Incidence of thyroid cancer in the Kingdom of Saudi Arabia, 2000–2010

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BACKGROUND: Thyroid cancer is the second most common malignancy among females at King Faisal Specialist Hospital and Research Centre (KFSH&RC) and in Saudi Arabia, accounting for about 11% of all newly diagnosed female cancers in the country in 2008. Over the past several decades, an increasing incidence of thyroid cancer has been reported in the Kingdom of Saudi Arabia. There are no comprehensive clinical epidemiological data for the trends of thyroid cancer incidence compared to the global incidence. This report reviews the thyroid cancer incidence in KFSH&RC and compares that with Saudi Arabia, the Gulf region, North America and globally from 2000 to 2010.

METHODS: Retrospective review of patients with thyroid cancer was carried out from 2000 to 2010, using the hospital Tumor Registry program as per the American College of Surgeons standards. Trends and patterns of all well-known prognostic factors were sub-stratified by age, stage and grade.

RESULTS: A total of 2292 patients with thyroid cancer were treated at KFSH&RC, Riyadh, Saudi Arabia, from 2000 to 2010. Thyroid cancer constitutes about 9% of all malignancies and 12% of all female malignancies at KFSH&RC, which are significantly higher compared to the USA, where thyroid cancer represents only 2.9% of all malignancies and 4.6% of all female malignancies. Papillary adenocarcinoma was the most common histological subtype followed by papillary carcinoma, follicular variant. Median age at diagnosis was 40 for females and 44 years for males. Overall Age-Standardized Incidence Rate (ASR) was 4.4/100,000 (6.8 for female and 2/100,000 for males) in the Kingdom in 2008. Median age at diagnosis was 38 years and the highest incidence was in the 30–39 year age group in KFSH&RC. About 48% of patients presented in the localized stage and 60% underwent combined modality treatment consisting of surgery, radiation and hormonal therapy. There was significantly increased incidence among females as compared to males. The age-adjusted thyroid cancer incidence rates from 2000 to 2010 varied three-fold more for females than for males. Considerable geographical variations were present in thyroid cancer incidence in Saudi Arabia.

CONCLUSION: Thyroid cancer incidence rates have increased exponentially between 2000 and 2010 and there is significant geographical variation in the incidence of thyroid cancer throughout the Kingdom. Thyroid cancer has become the second most common cancer among young Saudi women with a male to female ratio at 0.3:1. Rising incidence of thyroid cancer in Saudi Arabia may be due to the increased detection and diagnosis of the thyroid cancers and not only an increase in the true occurrence of thyroid cancer. More studies are required to determine this significant difference at the molecular level.
Thyroid cancer is the second most common malignancy among women in King Faisal Specialist Hospital & Research Centre (KFSH&RC). It encompasses 8.8% of all malignancies and 12% of female malignant cancers. Thyroid cancer is significantly less common among males with a male to female ratio of 0.3:1.

According to the 2008 Saudi Cancer Registry report, there were a total of 727 cases of thyroid cancers; 606 among Saudis and 121 among non-Saudis. Among Saudis, thyroid cancer accounted for 6.8% of all newly diagnosed cases that year. This cancer was ranked the second most common cancer among females, and thirteenth among males affecting 131 (21.6%) males and 475 (78.4%) females. The male to female ratio was 28:100. The overall ASR was 4.4/100,000 (2/100,000 for males and 6.8/100,000 for females). The five regions with the highest ASR were Tabuk (6/100,000), the Eastern Region (5.9/100,000), Riyadh (5.8/100,000), Qassim (5.7/100,000), and the Northern Region (4.9/100,000).

The age distribution of thyroid cancer differs from most other cancers, with thyroid malignancies occurring at an earlier age. The median age at diagnosis was 44 years among males and 40 years among females. The most common histological type of thyroid cancer was papillary adenocarcinoma.

At the regional level, thyroid cancer is the fifth most common cancer in Gulf Cooperation Council (GCC) countries. A total of 5587 cases (5.9%) were diagnosed between 1998 and 2007. The overall ASR was 1.8 and 5.9 per 100,000 for males and females respectively. Thyroid cancer has a significantly higher incident rate among females in all GCC countries and is the second most common malignancy among women. Qatari women have the highest incidence of thyroid cancer (ASR 10.9/100,000). Incidence of thyroid cancer continues to increase in GCC countries with a 24% increase in males and a 63% increase among females over the ten year period.

In the United States, thyroid cancer constitutes 2.9% of all cancer cases and 4.6% of all female malignancies, making it the fifth most common cancer among females. In 2012, it was estimated that a total of 56,460 new cases (77% among females and 17% in males) and 1780 deaths will occur due to thyroid cancer. The incidence rate has been increasing significantly since the mid-1990s and has become the fastest increasing cancer in males and females.

