

## ARTICLE

# Review of COPD in Middle East and Gulf countries

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### Abstract

Incidence of COPD is increasing and becoming a concern worldwide. Eastern Mediterranean Region happens to follow the same trend showing the highest percentage increase in the last few years. The purpose of this review article was to study burden of the disease in the region with reference to the research done so far. Data was compared with regards to prevalence, risk factors and study design with rest of the world to identify similarities and differences between Middle East countries and the West. The goal of this review is to establish good insight into the challenges associated with COPD and subsequently develop public awareness and health policies to try and encounter it effectively. It is obvious that more studies are needed with uniform methodology across the region. Risk factors for COPD seem to be similar with the rest of the world with slight cultural differences having some impact. The economic burden of COPD in the region was also reviewed which was found to be quite high.

**Keywords:** COPD, Middle East countries, Gulf countries, prevalence of smoking, shisha, medwakh, bakhour

## **1. Introduction:**

More than 3 million people died of Chronic Obstructive Pulmonary Disease (COPD) in 2012, representing 6% of all global deaths that year. More than 90% of COPD deaths occur in low- and middle-income countries.

COPD primary cause is tobacco smoke (through tobacco use or second-hand smoke). Currently the disease affects men and women almost equally, due in part to increased tobacco use among women in high-income countries. Even when there's no cure for COPD, available treatments are able to slow its progression. According to WHO estimates, 65 million people suffer from moderate to severe COPD—such estimates show that by 2030 COPD will be the third leading death cause worldwide.<sup>1</sup>

A systemic meta-analysis of spirometry-based investigations (including 123 studies) across the world performed from January 1990 to December 2010, including individuals 30 years old or more showed a global COPD growing prevalence; main results may be summarized as follow:

- Global prevalence increased from 227 million cases in 1990 to 384 million cases in 2010 which represents a 68.9% increase along such time frame.
- Overall prevalence in men was 14.3% compared to 7.6% in women
- Eastern Mediterranean Region (EMR) showed the highest percentage increase (118.7%).

## **2. COPD Burden in MENA region:**

There is a paucity of studies in Africa, South East Asia and Eastern Mediterranean Region (EMR).<sup>2</sup> For the purpose of this review,

PubMed was searched for articles related to COPD burden in the Middle East and North Africa (MENA) region / Eastern Mediterranean Region (EMR).

Twelve studies were shortlisted. The largest regional study was BREATHE carried on 11 countries.<sup>3</sup> COPD prevalence in the MENA region was 3.6% ranging from 1.9% in United Arab Emirates (UAE) to 6.1% in Syria.<sup>3</sup>

On a post bronchodilator, spirometry based study AlZaabi et al<sup>4</sup> estimated prevalence in UAE to be 3.7% while another study in Dubai estimated COPD prevalence much higher at 12.9%.<sup>5</sup> This difference can be explained due the fact that the latter study was based on pre-bronchodilator definition which at certain point is not able to differentiate a substantial group of asthma patients from COPD leading to a prevalence overestimation.

Three studies in Saudi showed prevalence ranging from 2.4% to 14.2%.<sup>3,6,7</sup> The highest prevalence study was conducted in high-risk patients (smokers presenting to primary health clinics) instead of general population which could lead to overestimated results because of selection bias.

This difference was also noted in Jordan with prevalence of COPD being 5.4% (BREATHE study in general population)<sup>3</sup> vs. 8.2% in a study by AlOmari et al (done in male smoker subjects).<sup>8</sup>

Again, a study conducted on high risk population in Egypt integrated by smokers, occupational exposure and biomass fuel combustion exposure estimated a three-fold higher COPD prevalence in 9.6% vs. 3.5% in BREATHE.<sup>3,9</sup>

A spirometry based study in Egypt estimated the prevalence to be 6.6% compared to 3.5% in BREATHE.<sup>3,10</sup> Similarly, prevalence in Lebanon was 5.3% in BREATHE<sup>3</sup>, a questionnaire based research against 9.7% in

another study conducted using COPD post-bronchodilator definition.<sup>11</sup> Obviously spirometry-based studies produced a higher prevalence in comparison to the questionnaire-based studies.

