Research Article

National Burden of Cancers in Tunisia: A Disability Adjusted Life–year Approach

Houda Ben Ayed[1,*], Mohamed Hsairi[2], Sourour Yaich[1], Habib Feki[1], Jihene Jedidi[1], Raouf Karray[1], Mondher Kassis[1], Jamel Damak[1]

[1]*Community Health and Epidemiology Department, Hedi Chaker University Hospital, University of Sfax, Tunisia*
[2]*Department of Epidemiology, Salah Azaiez Institute of Tunis, Tunisia*

ARTICLE INFO

ABSTRACT

Cancer places a considerable burden on society that is reflected in both economic and humanitarian costs. We aimed to estimate the disease burden of cancers in Tunisia using the Disability Adjusted Life Years (DALYs) as a health measure. We performed the methodology suggested in the Global Burden of Disease. The DALYs were calculated as the arithmetic addition of Years of Life Lost (YLLs) and years lived with disability. National cancer data for all cancers were extracted from the GLOBOCAN database 2012. The overall age-standardized incidence rate was 127/100,000 males and 96/100,000 females. The total number of DALYs was 60,678.33 and 47,326.36 in males and females, respectively. Ranked by the age-standardized DALY rate, the top three cancers were lung (463.6/100,000 population), prostate (128/100,000 population), and colorectum (117.5/100,000 population) in males and breast (241/100,000 population), colorectum (111.7/100,000 population), and ovary cancer (86.5/100,000 population) in females. Among males, cancers with the highest YLL/DALY ratio were pancreas (93.95%), stomach (94%), and leukemia (93.5%). For females, ovary (96%), esophagus (94.4%), and stomach (94.4%) had the highest proportion of YLL toward DALY. According to age groups, brain and nervous system cancer, leukemia, and non-Hodgkin lymphoma were ranked first, second, or third in both sexes until the age of 30 years. Our study provides an insight into the magnitude of the disease burden of cancers in Tunisia. There is an urgent need to emphasize on cancer prevention, screening, early diagnosis, and curative care, notably for breast and lung cancers.

1. INTRODUCTION

Cancer is an eminent health problem and the second leading cause of deaths worldwide behind cardiovascular diseases [1]. The World Health Organization (WHO) estimated 9.6 million cancer deaths globally, of which approximately 70% occur in low- and middle-income countries [2]. Despite the advances in timely diagnosis and medical treatment, the burden of cancers is expected to almost double by 2030, with an estimated 22 million new cancer cases and 13.1 million deaths in 2030 worldwide [3]. The main factors explaining this increasing magnitude of cancer are population growth and aging, as well as economic and lifestyle changes. Despite the high burden of cancer worldwide, the "war on cancer" has not been won.

Survival rates are better in high-income countries in comparison to other countries; however, these rates vary between and within high-income countries [4–6]. In low-income countries, there are many barriers for cancer prevention and early detection programs to reduce incidence and mortality [7]. In African countries, although cancer is an increasing problem because of aging and economic transition, it continues to receive a relatively low public health priority, largely because of limited resources and other pressing public health problems, including communicable diseases. According to the GLOBOCAN data, there were 847,000 new cancer cases (6% of the world total) and 591,000 deaths (7.2% of the world total) in 54 countries of Africa in 2012, with about three-quarters recorded in 47 countries of sub-Saharan Africa [8]. The number of annual cancer cases and deaths are likely to increase in Africa by at least 70% by 2030 [8].

Tunisia is a country in the Maghreb region of North Africa and is located on the southern shore of the Mediterranean, covering 163,610 km², with about 11 million inhabitants [9]. In Tunisia, a review of the epidemiological profile shows that non-communicable diseases now exceed communicable and traditional infectious diseases as the main causes of morbidity (70.8% of cases) and mortality (79.7% of deaths) [10]. The Age-standardized Incidence Rate (ASIR) of all cancers was 115.4/100,000 population-year for both sexes [11]. The economic impact of cancer is very important with a high burden on the Tunisian society that is reflected in both economic and humanitarian costs. The full extent of these costs is shown in time lost owing to premature death and the disability resulting from diagnosis and treatment. Therefore, assessment of cancers burden provides valuable and accurate data to identify decisions related to health planning and to prioritize preventive strategies accordingly. Estimates of the burden of cancer worldwide are produced annually as part of the Global Burden of Disease (GBD) study. In light of this, this study aimed to provide an update

on the magnitude of cancers in Tunisia and to assess the cancer burden at a national level, using the Disability Adjusted Life Years (DALYs) as a health measure.

2. MATERIALS AND METHODS

2.1. Cancer Data Source

Calculation of DALYs requires global estimates of cancer incidence and mortality. The national incidence and mortality rates according to age and sex for all cancers were extracted from GLOBOCAN 2012 [12]. This database provides estimates of worldwide incidence and mortality from 27 major cancers and for all cancers combined for 2012, available at the GLOBOCAN series of the International Agency for Research on Cancer [12]. Malignant tumors included in this analysis were all cancers except Non-Melanoma skin cancer (International Classification of Diseases 10th revision, ICD-10: C00–97 except C44): Lip, Oral Cavity (C00–08), Nasopharynx (C11), Other Pharynx (C09–10, C12–14), Esophagus (C15), Stomach (C16), Colorectum (C18–21), Liver (C22), Gallbladder (C23–24), Pancreas (C25), Larynx (C32), Lung (C33–34), Melanoma of Skin (C43), Kaposi Sarcoma (C46), Breast (C50), Cervix Uteri (C53), Corpus Uteri (C54), Ovary (C56), Prostate (C61), Testis (C62), Bladder (C67), Brain, Nervous System (C70–72), Thyroid (C73), Hodgkin Lymphoma (C81), Non-Hodgkin Lymphoma (C82–85, C96), Multiple Myeloma (C88 + C90), and Leukemia (C91–95).

