RESEARCH ARTICLE

Editorial Process: Submission:06/13/2021 Acceptance:09/06/2022

Epidemiology of Bladder Cancer in the Arab World: 2019 Global Burden of Disease Data

Ibrahim Al Saidi[1], Ali Mohamedabugroon[1], Amer Sawalha[1]*, Iyad Sultan[2]

Abstract

Background: Urinary bladder cancer (UBC) has unique epidemiology. It is well known that some Arab countries have higher incidence of UBC due to certain risk factors, including schistosomiasis and smoking. **Methods:** We systematically reviewed the Global Burden of Disease study (GBD) database for the year 2019. We queried GBD study database using results tool for UBC in the 22 Arab countries and compared the age-standardized incidence rate (ASIR), death rate (ASDR), mortality-to-incidence ratio (MIR) and Disability-Adjusted Life Years (ASDALYs) in Arab countries with global values. **Results:** The Arab population represents 5.6% of the global population. There was an estimated number of 27,503 patients diagnosed with UBC in 2019 in the Arab world. The ASIR for developing UBC in the Arab countries was 9.9/100,000; which is higher than the average global ASIR (6.5/100,000). Specifically, the ASIR was higher than the global average in 11 out of the 22 Arab countries. Notably, the age-specific incidence in Egypt showed that younger individuals had higher incidence of UBC than other countries, reflecting unique epidemiology. It is estimated that 10,532 patients died of UBC in the Arab world in 2019. The average mortality-to-incidence ratio (MIR) was estimated to be 0.448. The burden of UBC as estimated by the number of DALYs in the Arab world was 272,976 years representing 4% of cancer burden in Arab countries and 6.2% of the global DALYs related to UBC. **Conclusion:** UBC has high incidence in many Arab countries, particularly in North Africa. Risk factors are known and are modifiable, making prevention the most optimal way to reduce disease burden. High MIR in many Arab countries reflects suboptimal management and a window for improvement.

Keywords: Arab World- urinary bladder neoplasms- incidence- quality-adjusted life years- global burden of disease

Asian Pac J Cancer Prev, **23 (9)**, 2907-2919

Introduction

Urinary bladder cancer (UBC) ranks the 9th most commonly diagnosed cancer globally; 7th most common cancer in men and the 17th most common cancer in women (Ploeg et al., 2009). Most cases of UBC are associated with schistosomiasis are squamous cell carcinoma (SCC), while those associated with smoking are transitional cell carcinoma (TCC) (Jemal et al., 2011).

Data on the incidence of UBC are difficult to interpret because of the changing classifications among different sources (Parkin, 2008). UBC incidence is three to four times more common in developed countries relative to developing countries (Ploeg et al., 2009). However, the incidence is decreasing in developed countries, and increasing in developing countries (Pakzad et al., 2015). Similarly, mortality rates are, for the most part, decreasing in developed countries whereas trends in developing countries are more variable (Parkin, 2008).

A study investigating cancer incidence, mortality rates, and their relationship with the Human Development Index (HDI) in the world illustrated the five countries with the highest age-standardized incidence rate (ASIR) per 100,000 were Belgium (17.5), Lebanon (16.6) Malta (15.8), Turkey (15.2), and Denmark (14.4). In general, there was a positive linear relationship between the standardized incidence rate and income (r=0.653, P<0.001). Notably, the five countries that had the highest age-standardized death rates (ASDR) per 100,000 were Turkey (6.6), Egypt (6.5), Iraq (6.3), Lebanon (6.3), and Mali (5.2) (Mahdavifar et al., 2016).

There is paucity of data regarding the burden of UBC in the Arab world. More data is needed to provide up-to-date information for further research on the topic. In this study, we systematically reviewed the data provided by the Global Burden of Disease (GBD) online database to calculate the most recent epidemiological metrics and compare them with those in the literature, thus setting ground for future research which would improve the management of UBC.

Materials and Methods

Arab countries were selected based on membership

*[1]School of Medicine, University of Jordan, Amman, Jordan. [2] Department of Pediatric Hematology and Oncology, King Hussein Cancer Center, Amman, Jordan. *For Correspondence: amer.m.sawalha@gmail.com*

to the Arab League (2013). They included the following countries: Jordan, Syria, Lebanon, Palestine, Saudi Arabia, Iraq, Kuwait, Qatar, Bahrain, United Arab Emirates (UAE), Oman, Yemen, Egypt, Sudan, Libya, Algeria, Tunisia, Morocco, Djibouti, Somalia, Mauritania, and Comoros. The literature was thoroughly reviewed for papers containing any of these countries and the phrase "bladder cancer".

We queried the GBD results tool for bladder cancer data in Arab countries for the year 2019 (Network, 2017).

The resulting Table was uploaded to a Microsoft Excel spreadsheet and R program (v.3.6.0) for further analysis. Of note, we used the GBD sociodemographic index (SDI) to categorize Arab countries. This index reflects average income, fertility and level of education of each country.

Similar to other global databases, the GBD uses modelling to estimate the incidence and mortality of different diseases. Regions with similar geography, demographics and income are used to impute unavailable data, the estimated mortality-to-incidence ratio (MIR) is used to predict incidence using causes of death as provided by death certificate. The Disability-Adjusted Life Years (DALY) is an important metric that reflects years lost because of death and/or disability. To calculate DALYs, cancer-related disability is spread over 4 sequalae of equal weight that reflect disease diagnosis, treatment, metastasis and relapse.

The prevalence of smoking was obtained from the World Development Indicators Data published by the World Health Organization . The population numbers were obtained from the World Bank Open Data .

To compare the ASIR, ASDR, and ASDALYs of bladder cancer in Arab countries to the global values, a one-sample student t-test was used, with global ASIR, ASDR, and ASDALYs as the reference values respectively. Spearman correlation was used to analyze the relation between smoking prevalence and bladder cancer incidence which is illustrated in the Figures.

To obtain ASIR, ASDR and ASDALYs for Arab countries as a group, the corresponding value was multiplied by each country population and the sum was divided by the total Arab population. Mortality-to-incidence ratio (MIR) was obtained by dividing the number of deaths attributed to bladder cancer by the number of patients diagnosed.

Results

Incidence

It is estimated that 524,304 patients were diagnosed with UBC in 2019 globally, of those, 27,503 (5.2%) were diagnosed in Arab countries making it the 4th most common neoplasm in the Arab World (Table 1 and 2). Globally, UBC has an ASIR of 6.52/100,000, whereas ASIR for developing UBC in Arab countries was (9.9/100,000); with males (16/100,000) having much higher incidence than females (3.6/100,000) (Table 2, 3). There was no significant difference in the ASIR between the Arab World and the Global ASIR (p=0.1) (Figure 4 A). Lebanon had the highest ASIR in the Arab world (30.1/100,000), which was followed by Egypt (19.1/100,000), Iraq (13.8/100,000), United Arab Emirates and Qatar (12.2/100,000), Libya (11.4/100,000), Bahrain (11.3/100,000), Kuwait (10.7/100,000), Tunisia (10.6/100,000), Jordan (8.7/100,000), and Palestine (7.5/100,000). These 11 countries had an ASIR higher than the global value (6.5/100,000). Lowest ASIRs were recorded in Somalia (2.4/100,000), Comoros (2.7/100,000) and Mauritania (3.1/100,000) (Table 2). Similar to global statistics, males had higher ASIR than

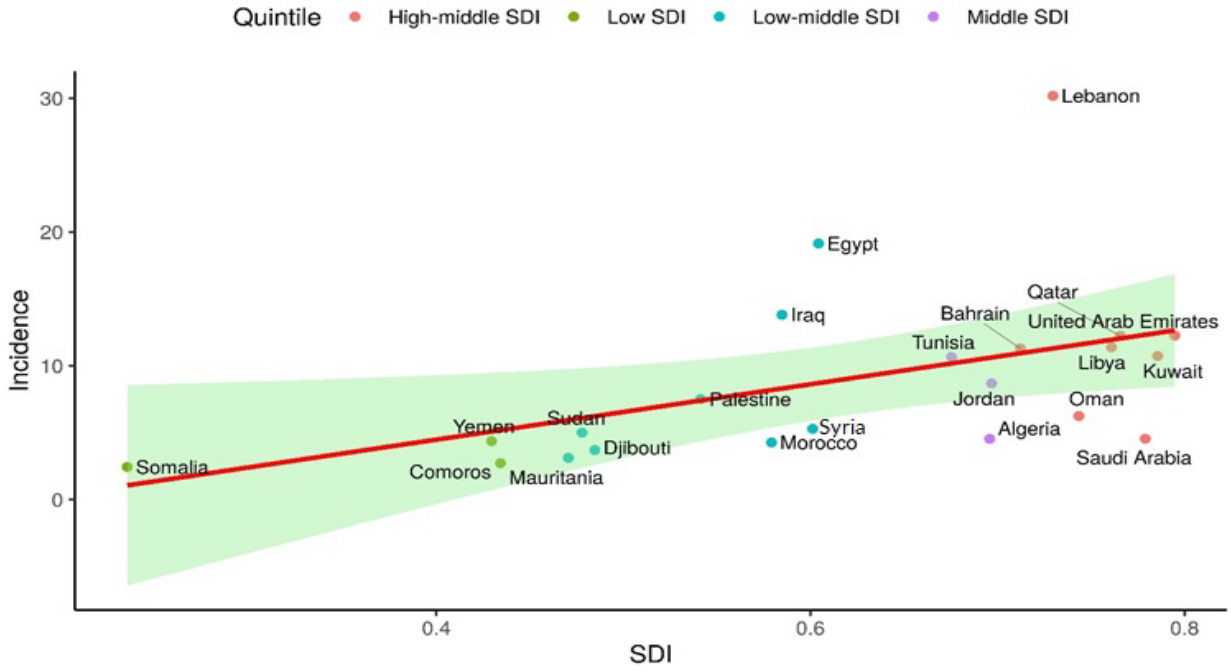

Figure 1. Scatter Plot of Age Standardized Incidence (ASIR) of Bladder Cancer in Arab Countries with Regression Line (Red Line) and Standard Error (Green Shaded Area)

