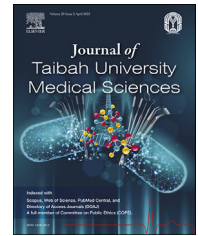




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Original Article

Trends of thyroid cancer in children and adolescents over 23 Years in KSA



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المخلص

أهداف البحث: هدفت هذه الدراسة إلى تحديد معدل الإصابة بسرطان الغدة الدرقية لدى الأطفال والمراهقين في المملكة العربية السعودية على مدى فترة ٢٣ عاما.

طريقة البحث: تم استخراج البيانات من السجل الوطني السعودي للسرطان، والتي تغطي جميع حالات سرطان الغدة الدرقية من عام ١٩٩٤ إلى عام ٢٠١٧ لدى الأفراد الذين تتراوح أعمارهم بين صفر و ١٩ عاما.

النتائج: تم تشخيص إجمالي ٧٠٦ مريضا بسرطان الغدة الدرقية خلال فترة الدراسة، وكان ٨٦,٣٪ منهم مواطنين سعوديين. حدث أعلى معدل للإصابة (١١٤ حالة) بين عامي ٢٠١٢ و ٢٠١٤. لوحظ أدنى معدل إصابة خام في الفترة من ١٩٩٤ إلى ١٩٩٦ (٤,٤٥ لكل ١٠,٠٠٠). والجدير بالذكر أن معدل الإصابة الخام كان الأعلى بين المرضى الذين تتراوح أعمارهم بين ١٥ و ١٦ عاما (٢٦,٧ لكل ١٠,٠٠٠).

تأثرت الإناث بشكل غير متناسب بسرطان الغدة الدرقية، حيث بلغ متوسط معدل الإصابة ٤٥ لكل ١٠,٠٠٠ مقارنة بـ ٨,٢ لكل ١٠,٠٠٠ لدى الذكور. من الناحية الجغرافية، سجلت منطقة الرياض أعلى معدل إصابة، وخاصة في عام ٢٠٠٤ (٦,٩ لكل ١٠,٠٠٠)، و ٢٠١٦ (١٥,٤ لكل ١٠,٠٠٠)، و ٢٠١٧ (١٥,١ لكل ١٠,٠٠٠).

الاستنتاجات: كشفت البيانات عن زيادة ثلاثة أضعاف في معدل الإصابة بسرطان الغدة الدرقية بين الأطفال والمراهقين في المملكة العربية السعودية من عام ١٩٩٤ إلى عام ٢٠١٧، مع فترة الذروة بين عامي ٢٠١٢ و ٢٠١٤. وهناك

حاجة إلى مزيد من الدراسات للتحقيق في العوامل التي تساهم في هذا الاتجاه المتزايد.

الكلمات المفتاحية: المراهقون؛ الإصابة؛ طب الأطفال؛ المملكة العربية السعودية؛ سرطان الغدة الدرقية

Abstract

Objective: This study aimed to determine the incidence of thyroid cancer (TC) in children and adolescents in the Kingdom of Saudi Arabia (KSA) during 23 years from 1994 to 2017.

Methods: Data were extracted from the Saudi National Cancer Registry for individuals aged 0–19 years diagnosed with TC from 1994 to 2017. TC incidence was retrospectively analyzed, age standardized for the Saudi Arabian population, and expressed per 100,000 people based on sex, nationality (Saudi and non-Saudi), and age at diagnosis (0–4, 5–9, 10–14, and 15–19 years). Data regarding the type of TC and tumor, node, and metastasis staging were excluded due to incomplete information.

Results: Overall, 706 patients were diagnosed with TC during the study period and 86.3 % were from KSA. The highest incidence (114) was observed between 2012 and 2014. The lowest crude incidence rate (CIR) was observed in 1994–1996 (4.45/100,000), and the CIR was highest among patients aged 15–16 years (26.7/100,000). Women were disproportionately affected by TC, with an average CIR of 45/100,000 compared with 8.2/100,000 in men. Geographically, Riyadh had the highest CIR, particularly in 2004 (6.9/100,000), 2016 (15.4/100,000), and 2017 (15.1/100,000).

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Conclusion: A three-fold increase was observed in the incidence of TC among children and adolescents in KSA from 1994 to 2017, reaching a peak between 2012 and 2014. Further studies are warranted to investigate the factors that contributed to this increasing trend.