Burden of Obstructive Lung Disease studies (BOLD), to best of our knowledge were conducted in 3 countries within the region. Estimated prevalence in Tunisia,<sup>12</sup> Saudi Arab<sup>7</sup> and Morocco was 7.8%,<sup>13</sup> 4.2% and 12.6% in comparison to BREATHE where such prevalence were 3.7%, 2.4 and 2.2% respectively. Under reporting of mild symptoms, smoking prevalence, especially in female patients (COPD diagnosis criteria in BREATHE) and difference in methodology could partially account for this difference.

Estimated gender and age prevalence also showed varied results. All included studies demonstrated either a statistically significant increased prevalence in male over female patients<sup>3, 7, 11</sup> or no difference at all.<sup>4, 5, 10</sup> This inconsistency can be explained by the wide variation of smoking prevalence in females within the region, difference in cultural background as well as diverse exposure to other risk factors like biomass fuel. In some studies older age was associated with higher COPD prevalence.<sup>4, 10-13</sup> GOLD stage II (moderate) COPD was found to have the highest prevalence in most of staged population studies.<sup>4-13</sup>

### **3. Current COPD Epidemiological Profile in the Region:**

#### **3.1 What is common?**

There is substantial variation in disease trends between different world regions, both globally and regionally. Smoking is COPD most important risk factor. To assess the relationship between smoking and COPD prevalence a

comparison was made among different studies carried out worldwide and those of MENA region. As already mentioned there were critical differences in the study groups, methodology, and definitions.

In 2015, over 1.1 billion people smoked tobacco. Although it is declining worldwide and in many countries, tobacco smoking prevalence appears to be increasing in the WHO Eastern Mediterranean Region and the African Region.<sup>14</sup>

BOLD study (from 14 countries worldwide) estimated smoking prevalence of 57.1% and COPD (Stage 2 or higher) of 8.1%.<sup>15</sup> Similarly, PLATINO study ("Proyecto Latinoamericano de Investigacion en Obstruccion Pulmonar- Latin American Lung obstruction Investigation- conducted in 5 Latin American countries) estimated smoking prevalence (results of 5 countries average) on 56.8% with a COPD average prevalence of 9.04%.<sup>16</sup>

The Continuing to Confront COPD survey (updated version) from 13 countries estimated smoking prevalence on 65% and COPD on 8.2%.<sup>17</sup>

BREATHE, the only large multi-regional study for COPD prevalence in MENA region and adapted from Confronting survey, estimated a smoking prevalence of 31.2% while COPD was 3.6%.<sup>3</sup>

For the sake of comparison, smoking prevalence was almost double in the west as compared to the MENA region with COPD prevalence following the same trend. Needless to say, this is only a rough estimate to support previously well-established fact that smoking is COPD most common risk factor with proportional prevalence increase.

#### **3.2 What is different?**

The COPD prevalence difference, globally or regionally, may be explained as follows:

### **3.2a Studies Comparison:**

There is concern that COPD burden has been underestimated in the region, due to over-reliance on doctor's diagnosis-; that's because many diagnoses were not based on spirometry and international diagnostic guidelines but only on clinical appreciation.<sup>18</sup>

#### **Spirometry vs. questionnaire based:**

BOLD and PLATINO were both spirometry-based researches. Eleven similar studies (spirometry based) from MENA region were reviewed. First study ever in the region was published by Alzaabi et al<sup>4</sup> in 2011 and results were comparable to the largest questionnaire based BREATHE study in the MENA region.<sup>3</sup> Three were based on BOLD protocol: Hajjaj et al in Saudi,<sup>7</sup> Daldoul et al in Tunisia,<sup>12</sup> and Rhazi et al.<sup>13</sup> The other studies<sup>5,6,8-11</sup> have already been described above.

