# RECENT PATTERNS OF BLADDER CANCER INCIDENCE AND MORTALITY: A GLOBAL OVERVIEW

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**Abstract – Objective:** Bladder cancer is the twelfth leading cancer and the fifteenth leading cancer-causing death worldwide. The present study was conducted to investigate recent patterns of bladder cancer incidence and mortality worldwide.

**Patients and Methods:** In the present study, information on the incidence and mortality of bladder cancer in different regions of the world was extracted from the International Agency for Research on Cancer (IARC) (GLOBOCAN, 2018). We provided the Age-Standardized Incidence Rate (ASIR) and Age Standardized Mortality Rate (ASMR) of bladder cancer per 100,000 population.

**Results:** During 2018, 549,393 new cases of bladder cancer were diagnosed worldwide, 125,311 (22.80%) of whom were female and 424,082 (77.19%) were male. In general, the global ASIR of bladder cancer was 5.7 (2.4 in women and 9.6 in men). There were also 199,922 deaths from bladder cancer, 51,652 (25.83%) of whom were female and 148,280 (74.16%) were male. The global ASMR of bladder cancer was 1.9 (0.87 in women and 3.2 in men).

**Conclusions:** The highest ASIR of bladder cancer was observed in North America, in regions with very high Human Development Index (HDI) and in Europe. The highest mortality due to bladder cancer was observed in Europe, in regions with very high human development index and in EMRO.

**KEYWORDS:** Patterns, Bladder Cancer, Incidence, Mortality.

**LIST OF ABBREVIATIONS:** WHO: World Health Organization; IARC: International Agency for Research on Cancer; HDI: Human Development Index; ASIR: Age- Standardized Incidence Rate; ASMR: Age- Standardized Mortality Rate; AFRO: WHO Africa region; PAHO; WHO Americas region; EMRO: WHO East Mediterranean region; EURO: WHO Europe region; SEARO: WHO South-East Asia region; WPRO: WHO Western Pacific region; BC: Bladder Cancer.

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#### INTRODUCTION

Non-communicable diseases such as cancers are now among the most important causes of mortality in humans<sup>1</sup>. Many studies have been conducted on the causes of increased incidence of cancers<sup>2,3</sup>. Based on these results, this is due to the increased mean age of human communities and unhealthy behaviors, especially smoking, inaccurate nutritional patterns and physical inactivity<sup>4,5</sup>. Cancer is currently the main cause of mortality in some developed countries<sup>6</sup>. In developing countries, cancer is the second or third leading cause of death after cardiovascular diseases<sup>7</sup>. Therefore, cancer is considered as a major health problem worldwide<sup>8</sup>. In the United States, one in every four deaths occurs due to cancer<sup>9</sup>.

Bladder cancer is the twelfth leading cancer and the fifteenth leading cancer causing death worldwide<sup>10</sup>. In addition, bladder cancer is the eighth leading cancer among women and the fourth leading cancer among men in Western countries11. The Age-Standardized Incidence Rate (ASIR) of bladder cancer is estimated to be 26.9 and 5 per 100,000 population in men and women in EURO countries, respectively<sup>12</sup>. The incidence of this cancer is high in North America, the Eastern Mediterranean, Southern and Western Europe, and some regions of North Africa. The highest mortality rate from bladder cancer has been reported in Egypt<sup>13</sup>. In all races, the incidence of bladder cancer is 3-4 times higher in men than in women, and the incidence of this disease increases with aging<sup>14</sup>. The well-known risk factors for bladder cancer include smoking, unhealthy nutrition, physical inactivity, occupational exposure to aromatic amines, schistosomiasis, hair dve, and contaminants in drinking water<sup>15</sup>. Potential risk factors for this cancer include adverse drug complications and side effects, geographical location and poor economic and social conditions<sup>16,17</sup>.

More than 420,000 new cases and over 165,000 mortalities from bladder cancer are annually reported worldwide<sup>18</sup>. Global geographical distribution of incidence and mortality of bladder cancer widely varies, mainly due to diverse risk factors for this cancer in different regions of the world<sup>18</sup>. The incidence and mortality of bladder cancer are higher in developed countries than in developing countries<sup>15,19</sup>, so that the ASIR and ASMR of bladder cancer per 100,000 population are 9.5 and 2.5 in more developed regions and 3.3 and 1.6 in less developed regions, respectively<sup>7</sup>. According to the available evidence, it has been estimated that the incidence of bladder cancer will rise, especially in developing countries, in the upcoming years<sup>15</sup>. In the United States, the rates of incidence and mortality of bladder cancer were nearly constant in men, but descending in women from 1997 to 2006. Since the information about the incidence and mortality from this cancer can be useful for research activities and health planning, the present study was conducted to investigate the recent patterns of bladder cancer incidence and mortality worldwide.

#### **PATIENTS AND METHODS**

To conduct this study, the data on the incidence and mortality of bladder cancer in 184 countries were drawn from the International Agency for Research on Cancer (IARC) (GLOBOCAN, 2018). GLOBOCAN is a database on various types of cancers that has been created by the World Health Organization (WHO). It covers information on the number, raw rates, and age-standardized incidence, prevalence and mortality from cancer in different regions and countries.

The present study classified and reported the data on the Age-Standardized Incidence Rate (ASIR) and Age Standardized Mortality Rate (ASMR) of bladder cancer for the continents (Asia, Africa, Oceania, Northern America, Latin America and Caribbean and Europe), world regions based on the development level (less developed regions and more developed regions), Human Development Index (HDI) (low, medium, high, very high), China and India, and the WHO regions [East Mediterranean region (EMRO), Africa region (AFRO), Europe region (EURO), Americas region (PAHO), Western Pacific region (WPRO) and South-East Asia region (SEARO)]. We provided the information about the incidence and mortality of bladder cancer based on the number, raw rates and the age-standardized rates in 2018. The ASIR and ASMR of bladder cancer were expressed per 100,000 population. Detailed descriptions of applied methods have been presented in previous studies<sup>20-23</sup>.

