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Emergence of Antimicrobial Resistance in the Arab Countries

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The impact of antimicrobial resistance (AMR) is a global issue of great concern. The prevalence of multidrug resistant (MDR) pathogens has increased worldwide, including in countries of the Arab league[1]. There is heavy international travel to these countries due to the large population of expatriates and to the annual pilgrimage to the holy city of Mecca, which contributes to the spread of AMR organisms such as MDR *Acinetobacter baumannii* and NDM producing *Escherichia coli*[2], with high rates of ceftazidime resistance and septicaemia episodes[2].

A recent review addressing some of the WHO MDR priority pathogens summarised the published literature over a period extending from 2008 and 2017 on the commonly encountered MDR pathogens from 14 countries of the Arab League[1] (**Figure**). Starting with extended-spectrum beta-lactamase (ESBL) producing bacteria, overall rates were reported as 25% in Kuwait, 17% in Qatar, 7% in Saudi Arabia, 4% in Oman, 66% in Palestinian territories, 54% in Syria, 47% in Iraq, 45% in Jordan, 31% in Lebanon, 55% in Egypt, 35% in Sudan, 9% in Tunisia and Morocco, and 14% in Algeria[1]. However, a much higher rate was observed in some institutes, such as one from Saudi Arabia that had 29% ESBL rates among *E. coli* and 65% among *Klebsiella pneumoniae*[2].

> ***"Incidence rates of ESBL-producing E. coli and K. pneumoniae among urinary tract infections and intra-abdominal infections from Lebanon and Jordan increased by about 20% from 2011 to 2015."***

Similarly, rates were recently reported from the Study for Monitoring Antimicrobial Resistance Trends (SMART), which found that the rates of ESBL-producing *E. coli* and *K. pneumoniae* among urinary tract infections and intra-abdominal infections from Lebanon and Jordan increased by about 20% from 2011 to 2015[3].

A wide range of resistance genes has been reported from ESBL-producing Enterobacteriaceae in the region. However, a predominance of the *ctx-M* gene was observed[1] with CTX-M-15 as the most prevalent enzyme produced in isolates from Lebanon and Jordan[3].

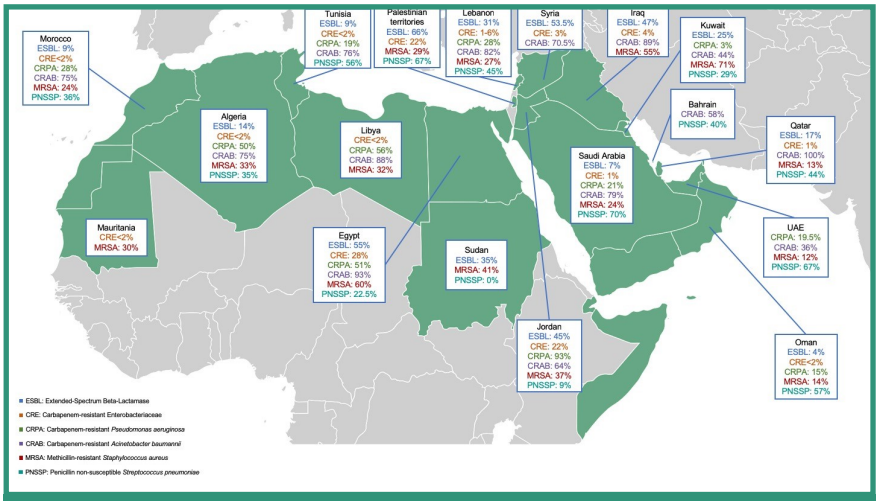
As for carbapenem-resistant Enterobacteriaceae (CRE), mostly *E. coli* and *Klebsiella* spp., their prevalence was found to be 1% in Saudi Arabia, Qatar and Lebanon, 3% in Syria, 4% in Iraq, 22% in Palestinian territories and Jordan, and 28% in Egypt[1]. Algeria, Libya, Morocco, Mauritania, Tunisia and Oman have a CRE prevalence of 2% or less[1]. More recently, many tertiary care centres across the region have observed an increase in the rate of CREs, reaching 7.3% in *Klebsiella* spp. and 5% in *E. coli* in a study from Lebanon[4].

