

Lung Cancer in the Middle East and North Africa Region



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Despite being an easily preventable disease, as more than 85% of the cases are caused by smoking, lung cancer has been the leading cause of cancer death worldwide since 1987. Especially in developing countries, the incidence of lung cancer is increasing drastically due to the increased use of tobacco products. Many Western countries have managed to control the prevalence of smoking leading to a reduction in lung cancer incidence. However, with a combined population of approximately 360 million in the Middle East and North African (MENA) region, up to 46% of the populations continue to smoke and more people are picking up the deadly habit. The challenges in the MENA countries are not just related to the increasing rate of incidence which reflects a failure in primary prevention, but also in the diagnosis and management of the affected patients; especially in lieu of recent advances and availability of more “expensive” management options.

In this editorial, we present the status of lung cancer in terms of burden, management patterns, available resources, and challenges in the MENA region. For the purpose of this paper, the MENA region covers countries in the Arab League including the Gulf Cooperation Council (GCC) countries (Kingdom of Saudi Arabia, United Arab Emirates, Oman, Qatar, Kuwait, and Bahrain), Yemen, Iraq, Levant region (Syria, Lebanon, and Jordan), North Africa (Libya, Tunisia, Algeria, and Morocco) and Egypt (although it is classified as a North African country, it will be discussed individually due to its large population size) (Fig. 1). Although all of these countries fall under the umbrella of the Arab League, they are at different social and economic levels ranging from more affluent countries to those that are classified as low-income countries by the World Bank.

Lung Cancer Epidemiology

The age-standardized rate (ASR) of lung cancer in the MENA region is less than international rates with a range between 4.2 per 100,000 in Yemen and 23 per 100,000 in Lebanon (Tables 1 and 2; Fig. 2).¹ The lack of

comprehensive up-to-date population registries in many countries in the region represents a major challenge to obtain accurate data about cancer incidence in general. Therefore, sources of epidemiologic data may include national registries, local registries, and international registries. However, available literature suggests variation in ASR, more male predominance, and presentation at advanced stages. Lung cancer ranked among the top 10 cancers in all but one country (Table 2).

The estimated numbers of new lung cancer cases in 2018 were 79,887. Despite significant advances in understanding and treating lung cancer, the 5-year relative survival rate in MENA is only 8%. The highest death percentages were observed in Morocco and Tunisia, whereas the lowest were in Yemen and Egypt.

The majority of lung cancer patients present at an advanced stage in the region. For example, in Yemen, the median age of diagnosis with lung cancer in Yemen was

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Figure 1. Countries of Middle East and North Africa region.

60 years, and almost 75% of lung cancer patients in the country were presenting with stages III and IV.² Consequently, due to the poor use of proper therapy, the mean survival time post-chemotherapy does not exceed 40 weeks. Moreover, there were no major differences in the laterality of the cancer in the lungs.

Smoking Epidemiology

Smoking in the MENA region is highly prevalent (Table 3), ranging from 14.7% in Oman to 46.9% in Jordan for males, and from 0.2% in Oman and Egypt to 34% in Lebanon for females, according to the WHO. The

Table 1. ASR of Lung Cancer Internationally and in the MENA Region

Population	Number	ASR
World	2093876	22.5
China	774323	35.1
United States	227356	35.1
United Kingdom	52320	32.5
France	47133	36.1
Morocco	6488	17.2
Egypt	6045	7.6
Algeria	3835	10.1
Syrian Arab Republic	2144	16.9
Iraq	2123	10.7
Tunisia	1909	13.9
Lebanon	1641	23.2
Jordan	1141	18.4
Saudi Arabia	923	4.3
Libya	668	14
Yemen	567	4.2
United Arab Emirates	190	6.3
Kuwait	158	7.3
Oman	112	4.7
Bahrain	81	11.6
Qatar	73	8.9

Data from International Agency for Research on Cancer /WHO.²¹
ASR, age-standardized rate; MENA, Middle East and North Africa region.