2.2. Disease Modeling

We used the methodology described in the GBD study [13]. The GBD provides a standardized analytical approach for estimating Years Lived with Disability (YLDs), Years of Life Lost (YLLs), and DALYs by age and sex. For disease modeling, we used DISMOD II (free, available by the WHO, from the website, http://www.who.int/evidence/dismod/) software, a statistical method performing a Bayesian metaregression tool that synthesizes sparse and heterogeneous epidemiological data for non-fatal outcomes [14]. DISMOD II requires three disease input variables as well as the total general mortality rate and population number for the population under study. In our study, cancer incidence, cancer specific mortality, and case-fatality rates were input variables. We obtained the total population structure by age and sex for 2012 from the National Institute of Statistics [9]. For the national mortality data of 2012, they were recorded from the WHO Life Tables by Country [15]. Next, the output of DISMOD II was used for calculating the disease duration of each cancer. All calculations were done separately for males and females. The GLOBOCAN 2012 data partitioned incidence and mortality into 10 age groups: 0–14, 15–39, 40–44, 45–49, 50–54, 55–59, 60–64, 65–69, 70–74, and 75+ years. Because YLLs, YLDs, and DALYs calculation requires other distribution by age group, DISMOD II was used to calculate incidence, mortality rates, and disease duration accordingly in all selected age groups.

2.3. Years of Life Lost

Age-specific YLLs caused by premature mortality by cancer were estimated by multiplying the estimated number of cancer deaths by age with the normative standard life expectancy at each age of death [16]. We derived estimated deaths from the GLOBOCAN 2012 data [12]. We used the WHO standard expected years of life to calculate the years of premature death [17].

2.4. Years Lived with Disability

The incidence of each malignant tumor was multiplied by the average duration (years) of the disease and the corresponding Disability Weight (DW) to compute the YLDs.

Years lived with disability depend on the number of new cases, disease duration, and assigned DW. We used the DW of cancers from a recently published study, which calculated the DWs for 228 causes [18].

2.5. Disability Adjusted Life Years

Disability adjusted life years were calculated by summing YLLs and YLDs of each cancer by sex and age group. According to standard convention, DALYs are age weighted and are discounted for time preference. Age weighting means that years lived at youngest and oldest age are given less weight and discounting means that future life years are assigned less value than now [19]. In the present analysis, the next parameters were fixed: discount rate (r) = 0.03, age weighting (β) = 0.04, adjustment constant for age weights (C) = 0.1658, and age weighting modulation (K) = 0 [20]. We used the DALYs Template of WHO for estimating YLDs, YLLs, and DALYs for all sites of cancer. DALYs were estimated for each cancer site by sex and age groups provided by the WHO templates (0–4, 5–14, 15–29, 30–44, 45–59, 60–69, 70–79, and ≥80 years) [21]. Then, YLDs, YLLs, and DALYs were divided by the Tunisian population of 2012 stratified by age and sex to calculate sex- and age-specific rates per 100,000 population. Age-standardized Rates (ASRs) of YLD, YLL, and DALY per 100,000 person-years (py) of 2012 were calculated based on the GBD reference population [22]. ASR of DALY was used to rank the leading causes of cancer burden by sex and age group.

2.6. Ethical Considerations

This study was approved by the Institutional Review Board of Hedi Chaker University Hospital, University of Sfax, Sfax, Tunisia. Data regarding the identification of individuals included in the study sample were omitted in order to preserve their anonymity.

3. RESULTS

3.1. Cancer Incidence and Mortality

For all cancers except non-melanoma skin cancer, 12,189 new cases and 7339 related deaths were reported in 2012. The overall ASIR was 127/100,000 py for males and 95.7/100,000 py for females. Among men, lung cancer posted the highest ASIR (31.1/100,000 py), followed by bladder (15.3/100,000 py), and colorectum cancer (11.9/100,000 py). For females, the most common incident cancers were breast cancer (ASIR = 31.8/100,000 py),

colorectum cancer (ASIR = 10/100,000 py), and cervix uteri cancer (ASIR = 4.8/100,000 py). Regarding mortality, the overall Age-standardized Mortality Rate (ASDR) was 84.1/100,000 and 49.3/100,000 py for males and females, respectively. The most common leading cancer deaths in males were lung cancer (ASDR = 27.8/100,000 py), colorectum cancer (ASDR = 7/100,000 py), and bladder (ASIR = 6.5/100,000 py) cancer. In females, the leading cancer deaths were breast cancer (ASDR = 10.8/100,000 py), colorectum cancer (ASDR = 5.9/100,000 py), and leukemia (ASDR = 2.9/100,000 py) (Table 1).

3.2. YLLs and YLDs by Sex

Overall, the total number of YLDs attributable to cancers was higher among males than in females (7648.7 vs. 5224.7); the same results were observed for YLLs (53,029.6 vs. 42,101.6). According to cancer site, the highest burden of male cancer in terms of YLDs were prostate cancer (YLDs = 2362.15), followed by lung cancer (YLDs = 1498.25), with an estimated ASR of 56.54/100,000 and 33.13/100,000 py, respectively. For females, the highest number of YLDs was observed for breast cancer (YLDs = 1609.44) and thyroid cancer (YLDs = 719.15), with ASRs of 29.48/100,000 and 12.13/100,000 py, respectively (Table 2).