Keywords: Adolescents; Incidence; Pediatrics; Saudi Arabia; Thyroid cancer

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Introduction

Thyroid cancer (TC) is the most common endocrine malignancy in adults in the Kingdom of Saudi Arabia (KSA), although it is uncommon in pediatric populations. The incidence rate of TC increased steadily among adults from 5.4 % in 1994 to 8 % in 2017.¹ TC predominantly affects adult women, with a male-to-female ratio of 0.3:1.² The global TC incidence remains lower among children and adolescents than in adults, accounting for just 1.5–3% of all other malignancies,³ but a notable rise was observed within this age group (0–19 years) in recent years.⁴ Despite this increase, the mortality rate has remained low and stable for several years.⁵

In children and adolescents, TC typically presents as a palpable thyroid nodule, although most patients remain asymptomatic and are diagnosed incidentally during routine neck imaging.^{4–6} TC behavior varies significantly, where most types are indolent, slow-growing tumors, but some are highly aggressive with increased mortality rates.⁷ The predominant histological subtype is papillary adenocarcinoma, followed by papillary carcinoma and the follicular variant.² The precise etiology that underlies this shifting trend remains unclear.

Determining the patterns and trends in TC incidence in KSA is crucial for understanding how its prevalence has evolved across different regions and for identifying the factors that drive these changes. This study aimed to assess the incidence of TC among pediatric and adolescent populations in KSA to advance our understanding of this disease.

Methods

The estimated population of KSA when data were extracted from the Cancer Registry was 32,612,846. Among the total population, 20,427,576 were Saudi nationals comprising 10,404,865 (51 %) men and 10,022,711 (49 %) women. KSA is divided into five main regions: central, western, eastern, Almadinah Almunawwarah and northern, and southern regions.

The data used for this study were obtained from the Saudi Cancer Registry, a national population-based registry. Cancer is a notifiable disease in KSA, so the registry provides comprehensive access to data from healthcare institutions nationwide, including the Ministry of Health, government and private hospitals, laboratories, and clinics. Data were

carefully extracted from the medical records based on histopathological and clinical diagnoses.

The collected data encompassed a wide range of patient information, including sex, age, address, and nationality. In addition, comprehensive tumor details were documented, including incidence date, source of information, basis of diagnosis, site, histology, stage, and behavior. The cancer types and diagnoses were coded according to the International Classification of Diseases for Oncology and World Health Organization guidelines.

This study retrospectively analyzed the incidence of TC from 1994 to 2017. Only children and adolescents aged 0–19 years who were diagnosed with TC were included in the analysis. Patients with secondary cases of TC were excluded due to the established influence of radiotherapy on TC risk.^{5,8}

This study was approved by the Research Ethics Committee of Taibah University (IRB number: 00010413).

The calculated incidence rate of TC was age standardized to the Saudi Arabian population and expressed per 100,000 people based on sex, nationality (Saudi and non-Saudi), and age at diagnosis (0–4, 5–9, 10–14, and 15–19 years). The type of TC and tumor, node, and metastasis staging were not included because some related data were missing.

Statistical analysis

All of the collected information was initially recorded on a Microsoft Excel spreadsheet and subsequently transferred for analysis using the IBM Statistical Package for Social Sciences version 23 (SPSS Inc., Chicago, IL, USA). Trends in TC incidence rates between 1994 and 2017 were estimated, tabulated, and presented graphically using three-year moving averages (0–4, 5–9, 10–14, and 15–19 years).

The crude incidence rate (CIR) was calculated as the total number of TC cases divided by 100,000 individuals. The CIR was further stratified by age, sex, and nationality (Saudi and non-Saudi). All rates were age adjusted according to the World Standard Population (Doll et al., 1966) and expressed per 100,000 person-years.

Results

Our analysis identified 706 cases of TC in children and adolescents aged 0–19 years between 1994 and 2017. Over 86 % of these cases were observed among Saudi citizens. Among the top 10 most prevalent cancer types, TC ranked as the second most common cancer among Saudi females based on the 2017 cancer registry report.

Trend analysis indicated an increasing incidence of TC. Only 60 cases were documented in 1994–1996, whereas 114 cases were reported in 2012–2014, which was the highest number during the 23-year study period (Figure 1).