In Europe, it was estimated that there will be 24,800 new cases of thyroid cancer and approximately 3890 deaths among women and 2103 among men due to thyroid cancer in 2007. Worldwide, thyroid cancer is the ninth most common cancer among females with an estimated incidence of 163,968 new cases and 24,177 deaths among women in 2008. The global ASR for thyroid cancer among females is 4.6/100,000.

### RESULTS

In the Kingdom of Saudi Arabia, thyroid cancer is the second most frequent cancer among females after breast cancer with a male to female ratio of 28:100, with significant prevalence among females. Thyroid cancer patients treated at the KFSH&RC from 2000 to 2010 comprised 76.3% females and 23.7% males.

#### Histopathology

At KFSH&RC, histopathological confirmation revealed 72% papillary adenocarcinoma and 13.6% mixed papillary and follicular carcinoma, 2.1% papillary microcarcinoma, 1.2% papillary carcinoma columnar cell, and 0.7% papillary carcinoma encapsulated (Table 1). In comparison, most of the patients in Saudi Arabia were histopathologically confirmed papillary adenocarcinoma (58%), as per the Saudi Cancer Registry, 2008 Cancer Incidence Report.

#### Age

The highest incidence of thyroid cancer was between 30–39 years of age and the median age of thyroid cancer patients was 38 years, as shown in Table 2. From 1975 to 2010, patients aged 15–39 years at
diagnosis contributed a substantial proportion of thyroid cancers to about 50% of all thyroid cancer cases. The highest incidence of thyroid cancer was in the 30–39 year age group (Figure 3). In comparison, the average age group for developing any cancer in Saudi Arabia was 45–59 years. However, thyroid cancer has struck males and females at a significantly younger age group: between the ages of 35 and 45 years. The median age for thyroid cancer patients in Saudi Arabia is 40 years among females and 44 years among males (Figure 2).

Stage
All thyroid cancers were staged according to the International Union Against Cancer (UICC), TNM staging and American Joint Commission on Cancer (AJCC) system. Most patients in Saudi Arabia presented in the localized/regional stage of thyroid cancer as shown in Figure 4. In KFSH&RC, between 2000 and 2010, the majority of the thyroid cancer patients (48%) were diagnosed in localized stage, as shown in Table 3. However, from 1975 to 2010, about 40.5% of thyroid cancers were diagnosed in

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**Figure 1.** Global incidence of thyroid cancer among females (courtesy of GLOBOCAN 2008, IARC, WHO).

**Table 1.** Histopathological distribution of thyroid cancers in KFSH&RC.

| Pathology                        | Total |  | Females |  | Males |  |
|----------------------------------|-------|  |---------|  |-------|  |
|                                  | n     | % | n       | % | n     | % |
| Papillary carcinoma              | 2063  | 90.01 | 1600 | 91.54 | 463 | 85.12 |
| Follicular carcinoma             | 117   | 5.1 | 85 | 4.86 | 32 | 5.88 |
| Follicular adenocarcinoma NOS    | 73    | 3.18 | 52 | 2.97 | 21 | 3.86 |
| Oncytic adenocarcinoma           | 32    | 1.40 | 21 | 1.20 | 11 | 2.02 |
| Follicular carcinoma minimal invasive | 12    | 0.52 | 12 | 0.69 | 0 | 0 |
| Medullary carcinoma NOS          | 52    | 2.27 | 28 | 1.6 | 24 | 4.41 |
| Carcinoma anaplastic NOS         | 33    | 1.44 | 19 | 1.09 | 14 | 2.57 |
| Others                           | 27    | 1.18 | 16 | 0.92 | 11 | 2.02 |
| Carcinoma NOS                    | 8     | 0.35 | 4 | 0.23 | 4 | 0.74 |
| Carcinoma undifferentiated NOS   | 3     | 0.13 | 1 | 0.06 | 2 | 0.37 |
| Neoplasm malignant               | 2     | 0.09 | 2 | 0.11 | 0 | 0.00 |
| Non encapsulated sclerosing carcinoma | 2    | 0.09 | 1 | 0.06 | 1 | 0.18 |
| Adenocarcinoma NOS               | 1     | 0.04 | 0 | 0.00 | 1 | 0.18 |
| All others                        | 11    | 0.48 | 8 | 0.46 | 3 | 0.55 |
| Total                            | 2292  | 100% | 1748 | 100% | 544 | 100% |
localized stage and 39.7% were diagnosed in regional stage (Figure 5).

**Treatment**

About 60% patients received multimodality treatment consisting of surgery, combined with radiation and hormonal therapy. A combination of surgery and hormonal therapy was administered to about 22.8% and surgery alone was given to 7% of the patients. Surgery and radiation therapy combination was given to 5.3% of the patients compared to radiotherapy alone that was given to only 0.8% of the patients. A summary of treatment is presented in Table 4.