Regarding the distribution of cancer YLL rate, for males, lung, colorectum, and bladder cancers had the highest ASR (430.43,

106.63, and 87.61 per 100,000 py, respectively). For females, the highest ASR of YLL were attributed to breast cancer (ASR = 211.26/100,000 py), colorectum cancer (ASR = 102.49/100,000 py), and ovary cancer (ASR = 82.7/100,000 py) (Table 2).

3.3. Disability Adjusted Life Years

The cancer-attributable ASR of DALYs in 2012 was higher in males compared to females (1328.18 vs. 939.98/100,000 py).

Among males, lung, colorectal, and prostate cancers were responsible for more than half of the total DALYs (35.46%, 8.84%, and 8.44%, respectively). For females, breast, colorectum, and ovary cancers were the main contributors to the total DALYs, accounting for 27.15%, 11.49%, and 9.67%, respectively. Hematologic malignancies, including Hodgkin lymphoma, non-Hodgkin lymphoma, multiple myeloma, and leukemia accounted for 12.9% in males and 15.18% in females of the total DALYs (Table 3).

The highest rates in male were observed for lung cancer (ASR = 463.56/100,000 py), followed by prostate cancer (ASR = 128.04/100,000 py), and colorectum cancer (ASR = 117.52/100,000 py). Among females, breast cancer (ASR = 240.74/100,000 py), colorectum cancer (ASR = 111.69/100,000 py), and ovary cancers (ASR = 86.47/100,000 py) were the leading causes of cancer burden (Table 3).

Table 1 | Cancer incidence and mortality by sex: results from GLOBOCAN 2012

Cancer sites (ICD-10)	Males				Females			
	Incident cases	ASIR	Deaths	ASDR	Incident cases	ASIR	Deaths	ASDR
All sites	6745	127	4511	84.1	5444	95.7	2828	49.3
Bladder (C67)	814	15.3	356	6.5	104	1.7	46	0.7
Brain, nervous system (C70–72)	129	2.4	79	1.5	100	1.8	61	1.1
Colorectum (C18–21)	631	11.9	379	7.0	572	10	342	5.9
Gallbladder (C23–24)	94	1.8	87	1.7	142	2.5	132	2.3
Hodgkin lymphoma (C81)	124	2.2	59	1.1	89	1.6	41	0.7
Kaposi Sarcoma (C46)	28	0.5	13	0.2	22	0.4	10	0.2
Kidney (C64–66)	134	2.6	90	1.7	103	1.9	70	1.3
Larynx (C32)	314	6.0	129	2.5	20	0.4	8	0.1
Leukemia (C91–95)	220	4.2	170	3.2	198	3.7	158	2.9
Lip, oral cavity (C00–08)	146	2.7	47	0.9	90	1.5	32	0.5
Liver (C22)	70	1.4	67	1.3	44	0.8	40	0.7
Lung (C33–34)	1631	31.1	1461	27.8	98	1.7	91	1.6
Melanoma of skin (C43)	27	0.5	12	0.2	31	0.5	12	0.2
Multiple myeloma (C88 + C90)	64	1.2	50	0.9	79	1.4	62	1.1
Nasopharynx (C11)	184	3.3	93	1.7	68	1.2	36	0.7
Non-Hodgkin lymphoma (C82–85, C96)	328	6.1	203	3.8	239	4.2	150	2.6
Esophagus (C15)	30	0.6	28	0.5	28	0.5	27	0.5
Other pharynx (C09–10, C12–14)	47	0.9	33	0.6	26	0.5	19	0.3
Pancreas (C25)	134	2.6	131	2.5	80	1.4	75	1.3
Prostate (C61)	618	11.3	353	5.9	–	–	–	–
Stomach (C16)	287	5.4	244	4.5	183	3.2	157	2.7
Testis (C62)	28	0.5	11	0.2	–	–	–	–
Thyroid (C73)	48	0.9	17	0.3	182	3.1	52	0.8
Breast (C50)	–	–	–	–	1826	31.8	624	10.8
Cervix uteri (C53)	–	–	–	–	265	4.8	103	1.9
Corpus uteri (C54)	–	–	–	–	183	3.3	46	0.8
Ovary (C56)	–	–	–	–	237	4.2	155	2.8

ASIR, age-standardized incidence rate per 100,000 population; ASDR, age-standardized death rate per 100,000 population; ICD-10, International Classification of Diseases, 10th revision.

Table 2 | Number and age-standardized rates of years of life lost, years lived with disability of cancers by sex

