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Pattern and temporal profile of thyroid carcinoma in the Kingdom of Saudi Arabia: A review and meta-analysis

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REVIEW

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ABSTRACT

Background

There is an increasing rate of thyroid carcinoma in the developed world attributed mainly to over-diagnosis due to healthcare improvement. Saudi Arabia has made health a top priority, an increasing rate of over diagnosis is expected.

Aims

The current review assessed the trends, spatial distribution, and epidemiology of thyroid carcinoma in the Kingdom of Saudi Arabia.

Methods

A systematic electronic search was conducted in PubMed and Google Scholar for relevant articles. All human studies published during the period 2009-December 2019 including Epub and ahead of print were eligible. The keywords thyroid carcinoma, thyroid lesion, Saudi Arabia, prevalence, and incidence were used in different combinations, among the three hundred fifty-four articles identified, twenty-three full text were assessed and only seventeen studies were included. Then the author's names, year and region of publication, the study type, period of study, and the result were recorded. The Statistical Package for Social Sciences (SPSS, IBM, version 20, New York was used for data analysis.

Results

Seventeen articles were included (9754 patient, age 44.53±5.42 years); women outmoded men and showed younger age (36.59 years), papillary carcinoma was the commonest sub-variant of carcinoma (75.62±17.53, age 52.3 years) followed by follicular (6.52±2.92). An increasing trend was observed all over the Kingdom, but not consistent in all-region.

Conclusion

An increasing rate of thyroid carcinoma was evident in the Kingdom of Saudi Arabia, the commonest being papillary carcinoma. Females were more commonly affected at a younger age group. Further National studies assessing whether the increased rate is due to over-diagnosis or other risk factors are highly recommended.

Key Words

Thyroid carcinoma, age groups, types, healthcare

What this review adds:

1. What is known about this subject?

There is an increasing rate of thyroid carcinoma in the developed world mainly due to over-diagnosis, papillary carcinoma is the commonest and women were more likely to acquire the disease.

2. What new information is offered in this review?

This is the first review and meta-analysis that gave a broad insight regarding thyroid carcinoma epidemiology, spatial distribution, and dynamic in the Kingdom of Saudi Arabia. The different dynamics of thyroid carcinoma in different region with improvement overtime and deterioration in others. The improvement observed in areas with comparatively low diagnostic yield and deterioration of others with the same facilities raised the questions of there may be other factors including health awareness programs

or other risk factors.

3. What are the implications for research, policy, or practice?

An urgent National surveys assessing the status of health awareness regarding thyroid cancer in Saudi Arabia and looking for modifiable risk factors to reduce the prevalence of thyroid cancer.

Introduction

Thyroid cancer is on the rise worldwide and the Kingdom of Saudi Arabia is not exceptional, fortunately, this is not mirrored by increasing mortality globally. In contrast, an increasing death accompanied the surge of thyroid cancer in Saudi Arabia during the period from 1990 to 2016. Although the risk factors behind the increasing thyroid cancer in Saudi Arabia remained to be elucidated, the increasing number of the population and the better diagnosis and early detection may not be enough to explain the high jump observed.[1]

A review conducted in the Gulf Cooperation Council (GCC) states in 2007 showed that thyroid carcinoma is the second most common malignancy in the Kingdom of Saudi Arabia and women during the fertile period were the most commonly affected. Papillary carcinoma is the most prevalent histological type followed by follicular variant.[2] A study conducted in Saudi Arabia and involved 14,336 showed that thyroid carcinoma constituted 11.7 per cent of all cancer with the Eastern region and Riyadh displaying the highest, while Hail and Jazan displaying the lowest age-standardized and age-specific incidence rates of all cancer.[3] To our best of knowledge, this is the first review and meta-analysis that gave a broad insight regarding thyroid carcinoma epidemiology, spatial distribution, and dynamic in the Kingdom of Saudi Arabia. Thud we conducted this review to determine the pattern and temporal profile of thyroid malignancy in Saudi Arabia.