#### **Difference in study groups:**

Within the MENA region, significant variation in study groups can explain COPD prevalence differences among different studies-; for example, 3 studies conducted in Saudi Arab found prevalence as follows:

14.2% – among smokers<sup>6</sup>

2.4% – BREATHE study questionnaire based<sup>3</sup>

4.2% – BOLD protocol.<sup>7</sup>

### **3.2b Risk Factors Comparison:**

Cigarette smoking is the most important single risk factor COPD development. However a substantive disease burden occurs in the absence of smoking, especially among younger persons, women, and residents of developing countries. Population-attributable fraction for smoking as a cause of COPD was found to be less than 80% in a review summary published by the American Thoracic Society (ATS) *ad hoc* subcommittee known as Environmental

and Occupational Health Committee, it was indicated that a substantial burden of disease is attributable to nonsmoking risk factors.<sup>19</sup>

Specific genetic syndromes and occupational exposures were causally related to COPD development. Traffic and other outdoor pollution, secondhand smoke, biomass smoke are all COPD associated risk factors. On the other hand chronic asthma and tuberculosis are associated with irreversible loss of lung function, but it remains uncertain about whether there are important phenotypic differences compared with COPD as it is typically encountered in clinical settings.<sup>19</sup>

#### **Tobacco smoking:**

In 2000, WHO estimated the rate of mortality from smoking in the adult population (age more than 30 years) to be 19% in industrialized countries and 9% in developing countries.<sup>20</sup> Tageldin et al<sup>21</sup> estimated adjusted smoking prevalence to be 31.2% in the MENA region. Highest rates were observed in Jordan, Lebanon, Syria and Turkey. Significant variation was observed in the MENA region for estimated smoking prevalence between countries ranging from 15.3% in Morocco to 53.9% in Lebanon.

Sex smoking prevalence ranged from 29.7% in Morocco to 61% in Turkey in men and 1.4% in Morocco to 47.3% in Lebanon in women. Gender differences could be attributed to women having limited access to public places, religious and cultural beliefs, as well social stigma. However, an increasing trend on women smoking may be seen due to increased marketing of cigarettes, social status, more professionally active women, and region westernization.<sup>21</sup>

Smoking in the MENA region (particularly Shisha – water pipe smoking) is a part of the culture. Lack of rules and regulations to ban

smoking in public places contributes to smoking high prevalence of smoking.<sup>22</sup> Water pipe smoking deserves special mention in this region as it may increase not only COPD risk but also lung cancer and other respiratory problems.<sup>23-25</sup>

Water – pipe use prevalence is high in the Eastern Mediterranean Region. A national survey in Kuwait showed that 57% of men and 69% of women had used water pipe at least once. Water pipe use is also common in Egypt, where 22% of 6762 men from two rural villages reported current or past use. Recent data from the EMR show that a substantial numbers of adolescents and young adults are now smoking water pipes. In Syria, for example, about half of university students report to have ever used a water pipe and about a quarter of males currently use it. The picture is similar in Lebanon, where, of 1964 Beirut university students, 30.6% of men and 23.4% of women reported current, weekly water pipe use in 2001. Across several EMR countries, about 10–18% of 13–15 year old people use tobacco products other than cigarettes, most likely water pipe.<sup>23</sup>

A systemic review of water pipe use on health outcomes published in 2016 showed chronic bronchitis and chronic obstructive pulmonary disease (COPD) were significantly associated ( $P < 0.05$ ) with water pipe use.<sup>3,25-28</sup> Passive water pipe was significantly ( $P < 0.05$ ) associated with COPD in one study<sup>28</sup> and was a significant ( $P < 0.05$ ) risk for developing COPD in another.<sup>25</sup> A large study in the UAE nationals found smoking prevalence to be most common in younger group with increasing trend in medwakh use among young population.<sup>29</sup> Passive smoking was also found

to be COPD risk factor in developed<sup>19</sup> and developing countries.<sup>30</sup>

#### **Factors other than smoking:**

COPD Prevalence among never-smokers is estimated to be 3-15%<sup>15, 16, 19</sup> further validating the role of other risk factors. A cross-sectional study in Lebanon revealed that 3.4% of nonsmokers had COPD (GOLD stage I) and 11.75% had chronic bronchitis. Lower prevalence in nonsmokers in MENA compared to other world areas could be a younger demographic structure in developing countries.<sup>31</sup> Tunisian BOLD study estimated a prevalence of 4.7% (GOLD stage 1) among nonsmokers (45% of COPD in the study were nonsmokers).<sup>32</sup>

#### **Outdoor pollution and urbanization:**

There is strong evidence supporting the association between outdoor pollution and decreased pulmonary function growth during childhood and adolescence,<sup>33-35</sup> though there are fewer studies that defined COPD by spirometry.