Tobacco Free Initiative (which was launched in 1998 to focus international attention, resources, and action on the tobacco epidemic) referred to an increase in the number of adults using tobacco in the Eastern Mediterranean region. Forty-two percent of adults in the region use tobacco; that figure is expected to reach 62% by 2025. Citizens of eastern Mediterranean countries pick up the habit earlier than any other area of the world, with 21.3% of 13-to 15-year-old males smoking. In Tunisia, 22.2% more men suffer tobacco-related deaths than in average middle-income countries.³

The smoking prevalence in general is predominantly affected by social and economic status, marital status, and education levels and age. However, the biggest factor in the region is sex. Socially, smoking is viewed as inappropriate and shameful for women. However, possibly under the influence of globalization, media, and marketing, there is a rapid increase in the prevalence of smoking around the MENA region in women. There is also a noticeable increase in the number of women joining the workforce and seeking higher education. These two factors are associated with higher incidence of smoking in women.⁴ However, a study performed in Jordanian women showed that a higher-level education was protective against cigarette smoking, whereas household wealth was a risk factor.⁵

Smoking in GCC

As with most countries in the MENA region, the prevalence of smoking among males in the GCC is higher than that of their female counterparts. Both the highest rate of smoking in males and females are found in Kuwait.⁶ Of particular notice, smoking among physicians is high in the GCC compared to western countries such as the United States and the United Kingdom with rates less than 10% and more comparable with France and Japan, ranging from 26% in Bahrain to 46% in Kuwait.^{7,8} These

Table 2. Lung Cancer Epidemiology in MENA in 2018, Compared to Global Lung Cancer Rate of 11.6%

Countries	Population	All New Cancers	New Lung Cancer No. n (%)	Rank of Lung Cancer	Lung Cancer Deaths n (%)	5-Year Prevalent Cases
Kingdom of Saudi Arabia	33,554,333	24,485	923 (4.06)	8 th	779 (8.1)	1,010
United Arab Emirates	9,541,612	4,707	190 (4.3)	6 th	183 (9.4)	216
Bahrain	1,566,994	1,048	81 (8.3)	2 nd	76 (13.7)	82
Oman	4,829,946	3,322	112 (3.7)	11 th	108 (7.2)	115
Kuwait	4,197,125	3,582	158 (4.7)	7 th	143 (9.3)	166
Qatar	2,694,843	1,260	73 (6.4)	5 th	68 (11.3)	78
Yemen	28,915,286	13,182	567 (4.8)	9 th	565 (6.9)	578
Iraq	39,339,754	25,320	2,123 (8.4)	2 nd	2,066 (16.5)	2,039
Syria	18,284,423	23,170	2,144 (9.3)	2 nd	2,107 (4.3)	1,998
Jordan	9,903,798	10,898	1,141 (10.5)	2 nd	1,022 (5.6)	1,049
Lebanon	6,093,510	17,294	1,641 (9.5)	3 rd	1,490 (5.3)	1,573
Morocco	36,191,813	52,783	6,488 (13.5)	2 nd	6,397 (21.9)	6,022
Tunisia	11,659,175	15,894	1,909 (13.3)	2 nd	1,822 (20.4)	1,780
Algeria	42,008,056	53,076	3,835 (8.04)	2 nd	3,826 (15.0)	3,654
Libya	6,470,954	6,308	2457 (7.9)	2 nd	295 (9.7)	1,022
Egypt	99,375,745	128,892	56,045 (5.2)	5 th	5,674 (7.3)	5,902

Data from International Agency for Research on Cancer/WHO.²¹ MENA, Middle East and North Africa region.

rates are lower than numbers found in other developing countries such as China, Turkey, and India with prevalence of approximately 50%.⁹

Smoking in Yemen

Although the overall rate of lung cancer in Yemen was the lowest compared to other nearby GCC countries, prevalence of smoking in Yemeni males over the age of 15 is increasing.¹⁰ The latest WHO report on the global tobacco epidemic, 2017, has reported an increased

prevalence rate of tobacco smokers in Yemen by 18.7%.⁶ Moreover, the Global Youth Tobacco Survey found an ever-smoker prevalence of 10.6% for girls and 19.8% for boys aged 13 to 15 years. A random sample of adults in Sana’a found a figure of 34.45%. Another survey of university students found rates of 25% for male students and 12% for female students. Cigarette smoking and waterpipe (also known as narghile, shisha, or hookah) was found to occur during Khat sessions using locally grown plant leaves; those leaves are now known as Khat