Methods

Eligibility criteria according to PICOS

1. Types of studies: All human studies investigating thyroid carcinoma in the Kingdom of Saudi Arabia in the last ten years (2009-December 2019) and published in the English language were included. Studies on animals and studies in languages other than English were excluded.
2. Types of participants: Studies in which participants were children or adults with thyroid carcinoma
3. Types of outcomes measures: Studies assessing at least one the following outcome measures were eligible:
   - Spatial distribution around the Kingdom of Saudi Arabia
   - Rising or decreasing trends of thyroid carcinoma
   - Types and age distribution of thyroid carcinoma in the Kingdom

Information sources and search methods

The PubMed database and the first hundred articles in Google Scholar were systematically searched for relevant articles from 2009 to 1st December 2019 using the following search terms “incidence” AND “thyroid carcinoma, Saudi Arabia”, or “prevalence” AND “thyroid carcinoma, Saudi Arabia”, and thyroid lesion, Saudi Arabia. The filter was set to English publications and to “Children or adults)”.

Study selection and data extraction

The results retrieved were searched manually for relevant articles. Two authors (I.A, H.M) screened all the titles and abstracts available and excluded the irrelevant reports. They independently checked all the retrieved articles for eligibility according to the mentioned selection criteria. The authors extracted the data, then the author's names, year and region of publication, the study type, period of study, and the result were reported. We did not assess the risk of bias (all the studies were retrospective). The PRISMA Chart was used in the current survey, in spite of being mainly for randomized controlled trials. However, it can be used for other reviews Figure 1.

Results

There were three hundred fifty-four studies, (Pub med=254 and the first 100 articles in Google Scholar), twenty-three full text were screened and only seventeen fulfilled the inclusion and exclusion criteria (9754 patient included). Thirteen studies were regional, while seven used registries from the whole Kingdom, twelve retrospective study and one review of thyroid lesions (benign and malignant). The studies showed and increasing rates of thyroid malignancy all over the Kingdom especially Riyadh, Tabuk City, and Eastern Provinces. A dynamic within the increasing rates was observed (decreased in the Northern Region and increased in some South Areas). Women were more affected with a tendency towards younger age (36.9 years *vs.* 44.53±5.42), papillary carcinoma was the commonest malignancy subtype followed by follicular and Hurthle cell (75.62 per cent, 6.52 per cent, and 2.85 per cent respectively), while lymphoma (1.55 per cent), anaplastic (0.8 per cent), and medullary carcinoma (0.8 per cent) were less common. Tables 1 & 2 depicted the pattern of thyroid carcinoma in the Kingdom of Saudi Arabia.

Discussion

In the present study, Al-shraim et al.[4] conducted a retrospective study during the period 1998–2007 in Abha City and found that the commonest thyroid carcinoma is papillary followed by follicular, the mean age was 41.35+/-15.52 for males and 36.59+/-13.28 years for women, Refeidi and colleagues[5] conducted a retrospective study during the same period and published two years later and supported the above findings. However, Refeidi et al. stated that the Bethesda system facilitated a more consistent approach for patients' management.[6] A registry-based study (2000-2010) published in Riyadh[7] found that thyroid carcinoma stands second among all malignancies in women with a median age of 38 years (constituted 9 per cent of all malignancies and 12 per cent of all female malignancies, M/F ratio=0.3:1). Also, the survey noted an increasing rate of thyroid malignancy attributed to an increased detection rate. Spatial autocorrelation analyses of population-based records from the whole Kingdom[8] observed significant clusters of thyroid cancers in females in the Eastern and Riyadh regions.