Table 1. Ranking of Different Neoplasms in the Arab World countries According to Incidence, Deaths, and DALYs as per GBD 2019 Data

Neoplasms	Incidence	Incidence Rank	Deaths	Death Rank	DALYs	DALY Rank
Breast cancer	63044.47	1	24942.64	2	880406.62	1
Tracheal, bronchus, and lung cancer	32591.71	2	32891.51	1	879785.9	2
Colon and rectum cancer	31109.70	3	21019.11	3	576745.47	4
Bladder cancer	27503.28	4	10532.37	8	272975.85	10
Leukemia	23443.17	5	14806.52	6	629018.34	3
Prostate cancer	23336.10	6	10285.12	9	195720.85	12
Liver cancer	20980.67	7	20364.64	4	575401.07	5
Stomach cancer	17292.19	8	16646.65	5	442945.52	6
Brain and central nervous system cancer	14364.16	9	9412.75	10	413810.85	7
Non-melanoma skin cancer	14326.97	10	884.44	25	20837.93	26
Non-Hodgkin lymphoma	12771.84	11	8137.36	11	288677.12	9
Thyroid cancer	12498.14	12	1448.72	23	50079.05	23
Cervical cancer	12383.13	13	6212.86	12	211470.71	11
Pancreatic cancer	11776.74	14	11716.38	7	315469.47	8
Kidney cancer	8628.01	15	3317.12	17	108304.65	16
Ovarian cancer	7739.61	16	4597.99	14	150927.86	14
Uterine cancer	6622.22	17	1852.24	21	53671.41	22
Larynx cancer	6253.28	18	4448.7	15	126449.11	15
Esophageal cancer	5821.08	19	5799.19	13	162044.38	13
Nasopharynx cancer	5260.98	20	2446.93	20	86489.59	18
Lip and oral cavity cancer	4616.04	21	2486.76	19	74594.13	20
Gallbladder and biliary tract cancer	4439.36	22	4072.12	16	101825.09	17
Hodgkin lymphoma	3696.82	23	1479.59	22	67544.46	21
Multiple myeloma	3617.39	24	2902.2	18	77222.02	19
Testicular cancer	2830.69	25	227.73	28	14085.31	27
Malignant skin melanoma	1531.81	26	722.99	26	23889.11	25
Other pharynx cancer	1393.37	27	1081.89	24	32302.91	24
Mesothelioma	318.80	28	247.43	27	8042.21	28

females in all Arab countries. Average male: female ratio in Arab countries is (4.4:1) and ranged from 1.6:1 in Somalia to 9.3:1 in Tunisia.

In general, the incidence of UBC increases with age in all Arab countries. It is noteworthy that the incidence rate of UBC in Egypt and Morocco declines in individuals 75-79 years old then continues to rise in older individuals. Egypt has the highest incidence for individuals 20-64 years old showing unique epidemiology where young patients are highly affected unlike other Arab countries. For individuals between 65-79 years, Iraq takes the lead in the incidence rate. After the age of 80, Qatar takes the lead, followed by Bahrain, Kuwait, Iraq and Tunisia (Figure 1).

Deaths

The number of patients dying with UBC in Arab countries was estimated to be 10,532 in 2019 making it the 8th most common cause of death due to neoplasms in the Arab World (Table 1). Countries with the highest number of UBC-related deaths were Egypt (4844), Iraq (1265), Morocco (630), Algeria (600), Lebanon (536). The ASDR of UBC in the Arab countries was greater than that of the Global ASDR (4.7 and 2.9 per 100,000 respectively). There was a significant difference in the ASDR between the Arab World and the Global ASDR (p=0.02) (Figure 4 B). The highest ASDR was seen in Lebanon (10.4 per 100,000), followed by Egypt (7.8 per 100,000), and Iraq (6.8 per 100,000). Saudi Arabia and Syria had the lowest ASDR (1.66 and 2.08 per 100,000, respectively) (Table 4). Similar to ASIR, ASDR for males was higher than that of females in all Arab countries (Table 3).

DALYs

The total number of annual DALYs related to UBC in Arab countries was estimated to be 272,976 which makes it the 10th most common cause of DALYs due to neoplasm (Table 1). Since the global DALYs were found to be 4,392,583, this means Arab countries represent 6.21% of the global DALYs. Egypt and Lebanon had the highest ASDALYs amongst all Arab countries (201.7 and 192.7 per 100,000, respectively), almost 4 folds that of Global ASDALYs (54.2 per 100,000). On the other hand, Saudi Arabia and Algeria recorded the lowest ASDALYs (33 and 39.4 per 100,000, respectively). There was a significant difference between the ASDALYs in the Arab World (99.2) and the Global ASDALYs (54.2), (p=0.03) (Table 4).

Table 2. Age-Standardized Incidence Rates (ASIR per 100,000) and Crude Incidence Rates (per 100,000) of Bladder Cancer in Arab Countries Compared to Global and Different Sociodemographic index (SDI) Levels

Country/Region	ASIR	Number	Incidence Rate
Algeria	4.547	1390.690	174.621
Bahrain	11.303	81.683	480.319
Comoros	2.731	12.523	107.642
Djibouti	3.710	19.393	145.879
Egypt	19.142	13736.161	578.166
Iraq	13.817	2940.165	537.884
Jordan	8.695	532.211	335.826
Kuwait	10.735	245.480	431.737
Lebanon	30.183	1574.175	1188.374
Libya	11.391	545.607	437.898
Mauritania	3.131	61.289	123.800
Morocco	4.276	1256.646	166.255
Oman	6.250	96.251	251.972
Palestine	7.516	164.628	289.663
Qatar	12.239	62.325	510.537
Saudi Arabia	4.561	817.547	170.331
Somalia	2.449	142.807	94.461
Sudan	5.008	863.674	196.338
Syrian Arab Republic	4.569	539.398	167.356
Tunisia	10.662	1308.544	415.219
United Arab Emirates	12.266	576.134	444.338
Yemen	4.374	535.947	169.364
Global	6.524	524304.568	258.114
High SDI	9.922	191916.317	395.153
High-middle SDI	8.745	177587.384	341.856
Middle SDI	3.845	93521.001	141.158
Low-middle SDI	2.639	34352.065	101.095
Low SDI	3.026	14392.494	117.314

MIR

Mortality-Incidence Ratio (MIR) of bladder cancer globally is 0.436, compared to 0.448 which is the average MIR of Arab countries. Seven of the Arab countries had a MIR higher than the global value. These include Somalia, Comoros, Mauritania, Djibouti, Yemen, Sudan and Morocco which had MIR values ranging from 0.5 to 0.85. There was an inversely proportional relationship between SDI and MIR, (correlation coefficient = -0.9, $p<0.0001$). (Table 4, 5). Overall, MIR was higher in females in all Arab Countries. Three countries recorded the highest MIR values for both males and females: Somalia (0.83 and 0.86, respectively), followed by Comoros (0.81 and 0.82, respectively), and Mauritania (0.73 and 0.76, respectively). The lowest MIR was recorded in Saudi Arabia for both males and females (0.23 and 0.34, respectively) (Table 5).