Cancer	Male				Female			
	YLDs		YLLs		YLDs		YLLs	
	N	Rate[a]	N	Rate[a]	N	Rate[a]	N	Rate[a]
All sites	7648.7	170.42	53,029.6	1157.76	5224.7	99.46	42,101.6	840.52
Bladder (C67)	686.41	15.94	3678.55	87.61	91.89	2.08	476.41	11.25
Brain, nervous system (C70–72)	117.72	2.25	1599.27	31.11	91.42	1.69	1262.99	23.51
Colorectum (C18–21)	495.07	10.89	4870.21	106.63	448.97	9.2	4990.94	102.49
Gallbladder (C23–24)	83.85	1.94	1022.14	23.37	122.85	2.67	1689.49	36.46
Hodgkin lymphoma (C81)	110.57	2.05	959.76	18.97	80.13	1.44	707.07	13.45
Kaposi Sarcoma (C46)	46.17	0.94	115.68	3	78.83	1.5	107.38	2.51
Kidney (C64–66)	108.18	2.36	1234.55	27.12	84.93	1.69	1178.18	24.74
Larynx (C32)	317.21	6.83	1696.62	37.2	138.64	2.53	104.66	2.24
Leukemia (C91–95)	188.33	3.93	2694.88	55.02	170.61	3.45	2866.59	57.88
Lip, oral cavity (C00–08)	150.33	3.26	616.42	13.29	92.15	1.93	427.71	8.94
Liver (C22)	307.04	6.54	913.47	20.66	45.93	0.98	664.48	14.28
Lung (C33–34)	1498.25	33.13	20,018.79	430.43	89.82	1.87	1402.45	28.33
Melanoma of skin (C43)	51.62	1.05	159.79	3.35	74.38	1.40	158.39	3.29
Multiple myeloma (C88 + C90)	51.7	1.14	590.73	13.21	74.68	1.51	841.92	17.77
Nasopharynx (C11)	165.81	3.17	913.47	20.66	83.06	1.58	664.48	14.28
Non-Hodgkin lymphoma (C82–85, C96)	260.20	5.32	2971.5	62.04	185.05	3.74	2258.68	46.84
Esophagus (C15)	42.22	0.87	397.35	8.55	22.76	0.49	386.96	7.99
Other pharynx (C09–10, C12–14)	64.57	1.34	385	9.05	23.32	0.42	376.97	6.8
Pancreas (C25)	120.13	2.63	1865.76	39.34	72.52	1.60	953.57	20.82
Prostate (C61)	211.47	4.58	3185.77	68.22	132.11	2.73	2238.8	45.68
Stomach (C16)	167.54	3.01	137.39	3.27	719.15	12.13	480.18	10.93
Testis (C62)	2362.15	56.54	2762.08	71.5	–	–	–	–
Thyroid (C73)	42.14	0.72	240.42	4.17	–	–	–	–
Breast (C50)	–	–	–	–	1609.44	29.48	11,240.16	211.26
Cervix uteri (C53)	–	–	–	–	235.65	4.49	1657.62	33.18
Corpus uteri (C54)	–	–	–	–	264.15	5.09	579.77	12.90
Ovary (C56)	–	–	–	–	192.27	3.77	4385.77	82.7

[a]Rate per 100,000 population. *N*, number; YLLs, years of life lost; YLDs, years lived with disability.

3.4. Proportional Contribution of YLLs toward DALYs

Years of life lost contributed to a high proportion of DALYs (87.3% for males and 89.0% for females). Among males, cancers with the highest YLL proportions of DALYs were observed for pancreas (93.95%), stomach (93.78%), and leukemia (93.47%). For females, the highest proportions were observed for ovary (95.8%), followed by esophagus (94.45%) and stomach cancers (94.43%) (Table 3).

3.5. DALYs Rank for the Top Five Cancer Types by Sex and Age Group

Brain and nervous system cancer, leukemia, and non-Hodgkin lymphoma were ranked first, second, or third, respectively, in both sexes until the age of 30 years. For childhood cancers (0–14 years), the top cancer was leukemia for both sexes, with a higher ASR of DALY among females (>60/100,000 py). As for younger adults (15–44 years) as well as older adults (>44 years), breast and lung cancers had the highest ASR of DALY among females and males, respectively. Globally, from 30 to 70 years, lung, colorectum, and stomach cancers as well as non-Hodgkin lymphoma had a higher ASR of DALY than other cancers for males, whereas in females, breast, ovary, colorectum, and stomach cancers had the highest

burden in terms of ASR of DALY in this age group. As for patients older than 70 years, lung, prostate, and bladder cancers were the top three cancers in males. For females of this age group, breast cancer, colorectum cancer, and non-Hodgkin lymphoma consistently produced a higher burden compared with other cancers (Table 4).

4. DISCUSSION

To the best of our knowledge, this is the first study to assess, on the basis of a retrospective analysis of the GLOBOCAN data, the burden of cancer in Tunisia using DALYs as a unified health measure, which combines incidence and mortality data. This approach for disease burden estimates is greatly beneficial to monitor services and conduct health economic analyses such as cost-effectiveness studies.

In our study, the global burden of all cancers in terms of ASR of DALY was 1328.18/100,000 py in males and 939.98/100,000 py in females. Higher levels of DALY ASR were reported in the GBD study of 2016, in which cancers accounted for 213 million and 221 thousand DALYs, with an overall ASR of 3024.9/100,000 py [23]. In the African continent, the burden of cancers had significantly increased during the past two decades [24]. When compared with other countries within the Eastern Mediterranean Region (EMR), the Tunisian global ASR of DALY of all cancer sites was close to

Table 3 | Number and age-standardized rates of disability adjusted life years (DALYs), proportion of total DALYs, and proportional distribution of years of life lost towards DALYs of cancers

