Prostate Cancer in the Arab World: A View From the Inside

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Abstract

The rates of prostate cancer vary by more than 50-fold across different international populations. The aim of this review was to explore the differences in epidemiology and risk factors between the Middle Eastern Arab countries and some of the developed countries in Europe and North America. The age-standardized incidence rate of prostate cancer in the Arab countries is still lower than that in the Western countries, but is steadily increasing with time. Several factors come into play to explain this difference. There are healthcare systems-related factors such as the lack of good population-based registries, and population-related factors. The latter include the relatively young age structure in the Arab countries, lower reported androgen and prostate-specific antigen levels in Arab men, the effect of genetic differences on prostate cancer risk, the metabolic syndrome paradox, and the protective effect of the Mediterranean diet on a subset of the Arab population. In conclusion, the study of prostate cancer in the Arab world represents a challenge with the currently available cancer care systems and the increase in the burden of the disease. A multinational prospective study to investigate the epidemiology of prostate cancer in the Middle East, with specific attention to country/geographic variability along with a comparative analysis to that of the Western hemisphere is needed.

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Introduction

Prostate cancer is the number one cancer in developed countries and the second most common cancer among men worldwide.1 The rates of prostate cancer vary by more than 50-fold between different international populations.2 This has been associated with variations in screening practices and the difference in the magnitude of various prostate cancer risk factors in each population. In this review we focus on the epidemiology of prostate cancer in the Middle East and provide an analysis of the possible factors that affect the difference in incidence of prostate cancer between developed countries such as the United States of America (US) and the Middle Eastern Arab region.

Evidence Acquisition

A literature search in English was performed using PubMed and Google Scholar in January 2015 using the following search terms: “prostate cancer,” “epidemiology OR risk factors,” and “Middle East OR Arab.” Relevant articles, from 1984 to 2015, on prostate cancer in the Arab world were selected. Special attention was given to studies that investigated the disease epidemiology and risk factors in the Arab world.

Epidemiology in the Middle East

The incidence of prostate cancer is low in Asia, intermediate in most of Africa and Eastern Europe, and high in Western Europe and North America.3 As for the incidence in Middle Eastern Arab men, the age-standardized incidence rate (ASIR), as low as 3 per 100,000, was recorded in Qatar in 2006,4 compared with an ASIR of 147.8 per 100,000 in the US,5 according to the Surveillance, Epidemiology, and End Results (SEER) database.

The low incidence of prostate cancer among men of Middle Eastern origin is also evident in the first-generation immigrants in several countries such as Australia,6 Sweden,7 and The Netherlands,8 and in California.9 However, of note is that this difference tends to diminish with each generation.6,9 For example,
when Nasseri et al studied cancer incidence in the Middle Eastern Arab population in California, they found that the prostate cancer rate was 11-fold higher in the Arab individuals in California than the reported rates from the Middle Eastern countries themselves. The authors attributed this to several factors including acculturation to the lifestyle of the host country and possible underreporting of good quality data in most of the Middle Eastern countries because of the lack of organized cancer-based registries.

Figure 1 shows the lower ASIR of prostate cancer in the Middle East and North Africa (MENA) countries compared with Western countries such as the US based on GLOBOCAN 2012 data. In 2005, during the sixth International Consultation on Prostate Cancer and Prostatic Diseases, sponsored by the International Union Against Cancer, concerns were raised regarding the future increase in the incidence of prostate cancer in Asia and the Middle East. This notion was spurred by the observed trends of prostate cancer in the Middle East and Southeast Asia. The meeting synopsis clearly depicted an alarming increase in the incidence rate in Lebanon, exceeding that of Korea and Japan.

Although the incidence and mortality rates for prostate cancer in the US and other developed countries are decreasing, the limited reports from the Middle East have shown an unexpected increase in incidence and mortality rates for prostate cancer in our part of the world. In Lebanon for example, the ASIR increased from 29.9 per 100,000 in 2003 to 39.2 per 100,000 in 2008. As for the survival, several studies have used the age-standardized mortality rate (ASMR) to ASIR ratio, known as the mortality rate to incidence rate ratio (MR:IR), as an indicator of survival. Table 1 shows the ASIR and ASMR of several countries in the MENA region compared with European countries, the US, and Japan, based on the GLOBOCAN 2012 database on prostate cancer. Based on this, Shahait et al used the MR:IR ratio, from the GLOBOCAN 2012 database on prostate cancer (MR:IR ratio being inversely proportional to the survival), and they found that the population-averaged MR:IR ratio was 0.5 in the MENA region.
weighed against 0.09 in the US (Figure 2). These data suggest that mortality from prostate cancer in our part of the world, the MENA region, is approximately 5.6 times that of the US.