#### **RESULTS**

# The ASIR and ASMR of bladder cancer worldwide

A total of 549,393 new cases of bladder cancer were diagnosed worldwide in 2018, of whom 125,311 (22.80%) individuals were female and 424,082 (77.19%) ones were male. The global ASIR of bladder cancer was 5.7 (2.4 in women and 9.6 in men). There were also 199,922 deaths from bladder cancer, 51,652 (25.83%) of whom were female and 148,280 (74.16%) were male. The global ASMR of bladder cancer was 1.9 (0.87 in women and 3.2 in men).

# Bladder cancer incidence and mortality according to continents

The ASIR of bladder cancer was 11.9 in North America (5.1 in women and 19.7 in men), 11.3 in Europe (4.3 in women and 20.2 in men), 5 in Oceania

(2.1 in women and 8.4 in men), 3.6 in Asia (1.5 in women and 6 in men), 3.7 in Latin America and the Caribbean (2.0 in women and 6.3 in men), and 4.0 in Africa (2.2 in women and 6.2 in men). The highest incidence rate of bladder cancer was observed in North America and the lowest rate was observed in Asia. From among all cases of this disease worldwide, 36.2% occurred in Asia, 35.9% in Europe, 16.7% in North America, 5.3% in Latin America and the Caribbean, 5.3% in Africa and 0.69% in Oceania (Table 1 and Figure 1 and 2).

The ASMR of bladder cancer was 2.2 in North America (1.1 in women and 3.6 in men), 3 in Europe (1.2 in women and 5.6 in men), 2.1 in Oceania (1.0 in women and 3.4 in men), 1.5 in Asia (0.66 in women and 2.8 in men), 1.4 in Latin America and the Caribbean (0.76 in women and 2.2 in men), and 2.4 in Africa (1.4 in women and 3.6 in men). The highest percentage of mortality from bladder cancer was seen in Asia and the lowest was observed in Oceania, Latin America and the Caribbean, so that 42.4% of deaths were seen in Asia, 32.5% in Europe, 10.1% in North America, 8.2% in Africa, 5.9% in Latin America and the Caribbean, and 0.91% in Oceania (Table 2 and Figure 1 and 2).

# The ASIR and ASMR of bladder cancer based on the WHO classification

The ASIR of bladder cancer was obtained 4.3 in WPRO (1.8 in women and 7 in men), 10.9 in EURO (4.1 in women and 19.8 in men), 7.7 in PAHO (3.5 in women and 12.8 in men), 1.8 in SEARO (0.74 in women and 2.9 in men), 6.6 in EMRO (2.7 in women and 10.5 in men), and 2.7 in AFRO (1.8 in women and 3.7 in men). Of all cases of bladder cancer, 24.6% were observed in WPRO, 38.6% in EURO, 22% in PAHO, 6.1% in SEARO, 5.8% in EMRO and 2.8% in AFRO (Table 1 and Figure 3 and 4).

The ASMR of bladder cancer was obtained 1.6 in the WPRO (0.75 in women and 2.6 in men), 3 in EURO (1.1 in women and 5.6 in men), 1.8 in PAHO (0.91 in women and 2.9 in men), 0.96 in SEARO (0.39 in women and 1.6 in men), 3.1 in EMRO (1.3 in women and 4.9 in men), and 1.7 in AFRO (1.3 in women and 2.1 in men). Of all cases of mortality from bladder cancer, 27.7% were observed in WPRO, 35.5% in EURO, 16% in PAHO, 9% in SEARO, 7.3% in EMRO and 4.5% in AFRO (Table 2).

# Incidence and mortality of bladder cancer based on the HDI

The ASIR of bladder cancer was obtained 10.5 in regions with very high HDI (4.2 in women and 18.1 in men), 2.3 in regions with medium HDI (1 in

women and 3 in men), 4.3 in regions with high HDI (1.8 in women and 7.1 in men), and 2.4 in regions with low HDI (1.8 in women and 3.1 in men), 1.5 in India (0.65 in women and 2.4 in men) and 3.7 in China (1.6 in women and 5.9 in men). Of all cases of bladder cancer, 60.31% were observed in regions with very high HDI, 12.34% in regions with high HDI, 6.64% in regions with medium HDI, 2.26% in regions with low HDI, 14.98 % in China and 3.44% in India (Table 1).

The ASMR of bladder cancer was obtained 2.5 in regions with very high HDI (1.1 in women and 4.3 in men), 1.7 in regions with high HDI (0.76 in women and 2.9 in men), 1.2 in regions with medium HDI (0.54 in women and 2 in men), 1.6 in regions with low HDI (1.3 in women and 2 in men), 1.6 in China (0.76 in women and 2.6 in men) and 0.82 in India (0.33 in women and 1.3 in men). Of all cases of bladder cancer mortality, 48.89% were observed in regions with very high HDI, 13.21% in regions with high HDI, 9.71% in regions with medium HDI, 3.93% in regions with low HDI, 19.12 % in China and 5.11% in India (Table 2).

#### **DISCUSSION**

The present study was conducted using the 2018 GLOBOCAN PROJECT data of the WHO to investigate the geographical distribution of incidence and mortality of bladder cancer based on economic, political and geographical divisions at an international scale. In general, 549,393 new cases of bladder cancer were observed across the world in 2018. The ASIR of bladder cancer was 5.7 per 100,000 population worldwide (2.4 in women and 9.6 in men). Furthermore, 199,922 mortalities from this disease occurred in this year. The global ASMR of bladder cancer was 1.9 worldwide (0.87 in females and 3.2 in males).

Typically, men are 4-5 times more likely to be diagnosed with bladder cancer than women<sup>24,25</sup>. In the present study, 76.87% of incidence and 74.54% of mortality from bladder cancer were found to occur in males. In a study by Pakzad et al<sup>26</sup> on the Asian countries, 68.7% of bladder cancer incidence and 67% of deaths from it occurred in men, so that the sex ratio (male to female) of incidence was obtained 2.19, and the sex ratio of mortality was obtained 2.03. These results are consistent with the findings of other studies on bladder cancer in Spain<sup>27</sup>, England<sup>28</sup>, Canada<sup>29</sup> and Pakistan<sup>30</sup>, indicating greater incidence and mortality from bladder cancer in men due to the higher prevalence of smoking and higher occupational exposure to risk factors of the disease among them<sup>31</sup>.