A study conducted in Dammam (Eastern Saudi Arabia)[9] found that the risk of malignancy increased with each increase in the Bethesda System for Reporting Thyroid Cytopathology category (I-VI), Albasri et al.[10] published a retrospective cohort in Al-Madinah region (West Saudi Arabia) and concluded an increasing rate of thyroid malignancy (Follicular adenoma 3.7 per cent, papillary carcinoma 80.2 per cent, Hurthle 2.5 per cent, and mean age 39.7 years), Alghamdi et al.[11] used the registry of the Kingdom during the period 2001–2008 in which a large sample size was reported (2930) and concluded that: Age-standardized incidence rate was highest in Riyadh (Central) followed by Tabuk (North-East), and Eastern Region, while Jazan (South) and Jouf (North) had the lowest average, the authors also observed a slight increase in the Age-standardized incidence rate and crude standard rate (highest in Qasim Region). A retrospective comparative study[12] conducted among twenty-seven children and one hundred-thirty adult controls found more complications and decreased survival among children, a lower survival rate was also observed when metachronous second primary malignancies are detected in differentiated thyroid carcinoma (DTC),[13] similar poor prognosis was observed when tall cell variant of papillary thyroid carcinoma (PTC) was detected,[14] the obvious poor prognosis with age above 60 years was supported by Al-Qahtani and colleagues from Riyadh,[15] Al-Dawish et al.[16] investigated the thyroid nodules in Riadh Central Region and found 33.6 per cent were malignant, the ages ranged from 13–45 years, 89.6 per cent were papillary, 8.9 per cent follicular, medullary (0.8 per cent), and anaplastic (0.8 per cent). Bethesda VI category was the commonest followed by Bethesda IV.

It is interesting to note that, the largest registry-based study[17] used data from the whole Kingdom (7679 patients during the period 2001–2013) observed the opposite to its comparators (other studies in Saudi Arabia). The study observed an increased incidence in Najran (South) and a drop in thyroid malignancy in Tabuk (North-west) and the Northern Region. The above result needs a special focus on possible socio-demographic factors during the period from 2008–2013 that may explain the increasing rates in areas observed to have low risk and a drop in high incidence areas observed during the period 1998–2008 with an overlap during the period from 2001–2008. The dynamic of cancer shown by the current review cannot be explained by genetic factors alone or even by arrivals and mobility. It is important to note that Al-Ahmadi & Al-Zahrani and Alghamdi et al.[8,11] observation were among women. While Alshehri[17] found an overall increased rate and decreasing rate among females in Tabuk and Northern Provinces. We found three more recent studies since Alshehri published his retrospective registry-based study, Althubiti et al.[18] published a study using a National-based registry (1990–2016) and observed a twenty-six fold increasing rate. The findings of this study are alarming and necessitating un urgent studies investigating the various risk factors behind the observed high shift in thyroid carcinoma, a more recent retrospective study conducted among 456 patients in Jeddah (Western Region)[19] showed a 2.3 fold increasing rate. The Kingdom of Saudi Arabia is a vast country, the contradicting findings regarding thyroid carcinoma rates could be due to different practices in different region (there could be programs to reduce the high detection rate and vice versa). The observation of papillary thyroid carcinoma as the most common cause of thyroid lesions was confirmed by Saeed et al.[20]

The increasing rate of thyroid carcinoma observed in the Kingdom of Saudi Arabia is in similarity to the trends in the USA (with minor differences) in which the rate was stable before mid-1990s then increasing in 2014. The current findings were also similar to reports from the developed world. The increasing rate was attributed to over-diagnosis especially among women due to the introduction of advanced investigational modalities. However, the reduction in thyroid cancer observed in the United States during the periods 2000–2009 in women and 2009–2012 in men is not observed in the Kingdom of Saudi Arabia excluding Tabuk and Northern Region.[21-23] The results of the current meta-analysis call for further National studies

addressing the possibility of over-diagnosis and investigating the possible risk factors for thyroid malignancy.

Conclusion

There is an increasing rate of thyroid carcinoma in the Kingdom of Saudi Arabia with some reports showing decreasing rates. Papillary thyroid carcinoma was the commonest thyroid malignancy followed by follicular and Hurthle cell. Females were more affected than males and the reproductive age group was the commonest.

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PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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Figure 1: Flow diagram through the different phases of the systematic review (PRISMA flowchart)