Discussion

Results and Findings

Historically, UBC has an interesting epidemiology in the Arab world, particularly in North Africa. It is a very common malignancy in Egyptian males, which was previously attributed to Schistosomiasis, a major risk factor for squamous cell carcinoma (SCC). However, recent data shows a rise in transitional cell carcinoma (TCC) incidence attributed to smoking and a decline in the incidence of (SCC) owing to schistosomiasis among Egyptian males (Fedewa et al., 2009). According to a study by Bergmans et al which was done by collecting data from the SEER registry in the USA, it was found that in Arab males that migrated to America bladder cancer incidence was higher than in Hispanics and Blacks. This suggests that genetics may play a role in the etiology of the disease and its prevalence in the Arab world. (Bergmans

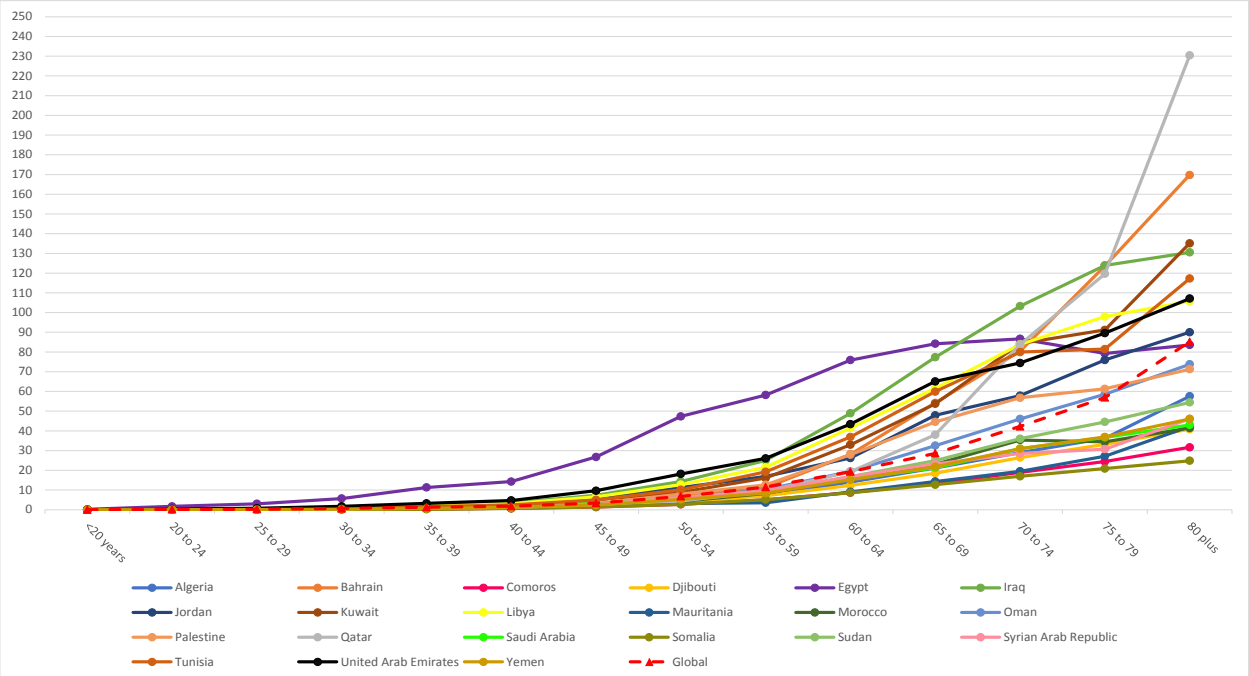

Figure 2. Age-Specific Incidence Rates of Bladder Cancer in Arab Countries. * Lebanon has been removed from this figure for better scaling.

Table 3. Gender Specific Age-standardized Incidence Rates (ASIR) and Death Rates (ASDR) for Urinary Bladder Cancer in Arab Countries

Country/Region	Males		Females	
	ASIR	ASDR	ASIR	ASDR
Algeria	7.337	3.449	1.526	0.979
Bahrain	17.571	7.839	3.785	2.326
Comoros	3.472	3.017	2.155	1.844
Djibouti	4.818	3.994	2.509	2.107
Egypt	30.707	11.637	5.616	3.087
Iraq	23.488	11.382	4.978	2.941
Jordan	14.806	5.878	2.003	1.114
Kuwait	15.209	4.982	3.932	1.787
Lebanon	53.974	17.454	10.748	4.751
Libya	19.548	8.987	2.986	1.683
Mauritania	4.464	3.558	1.774	1.451
Morocco	7.642	4.154	1.027	0.701
Oman	8.869	3.372	3.325	1.672
Palestine	14.152	6.972	2.074	1.265
Qatar	13.419	5.837	8.334	5.149
Saudi Arabia	6.473	2.26	1.741	0.844
Somalia	3.185	2.998	1.999	1.899
Sudan	7.518	4.649	1.99	1.473
Syrian Arab Republic	7.567	3.142	1.333	0.83
Tunisia	19.901	7.766	2.137	1.109
United Arab Emirates	15.606	7.059	3.893	2.39
Yemen	7.003	4.584	1.863	1.433
Global	11.28	5.094	2.663	1.357
High SDI	16.622	6.195	4.476	1.74
High-middle SDI	16.461	6.751	2.918	1.306
Middle SDI	6.372	3.554	1.63	0.972
Low-middle SDI	4.023	2.886	1.417	1.068
Low SDI	4.269	3.987	1.881	1.601

et al., 2014)

In the majority of Arab world countries data on bladder cancer is scarce. A study by Sharif-Askari (Sharif-Askari et al., 2018) on the incidence of UBC in Libya from (1983-2009) found age specific incidence for both genders to be higher than the age specific incidence globally. This study speculated that the incidence of Bladder cancer is expected to grow due to the rise in smoking populations, life expectancy, a shift to sedentary lifestyle, diabetes, and obesity. Our data illustrates that the age specific incidence and ASIR in Libya are indeed higher than the global values as seen in Table 2. Despite this finding, there was no significant difference in the ASIR between the Arab World and the Global ASIR (p=0.1) (Figure 4 A).

A study by Parkin et al showed that mortality rates are, for the most part, decreasing in developed countries and increasing in developing countries (albeit trends are more variable in developing countries). Noteworthy, the highest estimated mortality was in Egypt. (Parkin, 2008) This is supported by our results, where Egypt also had the highest number of deaths and MIR is higher in low SDI Arab countries, as shown in the data in Tables 4, 5.

Previous literature reveals that incidence rates in males are about fourfold that in females, this coincides with our results as seen in Table 3 (Ploeg et al., 2009). Recent data shows that mortality due to UBC caused by smoking increased in women, as opposed to men where the mortality has decreased in developed countries (Dy et al., 2017). Further evidence as shown by Mun et al reveals that women present with more advanced UBC and have stage-for-stage worse outcome compared with men. (Mun et al., 2019) This coincides with our results where a higher MIR is seen in women compared to men in all Arab countries (Table 5).

Risk Factors

UBC incidence increases with age, particularly in men, which increases its burden in older individuals. Environmental risk factors for UBC in Western countries are smoking and occupational exposures, whereas in

Figure 3 A. Map Representation of Disability adjusted lost years (DALYs) due to Bladder Cancer in the Arab World.

Table 4. Age-Standardized Disability-Adjusted Life Years (ASDALYs), Deaths (ASDR) and Mortality-Incidence Ratio (MIR) of Bladder Cancer in Arab Countries Compared to Global and Different Sociodemographic index (SDI) Levels

Country/Region	DALYs	ASDALYs	Deaths	ASDR	MIR
Algeria	12204.313	39.422	600.792	2.308	0.432
Bahrain	589.047	82.203	25.027	5.148	0.306
Comoros	218.449	45.767	10.216	2.349	0.816*
Djibouti	343.694	59.981	13.83	3.059	0.713*
Egypt	146006.404	201.754	4844.569	7.842	0.353
Iraq	28575.555	132.622	1265.337	6.85	0.43
Jordan	4149.817	67.726	179.471	3.618	0.337
Kuwait	1486.73	66.097	69.595	3.725	0.284
Lebanon	10051.597	192.745	536.118	10.38	0.341
Libya	5046.755	104.455	232.964	5.358	0.427
Mauritania	960.843	46.986	45.23	2.521	0.738*
Morocco	13632.953	45.585	629.929	2.384	0.501*
Oman	682.024	45.478	26.825	2.493	0.279
Palestine	1521.84	68.922	66.649	3.592	0.405
Qatar	375.706	78.213	13.773	5.739	0.221
Saudi Arabia	5811.828	32.93	203.468	1.662	0.249
Somalia	3166.278	48.043	121.28	2.305	0.849*
Sudan	10810.029	61.025	493.146	3.198	0.571*
Syrian Arab Republic	4789.598	40.1	203.835	2.08	0.378
Tunisia	9647.67	78.521	480.216	4.203	0.367
United Arab Emirates	5504.675	114.978	152.378	5.676	0.264
Yemen	7400.041	57.819	317.726	2.95	0.593*
Global	4392583.341	54.198	228734.501	2.942	0.436
High SDI	1247727.376	64.77	77040.136	3.606	0.401
High-middle SDI	1329958.706	65.238	69874.27	3.482	0.393
Middle SDI	1032346.548	42.017	47024.219	2.126	0.503*
Low-middle SDI	505458.044	37.534	22907.489	1.902	0.667*
Low SDI	274570.451	54.117	11756.897	2.726	0.817*

developing countries (namely countries in Africa and the Middle East) chronic infection with Schistosoma haematobium accounts for up to 50% of the total burden of the disease (Jemal et al., 2011). Nonetheless, cigarette

