 31st, 1988.

Materials and methods In 1985 a computerized tumor registry system was designed and became fully operational in 1987. Basic data for all cancer sites were obtained from all health facilities throughout the Eastern Region. All from available hospital-based data in Saudi Arabia. The crude incidence rate/100,000 population/year was computed by dividing the average yearly frequency of thyroid cancer by the corresponding population, and multiplying the quotient by a base of 100,000. The age specific incidence rates were calculated by dividing the average annual number of cases in each five year age interval, by the population at risk, in the same interval, and multiplying the quotient by a base of 100,000. To allow for international comparisons, the crude incidence rates were standardized for age in order to adjust for the differences in the population structure. Thus, the age standardized world incidence rates were computed by the direct standardization method, using the standard world population as described by Smith, and the age specific incidence rates of our registry. This rate standardization removes the confounding effect of age on the incidence rates of cancer. The Relative Age Standardized Rate is defined as the percent age standardized incidence rate of each type of cancer relative to the overall age standardized incidence rate of all cancer sites, excluding skin cancers (ICD-9: 173). This relative age standardized incidence rate was also calculated to allow for comparison of the relative burden of each type of cancer among different population-based cancer registries.

The means of continuous variable in categorized groups were compared using two-tailed Student-t test. Categorical data were analyzed by Chi-Square test. Rates were compared by z-test for the difference between two proportions. All data analysis was carried out using the Epi-Info and Statgraphics Software Statistical Packages.

Table 2 - Comparison of the different morphologic types of thyroid cancer between the Eastern Region (ER) and King Faisal Specialist Hospital (KFSH&RC) clinics.
**Results**  A total of 67 patients with thyroid cancer were identified during the two-year study period. Of these, 64% were Saudis and 70% were females. The male:female ratio among Saudis, 1:3.8, was significantly (p<0.05) lower than among non-Saudis, 1:1.2. The difference is still large after taking into account the corresponding population male:female ratio among Saudis and non-Sauds, which is respectively 1:1 and 1.9:1. The overall relative frequency rate was 4.3% among 1559 malignancies of all sites captured in the Eastern Region during the same period. The relative frequency rate for Saudi females, 7.1%, was significantly (p 0.001) higher than that for Saudi males, 1.3%. Similarly, the relative frequency rate for non-Saudi females, 9.3%, was higher than that of non-Saudi males, 4.1%, but the difference was not statistically significant (p >0.05). The crude incidence rate was 0.8/100,000 population/year for Saudi males, and 3.1 for Saudi females. The corresponding crude incidence rates among non-Saudi males and females were, respectively, 3.1 and 6.8/100,000 population/year. When the incidence rates were adjusted according to the world standard population (age standardized incidence rate) and the relative age standardized incidence rates were computed, thyroid cancer ranked fourth, 5.8%, among all cancer sites in Saudi females, and eighth, 5.2% among non-Saudi females. The relative age standardized incidence rates for Saudi males, 1.4%, and non-Saudi males, 1.5%, were low, and the disease was not among the top ten cancer sites in either of the two groups. All the five rates relative frequency rate, crude incidence rate, age standardized incidence rate, relative age standardized incidence rate and age specific incidence rates were consistently lower among Saudi males, compared to Saudi females, except for the age specific incidence rate of the age interval (65+).

The mean age (±SD) of the 67 patients was 42.3±15.8 years, with a median of 38 years. The mean age of Saudi males, 61.1±22.9 years, was significantly (p<0.05) higher than that of Saudi
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females, 40.1±13.9 years. This significant difference was not observed between non-Saudis males, 39.5±8.6 and females, 37.1±0.2. The mean age of Saudi males was, however, statistically significantly higher (p<0.05), than that of females, Table 1.

In order to study the trend of the incidence of thyroid cancer with age among Saudis, the age specific incidence rates were recalculated by ten-year age intervals due to the small number of cases. The age intervals started at 20 years and ended at 60 years and above. Comparison of the trend of the age specific incidence rate among Saudi males and females revealed a peculiar pattern, as shown in Figure 1. The rates among males were very low until the age of 40 years after which they showed a marked increase. In contrast, the rates among females were higher than those of males and they steadily increased until the age of 40 years after which they started to decline. At the age of 60 years and above, the age specific incidence rate of thyroid cancer among males, as was even higher than that among females, but the difference was not statistically significant.

Comparison of the different morphologic types of thyroid cancer in all nationalities, between the Eastern Region tumor registry and King Faisal Specialist Hospital and Research Center tumor registry, showed no significant differences, table 2. However, the relative frequency rate of thyroid cancer was significantly (p<0.05) higher in King Faisal Specialist Hospital tumor registry.