**TABLE 1.** The standardized incidence rate of bladder cancer in different regions of world in 2018.

Population		ΑII			Male			Female	
	Numbers	Crude Rate	ASR (W)	Numbers	Crude Rate	ASR (W)	Numbers	Crude Rate	ASR (W)
WHO Africa region (AFRO)	15113	1.4	2.7	9 438	1.8	3.7	5 675	1.1	1.8
WHO Americas region (PAHO)	120 787	11.9	7.7	90 730	18.1	12.8	30 057	5.9	3.5
WHO East Mediterranean region (EMRO)	31 983	4.6	9.9	25 433	7.1	10.5	6 550	1.9	2.7
WHO Europe region (EURO)	212 285	23	10.9	166 679	37.2	19.8	45 606	9.6	4.1
WHO South-East Asia region (SEARO)	33 727	1.7	1.8	26 466	2.6	2.9	7 261	0.75	0.74
WHO Western Pacific region (WPRO)	135 386	7	4.3	105 248	10.7	7	30 138	3.2	1.8
Africa	28 954	2.2	4	20 368	3.2	6.2	8 586	1.3	2.2
Asia	198 753	4.4	3.6	156 184	6.7	9	42 569	1.9	1.5
Europe	197 105	26.5	11.3	153 849	42.8	20.2	43 256	11.3	4.3
Latin America and the Caribbean	29 098	4.5	3.7	20 386	6.3	5.8	8 712	2.6	2
North America	91 689	25.2	11.9	70 344	39	19.7	21 345	11.6	5.1
Oceania	3 794	9.2	5	2 951	14.3	8.4	843	4.1	2.1
China	82 270	5.8	3.7	64 278	8.8	5.9	17 992	2.6	1.6
High HDI	67 774	6.1	4.3	52 505	9.4	7.1	15 269	2.7	1.8
India	18 926	1.4	1.5	14 729	2.1	2.4	4 197	0.64	0.65
Low HDI	12 443	1.2	2.4	7 542	1.5	3.1	4 901	96.0	1.8
Medium HDI	36 473	2	2.3	27 858	3	3.7	8 615	0.95	1
Very high HDI	331 216	23.9	10.5	256 945	37.5	18.1	74 271	10.6	4.2
High income	309 177	25.4	11	240 225	39.6	18.6	68 952	11.3	4.5
Low income	12 020	1.6	2.9	7 340	2	3.9	4 680	1.2	2.1
Low middle income	60 480	2	2.4	46 869	3.1	3.9	13 611	0.92	

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 TABLE 1 (CONTINUED). The standardized incidence rate of bladder cancer in different regions of world in 2018.

Population		All			Male			Female	
	Numbers	Crude Rate	ASR (W)	Numbers	Crude Rate	ASR (W)	Numbers	Crude Rate	ASR (W)
Upper middle income	164211	6.3	4.4	127260	9.6	7.3	36951	2.8	1.9
Australia and New Zealand	3558	12.1	5.3	2764	18.8	8.8	794	5.3	2.2
Caribbean	2721	6.2	4.3	1982	9.1	6.9	739	3.3	2.1
Central America	2682	1.5	1.5	1786	2	2.2	968	66.0	0.92
Central and Eastern Europe	47910	16.4	8.3	36561	26.6	16.1	11349	7.3	3.2
Eastern Africa	6192	1.4	2.8	3274	1.5	3.2	2918	1.3	2.4
Eastern Asia	128255	7.8	4.5	99717	11.8	7.3	28538	3.5	1.9
Melanesia	200	1.9	2.8	159	3	4.9	41	0.79	1.1
Micronesia	15	2.8	2.7	11	4.1	4.1	4	1.5	1.2
Middle Africa	953	0.57	1.2	503	9.0	1.3	450	0.53	1
North America	91689	25.2	11.9	70344	39	19.7	21345	11.6	5.1
Northern Africa	16509	6.9	8.4	13247	11.1	14.3	3262	2.8	3.2
Northern Europe	22827	21.8	8.7	16872	32.6	13.9	5955	11.2	4.2
Polynesia	21	3	3.1	17	4.8	5.2	4	1.2	1.2
South America	23695	5.5	4.4	16618	7.9	7	7077	3.3	2.3
South-Central Asia	34046	1.7	2	26710	2.6	3.2	7336	0.77	0.82
South-Eastern Asia	15553	2.4	2.4	12300	3.8	4.2	3253	66.0	0.91
Southern Africa	1763	2.7	3.3	1273	3.9	6.3	490	1.5	1.5
Southern Europe	69065	38.6	15.2	47473	63.5	26.5	11596	14.8	5.5
Western Africa	3537	0.93	1.8	2071	1.1	2.3	1466	0.77	1.4
Western Asia	20899	7.7	9.2	17457	12.3	16.4	3442	2.7	2.8
Western Europe	67299	34.7	13.2	52943	55.3	22.5	14356	14.6	5.1