The highest CIR was observed among adolescents aged 15–19 years, with 26.7 per 100,000 individuals among Saudi citizens and 13.2 per 100,000 individuals among non-Saudis. In this age group, Saudi women had the highest CIR of 45 per 100,000 individuals, which was over five times greater than that among their male counterparts, who had a CIR of 8.2 per 100,000. A similar disparity was observed among

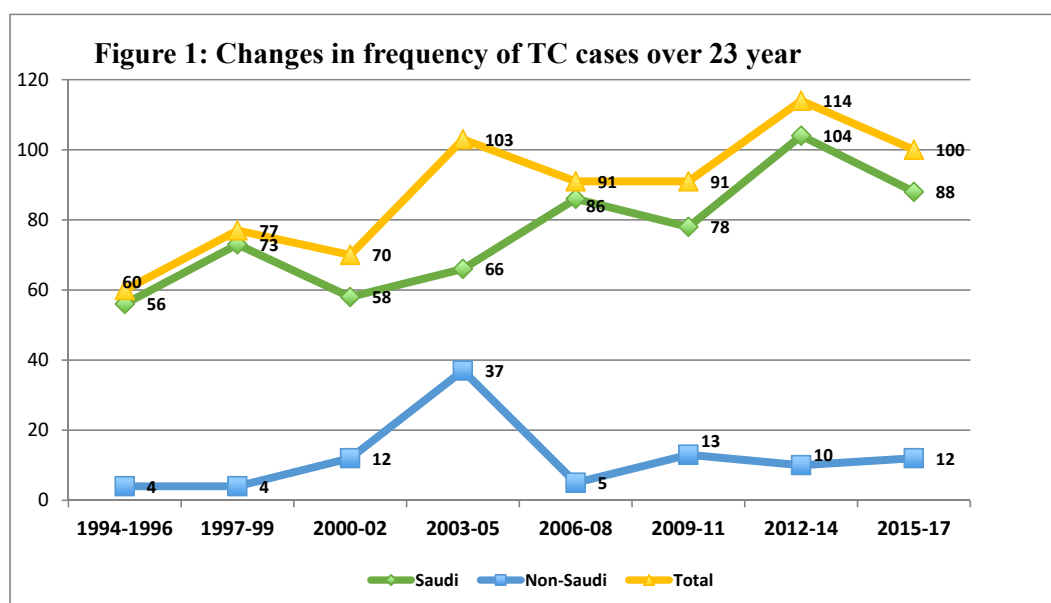


Figure 1: Changes in frequency of thyroid cancer cases over 23 years.

non-Saudis, where women had a CIR of 19.6 per 100,000 individuals and men had a CIR of 6.8 per 100,000 individuals (Figure 2).

Analysis of trends across study periods revealed that the highest CIR was documented in 2015–2017, reaching 8.95 per 100,000 individuals, whereas the lowest CIR was 4.9 per 100,000, reported in 2003–2005 (Figure 3). In 2000–2002, the CIR was higher among non-Saudis (4 per 100,000 individuals) compared with Saudis (3.45 per 100,000 individuals).

In 2004, the highest CIR (6.9 per 100,000 individuals) was recorded in Riyadh. In 2005, the CIR was higher than this amount in the northern region of KSA, with 8.1 per 100,000 individuals, representing 27 % of all women with TC nationwide. In 2010, some of the highest CIRs for both women (6.3 per 100,000) and men (1.8 per 100,000) were recorded in the Almadinah Almunawwarah region, accounting for 25 % of all thyroid cases in KSA. The highest CIRs for women in 2016 (15.4 per 100,000) and 2017 (15.1 per 100,000) were documented in Riyadh.