Cancer sites (ICD-10)	Male				Female			
	DALY		% of total DALY	YLL/DALY (%)	DALY		% of total DALY	YLL/DALY (%)
	N	Rate[a]			*N*	Rate[a]		
All sites	60,678.33	1328.18	100	87.3	47,326.33	939.98	100	88.96
Bladder (C67)	4364.96	103.55	7.19	84.27	568.3	13.33	1.2	83.83
Brain, nervous system (C70–72)	1716.99	33.36	2.83	93.14	1354.41	25.2	2.86	93.25
Colorectum (C18–21)	5365.28	117.52	8.84	90.77	5439.91	111.69	11.49	91.75
Gallbladder (C23–24)	1106	25.31	1.82	92.42	1812.34	39.13	3.83	93.22
Hodgkin lymphoma (C81)	1070.33	21.01	1.76	89.67	787.2	14.9	1.66	89.82
Kaposi sarcoma (C46)	161.84	3.93	0.27	71.48	186.22	4.01	0.39	57.66
Kidney (C64–66)	1342.74	29.48	2.21	91.94	1263.11	26.44	2.67	93.28
Larynx (C32)	2013.83	44.03	3.32	84.25	243.3	4.77	0.51	43.02
Leukemia (C91–95)	2883.22	58.95	4.75	93.47	3037.2	61.34	6.42	94.38
Lip, oral cavity (C00–08)	766.76	16.55	1.26	80.39	519.87	10.88	1.1	82.27
Liver (C22)	1220.51	27.2	2.01	74.84	710.41	15.26	1.5	93.53
Lung (C33–34)	21,517.04	463.56	35.46	93.04	1492.27	30.2	3.15	93.98
Melanoma of skin (C43)	211.41	4.4	0.35	75.58	232.77	4.69	0.49	68.05
Multiple myeloma (C88 + C90)	642.43	14.36	1.06	91.95	916.61	19.28	1.94	91.85
Nasopharynx (C11)	1079.28	23.83	1.78	84.64	747.54	15.86	1.58	88.89
Non-Hodgkin lymphoma (C82–85, C96)	3231.71	67.36	5.33	91.95	2443.73	50.58	5.16	92.43
Esophagus (C15)	439.58	9.42	0.72	90.39	409.71	8.48	0.87	94.45
Other pharynx (C09–10, C12–14)	449.57	10.38	0.74	85.64	400.29	7.22	0.85	94.17
Pancreas (C25)	1985.89	41.97	3.27	93.95	1026.09	22.42	2.17	92.93
Prostate (C61)	5124.23	128.04	8.44	53.9	–	–	–	–
Stomach (C16)	3397.24	72.8	5.6	93.78	2370.91	48.41	5.01	94.43
Testis (C62)	282.56	4.89	0.47	85.09	–	–	–	–
Thyroid (C73)	304.93	6.29	0.5	45.06	1199.33	23.06	2.53	40.04
Breast (C50)	–	–	–	–	12,849.6	240.74	27.15	87.47
Cervix uteri (C53)	–	–	–	–	1893.28	37.67	4	87.55
Corpus uteri (C54)	–	–	–	–	843.92	17.99	1.78	68.70
Ovary (C56)	–	–	–	–	4578.04	86.47	9.67	95.8

[a]Rate per 100,000 population. *N*, number; ICD-10, International Classification of Diseases, 10th revision; YLL, years of life lost.

Table 4 | Top five cancers ranked by disability adjusted life-year (DALY) rate according to sex and age groups

Age groups (years)	Sex	Cancer rank (DALY rate[a])				
		1	2	3	4	5
0–4	Male	Leukemia, 28.13	Brain nervous system, 27.43	Non-Hodgkin, 27.17	Kidney, 13.54	Hodgkin, 7.28
	Female	Leukemia, 65.21	Kidney, 28.38	Non-Hodgkin, 14.76	Nasopharynx, 8.58	Hodgkin, 7.65
5–14	Male	Leukemia, 36.48	Brain nervous system, 25.42	Non-Hodgkin, 14.80	Kidney, 14.27	Hodgkin, 7.73
	Female	Leukemia, 62.62	Kidney, 23.14	Non-Hodgkin, 15.92	Brain nervous system, 15.57	Ovary, 8.94
15–29	Male	Leukemia, 32.86	Non-Hodgkin, 24.55	Lung, 23.61	Brain nervous system, 18.05	Colorectum, 16.38
	Female	Breast, 120.81	Ovary, 34.04	Leukemia, 32.11	Colorectum, 23.66	Non-Hodgkin, 22.97
30–44	Male	Lung, 118.82	Non-Hodgkin, 34.32	Colorectum, 33.53	Leukemia, 31.23	Stomach, 23.75
	Female	Breast, 205.28	Ovary, 59.50	Colorectum, 45.99	Leukemia, 33.49	Stomach, 24.31
45–59	Male	Lung, 1079.33	Colorectum, 215.50	Stomach, 152.65	Non-Hodgkin, 115.20	Bladder, 107.83
	Female	Breast, 570.20	Ovary, 225.05	Colorectum, 204.61	Cervix, 93.10	Stomach, 74.96
60–69	Male	Lung, 2146.24	Colorectum, 504.71	Bladder, 452.34	Prostate, 438.03	Stomach, 304.53
	Female	Breast, 623.49	Colorectum, 404.49	Ovary, 254.62	Stomach, 170.90	Gallbladder, 168.13
70–79	Male	Lung, 1806.83	Prostate, 1427.74	Bladder, 828.57	Colorectum, 602.01	Stomach, 319.90
	Female	Breast, 600.82	Colorectum, 594.87	Non-Hodgkin, 271.15	Stomach, 262.19	Gallbladder, 252.88
80+	Male	Lung, 1006.33	Prostate, 976.49	Bladder, 558.96	Colorectum, 366.92	Stomach, 182.19
	Female	Colorectum, 339.12	Breast, 308.37	Non-Hodgkin, 164.27	Gallbladder,147.32	Stomach, 145.82

[a]Age-specific rate/100,00 population.

that of Saudi Arabia in both males (1300/100,000 py) and females (992/100,000 py) [25]. The high mortality rate of these malignant tumors in Tunisia could be explained in part probably by the high occurrence of late stages at the time of diagnosis and the low rate of cancer screening coverage, resulting in a diagnosis delay. Meanwhile, ASR of DALY was substantially lower than the rates observed in Afghanistan (ASR = 5066/100,000 py for males and ASR = 4260/100,000 py for females) and Somalia (4751/100,000 py for males and 4031/100,000 py for females). Moreover, it has been reported that the estimated values of cancers ASR of DALYs in Tunisia within the EMR countries were relatively higher than our rates (3445/100,000 py in males and 1878/100,000 py in females) [25]. This might be explicated, first, by the discount rate and the standard age weighting used in the computation of DALYs in this study, resulting in lower DALYs, and second, by the exclusion of "other neoplasms" group of cancers in our analysis, as opposed to the EMR study. Another possible explanation of the observed differences between GLOBOCAN and GBD could be the use of different methods to estimate cancer mortality. Whereas the GLOBOCAN methodology used survival models to estimate mortality [12], GBD used another model to estimate cancer incidence and mortality [13]. These discrepancies in the burden estimates underscore the need for improving the cancer registries as well as the causes of death surveillance system in Tunisia.