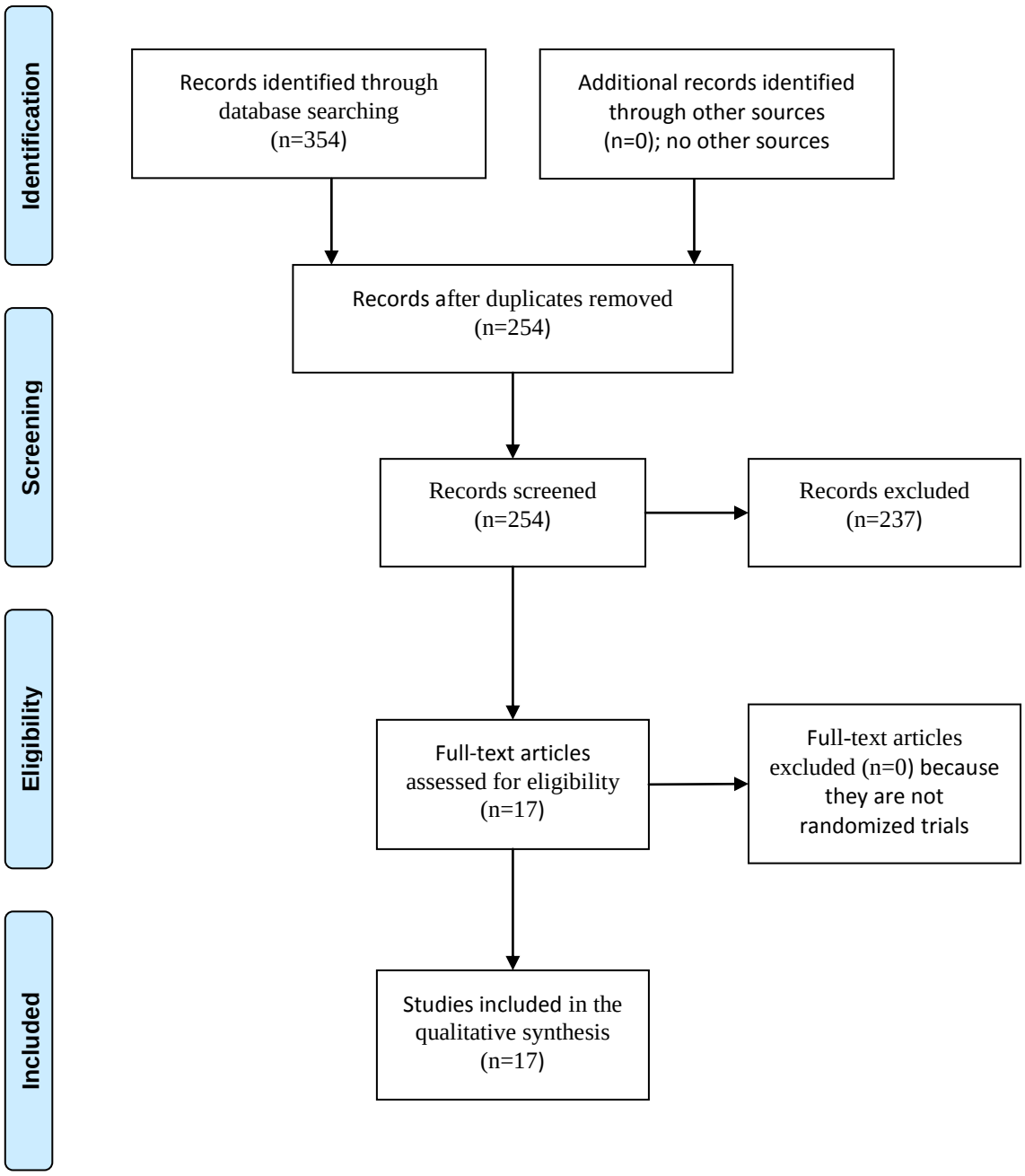

Table 1: the current status of thyroid carcinoma in Saudi Arabia

Author	Year	Region	Type	No of patients	period	Results
Al-shraim et al.	2010	Abha	Retrospective	516	1998 - 2007	Papillary thyroid carcinoma is the most common followed by follicular, age 41.35+/-15.52 for males and 36.59+/-13.28 for women
Refeidi et al.	2012	Abha	Retrospective	516	1998 - 2007	The mean age for males was 41.35+/-15.52 years compared to 36.59+/-13.28 Papillary carcinoma constituted 50%, follicular 4.3%, Lymphoma 1.1% Bethesda system facilitated a more consistent approach for patients' management.
Refeidi et al.	2012	Abha	Retrospective	516	1998 - 2007	Bethesda system facilitated a more consistent approach for patients' management.
Hussain et al.	2013	Riyadh	Retrospective, registry-based	2292 thyroid cancer patients	2000-2010	Thyroid cancer is the second most common cancer among young women constitutes about 9% of all malignancies and 12% of all female malignancies, M/F ratio=0.3:1, and an increasing rate observed attributed to increased detection Median age at diagnosis was 38years and the highest incidence was in the 30–39year age group
Al-Ahmadi &Al-Zahrani	2013	Saudi Arabia	Retrospective Population-based	Spatial autocorrelation analyses	1998-2004	Significant clusters of thyroid cancers in females in the Eastern and Riyadh regions
Al-Abbadi et al.	2013	Dammam	Retrospective	186 patients,		The risk of malignancy in our cohort increased with each increase in the Bethesda System for Reporting Thyroid Cytopathology category (I-VI)
Albasri et al.	2014	Al-Madinah region	Retrospective	292	2006-2013	Age 39.7, Follicular adenoma (3.7%) was the commonest benign tumour and papillary carcinoma (80.2%) was the commonest malignant lesion. Hurthle (2.5%) A slightly increasing trend of papillary carcinoma diagnosis was observed, most being diagnosed at an advanced stage
Alghamdi et al.	2015	Saudi Arabia	Retrospective from registry	2,930 women with thyroid cancer	2001-2008	The age-standardized incidence rate was highest in Riyadh followed by Tabuk, and Eastern Region, while Jazan and Jouf had the lowest average, There was a slight increase in the Age-standardized incidence rate and crude standard rate (highest in Qasim Region)