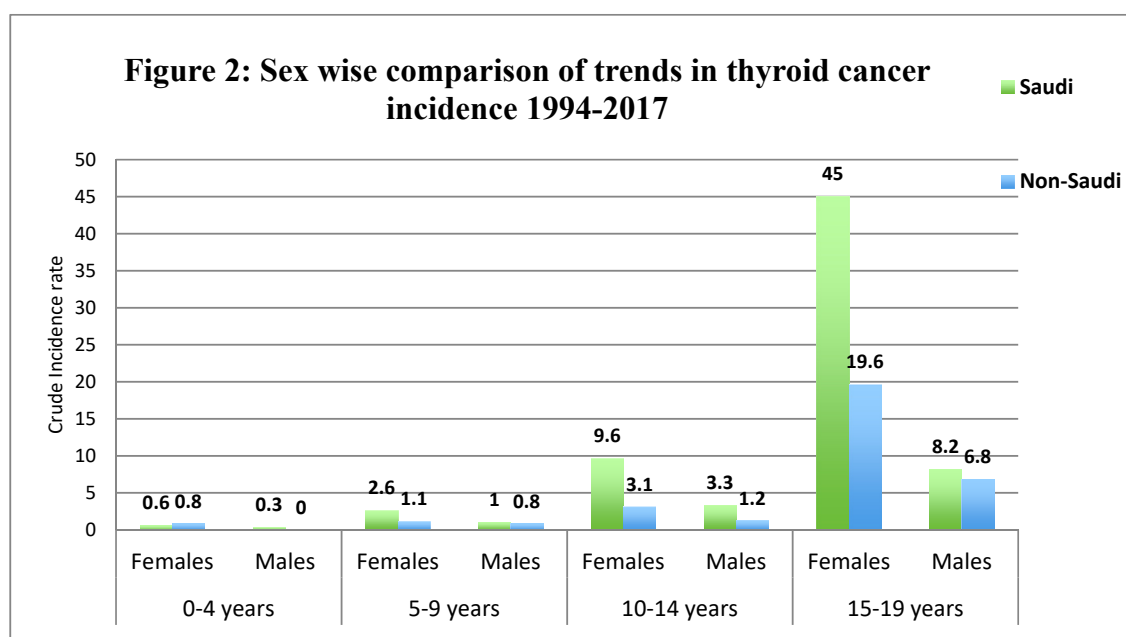


Figure 2: Sex based comparison of trends in thyroid cancer incidence during 1994–2017.

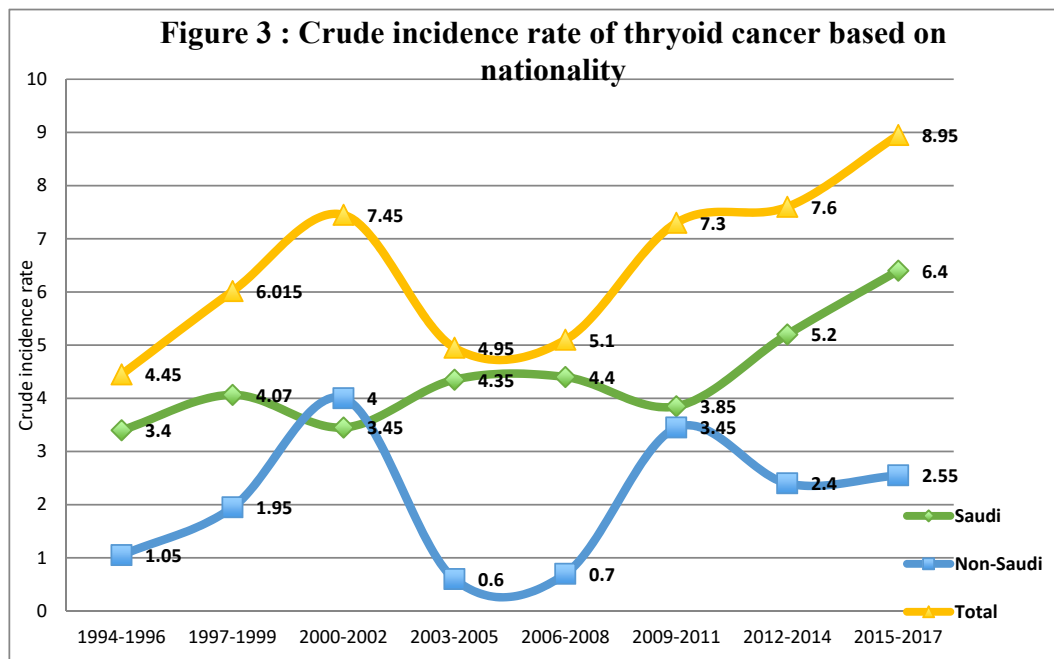


Figure 3: Crude incidence rate of thyroid cancer based on nationality.

Discussion

A previous study conducted by Hussain et al. in the Riyadh region showed that TC accounted for approximately 9 % of all adult malignancies and 12 % of all female malignancies.² These rates are considerably higher than those found in the United States, where TC accounts for only 2.9 % of all cancer types and 4.6 % of female malignancies.