The Study on Air Pollution and Lung Diseases in Adults (SAPALDIA), a cohort analysis, examined the association between the 11-year change in air quality and lung function decline among 8,047 adult subjects (4,742 had complete follow-up) with significant decline with higher PM<sub>10</sub>, measure of particular matter in the air.<sup>36</sup>

The Adventist Health and Smog (AHSMOG) cohort examined survey-based definitions of chronic bronchitis or emphysema only.<sup>37-38</sup> The German SALIA (Study on the influence of Air Pollution on Lung) study of women<sup>39</sup> showed higher PM<sub>10</sub> was related to an increased risk for COPD (GOLD stage 1 criteria). There is also

evidence of biological plausibility, supporting that exposure to air pollutants, such as particulate matter, O<sub>3</sub>, and NO<sub>2</sub>, can produce deleterious effects on the airway as well irreversible loss of pulmonary function and COPD over time.<sup>40</sup>

A case-control study in Lebanon found statistically significant association between outdoor pollution and chronic bronchitis. It concluded that living close to a busy road / power plant was linked to chronic bronchitis. Dubai was found to rank among the worst in the developed world using a pollutant score on account of two variables including volume of cars and emission from each vehicle.<sup>22</sup> Rapid urbanization and motorization are responsible for this situation. COPD prevalence was found to be higher in urban dwellers (60% of all cases) in 2010 in a meta-analysis of the WHO world regions.<sup>2</sup>

### **Biomass fuel:**

In developing countries, a significant proportion of COPD cases occur among never-smokers, especially in women cooking with open fire stoves. Fuel used in these stoves is collectively known as biomass, which includes wood, animal dung, and crop residues. These stoves emit high levels of multiple pollutants that are similar to those present in tobacco smoke with exposure mostly occurring during the entire life span.<sup>41</sup>

About half of world's population uses solid fuels for cooking-; Usage is even higher in rural areas (up to 80%) and particulate matter concentrations greatly exceed most governmental standards for outdoor air.<sup>19</sup>

Several case-control and cross-sectional studies, mostly from developing countries have

found a consistent association between cooking with biomass stoves and respiratory symptoms, chronic bronchitis, and chronic airflow obstruction with evidence of an exposure-response relationship (e.g., hours of cooking per day and number of years cooking with biomass.<sup>42-60</sup>

A study from Colombia found that biomass stove use for 10 or more years was associated with a greater risk of COPD (GOLD stage 1)-<sup>61</sup> while a study conducted in USA showed that exposure to wood smoke (barbeques, cooking stoves) increases chronic bronchitis risk in smokers (current or former).<sup>62</sup>

In the MENA region, a study in the UAE<sup>4</sup> showed that among COPD patients, biomass exposure was higher (33%) than other risk factors, including cigarette smoking (12% current, 12% former). An Egyptian study<sup>9</sup> showed a COPD (GOLD stage 1) prevalence of 11.2% of women exposed to biomass fuel- in fact 86.2% of the total females in the exposed group were nonsmokers.

### **Other exposures (occupational, Bakhour-Burning Arabian incense):**

In multiple high-quality epidemiological studies consistent associations have been observed between exposure to workplace agents and COPD.<sup>19</sup>

Prevalence of exposure to bakhour is high in the MENA region, particularly the Gulf- and it has been found as an exacerbating factor in asthma but not with COPD.<sup>4</sup>

### **Genetic factor:**

Alpha 1 anti-trypsin deficiency (AATD) accounts for 1-2% of COPD cases especially in the young.<sup>22</sup> There is very limited data available in the region to estimate prevalence of AATD.

One study in Saudi Arab concluded higher than expected prevalence of AATD allele in the Saudi population. Genetics has an important role on COPD prevalence and more studies need to be conducted.<sup>63</sup>

#### **Asthma and tuberculosis:**

Many studies have identified the presence of irreversible airway obstruction in asthmatic patients, including nonsmokers<sup>64-66</sup> with evidence that asthma longer duration may lead to a more severe chronic airway obstruction due to accelerated loss of pulmonary function.<sup>66-67</sup>

There is limited/suggestive evidence of an association between tuberculosis and chronic airflow obstruction. Evidence is weak to support any conclusion regarding a causal association between tuberculosis and COPD, worldwide as well in MENA region.