In Tables 3 and 4, the age specific incidence rates, crude incidence rates, age standardized incidence rates and relative age standardized incidence rates of thyroid cancer captured by our registry, among Saudi males and females, are compared with those of international population-based registries.

Comparisons of our figures with the international rates showed that the risk of thyroid cancer was relatively high among Saudi males and females. For males, the lowest age standardized incidence rate, 0.0, was reported by Netherlands tumor registry (Antilles less Aruba). The second lowest, 0.3, was from Spain tumor registry (Navarra). The highest age standardized

Table 4 - Comparison of age specific incidence rate (ASpR), crude incidence rate (CIR), age standardized incidence rate (ASR), and relative age standardized incidence rate (%ASR) of thyroid cancer (ICD-9-193) among Saudi and Non-Saudi females in the Eastern Region of Saudi Arabia with those of Kuwait and countries with the lowest and the highest ASR of thyroid cancer*.

<table>
<thead>
<tr>
<th>Registry</th>
<th>Freq*</th>
<th>0-5</th>
<th>10-15</th>
<th>20-25</th>
<th>30-35</th>
<th>40-45</th>
<th>50-55</th>
<th>60-65</th>
<th>CIR</th>
<th>ASR</th>
<th>%ASR</th>
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<tr>
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<td>1987-88</td>
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<tr>
<td>Saudi</td>
<td>34</td>
<td>.</td>
<td>.</td>
<td>2.9</td>
<td>5.4</td>
<td>9.5</td>
<td>7.8</td>
<td>8.5</td>
<td>24.3</td>
<td>14.0</td>
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<td>Non-Saudi</td>
<td>13</td>
<td>.</td>
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<td>6.2</td>
<td>7.5</td>
<td>19.4</td>
<td>6.8</td>
<td>12.4</td>
<td>22.2</td>
<td>90.9</td>
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<td>1979-82</td>
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<tr>
<td>Kuwaiti**</td>
<td>44</td>
<td>.</td>
<td>.</td>
<td>2.4</td>
<td>3.7</td>
<td>10.0</td>
<td>7.4</td>
<td>9.2</td>
<td>4.7</td>
<td>9.6</td>
<td>20.6</td>
</tr>
<tr>
<td>USA, Hawaii, Chinese: 1978-82**</td>
<td>56</td>
<td>.</td>
<td>.</td>
<td>2.9</td>
<td>9.6</td>
<td>21.0</td>
<td>20.7</td>
<td>26.5</td>
<td>25.8</td>
<td>24.9</td>
<td>69.1</td>
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<td>Spain, Navarra: 1978-82**</td>
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* Excluding tumor registries with no reported cases ** Source: Cancer incidence in five continents

**Source: Cancer incidence in five continents**

Position of the age standardized incidence rate (ASR) of thyroid cancer for female Saudis, Eastern Region, Kingdom of Saudi Arabia (1987-88) on the scale of thyroid cancer ASR of different international tumor registries*.
incidence rate, 8.8, was reported by USA, Hawaii (Chinese) tumor registry, table 3. Saudi males' age standardized incidence rate, 1.8, lies between the median, 1.3, and the third quartile, 1.9, on the international scale of thyroid cancer age standardized incidence rate for males.

For Saudi females, the age standardized incidence rate, 5.6, lies above the third quartile, 5.0, of age standardized incidence rate reported by international registries. In fact, it occupies the 23rd highest rank on the international scale of age standardized incidence rates among females, constructed from the rates reported by 137 population-based tumor registries, as shown in Table 4.

The position of the relative age standardized rates of Saudi males and females, on the international scale of thyroid cancer was also studied. It was found that both occupy a very high rank on this scale, eleventh highest for males and sixth highest for females.

Thyroid cancer claimed two of the 200 cancer deaths among male Saudis in the Eastern Region in 1987 and 1988, corresponding to relative frequency rate of cancer deaths of 1.0% and a mortality over morbidity ratio of 2.9 or 22.2%. However, no death due to thyroid cancer among female Saudis was reported during the same period.

**Discussion** It has been claimed that Saudi Arabia is "a medium risk area for thyroid cancer." Data from our registry have shown that the risk of thyroid cancer is high, especially among females. The female preponderance of thyroid cancer is a well known and established fact. In Saudi Arabia, a similar pattern was reported from Riyadh by Johansen and Woodhouse who had also reported a significantly higher age among males (58 years) compared to females (38 years), similar to our findings in this study. More recently, a female to male ratio of 2.5:1 has been reported in Riyadh. The increasing trend of age specific incidence rates with age, observed among Saudi males, was similarly seen in the tumor registry of Kuwait and the USA registry in Hawaii among Chinese, Table 3. For females, the trend of age specific incidence rates with advancing age, observed in our registry, is similar to that of Kuwait registry and the USA registry in Hawaii among Filipinos. However, the peak in these registries is at a later age (50-55) than that of our registry (45-50), as shown in Table 4. The pattern of the age distribution of thyroid cancer among Saudi females of our registry is compatible with the reported age peak of 30-50 years. The trends among Saudi males and females also give support to the etiological hypotheses of thyroid cancer, Figure 1. The increasing trend among Saudi females until the age of (40-50), observed in Table 4, supports the theory of the effect of the extra load of repeated pregnancies on the thyroid. It might be postulated that the increasing trend among males after the age of 40 years could be related to exposure to environmental factors, particularly exposure to radiation. A strong link between external radiation and benign as well as malignant thyroid tumors has been established by cohort and case-control studies.