Moreover, the limited data on the stage at presentation of prostate cancer in the Middle East report a more advanced stage in our part of the world compared with the US. Osman et al reported on prostate cancer in Saudi Arabia: of a cohort of 72 patients, 46 (64%) had extraprostatic disease at presentation. Of the 54 patients who had staging imaging, 27 (50%) had lymph node metastasis, 12 (22%) had pulmonary metastasis, and 6 (11%) had liver metastasis. This is contrary to the lower rate of extraprostatic disease in the US. According to the SEER database, out of a sample size of 2,795,592 men, 2,264,430 (81%) prostate cancer patients present with localized disease, 335,471 (12%) with regional lymph node metastasis, and only 111,824 (4%) with distant metastasis.

According to the available data it is difficult to determine whether this prediction of a worse stage and survival in the MENA Arab region compared with the US should be attributed to a different biology of the tumor or to the health care systems in those Arab countries or, most probably, to a combination of those different factors. Underreporting of incidence rates and overreporting of mortality rates and inaccuracies in mortality reports can lead to such inconsistencies. The incidence and mortality rates from prostate cancer are on the rise based on future projection models. Shamseddine et al published a report on the cancer trends in Lebanon, and showed that the incidence rate of prostate cancer is expected to increase from 42 per 100,000 in 2009 to 64 per

**Figure 2** The Mortality Rate to Incidence Rate Ratio of the Middle East and North Africa (MENA) Countries Compared With the United States (USA)

Abbreviation: UAE = United Arab Emirates.


**Figure 3** Ten-Year Cancer Incidence Projection of the 5 Most Common Cancers in Men (2009-2018)

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Factors That Affect Incidence

Several factors come into play to explain the lower ASIR of prostate cancer in the Middle Eastern Arab world. They can be divided into 2 main categories: factors related to the health care systems in our region and factors related to the different clinical characteristics of our population.

Factors Related to the Health Care System

The ASIR of prostate cancer reported from the Middle Eastern countries is affected by the access to health care, the quality of health services, and by the accuracy of the cancer registries. The lack of a population-based registry and a prospective oncology database across the Middle Eastern Arab world represents one of the main obstacles that hamper researchers’ ability to report on temporal trends of prostate cancer. It also impairs the efforts to translate that into quantitative evidence to spur governments and health care planners to implement adequate prostate cancer screening programs. Cultural awareness of prostate cancer and screening practices in the Middle East plays a role in affecting the rate of prostate cancer screening. A study performed by Araf et al showed that in the 3 studies conducted in Arab countries: Egypt, Saudi Arabia, and Jordan, participants had poor knowledge of prostate cancer screening practices.16

Although there have been some recent improvements in screening and earlier detection of disease in some Arab countries, such as Qatar, the overall acceptance of screening practices by the Middle Eastern Arab population is still below expectations.17 This might be because of the lack of health knowledge and inaccurate public beliefs in the benefits of screening.17 A survey of 1337 citizens in Saudi Arabia showed that 1,243 people, 92.6% of the subjects thought a physician’s recommendation is essential for them to undergo screening.18 However, in another study conducted in Saudi Arabia it was reported that only 110 out of 204 (54%) of the physicians practiced prostate cancer counseling and screening with their patients.19 A survey conducted in Jordan revealed that almost all believed that cancer screening results in earlier and easier treatment, but only 352 out of 3196, 11% of the participants performed any form of cancer screening.20 As for the screening practices in Lebanon, the recent increase in the incidence of prostate cancer has been partly attributed to better detection rates.21 However, similar to other Middle Eastern Arab countries, there are not specific national prostate cancer screening programs. This factor might have contributed to the lower ASIR detected in this part of the world. As for the mortality rate from prostate cancer, the data on whether screening programs decrease mortality is still controversial with some trials that showed no significant effect of screening on mortality from prostate cancer.22 It should be noted that in some of the low-income Arab countries like Lebanon and Jordan, with the limited financial resources, the welfare of patients and the society should be considered in the analysis of screening decisions.23

However, the lower ASIR of prostate cancer in the Middle Eastern Arab world is not only because of low screening rates. Several studies showed that even if the incidence of prostate cancer is higher in Arab immigrants to the US or Australia than the incidence reported in their native countries, it is still less than the incidence rates of the non-Arab locals in the host country.6,9 A recent review of the SEER program showed that Arab American men had a drastically lower incidence rate of prostate cancer compared with non-Arab white American and Hispanic men. This finding supports the suggestion that these ethnic differences cannot be solely explained by differences in the health care practices and cancer registration.