Al-Qahtani et al.	2015	Riyadh	Retrospective	157 (27 children *vs.* 130 adults controls)	2000-2012	More complications and decreased survival observed among children

Al-Qahtani et al.		Riyadh	Retrospective	823	2000-2012	Metachronous second primary malignancies when present with DTC lowered survival
Al-Qahtani et al.	2016	Riyadh	Retrospective	776 papillary thyroid carcinoma	2007-2015	The mean age of the cohort was 52.3 years with female predominance, tumour size was 3.62cm, overall 5-year survival 86.7%. Tall cell variant PTC is associated with aggressive biological behaviour.
Al-Qahtani et al.	2016	Riyadh	Retrospective comparative	370 (258 *vs.* 118)	2000-2012	Age 51.9 for group A and 68.6 for group B. Patients aged above 60 years with DTC showed poor prognosis
Al Dawish et al.	2017	Riyadh	Retrospective	1188 patients with thyroid nodules	2012-2014	33.6% were malignant, 13-45 age, 89.6%, 8.9%, 0.8% each for papillary, follicular, medullary, and anaplastic respectively. Bethesda VI category followed by Bethesda IV.
Alshehri et al.	2017	Saudi Arabia	Retrospective	7,670 thyroid cancer patients	2001-2013	Age 35-39, increasing incidence observed mainly in Najran, a drop was observed in Tabuk and Northern region
Althubiti et al.	2018	Saudi Arabia	Retrospective	Retrospective, registry-based	1990-2016	The incidence of thyroid cancer increased 26 fold attributed to change in socioeconomic status
Aljabri et al.	2018	Jeddah	Retrospective	456 patients	2000-2017	Mean age 45.2, papillary 82.7%, follicular 9.2%, Hurthle cell 3.2%, Lymphoma 2%, 2.3-fold increase observed.
Saeed et al.	2018	Mecca	A review of thyroid lesions			Mean age 43.35 Papillary carcinoma was the most common malignancy

Table 2: Ages and pathological distribution of thyroid carcinoma among the included studies

Character	**Mean±SD**
Age, thyroid carcinoma (range, 39.7-51.9 years)	44.53±5.42
Age (papillary carcinoma)	52.3
Age (women)	36.59
Frequency of thyroid cancer Papillary (range, 50-89.6%) Follicular (range, 3.7-9.2) Hurthle cell (range, 2.5-3.2%) Lymphoma (range, 1.1-2) Anaplastic carcinoma Medullary carcinoma	 75.62±17.53 6.52±2.92 2.85±0.49 1.55±0.63 0.8 0.8