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Population		All			Male			Female	
	Numbers	Crude Rate	ASR (W)	Numbers	Crude Rate	ASR (W)	Numbers	Crude Rate	ASR (W)
WHO Africa region (AFRO)	9 053	0.84	1.7	5 232	86.0	2.1	3 821	0.71	1.3
WHO Americas region (PAHO)	31 999	3.1	1.8	22 723	4.5	2.9	9 276	1.8	0.91
WHO East Mediterranean region (EMRO)	14 500	2.1	3.1	11 355	3.2	4.9	3 145	0.94	1.3
WHO Europe region (EURO)	70 932	7.7	3	54 254	12.1	5.6	16 678	3.5	1.1
WHO South-East Asia region (SEARO)	17 964	6.0	96.0	14 153	1.4	1.6	3 811	0.39	0.39
WHO Western Pacific region (WPRO)	55 434	2.9	1.6	40 518	4.1	2.6	14 916	1.6	0.75
Africa	16 464	1.3	2.4	10 982	1.7	3.6	5 482	0.85	1.4
Asia	84 669	1.9	1.5	63 937	2.8	2.4	20 732	0.93	99.0
Europe	64 966	8.7	3	49 309	13.7	5.6	15 657	4.1	1.2
Latin America and the Caribbean	11 772	1.8	1.4	8 048	2.5	2.2	3 724	1:1	0.76
North America	20 227	5.6	2.2	14 675	8.1	3.6	5 552	3	1.1
Oceania	1 824	4.4	2.1	1 319	6.4	3.4	505	2.4	1
China	38 208	2.7	1.6	28 692	3.9	2.6	9 516	1.4	0.76
High HDI	26 407	2.6	1.7	20 197	3.9	2.9	6 210	1.3	0.76
India	10 231	0.76	0.82	660 8	1.2	1.3	2 132	0.33	0.33
Low HDI	7 863	0.77	1.6	4 511	0.88	2	3 352	99.0	1.3
Medium HDI	19 415	1.1	1.2	14 673	1.6	2	4 742	0.51	0.54
Very high HDI	97 704	7	2.5	72 025	10.5	4.3	25 679	3.7	1:1
High income	88 943	7.3	2.5	65 237	10.8	4.2	23 706	3.9	1.1
Low income	7 253	0.97	1.8	4 139	1.1	2.3	3 114	0.83	1.4
Low middle income	32 356	1.1	1.3	25 080	1.6	2.1	7 276	0.49	0.53

 TABLE 2. The standardized mortality rate of bladder cancer in different regions of world in 2018.

 TABLE 2 (CONTINUED). The standardized mortality rate of bladder cancer in different regions of world in 2018.

Population		All			Male			Female	
	Numbers	Crude Rate	ASR (W)	Numbers	Crude Rate	ASR (W)	Numbers	Crude Rate	ASR (W)
Upper middle income	70 000	2.7	1.8	52 904	4	3	17 096	1.3	0.76
Australia and New Zealand	1 697	5.7	2.1	1 217	8.3	3.4	480	3.2	1.1
Caribbean	1 199	2.7	1.7	817	3.7	2.6	382	1.7	96.0
Central America	1 458	0.81	0.75	1 010	1.1	1.2	448	0.5	0.42
Central and Eastern Europe	18 436	6.3	2.8	14 373	10.5	9	4 063	2.6	0.92
Eastern Africa	4 024	0.93	1.9	1 999	0.93	2.1	2 025	0.93	1.7
Eastern Asia	51 583	3.1	1.6	37 682	4.5	2.6	13 901	1.7	0.77
Melanesia	106	1	1.6	85	1.6	2.8	21	0.41	0.57
Micronesia	7	1.3	1.4	S	1.9	2	2	92.0	0.7
Middle Africa	999	0.4	0.85	336	0.4	0.95	330	0.39	0.78
North America	20 227	5.6	2.2	14 675	8.1	3.6	5 552	3	1.1
Northern Africa	8 601	3.6	4.4	892 9	5.7	7.5	1 833	1.5	1.7
Northern Europe	8 925	8.5	2.6	6 189	12	4.2	2 736	5.2	1.4
Polynesia	14	2	2.1	12	3.4	3.7	2	0.59	0.63
South America	9 115	2.1	1.6	6 221	2.9	2.5	2 894	1.3	0.85
South-Central Asia	16 630	0.85	96.0	13 172	1.3	1.6	3 458	0.36	0.39
South-Eastern Asia	8 215	1.3	1.3	6 373	1.9	2.2	1 842	0.56	0.5
Southern Africa	988	1.3	1.7	604	1.9	3.2	282	0.84	0.88
Southern Europe	17 408	11.4	3.2	13 692	18.3	9	3 716	4.7	1.1
Western Africa	2 287	9.0	1.3	1 275	99.0	1.5	1 012	0.53	1
Western Asia	8 241	3	3.6	6 710	4.7	6.5	1 531	1.2	1.2
Western Europe	20 197	10.4	3	15 055	15.7	5.2	5 142	5.2	1.3

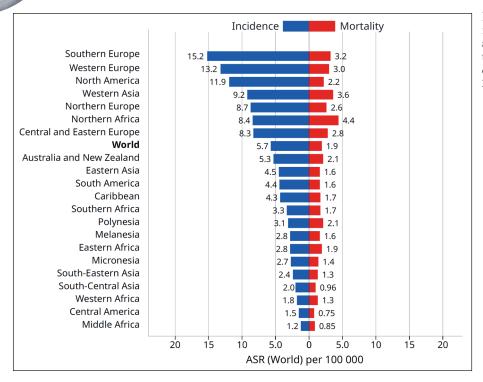
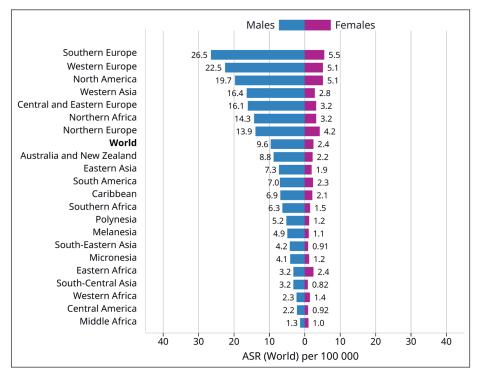


Fig. 1. The Age-Standardized Incidence Rate (ASIR) and Age Standardized Mortality Rate (ASMR) of Bladder cancer in the world in 2018.