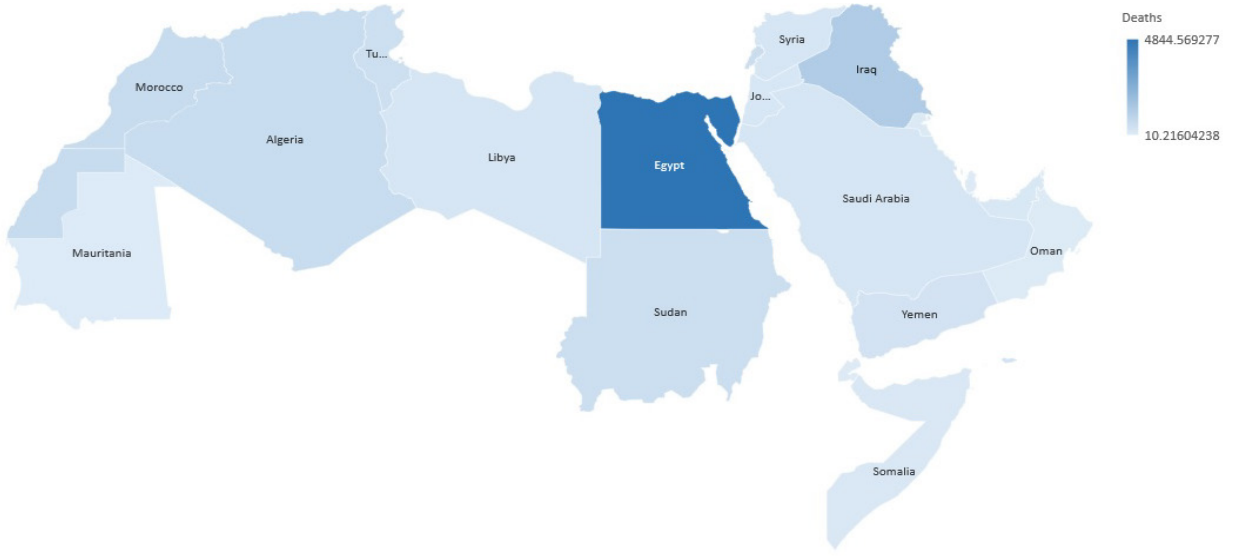

Figure 3 B. Map Representation of Annual Deaths due to Bladder Cancer in the Arab World.

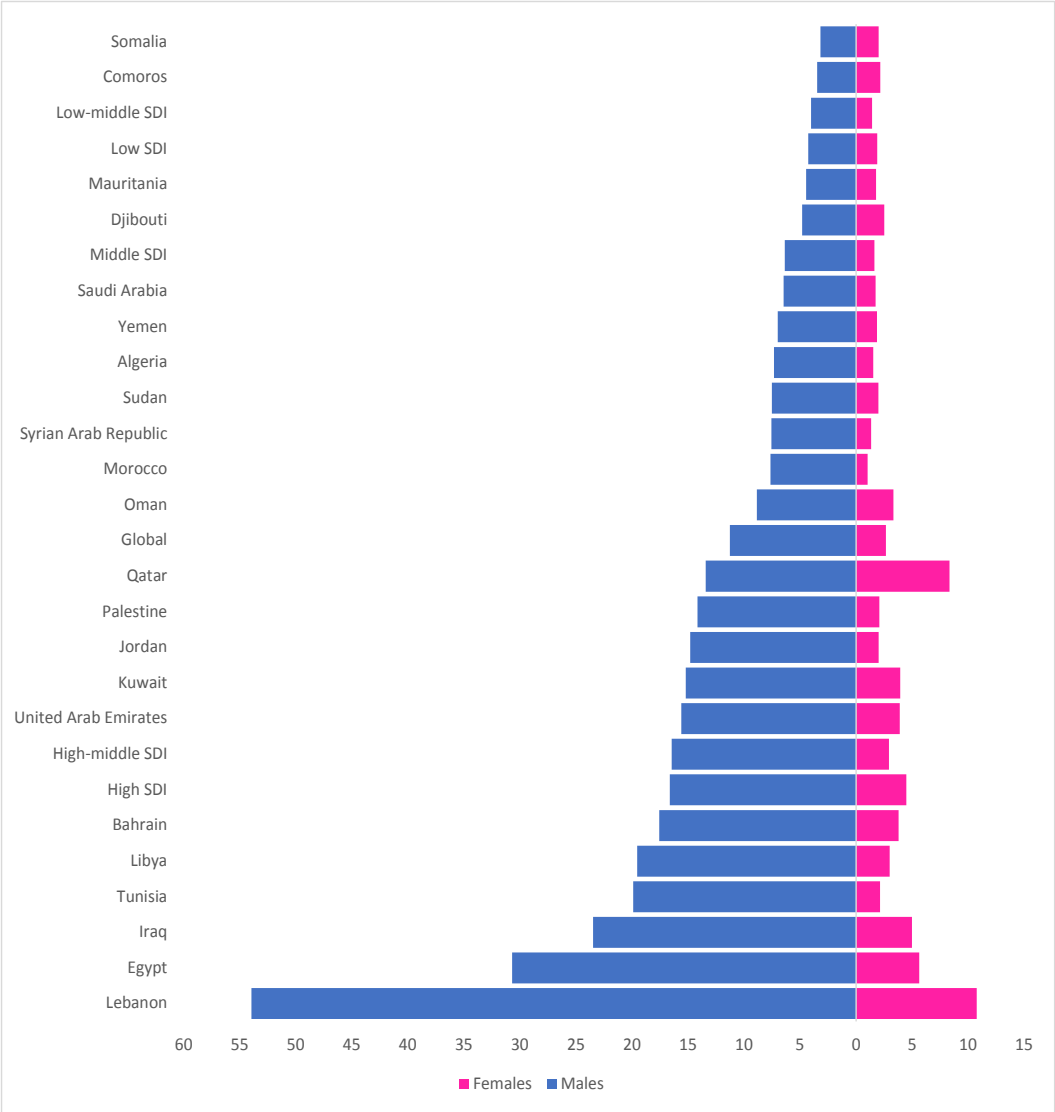

Figure 4. Population Pyramid showing Age-Standardized Incidence Rates (ASIR) for Bladder Cancer in Arab Countries

Table 5. Sociodemographic Index (SDI) of Arab Countries Alongside the General and Gender-specific Mortality-Incidence Ratio (MIR) of Bladder Cancer

Country/Region	2019 SDI	MIR	Males MIR	Females MIR
Algeria	0.652	0.432	0.412	0.538
Bahrain	0.751	0.306	0.285	0.47
Comoros	0.455	0.816	0.812	0.821
Djibouti	0.459	0.713	0.704	0.733
Egypt	0.658	0.353	0.336	0.464
Iraq	0.671	0.43	0.408	0.526
Jordan	0.731	0.337	0.323	0.455
Kuwait	0.851	0.284	0.269	0.362
Lebanon	0.708	0.341	0.316	0.441
Libya	0.709	0.427	0.413	0.516
Mauritania	0.496	0.738	0.729	0.760
Morocco	0.548	0.501	0.485	0.620
Oman	0.783	0.279	0.246	0.400
Palestine	0.588	0.405	0.382	0.545
Qatar	0.83	0.221	0.203	0.359
Saudi Arabia	0.805	0.249	0.232	0.344
Somalia	0.081	0.849	0.834	0.866
Sudan	0.515	0.571	0.552	0.654
Syrian Arab Republic	0.619	0.378	0.361	0.493
Tunisia	0.672	0.367	0.352	0.495
United Arab Emirates	0.88	0.264	0.256	0.386
Yemen	0.412	0.593	0.568	0.682
Global	0.65	0.436	0.415	0.511

smoking remains the most important risk factor worldwide while various occupational and environmental exposures to chemicals are also held responsible (Nesi et al., 2019). This is illustrated in our study by positive correlation between UBC-ASIR and smoking prevalence in males and females (Figure 7).