It has been reported that approximately 50-80% of all observed thyroid malignancies were papillary thyroid carcinoma and that they constituted 90% of the radiation-induced thyroid cancers. In the past, particularly in Europe and other parts of the world where iodine deficiency was endemic, a substantially large proportion of thyroid cancer was anaplastic. With the supplementation of table salt with iodine, a gradual shift to more papillary thyroid carcinoma was observed. Papillary carcinoma has been related to increased iodine intake, while thyroid nodules and follicular cancer were more frequently associated with low iodine intake. However, the relationship between dietary factors and thyroid cancer has been recently questioned.

In our series, 61% of all thyroid cancer cases were papillary type and 16% follicular, Table 2. These figures are slightly different from those of KFSH&RC, which were respectively 69% and 10%, but the difference is not statistically significant (p>0.05). Comparison with more recent data from KFSH&RC revealed a more prominent difference, where the percentages of papillary and follicular types were respectively 79.3% and 4.3%. The difference was even more striking when our figures were compared with those reported from the Saudi Arabian Armed Forces. Their figures for papillary and follicular types were 84% and 5% respectively, statistically significantly different from our figures (X² df=2 17.2486, p<0.0001). These two last centers
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are national referral centers located in the central region of the Kingdom where iodine deficiency is more probable than our coastal catchment area in the Eastern Region. This would have led to more papillary carcinoma in our series, but the opposite was observed. This paradox might be due to the fact that KFSH&RC and the Armed Forces Hospital are referral centers receiving cases from various regions of the Kingdom which might have affected the ratio of the various morphologic types. Moreover, differences in the application of the methods of classification of thyroid cancer might lead to some conflicting figures across various studies.10

Comparison of rates from the present study with international ones revealed that the relative position of our age standardized rates on the international scale of thyroid cancer is very high. This observed high risk based on age standardized rate as an indicator, is more reliable and factual than using the relative frequency rate. Our relative frequency rate of thyroid cancer among males was very low, 1.3%, with a very low ranking order as a site of cancer morbidity. However, after age standardization, the relative age standardized incidence rate of thyroid cancer in Saudi males, 1.4%, occupied the eleventh highest position among males on the international scale. The situation is even more serious for Saudi females whose relative age standardized incidence rate, 5.8%, occupied the sixth highest position among females on the international scale. Considering the absolute risk of thyroid cancer, the age standardized incidence rate of Saudi males, 1.8, comes above the median on the international scale. The risk is much higher among Saudi females whose age standardized incidence rate, 5.6, occupies the 23rd highest rank among thyroid cancer age standardized incidence rates for females reported from 137 international registries.13 The problem is even more apparent in our neighboring country, Kuwait, where Kuwaiti females relative age standardized incidence rate, 8.8%, had the second highest rank, and age standardized incidence rate, 6.3, had the tenth highest rank among females on the corresponding international scales.

It is interesting to notice that Asians and particularly Filipinos, in the tumor registries of the coastal regions of USA (Los Angeles, Hawaii, Detroit), occupied the highest ranks of thyroid cancer age standardized incidence rate and relative age standardized incidence rate for both genders. The age standardized incidence rates of thyroid cancer among migrant Filipinos in USA are even higher than those reported by the Philippines tumor registry.13 The common feature among all these is probably the high intake of iodine due to excessive fish consumption. Epidemiologic studies have shown an association between seafood consumption and risk of thyroid cancer.25 Migrants’ studies are needed to disentangle the effects of genetic and environmental factors on the occurrence of thyroid cancer. Also, larger epidemiological studies on thyroid cancer among Asians, especially Filipinos, in Saudi Arabia would help to elucidate these findings.

To conclude, all indicators of cancer incidence point to relatively high incidence rates of thyroid cancer in the Eastern Region of Saudi Arabia compared to other countries, especially among females. The burden of the problem is increased by its occurrence in the young productive age groups, peaking at the third and fourth decades of life. Although a sizable proportion of thyroid cancer cases are differentiated and potentially curable, the cost of therapy and the effects on the quality of life could be enormous. The identification of risk factors associated with thyroid cancer might help in the prevention of this disease.

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References