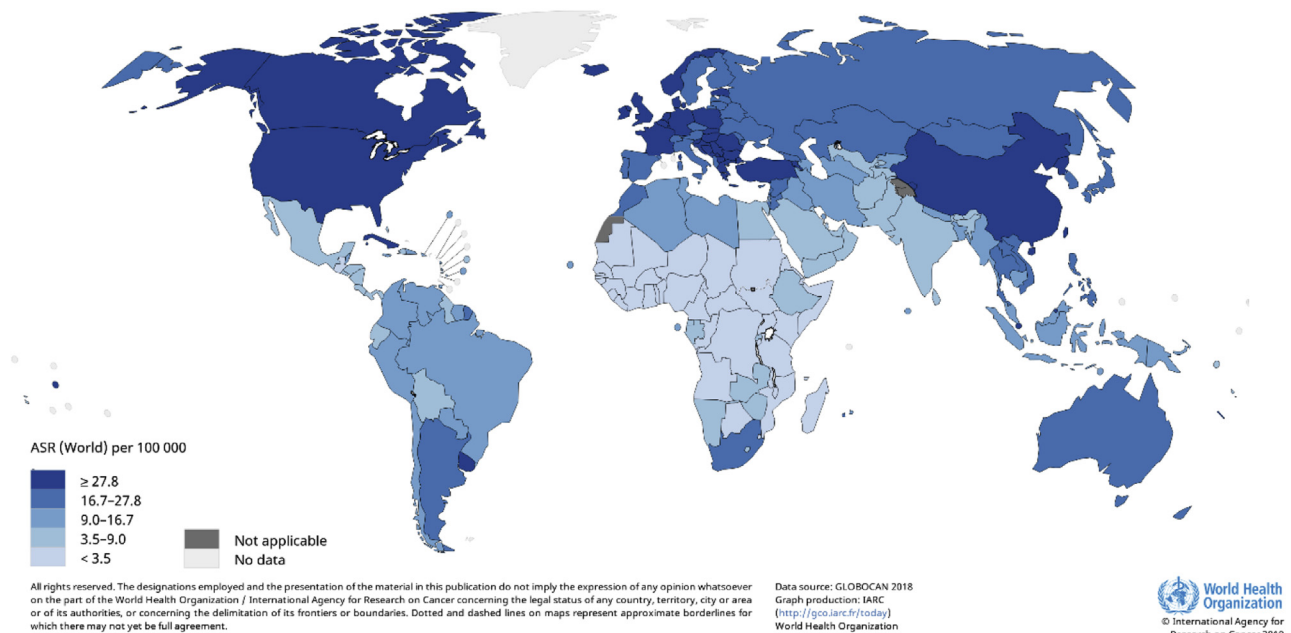


Figure 2. Estimated age-standardized incidence rates (world) in 2018, lung, both sexes, all ages.

Table 3. Tobacco Epidemiology in MENA Region Countries Extracted From the WHO Cancer Country Profiles for 2017

Countries	Smoking Prevalence Males, %	Smoking Prevalence Females, %	Tobacco Control Policy, Strategy or Action Plan	Smoke-Free Public Places	Tobacco Taxes of Retail Price, %
Kingdom of Saudi Arabia	23.7	1.5	Yes	6-7	≤25
United Arab Emirates	28.0	0.9	No	3-5	≤25
Bahrain	33.4	7.0	Yes	1-2	≤25
Oman	14.7	0.2	Yes	-	≤25
Kuwait	39.2	3.3	No	6-7	≤25
Qatar	21.3	0.6	Yes	1-2	≤25
Yemen	20.7	6.0	No	1-2	≤25
Iraq	30.8	4.5	Yes	1-2	≤25
Syria	N/A	N/A	Yes	6-7	51-75
Jordan	46.9	18.0	Yes	3-5	>75
Lebanon	43	34	Yes	All	26-50
Morocco	31.5	3.3	Yes	3-5	51-75
Tunisia	48.4	8.2	Yes	1-2	>75
Algeria	27.1	1.7	Yes	3-5	51-75
Libya	10.2	0.8	No	All	≤25
Egypt	46.4	0.2	Yes	3-5	51-75