According to cancer site, in Tunisia, lung and breast cancers were the leading causes of morbidity and mortality in males and females, respectively. A previous Tunisian study reported that lung, upper aerodigestive tract, and liver cancers had the highest values of YLLs among males (19,181, 4614, and 4466 YLLs, respectively) [26]. Among females, the same study showed that breast cancer, cervical cancer, and leukemia were the top three cancers in terms of YLLs (10,027, 3484, and 3131 YLLs, respectively) [26]. Similar results were reported in Burden of Cancer Study in the EMR, where the highest values of DALYs in thousands were attributed to lung (1013), leukemia (637), and liver cancer (448) among males, and breast (1314), followed by leukemia (498) and colorectum cancer (373) among females [25]. The GBD study reported that in 2016, lung (526.1/100,000 py), liver (295.2/100,000 py), and stomach cancers (262.9/100,000 py) were the leading causes of cancer burden in both sexes [23]. Similar to our results, a previous Indonesian study showed that lung cancer ranked first in terms of YLLs and DALYs [27]. A previous study conducted in Japan demonstrated that lung and stomach cancers accounted for the largest proportions of the burden (19.2% and 18.6% of total DALYs, respectively), followed by liver cancer (14.1%) and colorectal cancer (12.4%) [28]. In our study, colorectal cancer was ranked second among males. Similar patterns were noted in England, where the top three cancers responsible for the highest burden of disease were lung, colorectal, and breast cancers [29]. Likewise, the DALY rate of colorectal cancer had significantly increased between 1990 and 2015 among Brazilian men from 97.06 to 129.281/100,000 population [30]. It was 383.13/100,000 persons in Korea [31] and 250/100,000 persons in Lithuania, ranked as the third cancer within the European Countries [32]. Therefore, the national colorectal cancer service provision should be amplified, and a program for cancer prevention and control is highly recommended.

Among females, similar to our study results, the GBD study of 2016 reported that breast cancer was the most common incident cancer and the leading cause of cancer deaths and DALYs

(1.7 million incident cases, 535,000 deaths, and 14.9 million DALYs) [33]. The same findings were applied for African countries [34]. Another study conducted in The Netherlands showed that the total number of DALYs due to breast cancer in 2010 was estimated as 68,500, of which 50,000 were attributable to YLLs and 18,500 to YLDs [35]. Breast cancer posted the highest number of YLDs in Iran (594) [36], Mexico [37] (231.2), and India (668.052) [38]. Another study conducted in The Netherlands showed that the total number of DALYs due to breast cancer in 2010 was estimated as 68,500, of which 50,000 were attributable to YLLs and 18,500 to YLDs [35]. Likewise, it has been reported that breast cancer accounted for about 10% of all DALYs in the United States [39]. In 2012, a Korean study reported that the DALYs for breast cancer was 386.7 DALYs/100,000 female persons [31]. These findings were consistent with our results showing that breast cancer was the leading cancer in terms of female morbidity, mortality, and cancer burden. Given these results, the high burden of breast cancer could be accompanied by a substantial economic burden eventually caused by an increase in costs related to hospital and medical professional care, which could engender an increase in productivity losses owing to morbidity and premature mortality.

An important finding in this study must be highlighted: the YLLs had the major role in burden disease, which may reflect the poor prognosis after cancer diagnosis. In fact, this ratio varied by region and cancer site. A systematic review of the GBD 2008 reported that low-resource settings had consistently higher YLLs than did high-resource settings [40]. A previous study conducted in Iran showed that YLLs were the most important components of DALYs (93%) [36]. The highest YLL/DALY ratios were those of pancreatic cancer in males (93.95%) and ovarian cancer (95.8%) in females. In India, similar values were reported for pancreatic cancer (98% in males and 99% in females), whereas YLLs of ovarian cancer accounted for only 54.3% of the DALYs [38]. A possible explanation for this is that survival has not been improved for these cancers with poor prognosis, in spite of the diagnosis progress and the high-quality treatment. A previous research conducted in Australia showed that YLLs contributed to 78% of the overall DALYs related to cancer in 2001 [41]. Therefore, cancer primary prevention has to be seen in conjunction with expanding access to early detection and treatment to avoid later stages. The differences among studies in the YLL/DALY ratio might be attributable to variations in the age structure of the respective populations, the incidence/mortality ratio, or average age at onset or death [28].