The highest ASIR of bladder cancer was observed in regions with very high HDI (ASIR=10.5) and high HDI (ASIR=4.3), and the lowest ASIR of the disease was observed in regions with medium HDI (ASIR=2.3) and low HDI (ASIR=2.4). There was a big difference in the distribution of bladder cancer incidence worldwide, so that there was a difference of 7.5 times between regions with the highest and lowest ASIR of bladder cancer. The ASIR of bladder cancer was

higher in developed countries compared to developing regions. According to a research by Wong et al<sup>32</sup>, there is a significant correlation between the ASIR of bladder cancer and the HDI worldwide. With regards to the division of countries into four groups based on the HDI (very high HDI, high HDI, medium HDI and low HDI), the highest and lowest ASIR and ASMR of bladder cancer were seen in regions with very high HDI and low HDI, respectively.



**Fig. 2.** The Age-Standardized Incidence Rate (ASIR) of bladder cancer by gender in the world in 2018.

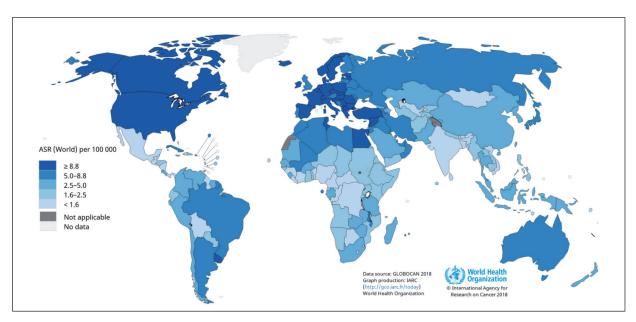


Fig. 3. Geographic distribution of new cases of bladder cancer worldwide in 2018.

The highest ASMR of bladder cancer was observed in regions with very high HDI (ASMR=2.5) and high HDI (ASMR=1.7), but the lowest mortality was observed in regions with medium HDI (ASMR=1.2) and low HDI (ASMR=1.6). There was a difference of 11.5 times between regions with the highest and lowest ASMR of bladder cancer<sup>33</sup>. According to a research by Wong et al<sup>32</sup>, a positive and significant correlation was observed between the HDI and ASMR of bladder cancer in men, but this correlation was not significant in women.

The high incidence of bladder cancer in developed regions with high or very high HDI can be attributed to the higher prevalence of obesity, tobacco smoking, alcohol consumption, and the overuse of red meat in these regions<sup>15,33</sup>. The WHO has warned about the high prevalence of these risk factors across the European countries<sup>34</sup>. The WHO report on the mortality attributable to tobacco, estimated the relative risk (RR) of mortality from bladder cancer due to tobacco smoking equal to 3 in men and 2.4 in women<sup>34</sup>. Although the prevalence of tobacco con-

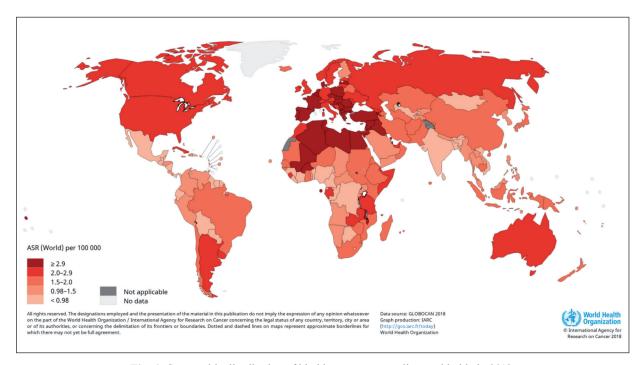


Fig. 4. Geographic distribution of bladder cancer mortality worldwide in 2018.

sumption is higher in developed countries than in other regions, these countries have designed and implemented applied programs to control and reduce smoking in the general population and particularly in the population at risk of cancer. These interventions have led to a decline in tobacco smoking in these societies; however, smoking has been rising in developing countries<sup>35,36</sup>. Given the role of tobacco as a risk factor for incidence and mortality of cancer, if developing countries do not design and implement effective interventions to reduce the prevalence of cigarette smoking, the ASIR and ASMR of bladder cancer will be raising in these regions in the upcoming years. Another reason for the high incidence of bladder cancer in developed regions of the world is the easier access of individuals to screening and diagnostic tests. Furthermore, people living in these regions are more environmentally and occupationally exposed to carcinogenic agents such as aromatic amines used in painting industry<sup>37</sup>.

Most bladder cancer cases are secondary to exposure to carcinogens through the gastrointestinal tract, respiratory system, or skin<sup>38</sup>. Risk factors for bladder cancer include smoking tobacco<sup>38</sup>, cannabis<sup>39</sup>, and opium<sup>40</sup>, lack of using adequate fruits and vegetables in the daily diet41, carbohydrate foods with high glycemic index and glycemic load<sup>42</sup>, alcohol use<sup>43</sup>, low hydration<sup>44</sup>, arsenic or trihalomethanes in drinking water<sup>45</sup>, physical inactivity, eating processed meats and low levels of vitamins A, D and E<sup>46</sup>, radiotherapy in cancer patients<sup>47</sup>, cyclophosphamide therapy<sup>48</sup>, pioglitazone treatment<sup>49</sup>, diabetes<sup>50</sup>, Schistosomiasis<sup>51</sup>, recurrent urinary tract infection<sup>52</sup>, family history of bladder cancer<sup>53</sup>, obesity<sup>46</sup> and genetic predisposition<sup>54</sup>. Varied distribution of bladder cancer risk factors appears to have led to differences in the geographical distribution of the disease across the globe.

The rate of mortality from bladder cancer has been declining over the past few years possibly due to the reduced incidence or early diagnosis of disease at primary stages when intervention and treatment measures are more effective<sup>32</sup>. Therefore, given the high incidence and mortality of bladder cancer worldwide, it is suggested that governments implement effective interventions as quickly as possible to reduce exposure to environmental, occupational and behavioral risk factors for the disease in the general population. It is also possible to improve the survival and prognosis of this type of cancer by providing necessary facilities and equipment for the early diagnosis and effective treatment. This study was designed and conducted based on the latest statistics of GLOBOCAN project. Despite the fact that this information is now the latest and most complete data on the incidence, prevalence, mortality and distribution of cancers across the world, the information was not obtained from all studied regions who did not have the same quality and precision, and thus it is expected that the number of new cases and mortality from cancer has been underestimated in less developed regions due to their unsatisfactory disease registration and reporting systems<sup>55</sup>.