#### **Gender:**

Across all WHO regions, COPD was more prevalent in men (14.3%) than women (7.6%) suggesting a higher risk profile among men.<sup>2</sup> Similar results were seen in MENA region- with men accounting for 5.2% prevalence against women with only 1.8%.<sup>3</sup>

Recently, due to increased tobacco consumption among women and higher risk of exposure to indoor pollution (such as biomass fuel used for cooking and heating) in Low and /or Middle Income Countries (LMIC) may reduce gender differences regarding this disease pattern.<sup>68</sup> For example, in the revised confronting survey of North America and Europe done in 2013, women (7.1%) had higher prevalence of COPD than men (6.2%) only in the US. Rest of the countries showed similar patterns, being men those with higher prevalence.<sup>17</sup>

#### **4. COPD Burden in terms of cost and health care resource consumption:**

COPD causes burden in terms of mortality, morbidity, high health care costs, disability and impaired quality of life.<sup>69</sup> The European Union reported direct cost from COPD over 38.6 billion Euros in 2005, representing about 3% of total health care expenditure.<sup>70,71</sup>

In 2010, US government spent nearly US\$ 49.9 billion on COPD including 29.5 billion on direct health care compared to US\$ 38 billion spent in 2005 of which direct health care costs represented US \$ 22 billion. Direct cost per patient in 2005 ranged from \$ 2700 to \$5900 annually.<sup>72,73</sup>

The burden in LMIC has been comparatively high owing to relatively low COPD awareness, challenged with COPD diagnosis and increased exposures to additional risk factors, like biomass fuel combustion.<sup>74</sup> With an increasing smoking prevalence in MENA region, especially among young as well a longer life expectancy, burden of COPD resource consumption is likely to increase.

Results of BREATHE study: (Monetary quantification was not possible due to wide variation in the region in terms of structure of health care provision)

- Physician consultation was the most frequent cause of health care resource use followed by emergency visits and hospitalizations with similar hierarchy seen in the developed countries.<sup>75-80</sup>
- Health care consumption showed proportional increase with GOLD severity.
- Frequency of symptoms, exacerbations and higher COPD Assessment Test (CAT) score resulted in higher burden in terms of resource consumption. Group D in CAT had the highest expenditure with six fold increase in hospitalization and emergency

visits. COPD Exacerbation was the major reason for physician consultation, hospitalization and emergency visits. This puts emphasis on having individualized approach in high risk patients to optimize COPD management and prevent exacerbations.

- Presence of co morbidities (mainly cardiovascular diseases and diabetes) showed an increased hospitalizations rate ( $p < 0.0001$ ) and hence a raise on resource consumption consistent with other studies.<sup>81,82</sup>
- Regional variation was observed within the MENA region which could be explained by differences in the health care systems (availability of health care facilities for the general population, reimbursement process etc.)<sup>83</sup>

## **5. Conclusions:**

COPD prevalence is high in this region but there is lack of accurate and reliable data on true prevalence. There is a paucity of studies in Africa, South East Asia and Eastern Mediterranean Region (EMR). There is concern that the prevalence of COPD has been underestimated in the region owing to overreliance on clinical diagnosis. In the available studies many COPD diagnoses are not based on spirometry and international

diagnostic guidelines but only on clinical appreciation. Within the MENA region, significant variation in study groups can explain differences in prevalence determined from the studies. ***More studies using uniform methodologies according to the guidelines are needed to describe true COPD prevalence in this region.*** There has been recent regional collaboration, COPVAR that studied symptom burden and impact of quality of life in severe COPD patients (GOLD C and D). Abstract data suggests high symptom burden with breathlessness being the most common complain.<sup>84</sup>

Smoking in the MENA region (particularly Shisha – water pipe smoking) is a part of the culture. The increasing smoking trend especially in young is alarming. Lack of rules and regulations to ban smoking in public places contributes to high prevalence of smoking. With this, burden of COPD resource consumption is likely to increase.

***Strict regulations such as smoking ban in public places should be implemented in order to reduce ill effects of smoking including COPD.*** As mentioned above, COPVAR abstract demonstrated that GOLD D patients (most severe group) had higher smoking prevalence than GOLD C. This is alarming given that despite declining quality of life and increased symptoms, COPD patients continue to smoke and steps to need to be taken to counter this.<sup>84</sup>



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