Data from WHO Report on The Global Tobacco Epidemic.⁶
MENA, Middle East and North Africa region.

and are scientifically known as *Catha edulis*.^{11,12} A recent study in Yemen reported that the majority (83.8%) of lung cancer cases were found in smokers (97% males versus 3% females).²

Smoking in North Africa

In Morocco, the prevalence of smoking is estimated at 18% among population older than 15 years, with nearly 41% of the population exposed to passive smoking. In Morocco, 31.5% of men and 3.3% of women are smokers. Morocco is considered one of the biggest consumers of tobacco in the Mediterranean area with more than 15 billion cigarettes consumed every year. Since 1996, Morocco has had an antismoking law (No. 15-91) which prohibits tobacco in some public areas and advertising of tobacco products, but so far without any implementing decree.¹³ In Algeria, the prevalence of smoking among those aged 15 years or older is 27% in men and 2% in women.¹⁴ In Tunisia, the proportion of smokers is 55% among men versus 5.6% among women.³

Smoking in Egypt

While much of the Arab world is plagued by tobacco consumption, the problem is especially dire in Egypt with 36.1% of the adult male populations smoking according to state statistics from the WHO's Tobacco Atlas, a global database on tobacco consumption.

The use of tobacco products in Egypt is widespread. Approximately 22% of the population are current smokers.⁶ Approximately 20 billion cigarettes are smoked annually in the country. Waterpipe and imported

tobacco use is also common. There is an increase in the prevalence of smoking in adolescents despite many attempts to prohibit smoking.

Screening and Prevention

The topic of lung cancer screening remains controversial in the region due to lack of local experience. Meanwhile substantially reducing lung cancer mortality by 20% and all-cause mortality by 6.7% with favorable impacts on smoking cessation rates, as shown in the National Lung Screening Trial, screening with low-dose chest computed tomography (CT) annually is not risk-free due to associated harm by unnecessary procedures, follow-ups, and anxiety for the patients. The yield and cost effectiveness of the screening is not well studied in the region especially in terms of potential benign, noncancerous findings. Therefore, in the MENA region, there is no national program offering mass screening using low-dose CT scans offered in any country, albeit some physicians may screen high-risk patients on an individual basis.

Lung cancer primary prevention through smoking cessation efforts usually takes the form of scattered community nongovernmental initiatives that offer help programs to smokers. Although there are laws in some countries to prevent smoking in work or public places, these laws are not usually enforced. There was a discussion of broad ban on smoking during Council of Arab Ministers of Health meeting including advertising and promotion of its products and derivatives in 2017; however, affirmative action has yet to be taken.

Diagnosis

Pathology

The pathologic diagnosis of lung cancer is available in all tertiary cancer facilities in the MENA region, and performing immunohistochemistry staining in-house is routine. However, testing for EGFR and ALK receptor tyrosine kinase (ALK) is performed most of the time on a send-out basis to referral laboratories in the country or internationally. Next-generation sequencing is being introduced in some countries on limited basis for selected patients. Programmed death ligand 1 (PD-L1) testing is available in most countries (Table 4).

Diagnostic Imaging

Imaging modalities by CT scans are available in all tertiary centers. In contrast, positron-emission tomography-CT is very limited (Table 4).

Surgical Approaches

There are many trained consultant thoracic surgeons who are managing lung cancer in tertiary hospitals. Their main work is dealing with early-stage lung cancer with curative intent surgery. However, they are also involved in obtaining diagnostic specimens, mediastinal staging, and metastatectomy.

In all centers, surgical indications are generally kept after a multidisciplinary consultation meeting, gathering all actors involved in the management of this disease.

The percentage of surgical patients remains unfortunately very low because of late diagnosis. Parenchymal resections with lymphadenectomy are usually performed by video-assisted thoracic surgery for early stages I and II. When operable, patients with stage III cancer benefit from open surgery with neoadjuvant and/or adjuvant chemotherapy and/or radiotherapy in most cases. Robotic-assisted surgery has not yet been introduced in most countries.