#### **CONCLUSIONS**

The highest ASIR of bladder cancer was observed in North America, Europe and regions with very high HDI. Besides that, the highest mortality from bladder cancer was observed in Europe, EMRO and regions with high and very high HDI.

#### **AUTHOR CONTRIBUTIONS**

All authors contributed to the study conception. MM, HS, MA, FAB and AMH collected and summarized the data. All authors contributed to drafting the first version of the manuscript. HSG, AS, AMH and KAB edited the first draft. All authors reviewed, revised and approved the final version of the manuscript.

#### CONFLICT OF INTEREST

The Authors declare that they have no conflict of interests.

#### **REFERENCES**

- Boutayeb A. The double burden of communicable and non-communicable diseases in developing countries. Trans R Soc Trop Med Hyg 2006; 100: 191-199.
- 2. Fitzmaurice C, Allen C, Barber RM, Barregard L, Bhutta ZA, Brenner H, Dicker DJ, Chimed-Orchir O, Dandona R, Dandona L, Fleming T, Forouzanfar MH, Hancock J, Hay RJ, Hunter-Merrill R, Huynh C, Hosgood HD, Johnson CO, Jonas JB, Khubchandani J, Kumar GA, Kutz M, Lan Q, Larson HJ, Liang X, Lim SS, Lopez AD, MacIntyre MF, Marczak L, Marquez N, Mokdad AH, Pinho C, Pourmalek F, Salomon JA, Sanabria JR, Sandar L, Sartorius B, Schwartz SM, Shackelford KA, Shibuya K, Sun J, Takahashi K, Vollset SE, Vos T, Wagner JA, Wang H, Westerman R, Zeeb H, Zoeckler L, Abd-Allah F, Ahmed MB, Alabed S, Alam NK, Aldhahri SF, Alem G, Alemayohu MA, Ali R, Al-Raddadi R, Amare A, Amoako Y, Artaman A, Asayesh H, Atnafu N, Awasthi A, Saleem HB, Barac A, Bedi N, Bensenor I, Berhane A, Bernabé E, Betsu B, Binagwaho A, Boneya D, Campos-Nonato I, Castañeda-Orjuela C, Catalá-López F, Chiang P, Chibueze C, Chitheer A, Choi JY, Cowie B, Damtew S, das Neves J, Dey S, Dharmaratne S, Dhillon P, Ding E, Driscoll T, Ekwueme D, Endries AY, Farvid M, Farzadfar F, Fernandes J, Fischer F, G/Hiwot TT, Gebru A, Gopalani S, Hailu A, Horino M, Horita N, Husseini A, Huybrechts I, Inoue M, Islami F, Jakovljevic M, James S, Javanbakht M, Jee SH, Kasaeian A, Kedir MS, Khader YS, Khang YH, Kim D, Leigh J, Linn S, Lunevicius R, El Razek HMA, Malekzadeh R, Malta DC, Marcenes W, Markos D, Melaku YA, Meles KG, Mendoza W, Mengiste DT,

- Meretoja TJ, Miller TR, Mohammad KA, Mohammadi A, Mohammed S, Moradi-Lakeh M, Nagel G, Nand D, Le Nguyen Q, Nolte S, Ogbo FA, Oladimeji KE, Oren E, Pa M, Park EK, Pereira DM, Plass D, Qorbani M, Radfar A, Rafay A, Rahman M, Rana SM, Søreide K, Satpathy M, Sawhney M, Sepanlou SG, Shaikh MA, She J, Shiue I, Shore HR, Shrime MG, So S, Soneji S, Stathopoulou V, Stroumpoulis K, Sufiyan MB, Sykes BL, Tabarés-Seisdedos R, Tadese F, Tedla BA, Tessema GA, Thakur JS, Tran BX, Ukwaja KN, Uzochukwu BSC, Vlassov VV, Weiderpass E, Wubshet Terefe M, Yebyo HG, Yimam HH, Yonemoto N, Younis MZ, Yu C, Zaidi Z, Zaki MES, Zenebe ZM, Murray CJL, Naghavi M. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 32 cancer groups, 1990 to 2015: a systematic analysis for the global burden of disease study. JAMA Oncol 2017; 3: 524-548.
- Jung KW, Won YJ, Oh CM, Kong HJ, Lee DH, Lee KH. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2014. Cancer Res Treat 2017; 49: 292-305.
- 4. Mohammadian M, Mahdavifar N, Mohammadian-Hafshejani A, Salehiniya H. Liver cancer in the world: epidemiology, incidence, mortality and risk factors. WCRJ 2018; 5: 1-15.
- Salehiniya H, Mohammadian M, Mohammadian-Hafshejani A, Mahdavifar N. Nasopharyngeal cancer in the world: epidemiology, incidence, mortality and risk factors. WCRJ 2018; 5: 1-7.
- Jemal A, Bray F, Center MM, Ferlay J, Ward E, Forman D. Global cancer statistics. CA Cancer J Clin 2011; 61: 69-90.
- Koosha A, Farahbakhsh M, Hakimi S, Abdolahi L, Golzari M, Farshad MS. Epidemiologic assessment of cancer disease in East Azerbaijan 2007. Journal Tabriz Uni Medi Scien 2010; 32: 15-22.
- Cabanes A, Vidal E, Aragones N, Perez-Gomez B, Pollan M, Lope V, López-Abente G. Cancer mortality trends in Spain: 1980-2007. Ann Oncol 2010; 21: 14-20
- Siegel R, DeSantis C, Jemal A. Colorectal cancer statistics, 2014. CA Cancer J Clin 2014; 64: 104-117.
- Chavan S, Bray F, Lortet-Tieulent J, Goodman M, Jemal A. International variations in bladder cancer incidence and mortality. Eur Urol 2014; 66: 59-73.
- 11. Grasso M. Bladder cancer: a major public health issue. Eur Urol 2008; 7: 505-510.
- 12. Ferlay J, Parkin DM, Steliarova-Foucher E. Estimates of cancer incidence and mortality in Europe in 2008. Eur J Cancer 2010; 46: 765-781.
- Antoni S, Ferlay J, Soerjomataram I, Znaor A, Jemal A, Bray F. Bladder cancer incidence and mortality: a global overview and recent trends. Eur Urol 2017; 71: 96-108.
- Ploeg M, Aben KK, Kiemeney LA. The present and future burden of urinary bladder cancer in the world. World J Urol 2009; 27: 289-293.
- Burger M, Catto JW, Dalbagni G, Grossman HB, Herr H, Karakiewicz P, Kassouf W, Kiemeney LA, La Vecchia C, Shariat S, Lotan Y. Epidemiology and risk factors of urothelial bladder cancer. Eur Urol 2013; 63: 234-241.
- Kirkali Z, Chan T, Manoharan M, Algaba F, Busch C, Cheng L, Kiemeney L, Kriegmair M, Montironi R, Murphy WM, Sesterhenn IA, Tachibana M, Weider J. Bladder cancer: epidemiology, staging and grading, and diagnosis. Urology 2005; 66: 4-34.
- Pelucchi C, Bosetti C, Negri E, Malvezzi M, La Vecchia C. Mechanisms of disease: the epidemiology of bladder cancer. Nat Clin Pract Urol 2006; 3: 327-340

