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Insights into the epidemiology of renal cell carcinoma in North Africa and the Middle East

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Abstract

Purpose: Recent improvements in the treatment of renal cell carcinoma (RCC), with the introduction of targeted agents, have increased the need of accurate data on its epidemiology. This descriptive study was designed to collate comprehensive information on RCC epidemiology from North Africa and the Middle East, which could provide the basis for further research.
Methods: A network of reference oncologists in North Africa and the Middle East were invited to share all available national and regional information on RCC epidemiology, captured in a comprehensive questionnaire. No statistical analysis was planned as the intention was to conduct a purely descriptive study
Results: The results reported that the incidence of RCC within the region is in the range of 0.9–2.35/100,000 for men (with Lebanon as an exception at 4.3/100,000 for men) and 0.5–1.7/100,000 for women, which is considerably lower than in Europe and the USA. No mortality or survival data are available. The age at diagnosis (mean <60 years) is lower than in Western countries and a high proportion of patients in North Africa and the Middle East (21–45%) have metastatic disease at diagnosis.
Conclusions: The information presented here provides a more complete and current picture of RCC in North Africa and the Middle East; however, there are still gaps in the data. Further research is needed to allow planning of treatment strategies and resource allocation.

Conflicts of Interest
The authors declare that there are no conflicts of interest associated with this work.

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Introduction

The global burden of disease has shifted from infectious diseases towards non-communicable conditions, among which cancer has become a frequent cause of morbidity and mortality in the developing world [1,2]. There has been a recent and continuing increase in the numbers of cancer cases and cancer deaths in low- and middle-income countries; more than 70% of all cancer deaths now occur in these countries [3].

Information on the epidemiology of cancer is essential to understand the risk factors, plan prevention and management

strategies, and allocate resources appropriately. However, although cancer epidemiology in North America and Europe is well researched, these areas represent only a fraction of the global population, and there is much less information available for the rest of the world. The International Agency for Research on Cancer GLOBOCAN project provides the most comprehensive, widely available, assessment of the global cancer burden and is a very valuable resource; this was recently updated in 2012 [4]. However, in many cases, the data are old and may have been extrapolated from a small region or from neighboring countries.

Although kidney cancer is responsible for only approximately 3% of all cancers in the Western world, it is an important urological cancer because of its poor prognosis [5–7]. Moreover, the incidence of kidney cancer is increasing in certain populations, including the in UK and the US, and is associated with significant mortality. Approximately 85% of kidney cancers are renal cell carcinomas (RCCs; adenocarcinomas arising in the renal parenchyma), with the remainder being mostly cancers of the renal pelvis. Most cases of RCC are clear cell carcinomas (80%) and other rarer subtypes include papillary RCC, chromophobe RCC, collecting duct carcinoma, and medullary carcinoma.

In recent years, the management of kidney cancer has evolved rapidly, with a shift in many countries towards earlier detection, resulting from the widespread use of better imaging techniques and with greater use of nephron-sparing surgery [7]. The introduction of targeted therapies for advanced and metastatic disease has improved the prognosis of RCC, with higher response rates and significant increases in progression-free survival compared with cytokine therapy [7,8]. These therapeutic changes have led to the development of new treatment guidelines [7,8]. The changing treatment landscape has increased the importance of collating accurate data on the epidemiology of RCC. The incidence of RCC varies widely (by as much as 10-fold) across the world [5], with the highest rates reported in Europe and North America and the lowest rates in Asia and Africa. Detailed and valid data are not currently available from Africa and the Middle East.

The Africa–Middle East Genitourinary Tumor Working Group was formed to improve the existing knowledge on key issues and challenges in genitourinary cancer in the region. A key priority for the group is to gain insights into the epidemiology of RCC, with the aim of optimizing treatment. The objective of this descriptive study was to collect available epidemiological data that could provide the basis for further research.

Materials and Methods

Contributing oncologists were asked to provide all available published and unpublished data on RCC in their countries. The information was captured in a questionnaire designed by the Africa–Middle East Genitourinary Tumor Working Group to determine the availability of epidemiologic data and to collect the following data:

- Type of existing cancer registry, information recorded, method of data collection
- RCC incidence and mortality rates
- Histological data
- Tumor node metastases (TNM) stage
- Age at diagnosis

Questionnaires were distributed between 2011 and 2012 to a network of reference oncologists across North Africa and the Middle East, identified through institutions, professional organizations, and personal contacts. Respondents provided the most recent information available on the epidemiology of RCC in their countries. Concerted efforts were made to collect information from a number of countries throughout the region; however, it was not possible to obtain information from many countries. No statistical analysis was planned as the intention was to conduct a purely descriptive study.

All participating physicians investigated all available resources in their country, with data collated from institutional records, national registries, and regional cancer registries. Data were collected over a period of 18 months from January 2011 to May 2012. A literature search was also conducted using PubMed to identify published information on RCC epidemiology in the region. Search terms included 'kidney cancer', 'renal cell carcinoma', and all relevant country names.