**DISCUSSION**

Thyroid cancer constitutes more than 90% of tumors of the endocrine system. There are several subtypes of thyroid cancers based upon histological characteristics, molecular and clinical features. Prognosis of thy-
Thyroid cancer varies widely from a five year survival rate of >98% for differentiated thyroid cancer to a four month median survival for anaplastic thyroid cancer. High vascularity, oncogenic mutations in the RAS, RAF and MEK pathway and oncogenicity by RET gene have resulted in multitarget inhibitors for various histological subtypes of thyroid cancers. Thyroid cancers in the Middle East are unique on a molecular level, particularly an increased amplification of the PIK3CA gene.

The incidence of thyroid cancer has increased significantly around the world. The rate increased from 3.6/100,000 in 1973 to 8.7/100,000 in 2002, without any change in the mortality rate. There were dramatic changes in the thyroid cancer incidence rates between 1973 and 1977 and between 1998 and 2002 from countries all around the globe. Thyroid cancer contributed 8.8% of all cancers diagnosed at KFSH&RC during 2010, which was significantly higher than the proportion in the United States (2.9%). The rate for females was at least three times as high as those for males and patients 30–39 years of age at diagnosis who contributed the largest proportion of cases, with 55% of all the cases below the age of 39 years. Papillary adenocarcinomas accounted for 72 of all thyroid cancers.

There is global difference in the incidence of thyroid cancer. In the US, thyroid cancer is the fifth most common cancer among women, while in Saudi Arabia, it is the second most common cancer among women. Risk factors include being female, history of goiter, family history of thyroid cancer, radiation exposure, certain genetic diseases, low dietary intake of iodine, overweight, environmental radiation, increased imaging or high levels of leptin in the body.

Thyroid cancer is a significant health care burden for the Kingdom of Saudi Arabia, prevalent in every region and encompassing each age group in the country. Exacerbated by western lifestyles and rapid urbanization due to major economic development in the country, the health care burden will continue to increase exponentially as social and cultural norms change. With no screening guidelines or well-defined screening method for early detection of thyroid cancer in the Kingdom, patients are generally detected in the later stages of the disease.
There are several possible explanations as to why thyroid cancer is significantly more frequent among women in Saudi Arabia compared to other countries around the world. The first possibility is iodine deficiency. It has been noticed that thyroid cancer is less frequently diagnosed in the US than in countries where iodine is not part of the diet. Iodine deficiency and endemic goiters are associated with increased risk of follicular thyroid cancer. Despite the lack of substantial data on iodine deficiency in the Arabian Peninsula, the existing research shows that Saudi Arabia has a slight amount of iodine deficiency, particularly in the south. Radiaton exposure, especially during childhood, is a significant risk factor for differentiated papillary carcinoma; radioactive fallout, depleted uranium, nuclear testing and the Chernobyl disaster are some of the well-known risk factors for thyroid cancer. Radiation exposure may also help predict prognosis of thyroid cancer. Leptin receptor expression may be a useful marker in predicting the stages of thyroid tumors in the Middle East region and help guide treatment and follow up.

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Excessive food intake leads to excessive leptin throughout the body. The amount of leptin, one of the molecules causing obesity, also plays a role in this increased frequency of thyroid cancer. Leptin may also help predict prognosis of thyroid cancer. Leptin receptor expression may be a useful marker in predicting the stages of thyroid tumors in the Middle East region and help guide treatment and follow up. Obesity in Saudi Arabia is high and remains an emerging public health issue. About 68.3% of the Saudi Arabian population are overweight.

Thyroid cancer rates in Saudi Arabia are well above those of industrialized nations and are expected to rise even higher due to population growth, compounded by the possible implications of an aging population, rapidly changing lifestyles including dietary habits, iodine deficiency, obesity, lack of exercise, and urbanization.

CONCLUSION

Thyroid cancer is the second most common malignancy among women in Saudi Arabia, with an exponential increase in the incidence rates over the last few years. The exact cause of this changing trend is unknown. However, several risk factors have been identified including iodine deficiency, family history, obesity, radiation exposure and high leptin levels. The escalating incidence of thyroid cancers in the Kingdom of Saudi Arabia may also be due to increased early detection and diagnosis of thyroid cancers for significant expansion of health care sector and outreach programs and not necessarily due to a true increase in the occurrence of thyroid cancers. The predominance of thyroid cancer in the Kingdom and the Gulf region necessitates prioritization at national and regional levels. Further clinical epidemiological research is needed to determine successful strategies for increasing awareness, screening, early detection, diagnosis and management in Saudi Arabia with unique cultural, racial and ethnic makeup as compared to the West. More studies are required to
determine the etiology, environmental factors and local characteristics of the disease in the Kingdom to determine the significance of the changing trends at molecular and genetic levels. This report is the first comprehensive evaluation on thyroid cancer from King Faisal Specialist Hospital & Research Centre and the Saudi Cancer Registry, looking into the increasing incidence, trends and patterns of thyroid cancer as a reference for defining future public health initiatives in cancer control in Saudi Arabia.

CONFLICT OF INTEREST STATEMENT

There is no conflict of interest and nothing to disclose.

REFERENCES