- Hassan TM, Al-Zahrani I. Bladder cancer: Analysis of the 2004 WHO classification in conjunction with pathological and geographic variables. African J Urol 2012; 18: 118-123.
- Fedewa SA, Soliman AS, Ismail K, Hablas A, Seifeldin IA, Ramadan M, Omar HG, Nriagu J, Wilson ML. Incidence analyses of bladder cancer in the Nile delta region of Egypt. Cancer Epidemiol 2009; 33: 176-1781
- Arabsalmani M, Mohammadian-Hafshejani A, Ghoncheh M, Hadadian F, Towhidi F, Vafaee K, Salehiniya H. Incidence and mortality of kidney cancers, and human development index in Asia; a matter of concern. J Nephropathol 2017; 6: 30-42.
- 21. Mohammadian M, Soroush A, Mohammadian-Hafshejani A, Towhidi F, Hadadian F, Salehiniya H. Incidence and mortality of liver cancer and their relationship with development in Asia. Asian Pac J Cancer Prev 2016; 17: 2041-2047.
- Rafiemanesh H, Mohammadian-Hafshejani A, Ghoncheh M, Sepehri Z, Shamlou R, Salehiniya H, Towhidi F, Makhsosi BR. Incidence and mortality of colorectal cancer and relationships with the human development index across the world. Asian Pac J Cancer Prev 2016; 17: 2465-2473.
- Shuja M, Farsani SI, Salehiniya H, Khazaei S, Mohammadian M, Aryaie M. Assessment the association between liver cancer incidence and mortality rate with human development index in the European countries in 2012. Biomed Res Therapy 2017; 4: 1185-1197.
- 24. Brookfield KF, Cheung MC, Gomez C, Yang R, Nieder AM, Lee DJ, Koniaris LG. Survival disparities among African American women with invasive bladder cancer in Florida. Cancer 2009; 115: 4196-209.
- 25. Whelan P. Survival from bladder cancer in England and Wales up to 2001. Br J Cancer 2008; 99: S90-92.
- Pakzad R, Mohammadian-Hafshejani A, Mohammadian M, Pakzad I, Safiri S, Khazaei S, Salehiniya H. Incidence and mortality of bladder cancer and their relationship with development in Asia. Asian Pac J Cancer Prev 2015; 16: 7365-7374.
- 27. Hita ER, Jiménez AV, Mellado PM, López JH, Sánchez EF, Grau JC. Descriptive study of bladder tumors in the district of Levante-Alto Almanzora. Actas Urol Esp 2001; 25: 415-421.
- Holick CN, Giovannucci EL, Stampfer MJ, Michaud DS. Prospective study of body mass index, height, physical activity and incidence of bladder cancer in US men and women. Int J Cancer 2007; 120: 140-146.
- McLellan R, French C, Bell D. Trends in the incidence of bladder cancer in Nova Scotia: a twenty-year perspective. Can J Urol 2003; 10: 1880-1884.
- 30. Nusrat J, Hamdani S, Burdy G, Khurshid A. Cancer urinary bladder--5 year experience at Cenar, Quetta. J Ayub Med Coll Abbottabad 2001; 13: 14-16.
- 31. Farahmand M, Almasi-Hashiani A. Epidemiology of bladder cancers in fars province, Southern Iran (2003-2008). J Kerman Uni Med Sci 2013; 20: 387-394.
- 32. Wong MC, Fung FD, Leung C, Cheung WW, Goggins WB, Ng C. The global epidemiology of bladder cancer: a joinpoint regression analysis of its incidence and mortality trends and projection. Sci Rep 2018; 8: 1129.
- 33. Gandomani HS, Tarazoj AA, Siri FH, karimi Rozveh A, Hosseini S, Borujeni NN, Mohammadian-Hafshejani A, Salehiniya H. Essentials of bladder cancer worldwide: incidence, mortality rate and risk factors. Biomed Res Ther 2017; 4: 1638-1655.