There is a well-established link between bladder cancer and schistosomiasis, which is highly prevalent in Egypt, Sudan and Yemen. A case-control study conducted in Egypt by Bedwani et al looked for an association between

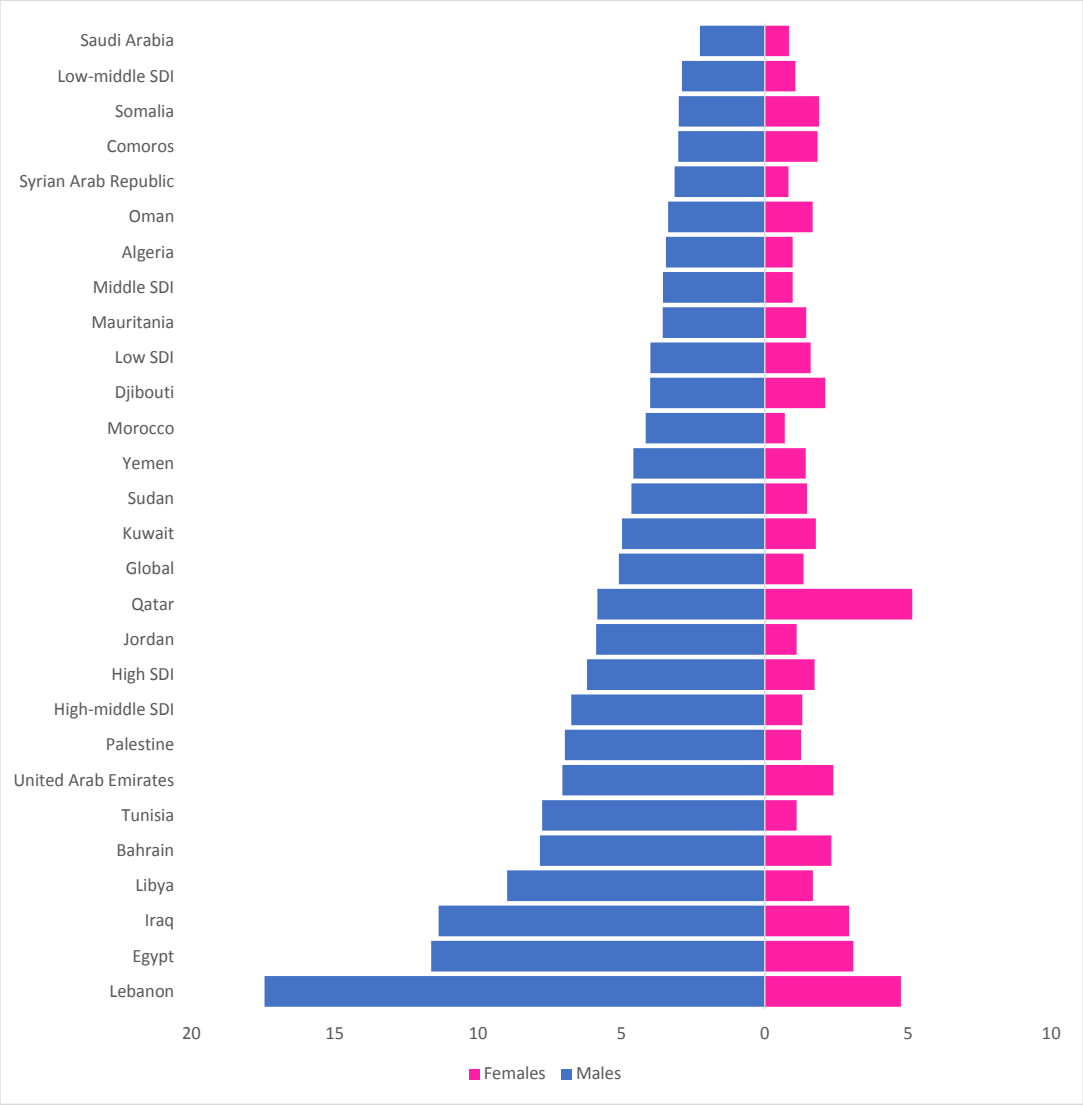

Figure 5. Population Pyramid showing Age-Standardized Death Rates (ASDR) for Bladder Cancer in Arab Countries

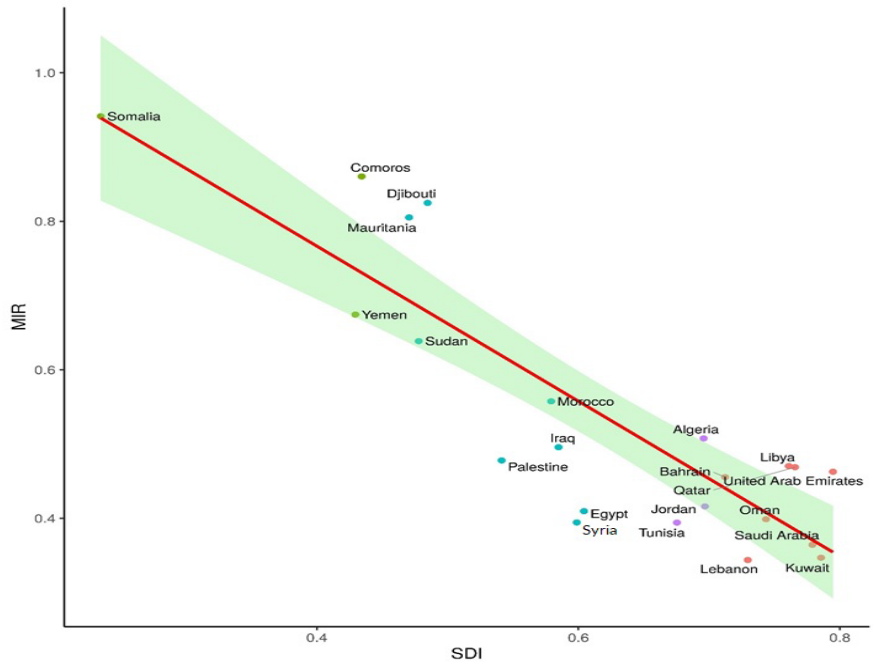

Figure 6. Scatter Plot Showing the Relation Between Sociodemographic Index (SDI) and Mortality-Incidence Ratio (MIR) of Arab countries with Regression Line (red line) and Standard Error (green shaded area)

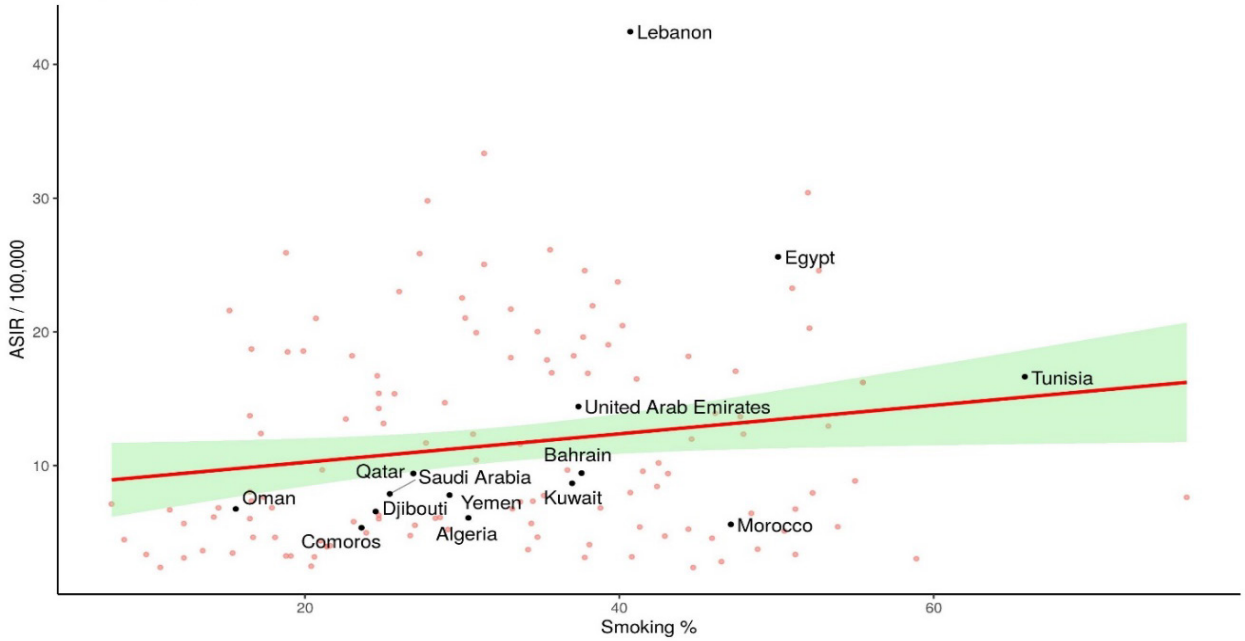

Figure 7 A. Scatter Plot Showing Relationship between Smoking and ASIR of UBC in Males with Regression Lines (red lines) and Standard Error (green shaded area).

the duration of exposure to urinary schistosomiasis and its risk of causing bladder cancer. The risk of developing UBC in subjects exposed to urinary schistosomiasis under the age of 15 years was higher with an Odds Ratio (OR) of 3.3, suggesting a duration-risk relationship. The (OR) was also 15.8 for male ever-smokers with a history of urinary schistosomiasis. All in all, this study concludes that tobacco smoking is a far greater risk factor for bladder cancer in Egypt, and a clinical history of urinary schistosomiasis accounts for only about 16% of bladder cancer cases of the Egyptian population (Bedwani et al., 1998).