Radiation Approaches

The access to radiation therapy varies among countries based on the available machines, the population, and the geographical distribution of the centers. The number of linear accelerators per country is shown in Table 5.

During early stages of cancer when surgery is not feasible, intensity-modulated radiation therapy or stereotactic radiotherapy is applied. In locally advanced stages, the standard treatment is concurrent chemoradiotherapy or, less often, radical radiotherapy.

Compared to the population numbers, there is a window for improvement for machines available in the region. In addition, there is a need to establish more training opportunities for radiation oncologists, medical physicists, and radiotherapists. For example, there is only one center in Yemen that offers radiotherapy. It is located in Sana'a, the capital. However, it does not address the long queue of patients who have been

Table 4. Availability of Diagnostic Testing in the MENA Region

	Pathology			PET Scan
	EGFR/ALK	NGS	PD-L1	No. of Machines
Kingdom of Saudi Arabia	Yes, routinely	Yes, infrequently	Yes, routinely in-house and send out	11
United Arab Emirates	Yes, routinely	Yes, infrequently	Yes	6
Bahrain	Yes	Yes,	Yes	1
Oman	Yes	Yes, infrequently	Yes	1
Kuwait	Yes	Yes, infrequently	Yes	6
Qatar	Yes	Yes, infrequently	Yes	2
Yemen	Not available	Not available	Not available	Not available
Iraq	Yes, EGFR routinely in-house; ALK, send out	Not available	Not available	3
Syria	Yes, routinely in-house	Not available	Yes, infrequently in-house	2
Jordan	Yes, routinely in-house	ROS1, yes, routinely in-house	Yes, routinely in-house	3
Lebanon	Yes, routinely in-house	Yes, infrequently in-house	Yes, routinely in-house	8
Morocco	Yes	Yes, sent out	Yes	?
Tunisia	Yes	Yes, sent out	Yes	?
Algeria		Yes, sent out	Yes	?
Libya	NA	NA	NA	NA
Egypt	Both (in-house and sent out)	Yes, infrequently in-house and sent out	Yes, in-house	>20

MENA, Middle East and North Africa region; ALK, ALK receptor tyrosine kinase; NGS, next-generation sequencing; PD-L1, programmed death ligand 1; PET, positron-emission tomography; NA, not available.

Table 5. Number of Radiation Therapy Centers and Linear Accelerators

Country	Radiation Therapy Centers	Linear Accelerators
Kingdom of Saudi Arabia	14	35
United Arab Emirates	3	5
Bahrain	1	2
Oman	1	2
Kuwait	1	4
Qatar	1	3
Yemen	1	2
Iraq	11	17
Syria	2	2
Jordan	5	13
Lebanon	11	16
Morocco	20	36
Tunisia	11	12
Algeria	15	34
Libya	3	2
Egypt	68	96

Data from Directory of Radiotherapy Centres (DIRAC).²²

waiting for a long time (more than 4 months). In Morocco, the type of radiation therapy most often used to treat lung cancer is three-dimensional conformal radiation therapy.

Systemic Therapy

The oncologists in the MENA region usually refer to the National Comprehensive Cancer Network guidelines and to a lesser extent to the European Society for Medical Oncology guidelines. Regional adaptations to the National Comprehensive Cancer Network lung cancer guidelines have been created repeatedly over the last 8 years.¹⁵ Patients with driver mutation are treated by targeted therapy based on the mutation and accessibility to the medications. Experience in the region with erlotinib is similar to the reported literature.¹⁶ Patients who have wild-type tumors usually receive chemotherapy and occasionally immune therapy. The EGFR mutation prevalence is different among the region populations with 12% of the cases positive in Lebanon, 21% in Morocco, more than 30% in the Gulf countries, and 27% in Egypt according to unpublished data.¹⁷⁻¹⁹