- 34. Mannami T, Iso H, Baba S, Sasaki S, Okada K, Konishi M, Tsugane S. Cigarette smoking and risk of stroke and its subtypes among middle-aged Japanese men and women: the JPHC Study Cohort I. Stroke 2004; 35: 1248-1253.
- 35. Mohammadian M, Sarrafzadegan N, Sadeghi M, Salehiniya H, Roohafza HR, Hosseini S, Khazaie S, Mohammadian-Hafshejani A. Factors associated with smoking initiation and continuation in Isfahan. J Mazandaran Uni Med Sci 2015; 25: 99-110.
- Shuja M, Sarrafzadegan N, Roohafza HR, Sadeghi M, Ghafari M, Mohammadian M, Mohammadian Hafshejani A. Factors associated with cigarette smoking in central parts of Iran. Asian Pac J Cancer Prev 2017; 18: 647-653.
- Kauppinen T, Toikkanen J, Pedersen D, Young R, Ahrens W, Boffetta P, Hansen J, Kromhout H, Maqueda Blasco J, Mirabelli D, de la Orden-Rivera V, Pannett B, Plato N, Savela A, Vincent R, Kogevinas M. Occupational exposure to carcinogens in the European Union. Occup Environ Med 2000; 57: 10-18.
- 38. Cumberbatch MGK, Noon AP. Epidemiology, aetiology and screening of bladder cancer. Transl Androl Urol 2019; 8: 5-11.
- Thomas AA, Wallner LP, Quinn VP, Slezak J, Van Den Eeden SK, Chien GW, Jacobsen SJ. Association between cannabis use and the risk of bladder cancer: results from the California Men's Health Study. Urology 2015; 85: 388-392.
- Afshari M, Janbabaei G, Bahrami MA, Moosazadeh M. Opium and bladder cancer: A systematic review and meta-analysis of the odds ratios for opium use and the risk of bladder cancer. PLoS One 2017; 12:e0178527.
- 41. Yao B, Yan Y, Ye X, Fang H, Xu H, Liu Y, Li S, Zhao Y. Intake of fruit and vegetables and risk of bladder cancer: a dose-response meta-analysis of observational studies. Cancer Causes Control 2014; 25: 1645-1658.
- 42. Augustin LSA, Taborelli M, Montella M, Libra M, La Vecchia C, Tavani A, Crispo A, Grimaldi M, Facchini G, Jenkins DJA, Botti G, Serraino D, Polesel J. Associations of dietary carbohydrates, glycaemic index and glycaemic load with risk of bladder cancer: a case-control study. Br J Nutr 2017; 118: 722-729.
- 43. Zaitsu M, Nakamura F, Toyokawa S, Tonooka A, Takeuchi T, Homma Y, Kobayashi Y. Risk of Alcohol Consumption in Bladder Cancer: Case-Control Study from a Nationwide Inpatient Database in Japan. Tohoku J Exp Med 2016; 239: 9-15.
- 44. Di Maso M, Bosetti C, Taborelli M, Montella M, Libra M, Zucchetto A, Turati F, Parpinel M, Negri E, Tavani A, Serraino D, Ferraroni M, La Vecchia C, Polesel J. Dietary water intake and bladder cancer risk: an Italian case-control study. Cancer Epidemiol 2016; 45: 151-156.
- 45. Villanueva CM, Cantor KP, Cordier S, Jaakkola JJ, King WD, Lynch CF, Porru S, Kogevinas M. Disinfection byproducts and bladder cancer: a pooled analysis. Epidemiology 2004; 15: 357-67.

- Al-Zalabani AH, Stewart KF, Wesselius A, Schols AM, Zeegers MP. Modifiable risk factors for the prevention of bladder cancer: a systematic review of metaanalyses. Eur J Epidemiol 2016; 31: 811-851.
- Abern MR, Dude AM, Tsivian M, Coogan CL. The characteristics of bladder cancer after radiotherapy for prostate cancer. Urol Oncol 2013; 31: 1628-1634.
- 48. Turner RM, Kwok CS, Chen-Turner C, Maduakor CA, Singh S, Loke YK. Thiazolidinediones and associated risk of bladder cancer: a systematic review and meta-analysis. Br J Clin Pharmacol 2014; 78: 258-273.
- 49. Lewis JD, Habel LA, Quesenberry CP, Strom BL, Peng T, Hedderson MM, Ehrlich SF, Mamtani R, Bilker W, Vaughn DJ, Nessel L, Van Den Eeden SK, Ferrara A. Pioglitazone use and risk of bladder cancer and other common cancers in persons with diabetes. JAMA 2015; 314: 265-277.
- 50. Zhu Z, Wang X, Shen Z, Lu Y, Zhong S, Xu C. Risk of bladder cancer in patients with diabetes mellitus: an updated meta-analysis of 36 observational studies. BMC Cancer 2013; 13: 310.
- Cumberbatch MGK, Jubber I, Black PC, Esperto F, Figueroa JD, Kamat AM, Kiemeney L, Lotan Y, Pang K, Silverman DT, Znaor A, Catto JWF. Epidemiology of bladder cancer: a systematic review and contemporary update of risk factors in 2018. Eur Urol 2018; 74: 784-795.
- 52. Lee WY, Sun LM, Lin CL, Liang JA, Chang YJ, Sung FC, Kao CH. Risk of prostate and bladder cancers in patients with spinal cord injury: a population-based cohort study. Urol Oncol 2014; 32: 51e1-7.
- 53. Turati F, Bosetti C, Polesel J, Serraino D, Montella M, Libra M, Facchini G, Ferraroni M, Tavani A, La Vecchia C, Negri E. Family history of cancer and the risk of bladder cancer: A case-control study from Italy. Cancer Epidemiol 2017; 48: 29-35.
- 54. Robertson AG, Kim J, Al-Ahmadie H, Bellmunt J, Guo G, Cherniack AD, Hinoue T, Laird PW, Hoadley KA, Akbani R, Castro MAA, Gibb EA, Kanchi RS, Gordenin DA, Shukla SA, Sanchez-Vega F, Hansel DE, Czerniak BA, Reuter VE, Su X, de Sa Carvalho B, Chagas VS, Mungall KL, Sadeghi S, Pedamallu CS, Lu Y, Klimczak LJ, Zhang J, Choo C, Ojesina Al, Bullman S, Leraas KM, Lichtenberg TM, Wu CJ, Schultz N, Getz G, Meyerson M, Mills GB, McConkey DJ; TCGA Research Network, Weinstein JN, Kwiatkowski DJ, Lerner SP. Comprehensive Molecular Characterization of Muscle-Invasive Bladder Cancer Cell 2017; 171: 540-556.
- 55. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, Parkin DM, Forman D, Bray F. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015; 136: E359-E86.