Results

Renal cell carcinoma epidemiology

The types of cancer registry and methods of data collection varied across the region. Jordan, Syria, Tunisia, Lebanon, and Saudi Arabia have national population-based registries, whereas Morocco, Algeria, and Libya have several regional registries. Saudi Arabia, UAE, Tunisia, and Libya have hospital-based registries. A variety of personnel are responsible for recording cancer data including pathologists, cancer registry staff/data managers, and clinicians with an interest in epidemiology.

Data on the incidence of RCC vary widely and are summarized in Table 1. The incidence varies between 0.9 and 4.4/100,000 for men and 0.5 and 1.7/100,000 for women. No mortality data are available for any country in the region except for Libya; the mortality rates for kidney cancer in Libya in 2004 were 0.91/100,000 in men and 0.65/100 000 in women.

In several countries, most cases are histologically verified (Lebanon, Algeria, Morocco, Jordan), but only limited histology data are available through existing registries. In many countries, no information is available on histologic subtypes and most cases are listed as RCC 'not otherwise specified'. Where data are available, there is a predominance of clear cell carcinoma: 79% in UAE and 68% in Morocco.

Table 1. Incidence rate of RCC in selected countries of Africa and the Middle East (cases per 100,000 population)

Incidence/100,000	Male	Female
Algeria	0.9	0.5
Tunisia	2.35	1.68
Morocco	1.13	1.09
Saudi Arabia[a]	1.6 (ASR 2.7)	1.0 (ASR 1.4)
UAE	NA	NA
Jordan	1.2	0.6
Lebanon	4.30	1.70
Syria	1.39	0.95
Libya[a]	2.07	0.91

[i]ncludes all kidney cancers. ASR, age standardized rate; RCC, renal cell carcinoma.

Information on stage at diagnosis is also limited (Table 2). Although the numbers of patients are very low, the results suggest that fewer patients are diagnosed at Stage 1 and a higher proportion have metastatic disease at diagnosis.

Data on age at diagnosis are available for four countries and show that RCC patients are typically in their mid-fifties at diagnosis. The mean age at diagnosis was 54.7 years, 50 years and 56.9 years in men and 51.9 years, 41.5 years and 57.6 years in UAE, Algeria and Jordan respectively; in Morocco the median age at diagnosis was 57 years in men and 53 years in women.

Discussion

This paper presents currently available data collected by RCC experts practicing in the region, including details of patient age and stage at diagnosis that have not previously been available. Although, it is acknowledged that there are many limitations to this study, the results reflect the most up-to-date and comprehensive information available, vital for future RCC research in the region.

The age-adjusted incidence rates for RCC reported here are broadly consistent with the rates reported in GLOBOCAN 2012 (summarized in Table 3) [4], and are also consistent with the data reported from Oman by Salim *et al.* [9]; these data are more recent and comprise of actual results rather than based on extrapolations. It is clear that the incidence of RCC in the North Africa–Middle East region is considerably lower than the typical rates observed in Western Europe and North America (6–15/100,000 in men and 3–7/100,000 in women). The Middle East Cancer Consortium project provides another source of information, but is also out of date (data from 1996 to 2001) [10]. In the case of Egypt, the Middle East Cancer Consortium reports incidence rates of 3.0/100,000 in men and 1.7/100,000 in women. However, these data are based on the Gharbiah Cancer Registry that covers only 3.4 million people from a total Egyptian population of 85 million.

Several papers have commented on the apparent lower incidence of RCC in this region compared with Europe and North America [9,11,12]. Factors that may contribute include possible under-diagnosis and under-reporting. However, existing differences in incidence of other tumor types, such as lung cancer, cannot be explained only by under-reporting. It seems likely that differences in environmental and genetic risk factors are responsible. The results of this survey confirm that, similar to other regions, there is a strong male predominance in the incidence of RCC; although, this difference is not as large as in Europe and North America where the incidence in men is

Table 2. TNM stage at diagnosis

	Tunisia n (%)	UAE n (%)	Jordan n (%)	Morocco n (%)	Libya n (%)	Saudi Arabia n (%)
Stage I	NA	93 (53)	41 (39.4)	2 (5)	2 (18)	(39)
Stage II			12 (11.6)	7 (18)	2 (18)	NA
Stage III				6 (15)	2 (18)	(17)
Stage IV	(16)	76 (43)	26 (25)	8 (21)	5 (45)	(25)
Unknown	NA	6 (3)	25 (24)	16 (41)	0	NA

NA, not available; TNM, tumor node metastases.