Other risk factors for UBC have been defined in the literature. For instance, a meta-analysis involving 14 prospective studies on 12,642 cases was conclusive of a strong direct non-linear relationship between bladder cancer risk and Body Mass Index (SRR = 1.03, 95% CI: 1.01-1.06, P-nonlinearity =0.031). Further conclusions from the study suggested that a dose-response relationship to the disease existed and amounted to be a 3.1% increase in UBC risk for each increment of 5kg/m2 (SRR: 1.10, 95% CI: 1.03-1.17) (Zhao et al., 2017). Another meta-analysis implicated that processed meat could be associated with an increased risk for bladder cancer. A positive association was noted only in case-control studies, while no association was observed in prospective

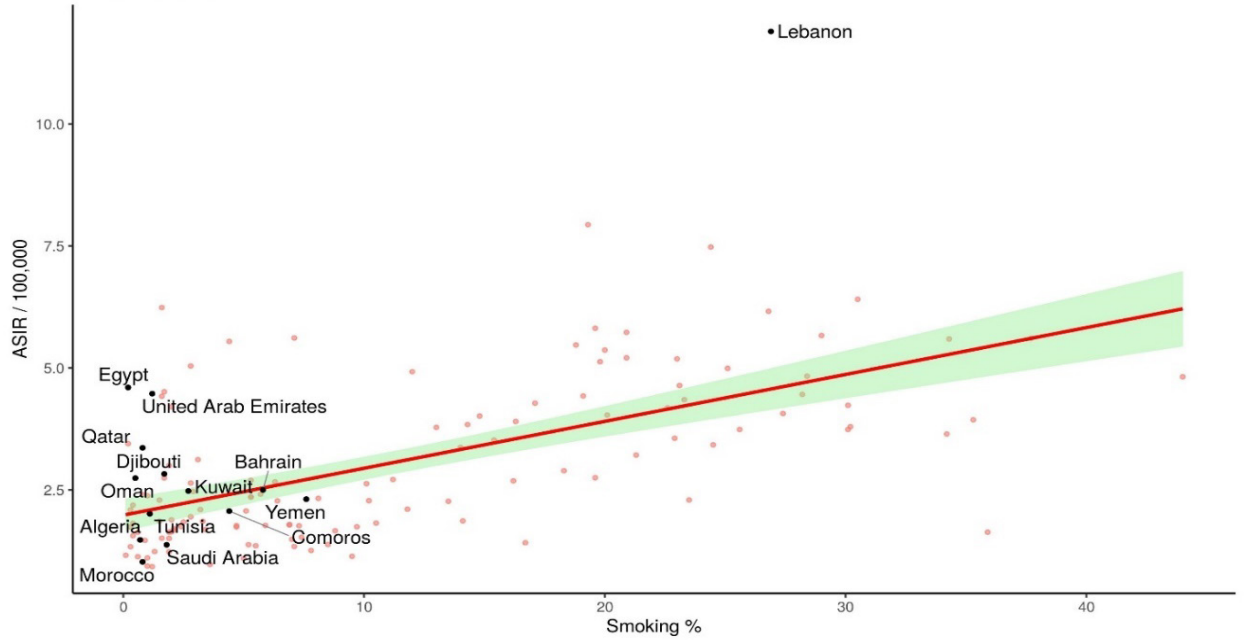

Figure 7 B. Scatter Plot Showing Relationship between Smoking and ASIR of UBC in Females with Regression Lines (red lines) and Standard Error (green shaded area).

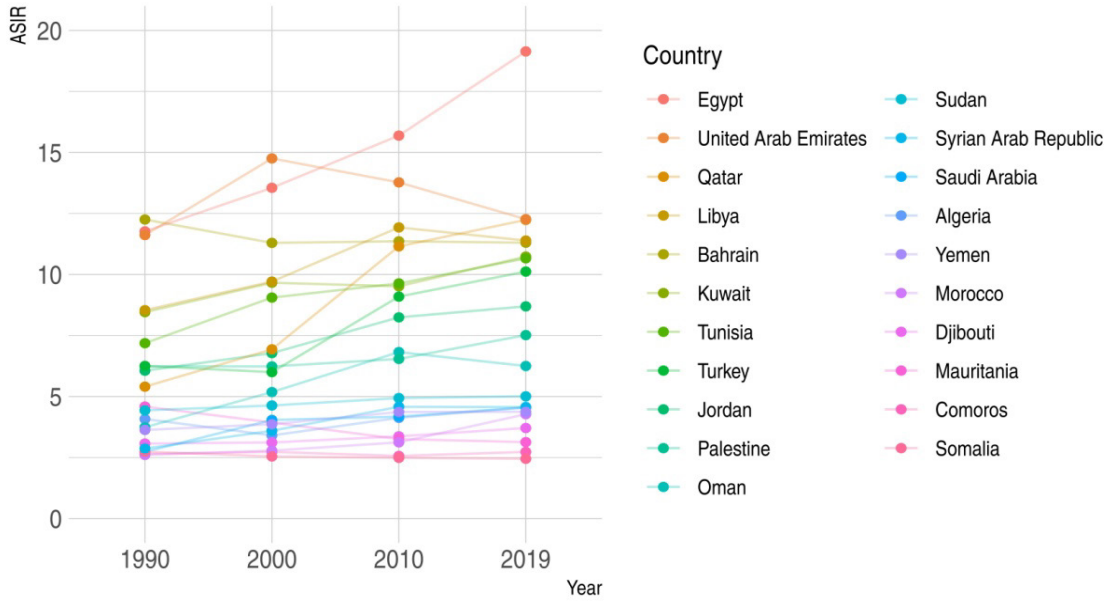

Figure 8 A. Line Graphs Representing ASIR in a Span of 30 Years from 1990-2019 across Arab Countries. *Lebanon has been removed from this figure for better scaling.

studies (Crippa et al., 2018). A study by Lippi et al shows that increased processed meat consumption was also associated with other malignancies such as colorectal, esophageal, and gastric cancers (Lippi et al., 2016). Ben Fradj et al., (2018) evaluated fatty acid plasma levels as a risk for developing UBC which revealed that palmitic acid was associated with increased risk and oleic acid with decreased risk of developing the disease. This highlights a possible protective effect of dietary modification.

According to evidence presented by Castelao et al., (2000) with the exception of pyrazolon derivatives, intake of NSAIDs showed an inverse dose-dependent association with risk of developing bladder cancer. This is believed to be due to the suppression of COX-1 activity which deprives the tumor of growth signals mediated by prostaglandins.

Statistically significant occupations with high risk of developing UBC were noted by Al-Zalabani et al., (2016) and included Relative Risk (RR) for tobacco workers (1.72), dye workers (1.58), and chimney sweeps (1.53). The combined probability of causation was 81.8 %. A study by Jemal et al., (2011) has shown a 14 fold variation in incidence internationally which implies that environmental factors may play a significant role in the development of bladder cancer.

Screening

An area of controversy in recent literature is application

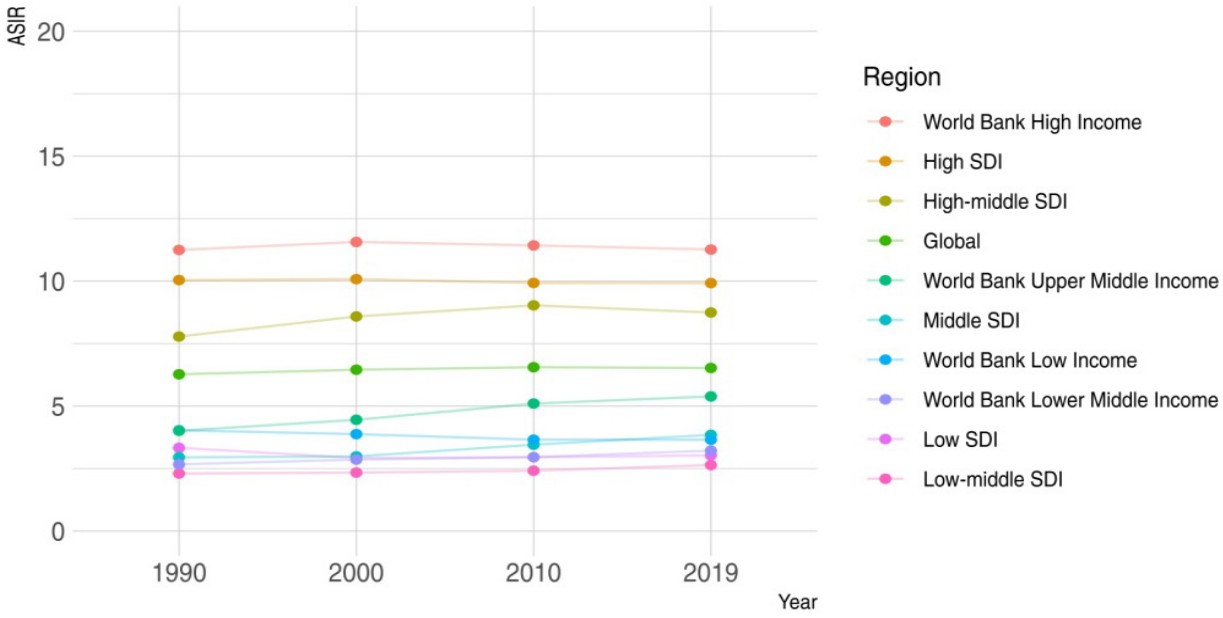

Figure 8 B. Line Graphs Representing ASIR in a Span of 30 Years from 1990-2019 across World Regions according to SDI and World Bank classifications (B).