Given these alarming rates and the substantial contribution of cancer to disease burden in our country, cancer control has to be among the top health policy priorities. Despite the advances in cancer screening and treatment approaches in the past decade, cancer burden is increasing because of the aging population and resulted in exploding costs. For this reason, risk factor reduction must be a priority in any cancer control effort. These factors are mostly lifestyle behaviors including tobacco use and dietary risk, obesity, and air pollution. There is an utmost need to emphasize on primordial, primary, secondary, and tertiary prevention. Our country has experienced effective preventive strategies to reduce this burden. Primordial and primary prevention include antismoking programs and promotion of smoke-free legislation as well as encouraging healthy lifestyle by increasing physical activity and healthy dietary habits. Other intervention strategies for primary prevention include vaccination against human papillomavirus

for cervical cancer prevention, treatment of hepatitis B and C, and vaccination against hepatitis B virus [42]. In Tunisia, cancer secondary prevention was mostly based on effective screening of breast, cervical and colorectal cancers as a substantial component of the cancer plans 2010–2014 and 2015–2019 [43]. In order to ensure effectiveness and sustainability of screening at a population level, strategic implementation should be coordinated at a national level and include health educational programs. Tertiary prevention consists of cancer treatment programs including curative and palliative care, which aim to improve patients' quality of life and avoid complication and sequelae. In addition, providing a suitable care requires multidisciplinary approaches such as laboratory, pathology, oncology, and radiology services.

The present study presents a reliable document to quantify the real burden of cancers at the national level in Tunisia, underscoring the need to expand cancer prevention, screening, and awareness programs. However, it has important limitations worth noting. First, reliability of cancer incidence and cancer-related mortality are major limitations because Tunisia lacks a national population-based cancer registry. Incidence data used in computing cancer burden was obtained from the GLOBOCAN project, and it was estimated from national mortality data and modelled survival. Second, from the perspective of the GBD study, the estimation of the distributions of the severity of sequelae and health states should be based on a population-based survey in calculating the YLDs, but the estimation of this study was based on DISMOD II software modeling, through estimating the disease duration and using a predefined disability weight for each cancer. This caused a problem in terms of the consistency of the study given that the sequelae were based on assessments of healthcare professionals. Another limitation for this study was the uncertainty engendered unavoidably in the process of the values estimation, which was not reflected in the results. This is a challenge that must be resolved in the future studies.

5. CONCLUSION

Our study provided an insight into the magnitude of the disease burden of cancers in Tunisia. The highest burden in terms of DALYs was observed in lung and breast cancers as well as cancers of the reproductive system. Our results are greatly interesting to quantify the burden of premature mortality and disability. These findings provide useful information for health-decision makers to plan, implement, and evaluate preventive measures for major cancers. Public health authorities should consequently benefit from this approach to evaluate potential health improvements gained by appropriate interventions or prevention programs.

CONFLICTS OF INTEREST

The authors declare they have no conflicts of interest.

AUTHORS' CONTRIBUTION

All authors revised the manuscript and gave their contribution to improve the paper. HBA, MH and SY gave substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data. HBA, MH, SY, JJ, HF and RK gave contribution in drafting the article or revising it critically for important intellectual content. HBA, MH, HF, RK, MK and JD gave final approval of the version to be published.

REFERENCES

[1] GBD 2015 Mortality and Causes of Death Collaborators. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet 2016;388;1459–544.

[2] WHO. Cancer 2018. Available from: https://www.who.int/news-room/fact-sheets/detail/cancer.

[3] Bray F, Jemal A, Grey N, Ferlay J, Forman D. Global cancer transitions according to the Human Development Index (2008–2030): a population-based study. Lancet Oncol 2012;13;790–801.

[4] Coleman MP. Cancer survival: global surveillance will stimulate health policy and improve equity. Lancet 2014;383;564–73.

[5] Stringhini S, Sabia S, Shipley M, Brunner E, Nabi H, Kivimaki M, et al. Association of socioeconomic position with health behaviors and mortality. JAMA 2010;303;1159–66.

[6] Stringhini S, Berkman L, Dugravot A, Ferrie JE, Marmot M, Kivimaki M, et al. Socioeconomic status, structural and functional measures of social support, and mortality: the British Whitehall II Cohort Study, 1985-2009. Am J Epidemiol 2012;175;1275–83.

[7] Vineis P, Wild CP. Global cancer patterns: causes and prevention. Lancet 2014;383;549–57.

[8] Parkin DM, Bray F, Ferlay J, Jemal A. Cancer in Africa 2012. Cancer Epidemiol Biomarkers Prev 2014;23;953–66.

[9] National Institute of Statistics. Tunisian population census 2012. 2013. Available from: www.ins.tn.

[10] Ben Romdhane H, Tlili F, Skhiri A, Zaman S, Phillimore P. Health system challenges of NCDs in Tunisia. Int J Public Health 2015;60;S39–S46.

[11] WHO. The Global Cancer Observatory, Tunisia. 2019. Available from: http://gco.iarc.fr/today/data/factsheets/populations/788-tunisia-fact-sheets.pdf.

[12] Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136;E359–E86.

[13] GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017;390;1211–59.

[14] Flaxman AD, Vos T, Murray CJL. An integrative metaregression framework for descriptive epidemiology. Seattle, WA: University of Washington Press; 2015.

[15] WHO. Life tables by country | Tunisia —statistics summary (2002–present), Available from: http://apps.who.int/gho/data/node.country.country-TUN?lang=en.

[16] GBD 2013 Mortality and Causes of Death Collaborators. Global, regional, and national age-sex specific all-cause and cause-specific mortality for 240 causes of death, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2015;385;117–71.

[17] WHO. Health Statistics and Information Systems, National tools; 2014. Available from: http://www.who.int/healthinfo/global_burden_disease/tools_national/en/.

[18] Ock M, Lee JY, Oh IH, Park H, Yoon SJ, Jo MW. Disability weights measurement for 228 causes of disease in the Korean Burden of Disease Study 2012. J Korean Med Sci 2016;31;S129–S38.