Table 3. GLOBOCAN 2012 data: incidence and mortality data for kidney cancer; rates per 100,000, all ages

	Male				Female			
	Incidence		Mortality[g]		Incidence		Mortality[g]	
	Crude	ASR	Crude	ASR	Crude	ASR	Crude	ASR
Algeria[a]	1.4	1.8	1.0	1.3	1.1	1.3	0.7	0.9
Egypt[a]	2.5	3.1	1.9	2.4	1.6	1.8	1.2	1.3
Jordan[b]	2.6	4.3	1.7	2.9	1.3	2.0	0.9	1.4
Lebanon[c]	4.8	4.8	3.0	3.0	1.9	1.8	1.2	1.1
Libya[d]	2.8	3.7	1.6	2.3	1.4	1.7	0.8	1.0
Morocco[e]	1.6	1.9	1.3	1.5	1.1	1.2	0.9	1.0
Saudi Arabia[b]	1.8	2.8	1.0	1.8	1.3	1.8	0.7	1.1
Syria[f]	2.8	4.0	2.1	3.1	1.6	2.2	1.2	1.6
Tunisia[a]	2.5	2.6	1.7	1.7	1.9	1.9	1.3	1.3
UAE[c]	0.7	2.6	0.3	1.6	0.9	1.8	0.3	0.7

[a]Incidence: estimated using high-quality regional data (coverage <10%). [b]Incidence: national data projected to 2012. [c]Incidence: national data, most recent data applied to 2012 population. [d]Incidence: one cancer registry (high quality; coverage <10%) used as representative. [e]Incidence: estimated as weighted average of local rates using regional data. [f]Incidence: no data; the rates are those of neighboring countries or registries in the same area. [g]All mortality rates are estimated, usually from national incidence estimates using modeled survival.
ASR: age standardized rate.

typically about twice that in women. Interestingly, a study from Nigeria seems to be the only published report worldwide showing a clear female predominance (male:female ratio 1:2.1) [13].

Cigarette smoking, obesity, and hypertension are well established as risk factors for RCC and there is some evidence implicating physical inactivity and dietary factors [5,14]. Recent changes in lifestyle in the Middle East and, to a lesser extent, in North Africa, may have an impact on the incidence of RCC in the future. Increasing obesity rates associated with Westernization of the diet and reduced physical activity are particularly relevant [15].

The information available on the histology of RCC in the region indicates that most cases are clear cell, in line with other countries. Accurate pathology reports are important to tailor treatment appropriately and provide quality patient care. In the case of RCC, an accurate histologic diagnosis is important because the response to targeted therapies may vary by subtype; most clinical trials of targeted agents have been limited to clear cell RCC [16,17]. The College of American Pathologists has developed protocols and checklists as educational tools to assist pathologists in the reporting of relevant information and these provide an example of good practice [18].

The limited results obtained on TNM stage at diagnosis (based on very small numbers) suggest that cases are most often diagnosed at an advanced stage, in contrast to Western countries where RCC is increasingly diagnosed incidentally and at an earlier stage [19,20].

Data collected confirm that RCC seems to occur at a younger age in this region, with the mean age at diagnosis typically in the fifties compared with the early to mid-sixties in Western countries [5,7,8,21]. The younger age at onset in Jordan and other Middle Eastern countries was also noted by Ghalayini *et al.*, who attributed it to the high proportion of young people in the population [12].

This survey confirms the lack of mortality data for RCC in this region, which was also documented by GLOBOCAN 2012. The mortality rates reported by GLOBOCAN and shown in Table 3 are estimates calculated from the incidence data using tumor site-specific survival information rather than actual clinical data. Mortality statistics provide a key indicator of the burden of a specific cancer type and collection of this information should be the responsibility of the national authorities. Due to the availability of new targeted agents to treat advanced and metastatic RCC, with the potential to improve survival and change metastatic RCC from a mainly untreatable disease into a chronic condition [22,23], access to accurate and up-to-date information on survival has become even more important. The current lack of reliable survival data makes it impossible to assess the impact of newer therapies on outcomes.

We recognize that this study has many weaknesses, including its purely descriptive nature, the limited detail provided by respondents, references to both kidney cancer and RCC, and the absence of data from sub-Saharan Africa. It is also possible that the results on stage and age at diagnosis may be unrepresentative of the population because urologists were not included. However, the epidemiologic information presented here provides a more complete and current picture of RCC in the region than has previously been available; nevertheless, there are still many gaps in the data. For example, information on trends over time was not collected and would have been of great interest. It is hoped that this paper will encourage further efforts to record and collate all relevant data on RCC from a wider range of countries throughout the region. A systematic approach is needed to ensure that nationally representative data are collected, with robust validation and quality control. Comprehensive and precise information is needed on the histology and TNM stage at diagnosis to allow planning of treatment strategies and resource allocation. Accurate mortality statistics are essential to allow assessment of the benefits of newer therapies, to target areas of need, and to develop programs that will further reduce the burden of cancer. In the future, it will be important for cancer registries to extend their remit to include data on treatments and outcomes that could potentially allow evaluation of different therapeutic strategies.

In parallel with this drive to collect more complete epidemiology data in Africa and the Middle East, efforts are also needed to prevent known risk factors, to improve access to targeted therapy, and to ensure all eligible patients receive optimal therapy.

Conclusion

The information presented here provides more insights into the epidemiology of RCC in North Africa and the Middle East than have been previously available, but also highlight the need for more comprehensive knowledge. Further research is needed to generate the data required to facilitate planning of treatment strategies and resource allocation.

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