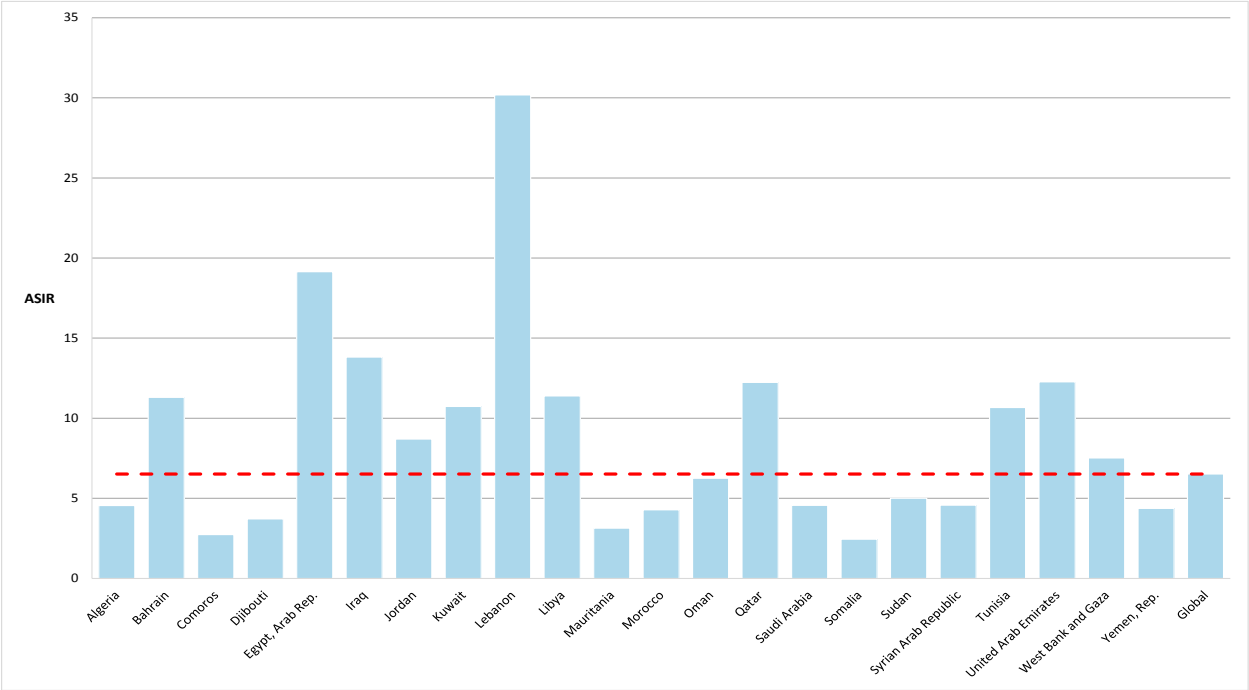

Figure 9 A. A Bar Plot Showing the Age Standardized Incidence Rate (ASIR) in Different Arab countries; red line represents average global rates.

of screening programs for UBC. A study by Britton et al., (1992) investigated the effectiveness of urine dipsticks as an initial test to detect early bladder cancer in men aged 60 years or more; 2,356 men were tested with a dipstick for hematuria and 474 had dipstick hematuria and 319 agreed to undergo further urological evaluation. An asymptomatic bladder tumor was found in only 17 men. Although urine dipstick as an initial test for hematuria is an inexpensive and simple screening test for bladder cancer, applying this to the general population as a screening method would produce a very large number of individuals requiring further investigations due to low specificity. Further research for effective screening programs for bladder cancer in the general population is required (Britton et al., 1992). Furthermore, comparison between patients who underwent screening using dipstick showed no difference in detection of bladder cancer compared to those who were unscreened (Messing et al., 1995).

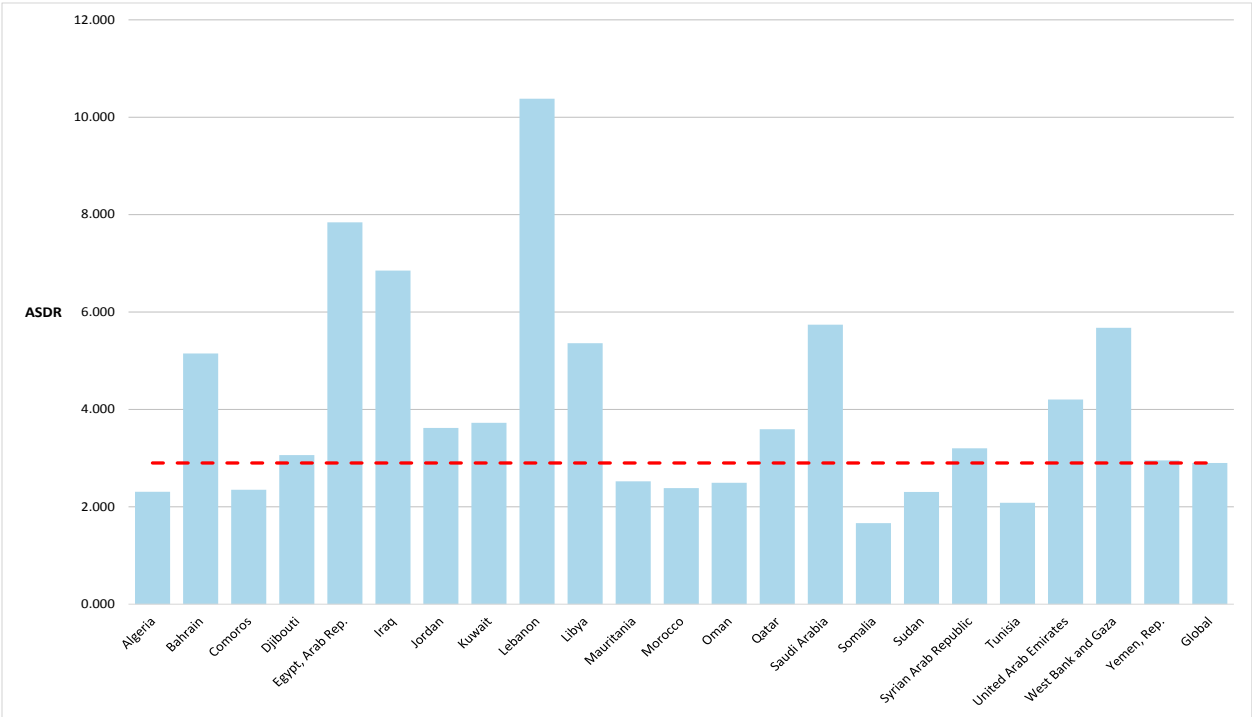

Figure 9 B. A Bar Plot Showing the Age-Standardized Death Rate (ASDR) in different Arab countries; red line represents average global rates.