[19] Murray CJ. Quantifying the burden of disease: the technical basis for disability-adjusted life years. Bull World Health Organ 1994;72;429–45.

[20] Devleesschauwer B, de Noordhout CM, Smit GSA, Duchateau L, Dorny P, Stein C, et al. Quantifying burden of disease to support public health policy in Belgium: opportunities and constraints. BMC Public Health 2014;14;1196.

[21] WHO. Global Cancer Observatory, Data and Methods, Cancer Today. Available from: https://gco.iarc.fr/today/data-sources-methods.

[22] GBD 2016 Mortality Collaborators. Global, regional, and national under-5 mortality, adult mortality, age-specific mortality, and life expectancy, 1970-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017;390;1084–150.

[23] GBD 2016 DALYs and HALE Collaborators. Global, regional, and national disability-adjusted life-years (DALYs) for 333 diseases and injuries and healthy life expectancy (HALE) for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2017;390;1260–344.

[24] Global Burden of Disease Cancer Collaboration, Fitzmaurice C, Allen C, Barber RM, Barregard L, et al. 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;524–48.

[25] GBD 2015 Eastern Mediterranean Region Cancer Collaborators. Burden of cancer in the Eastern Mediterranean Region, 2005–2015: findings from the Global Burden of Disease 2015 Study. Int J Public Health 2018;63;151–64.

[26] Gobrane HL-B, Hajjem S, Aounallah-Skhiri H, Achour N, Hsairi M. Mortalité par cancer en Tunisie: calcul des années de vies perdues. Sante Publique 2011;23;31–40.

[27] Kristina SA, Endarti D, Sendjaya N, Pramestuty O. Estimating the burden of cancers attributable to smoking using disability adjusted life years in Indonesia. Asian Pac J Cancer Prev 2016;17;1577–81.

[28] Pham TM, Kubo T, Fujino Y, Ozasa K, Matsuda S, Yoshimura T. Disability-adjusted life years (DALY) for cancer in Japan in 2000. J Epidemiol 2011;21;309–12.

[29] Jayatilleke N, Pashayan N, Powles JW. Burden of disease due to cancer in England and Wales. J Public Health (Oxf) 2012;34;287–95.

[30] Silva DAS, Tremblay MS, de Fatima Marinho de Souza M, Mooney M, Naghavi M, Malta DC. Mortality and years of life lost by colorectal cancer attributable to physical inactivity in Brazil (1990–2015): findings from the Global Burden of Disease Study. PLoS One 2018;13;e0190943.

[31] Gong YH, Yoon SJ, Jo MW, Kim A, Kim YA, Yoon J, et al. The burden of cancer in Korea during 2012: findings from a prevalence-based approach. J Korean Med Sci 2016;31;S168–S77.

[32] Lunevicius R, Poskus T, Samalavicius NE. National burden of colorectal cancer in Lithuania and the ranking of Lithuania within the 45 European nations. Oncol Lett 2015;10;433–8.

[33] Global Burden of Disease Cancer Collaboration; Fitzmaurice C, Akinyemiju TF, Al Lami FH, Alam T, Alizadeh-Navaei R, et al. Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 29 cancer groups, 1990 to 2016: a systematic analysis for the Global Burden of Disease Study. JAMA Oncol 2018;4;1553–68.

[34] Ginsburg O, Bray F, Coleman MP, Vanderpuye V, Eniu A, Kotha SR, et al. The global burden of women's cancers: a grand challenge in global health. Lancet 2017;389;847–60.

[35] Vondeling GT, Menezes GL, Dvortsin EP, Jansman FGA, Konings IR, Postma MJ, et al. Burden of early, advanced and metastatic breast cancer in The Netherlands. BMC Cancer 2018;18;262.

[36] Khajedaluee M, Dadgarmoghaddam M, Saeedi R, Izadi-Mood Z, Abrishami M, Zamani M. Mortality, morbidity, survival, and burden of top 9 cancers in a developing country. Razavi Int J Med 2014;2;e2073.

[37] Murillo-Zamora E, Mendoza-Cano O, Ríos-Silva M, Sánchez-Piña R, Higareda-Almaraz M, Higareda-Almaraz E, et al. Disability-adjusted life years for cancer in 2010-2014: a regional approach in Mexico. Int J Environ Res Public Health 2018;15;864.

[38] Murthy NS, Nandakumar BS, Pruthvish S, George PS, Mathew A. Disability adjusted life years for cancer patients in India. Asian Pac J Cancer Prev 2010;11;633–40.

[39] Lortet-Tieulent J, Soerjomataram I, Lin CC, Coebergh JWW, Jemal A. U.S. burden of cancer by race and ethnicity according to disability-adjusted life years. Am J Prev Med 2016;51;673–81.

[40] Soerjomataram I, Lortet-Tieulent J, Parkin DM, Ferlay J, Mathers C, Forman D, et al. Global burden of cancer in 2008: a systematic analysis of disability-adjusted life-years in 12 world regions. Lancet 2012;380;1840–50.

[41] Victorian Burden of Disease Study: mortality and morbidity in 2001. Melbourne: Public Health Group, Rural and Regional Health and Aged Care Services Division; 2005.

[42] Alavian SM, Haghbin H. Relative importance of hepatitis B and C viruses in hepatocellular carcinoma in EMRO countries and the Middle East: a systematic review. Hepat Mon 2016;16;e35106.

[43] Republic of Tunisia, Ministry of Health. Plan for the fight against cancer in Tunisia 2015-2019. Republic of Tunisia; 2015. Available from: http://www.iccp-portal.org/system/files/plans/Plan_pour_la_lutte_contre_le_cancer_2015-2019_Tunisie.pdf.