Population-Related Factors

Age. The age structure of the Middle Eastern population has changed over the past 20 years with a decrease in the fertility and mortality rates, yet it is still a relatively young population. A 2010 report from Yemen revealed that three-quarters of its population is younger than the age of 30 years and 46% younger than the age of 15 years; Yemen has the most youthful age structure in the world outside of sub-Saharan Africa.24 People in Yemen who are 65 years and older

Figure 4 The Expected Increase in the New Cases of Prostate Cancer in the Middle East and North Africa Region in 2020

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of new cases in 2020 (all ages)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>29,377</td>
</tr>
<tr>
<td>2020</td>
<td>38,562</td>
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</tbody>
</table>

Figure 5 The Expected Increase in Prostate Cancer Deaths in the Middle East and North Africa Region in 2020

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of cancer deaths in 2020 (all ages)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>13,422</td>
</tr>
<tr>
<td>2020</td>
<td>4,219</td>
</tr>
</tbody>
</table>

100,000 in 2018 (Figure 3).12 Based on GLOBOCAN 2012 data,11 prostate cancer incidence in the MENA region is expected to increase from 29,377 new cases in 2012 to 38,562 new prostate cancer cases in 2020 along with an increase in mortality from prostate cancer from 15,422 prostate cancer deaths in 2012 to 19,681 deaths in 2020 (Figures 4 and 5).

Hence, the importance of studying the possible factors that affect the incidence and mortality rates of prostate cancer in our part of the world. The factors related to treatment and mortality is beyond the scope of this review. The focus is on the factors that affect the incidence and current epidemiology of this disease in the Middle Eastern Arab countries.
make up 2.6% of the population. The same applies to other Arab countries like Saudi Arabia where 3.2% of the population are 65 years of age and older, in Egypt where 5% of the population is 65 years of age and older, and finally Lebanon and Morocco, which are considered to have an older population, with 6.7% and 6.3% older than or equal to 65 years of age, respectively.25 In contrast, 14.5% of the population of the US is 65 years of age or older.25

Hormonal Factors. Serum androgen levels in Arab men, including total testosterone, dehydroepiandrosterone sulfate, and androstenedione have been reported to be significantly lower compared with those reported in Caucasian men especially in early adulthood, the age range of 20 to 29 years.70

In one study performed on serum samples taken from Arab men mainly from Kuwait and Oman, it was shown that Middle Eastern Arab men have lower circulating levels of androgens than matched German (European) individuals and those newly diagnosed with prostate cancer among the Arab men had higher androgen levels than their healthy matched counterparts.26

As for the prostate-specific antigen (PSA) values in Arab men, the mean PSA values for Saudi men were also shown to be low.27 Moreover, although increased serum PSA level is commonly associated with prostate cancer, subclinical prostatitis is a significant source of high serum PSA in > 40% of men in Kuwait, which suggests the need for a locally applicable paradigm to identify prostate cancer.28

Other implicated factors in the development of prostate cancer are certain growth factors like insulin-like growth factor 1 (IGF-1). In a study performed in Kuwait, it was shown that there is a strong association between high IGF-1 levels and prostate cancer risk37 as has been found in the Chinese population30 and in some studies in Caucasians from Greece, Sweden, and the US.31-33 They also found that healthy Arab men have significantly lower serum IGF-1 levels compared with healthy Caucasian individuals.

Genetics. In Tunisia, in a case control study that enrolled 90 prostate cancer patients and 131 healthy Tunisians as controls, it was found that 3 consecutive regions on chromosomes 9, 17, and 22 that encompass 14 single nucleotide polymorphisms (SNPs) that are highly associated with prostate cancer. They investigated the presence of any similarities between Tunisian and Caucasian individuals and found that 17q21, containing signal transducer and activator of transcription 3 signaling factor, is common so this can be a promising prostate cancer marker in different ethnic populations. To also investigate whether these genetic findings in the Tunisian population can be replicated in other Arab individuals, they studied 155 unrelated prostate cancer patients and 182 healthy matched control participants from Saudi Arabia and Qatar. None of the SNPs found in the Tunisian participants was found in the other Arab individuals who were studied.

The genetic structure difference between North Africa and West Asia might explain the difficulty of replication of the findings of the Tunisian genome with genome of other Arab people from Qatar and Saudi Arabia.34

This finding along with the findings from several other studies explicitly show that MENA populations are genetically heterogeneous. Moreover, several studies point out the presence of genetic differences between the coastal populations and inland populations of the same countries.35-38

Metabolic Syndrome. The metabolic syndrome is pandemic, and its prevalence among Arab men ranges between 36.3% and 45.5%.39 Intriguingly, the Christian subpopulation of Lebanon has a high frequency of familial hypercholesterolemia (1 per 85 vs. 1 per 500 worldwide), which can be attributed to the founder effect.40

Diet. The Mediterranean diet, which is rich in antioxidants, phytoestrogens, polyunsaturated fat, and low fat content, has been shown to have a plausible effect against prostate cancer development.41,42 The dietary pattern in the Middle Eastern region has changed over the years as a result of urbanization and adoption of a Western lifestyle. Alas, there is an increase in the consumption of animal products and refined foods while there is a decrease in fruit and vegetable intake.43,44

Discussion

The health care- and population-related factors mentioned herein could contribute to a better understanding of the lower ASIR of prostate cancer in the Middle Eastern Arab world compared with the developed countries.