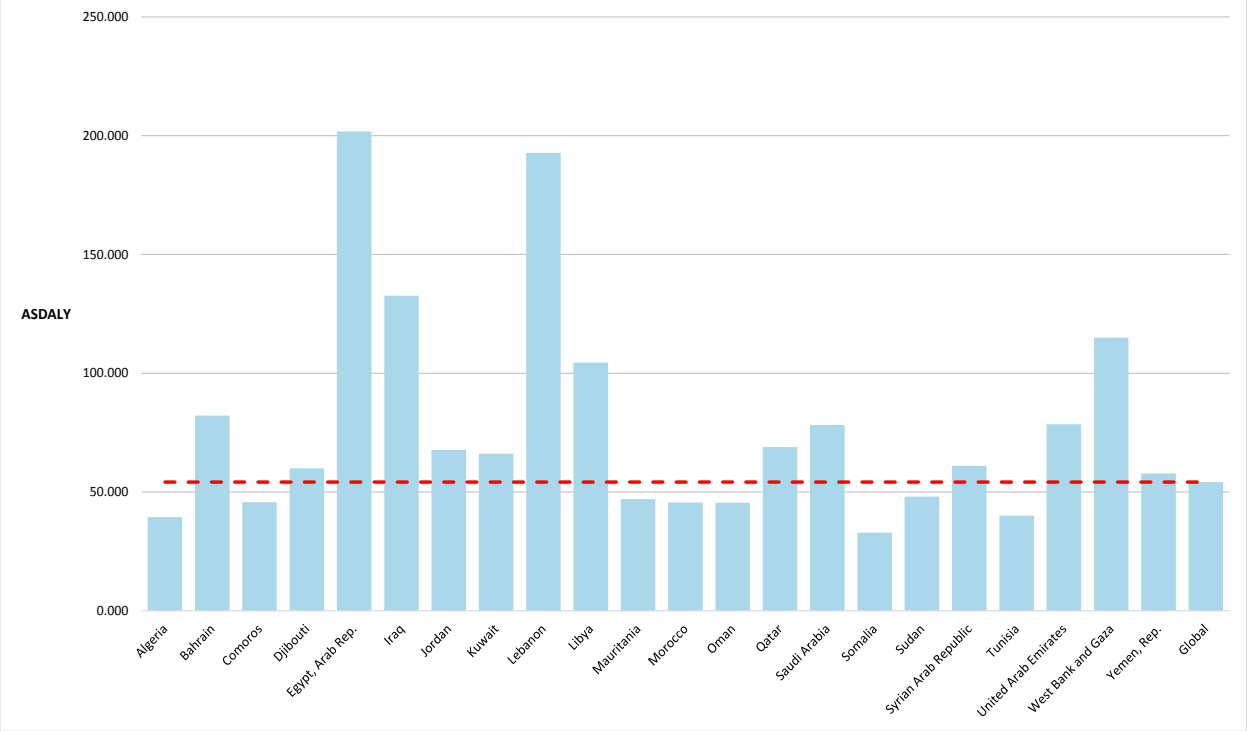

Figure 9 C. A Bar Plot Showing the Age-Standardized DALYs (ASDALYs) in different Arab countries; red line represents average global rates.

Ramakumar et al., (1999) suggested that urinary telomerase had a high combination of sensitivity and specificity (70 and 99%, respectively) for the screening of bladder cancer. Telomerase was found to be superior to cytology, dipstick and other cellular markers including BTA stat, NMP22, and FDP, for the prediction of UBC.

MIR

Due to lack of adequate data documentation of cancer patients in proper cancer registries in most Arab countries, MIR values were used in this study as a crude estimate of cancer survival in the Arab world. Although incidence and mortality rates for bladder cancer vary widely throughout the world, the MIR is higher in less developed countries (Greiman et al., 2017). This is supported by our data where the highest MIR for both males and females was recorded in Somalia (0.83 and 0.86 respectively), followed by Comoros (0.81 and 0.82 respectively), and Mauritania (0.73 and 0.76 respectively) which are all countries with a low SDI (SDI<0.5) (Table 5).

Treatment

Optimizing therapy of UBC requires the use of multimodal therapy, including chemotherapy, radiotherapy, surgery, and immunotherapy (Nadal and Bellmunt, 2019). Many Arab countries face difficulties in establishing multidisciplinary care and rely on scattered care to treat cancer. This haphazard approach in treatment (and screening) results in poor patient care, which is reflected by the significant difference in the ASDR and ASDALYs between the Arab World and the Global values (p=0.02 and p=0.03 respectively). Therefore, careful interventions to improve cancer care infrastructure in Arab countries must be implemented as soon as possible.

In conclusion, we showed that the incidence of UBC is high in multiple Arab Countries with predominance in males. High mortality and disability make this cancer a high priority for Arab countries. According to the GBD, UBC is the 4th most common cancer in the Arab World. It is the 8th most common cause of neoplastic death and the 10th most common cause of years of life lost due to disease. We aspire that this research will influence future researches into evaluating different screening methods for UBC in Arab countries, tackling different risk factors to decrease incidence, improving data collection and cancer registration and optimizing management schemes in order to decrease the burden of this disease.

Acknowledgements

The authors received no financial support for the research, authorship, and/or publication of this article.

Statement of Conflict of Interest

Ibrahim Al Saidi, Ali Mohamedabugroon, Amer Sawalha and Iyad Sultan declare that they have no conflict of interest.

Author Contribution Statement

Author 1 - Ibrahim Al Saidi
- Conceived and designed the analysis
- Wrote the paper: wrote the original draft of the paper

Author 2 – Ali Mohamedabugroon
- Performed the analysis
- Other contribution: reviewing and validating the draft

Author 3 – Amer Sawalha
- Collected the data: through Global Burden of Disease

Results Tool

• Contributed data and analysis tools

• Other contribution: reviewing and validating the draft

Author 4 – Iyad Sultan

• Other contributions: supervision and final approval of the version to be published

All data in this research was obtained from the Global Burden of Disease data available on their website.

References

Al-Zalabani AH, Stewart KF, Wesselius A, Schols AM, Zeegers MP (2016). Modifiable risk factors for the prevention of bladder cancer: a systematic review of meta-analyses. *Eur J Epidemiol*, **31**, 811-51.

Bedwani R, Renganathan E, El Kwhsky F, et al (1998). Schistosomiasis and the risk of bladder cancer in Alexandria, Egypt. *Br J Cancer*, **77**, 1186-9.

Ben Fradj MK, Ouanes Y, Hadj-Taieb S, et al (2018). Decreased Oleic Acid and Marine n− 3 Polyunsaturated Fatty Acids in Tunisian Patients with Urothelial Bladder Cancer. *Nutr Cancer*, **70**, 1043-50.

Bergmans R, Soliman AS, Ruterbusch J, et al (2014). Cancer incidence among arab americans in california, detroit, and new jersey SEER registries. *AM J Public Health*, **104**, 83-91.

Britton JP, Dowell AC, Whelan P, Harris CM (1992). A community study of bladder cancer screening by the detection of occult urinary bleeding. *J Urol*, **148**, 788-90.

Castelao JE, Yuan JM, Gago-Dominguez M, Yu MC, Ross RK (2000). Non-steroidal anti-inflammatory drugs and bladder cancer prevention. *Br J Cancer*, **82**, 1364-9.

Crippa A, Larsson SC, Discacciati A, Wolk A, Orsini N (2018). Red and processed meat consumption and risk of bladder cancer: a dose–response meta-analysis of epidemiological studies. *Eur J Nutr*, **57**, 689-701.

Dy GW, Gore JL, Forouzanfar MH, Naghavi M, Fitzmaurice C (2017). Global burden of urologic cancers, 1990–2013. *Eur Urol*, **71**, 437-46.

Fedewa SA, Soliman AS, Ismail K, et al (2009). Incidence analyses of bladder cancer in the Nile delta region of Egypt. *Cancer Epidemiol*, **33**, 176-81.

Greiman AK, Rosoff JS, Prasad SM (2017). Association of Human Development Index with global bladder, kidney, prostate and testis cancer incidence and mortality. *BJU Int*, **120**, 799-807.

Jemal A, Bray F, Center MM, et al (2011). Global cancer statistics. *CA Cancer J Clin*, **61**, 69-90.

Lippi G, Mattiuzzi C, Cervellin G (2016). Meat consumption and cancer risk: a critical review of published meta-analyses. *Crit Rev Oncol Hemat*, **97**, 1-14.

Mahdavifar N, Ghoncheh M, Pakzad R, Momenimovahed Z, Salehiniya H (2016). Epidemiology, incidence and mortality of bladder cancer and their relationship with the development index in the world. *Asian Pac Cancer Prev*, **17**, 381-6.

Messing EM, Young TB, Hunt VB, et al (1995). Comparison of bladder cancer outcome in men undergoing hematuria home screening versus those with standard clinical presentations. *Urology*, **45**, 387-97.

Mun DH, Kimura S, Shariat SF, Abufaraj M (2019). The impact of gender on oncologic outcomes of bladder cancer. *Curr Opin Urol*, **29**, 279-85.

Nadal R, Bellmunt J (2019). Management of metastatic bladder cancer. *Cancer Treat Rev*, **76**, 10-21.

Nesi G, Galli IC, Amorosi A, Santi R (2019). Environment and urinary bladder cancer. A historical perspective. *Pol J Pathtol*, **70**, 21-5.

Pakzad R, Mohammadian-Hafshejani A, Mohammadian M, et al (2015). Incidence and mortality of bladder cancer and their relationship with development in Asia. *Asian Pac Cancer Prev*, **16**, 7365-74.

Parkin DM (2008). The global burden of urinary bladder cancer. *Scand J Urol Nephrol*, **42**, 12-20.

Ploeg M, Aben KK, Kiemeney LA (2009). The present and future burden of urinary bladder cancer in the world. *World J Urol*, **27**, 289-93.

Ramakumar S, Bhuiyan J, Besse JA, et al (1999). Comparison of screening methods in the detection of bladder cancer. *J Urol*, **161**, 388-94.

Sharif-Askari NS, Bendardaf R, Sharif-Askari FS, et al (2018). Incidence of bladder cancer in Benghazi, Libya over the past three decades. *Sci Rep*, **8**, 1-5.

Zhao L, Tian X, Duan X, et al (2017). Association of body mass index with bladder cancer risk: a dose-response meta-analysis of prospective cohort studies. *Oncotarget*, **8**, 33990.