In the younger population, an increasing trend in the overall TC incidence was observed among Saudi Arabian children (0–19 years) from 2005 to 2017 in the present study, but particularly within the group aged 15–19 years. A similar increase was observed in the group aged 15–29 years,⁹ where the incidence peaked between 2012 and 2014. Compared with other countries in the region, an increased incidence rate of TC was observed in the United Arab Emirates between 2012 and 2015.¹⁰ This finding agrees with global data that indicate a rapid increase in the incidence of TC between 2008 and 2012 in 49 countries,⁴ although the underlying causes remain unclear.

Some studies have attributed this increase in the incidence of TC to improved detection using advanced technologies and highly sensitive methods,¹¹ but this does not explain the lack of a plateau trend in older age groups, which would be expected if this is the cause. It should be noted that the global incidence of cancer has increased sharply since 1975.¹² In addition, enhanced screening procedures have increased the number of adults diagnosed with TC.¹¹ Similar factors may have contributed to the trends in adolescents, but it is difficult to reconcile these effects with the pronounced observed sex differences. Bleyer et al. reported similar findings in the United States [9], implying that this trend is likely prevalent worldwide.

The increasing incidence of TC in teenagers and adolescents (15–29 years) is a concerning trend, with women diagnosed nearly three times more frequently than men.⁹ This gender disparity also extends to histological subtypes, where women have a higher percentage of follicular and papillary TC.¹¹ The underlying associated molecular factors remain elusive but further investigation is crucial to elucidate the mechanisms related to these observed differences.

In terms of the impact of nationality on the incidence of TC, the rate among Saudis was consistently higher than that among non-Saudis aged over 23 years, except in 2000–2002 when the CIR was only slightly higher among non-Saudis (4 per 100,000) compared with Saudis (3.45 per 100,000). However, no further details were available in the cancer registry. In addition, non-Saudis originate from different countries and ethnic groups worldwide, complicating their classification as a single group. This diversity makes it difficult to analyze the impact of nationality on the incidence rate.

Most pediatric malignancies, including those that occur during adolescence, are sporadic and arise from genetic mutations. However, the increasing incidence of TC in this age group suggests the influence of alternative factors, making it imperative to identify the genetic contributors to this increase. Sporadic mutations involved in TC include transformation, papillary thyroid carcinoma, neurotrophin receptor-tyrosine kinase chromosomal rearrangements, and BRAF mutation.¹³

Hormonal changes during adolescence may also contribute to sex-based disparities in TC incidence. In particular, polymorphisms in female sex hormones, particularly the estrogen receptor codon 594 polymorphism, are

strongly associated with TC development. These hormones play important roles in regulating gene expression and tumor cell biology.¹⁴

Furthermore, epidemiological research has identified childhood and adolescent obesity as a potential predictor of TC risk.¹⁵ In KSA, the obesity rates among females are higher than those in males in this age group, and thus this factor may have contributed to the observed sex-based differences in the incidence of TC.¹⁶

Other factors warrant further investigation, including exposure to ionizing radiation and environmental, dietary, and chemical factors.¹⁷ However, limited data are available about the survival and mortality rates regarding TC in this age group. Thus, it is important to conduct studies specifically in KSA by focusing on the survival and mortality rates among patients diagnosed with TC, as well as exploring the factors that might influence these rates to improve prognostic and patient outcomes. To the best of our knowledge, this is the first study in KSA to utilize government data from the Kingdom Cancer Registry. These data are representative of all regions in the country and include information from private and government sectors. In addition, the extensive time frame covered by these data is a major strength of this study. The Saudi Cancer Registry follows international guidelines for cancer diagnosis and management. However, a limitation of this study is that the data were extracted from the Cancer Registry without access to patient files, and thus some details were missing. Moreover, the diverse sources of data in the registry may have resulted in inter-observer bias.

Conclusion

The results obtained in this study highlight the substantial increase in the incidence of TC among children and adolescents in KSA from 1994 to 2017. This finding coincides with the substantial transformation in the country's healthcare sector, characterized by the establishment of numerous hospitals. Advances in diagnostic and screening practices probably contributed to the early detection of small and asymptomatic TCs, but further research is required to comprehensively understand the diverse factors associated with the observed increase.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical approval

This study was approved by the Research Ethics Committee of Taibah University (IRB number: 00010413).

Author contributions

R.S.A., L.A.A., R.F.A., G.T.A., H.Z.B., R.S.A. and S.A.A.

All authors accept responsibility for the entire content of this manuscript and have approved its submission.

The authors declare that this manuscript has not been published nor submitted for publication elsewhere. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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