Standard chemotherapy agents such as platinum, taxanes, and pemetrexed are available in all countries; however, the availability of targeted therapy and immunotherapy is much more limited (Table 6). For example, in Levant and Egypt, target therapy is only available in insurance-covered private sectors whereas immunotherapy is harder to reach. Access to first- and second-generation EGFR tyrosine kinase inhibitors (TKIs) is available in almost all countries with early use of third-generation TKIs especially in resistant disease. Treatment of ALK-positive disease also uses mainly

Table 6. Availability of Systemic Therapy in the Countries of the MENA

Medication	Use in the MENA
Standard chemotherapy agents: Platinum, taxanes, pemetrexed, topotecan, etoposide, vinorelbine, cyclophosphamide, vincristine, doxorubicin, etc.	Used routinely
Gefitinib/erlotinib	Routine
Afatinib	Less common
Osimeritinib	Early use in few countries
Crizotinib	Routine use
Alectinib	Early use in some countries
Ceritinib	Rare
Nivolumab	Used in second line irrespective of PD-L1
Pembrolizumab	Used first line PDL1>50% and recently sporadic use with chemotherapy. Used in Second line for PD-L>1%
Atezolizumab	Used in second line irrespective of PDL1, sporadic use in combination with chemo in first line
Cabozantinib, vandetanib, adotrastuzumab, dabrafenib, trametinib, dacomitinib, brigatinib, lorlatinib	Sporadic use

MENA, Middle East and North Africa region; PD-L1, programmed death ligand 1; PD-1, programmed death 1.

first-generation TKIs, and recently started using third-generation TKIs in some countries.

Immune therapy using checkpoint inhibitors is more often used in second-line and less in the first-line treatment, mainly for patients who are PD-L1-positive. A combination of checkpoint inhibitors with chemotherapy in the first-line setting is used sporadically.

Challenges

The challenges facing lung cancer management in the MENA region can be divided into three categories: prevention, diagnosis, and treatment.

Despite the adoption of the Framework Convention on Tobacco Control by most Arab countries, both cigarette smoking and the use of waterpipes are common in all countries in the region. There is a deficiency in the systematic approach to primary prevention through tobacco control programs and early detection of lung cancer which require both national policies and support in addition to education of health care professionals and the public. Efforts of the tobacco industry and the presence of poor law enforcement systems in most of Arab countries have delayed serious policy responses to the tobacco epidemic.

Some other factors that contribute to the issue include the low levels of awareness, affordability of tobacco products, low taxes, and availability of waterpipe smoking. Post-traumatic stress disorder and post-conflict effects might be factors to supporting the increase in smoking habits in the Levant countries, as highlighted by some of the researchers (in Iraq, Syria, and Lebanon, even in the Jordanian society which is suffering due to the increasing number of refugees).

Data on smoking prevalence are lacking uniformity in definition and inclusion criteria indicating an underutilizing population-based surveillance system to monitor the tobacco epidemic and prioritize areas of concern and action. In addition, there is a lack of reliable updated lung cancer epidemiologic data. It is essential to enhance population-based registries.

There is limited involvement of primary care physicians in lung cancer control efforts, as they play a crucial part in the front lines of primary prevention, in counseling patients about smoking cessation, or obtaining screening CT scans for high-risk patients.

There is also poor access to molecular profiling platforms of the tumor at a large scale. Although it is more available in some countries and tertiary centers of excellence, many patients will not realize the full benefits of precision oncology. Development of reference central laboratory in each country may help facilitate the access to these tests especially since the technology is getting cheaper and more convenient.

Management challenges are related to the difficulty in accessing the most recent targeted and immunotherapy agents due to the high cost and lack of uniform national approaches to cover the expenses for these medications. There are multiple approaches to improve access to these medications that can be followed at national levels and at the hospital level.²⁰

Access to radiation therapy is limited in certain countries and regions. Existing centers have the potential to improve the techniques offered, such as stereotactic radiosurgery. Access to palliative care is extremely limited as the field is new and has not matured enough, especially in terms of having adequately trained professionals.

In conclusion, lung cancer incidence varies among the countries in the region due to differences in smoking prevalence. There is also variation in access to certain diagnostic and therapeutic options. However, the interest in improving cancer care is encouraging and, hopefully, it will be translated into better patient care and outcome for all cancer patients.

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