Age is the most well established risk factor in prostate cancer, as is the case in most of other cancers. The probability of developing prostate cancer increases from 0.005% among individuals aged younger than 39 years to 2.2% (1 in 45) for those aged 40 to 59 years and 13.7% (1 in 7) for those aged 60 to 79 years.45 Based on that and on the previously discussed young age structure in the Middle Eastern Arab countries, age might be one of the factors that contribute to the relatively lower ASIR of prostate cancer in our part of the world, as shown in Table 1, and to the increasing trend of the disease at the same time.

As for the hormonal factors, the lower androgen levels in Arab men has been proposed as a protective mechanism against the development of prostate cancer. In other words, the prolonged duration of exposure to high androgen levels (ie, starting at an age younger than 30 years) in African American and Caucasian men compared with Arab and Chinese men might account for one of the factors that contribute to the low incidence of prostate cancer in such populations. Moreover, some studies have shown that IGFs are potent mutagens for a variety of cancer cells including prostate cancer cells because they stimulate cancer cell growth and suppress apoptosis.46 Thus, the lower IGF level in Middle Eastern men might be a possible explanation for the low incidence of prostate cancer in this group of Arab men.

Another factor that helps to explain the lower incidence in Middle Eastern Arab men is probably related to prostate cancer genetics being ethnic-specific as elaborated herein. There is also compelling evidence in the literature that shows a correlation between the metabolic syndrome and the risk of prostate cancer; clinically significant prostate cancer (defined as any Gleason pattern ≥ 4, > 50% involvement of a single biopsy core, or > 1 of 3 total number of cores involved) and intermediate- or high-grade prostate cancer.47 The high prevalence of the metabolic syndrome in the Arab world is paradoxical considering the low rates of prostate cancer in those countries. As for the finding of the metabolic derangement of hypercholesterolemia in the Lebanese Christian individuals, this has been used to partially explain the higher incidence of prostate cancer observed in Lebanon compared with other Arab countries.40
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Finally, the Mediterranean diet has been associated with low androstenedione, testosterone, and free testosterone levels. A systematic review on the effect of diet on prostate cancer risk, Ma and Chapman recommended a diet low in fats and rich in vegetables and fruits to decrease the risk of prostate cancer. Moreover, the recent shift in diet archetype is probably one of the culprits behind the increasing incidence of prostate cancer in the Middle East.

So, those factors combined interplay to affect the incidence of prostate cancer in the Middle Eastern Arab World that is recently on the increase. Even though the incidence is relatively still low in all of the Arab countries partly because of the previously mentioned causes, there are certain other causative factors that are specific to each country that necessitate more in-depth epidemiological studies on prostate cancer in the region.

The main limitations of this review are the following: all the studies used were retrospective, most had a limited sample size, and they were conducted in only specific countries from the MENA region. They might not apply to the whole population of Arab men. Moreover, the GLOBOCAN database and some of the other studies relied on either population-based cancer registries or projections from other countries rather than actual large-scale epidemiologic studies conducted in each of the countries included in this review. This results in a lower quality of data.

Accuracy in prostate cancer incidence and mortality rates in the Arab region is crucial to support more epidemiological studies. However, this might not be an easy task with the challenges that the Arab world is currently facing. The protracted war and armed conflicts that are being witnessed in several Arab countries have displaced populations and have led to fractured health care systems. In a report by Dewachti et al on this topic, he describes the importance of addressing what he calls “militarization of health care”—a process in which health care funds and health care professionals have been directed toward the preferential treatment of soldiers, which is similar to the situation in Bahrain, Libya, and Egypt among other Arab countries.

Conclusion

We can infer from the available studies that prostate cancer in the Arab world represents a challenge to the entire health care system that goes above and beyond registration issues. It suggests remaining weakens in the cancer care systems in these countries. However, despite the various challenges, the Arab world with its diverse genetic background provides us an opportunity to explore the effect of different factors on prostate cancer epidemiology across different countries. A multinational study to investigate the epidemiology of prostate cancer in depth in the Middle East, with specific attention to country and geographic variability and analysis comparative with that of the western hemisphere is needed. The analysis would include the study of demographic factors, disease-specific factors, and possibly serum and tissue markers. Such a study will enable us to better identify and understand the key risk factors unique to our region, and potential ways to decrease the increasing burden of prostate cancer.

Disclosure

The authors have stated that they have no conflicts of interest.

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