The most commonly produced carbapenemases in countries of the Arab League were NDM-1 (46%), OXA-48-like (32%), or both (9%),[1,3] and only a few *K. pneumoniae* carbapenemase (KPC) enzymes in Jordan, Saudi Arabia and Egypt[5]. In addition, resistance to quinolones was seen in a recent report from Lebanese hospitals, where ciprofloxacin susceptibility decreased from 58% to 52% in two years[6]. Recent reports from the region described emerging resistance to colistin, where Enterobacteriaceae were found to carry the *mcr1* gene on conjugative plasmids[7]. As for carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) isolates, data from the Gulf Cooperation Council (GCC) showed a CRPA prevalence of 20% in the United Arab Emirates (UAE), 15% in Oman, 21% in Saudi Arabia, and 3% in Kuwait. In the Levant, Jordan had a percentage of 93%, and it was 28% in Lebanon. In the African countries the highest prevalence was found in Egypt (51%) and Libya (56%), followed by Algeria (50%), and the lowest prevalence was found in Tunisia (19%) and Morocco (28%)[1].

The production of metallo-β-lactamases (mostly VIM and IMP) is the most important mechanism of carbapenem resistance in *P. aeruginosa* throughout the Arab League countries[1]. Other rare enzymes were also reported, such as PME-1 from Qatar[8]. Mutations in *gyrA* and *parC* were reported from Lebanon, and mutation of *oprD* enhancing porin loss was identified in Lebanon and Algeria[1,9].

A recent study from the GCC countries found that the most prevalent carbapenemase-encoding gene was blaVIM (39%).[10] *Acinetobacter* spp. seen in this region are mostly hospital-acquired and MDR[11] and particularly carbapenem-resistant[6]. The highest

prevalence of carbapenem-resistant *A. baumannii* (CRAB) in the GCC is in Qatar (100%), followed by 79% in Saudi Arabia, 58% in Bahrain, 44% in Kuwait and 36% in the UAE[1]. In the Levant, the highest CRAB prevalence was reported in Iraq (89%) and Lebanon (82%), followed by Syria (70%) and Jordan (64%). In the African countries, Egypt (93%) and Libya (88%) reported the highest resistance prevalence, followed by Algeria (75%), Morocco (75%) and Tunisia (76%)[1].



Prevalence of the resistance of some of the WHO Priority pathogens in the countries of the Arab League

Most of the CRAB isolates in the GCC were found to harbor the *bla*$_{OXA51}$ gene and 91% of them were also positive for *bla*$_{OXA-23}$, which is the most predominant gene in Lebanon also[12]. Most countries report polyclonal spread with the predominant carbapenemases being OXA-23 and OXA-24 and are associated with high-level resistance. Rapid emergence of NDM1[1,12] is also reported. Recently, colistin resistance was reported in *A. baumannii* isolates[1].

Meticillin-resistant *Staphylococcus aureus* (MRSA) has been extensively reported as a hospital-acquired pathogen in most countries of the Arab league[1]. In the GCC, MRSA rates were found to be 24% in Saudi Arabia, 14% in Oman, 13% in Qatar and 12% in UAE. In Kuwait, MRSA was isolated from 71% of diabetic foot cultures. In the Levant, MRSA rates were found to be 27% in Lebanon, 29% in Palestinian territories, 37% in Jordan and 55% in Iraq. In the African countries, the lowest rate of MRSA was in Morocco (24%), followed by Mauritania (30%), Libya (32%), Algeria (33%), Sudan (41%) and Egypt (60%)[1]. There is a predominance in the SCC*mec* IV strain[13,14] and the Pantone Valentine Leukocidin gene.[14] More than 20% of strains harbored the *tst1* gene.

Penicillin non-susceptible *Streptococcus pneumoniae* (PNSSP) was reported from the region and pertained to invasive and non-invasive pneumococcal diseases, as well as from healthy carriers and Hajj pilgrims[1]. The highest rate of PNSSP from the GCC countries was in Saudi Arabia (70%), then UAE (67%), Oman (57%), Bahrain (40%), Qatar (44%) and Kuwait (29%). In the Levant, Palestinian territories reported 67% PNSSP, followed by Lebanon (45%) and Jordan (9%). In Africa, PNSSP rates were 56% in Tunisia, 36% in Morocco, 35% in Algeria, 22% in Egypt and none in Sudan[1]. Different serotypes exist in the region with the most common being 19F, 23F, 6B and 19A.[15]

It is clear that AMR is quite prevalent among most countries of the Arab League. While the Global Antimicrobial Resistance Surveillance System (GLASS) report will publish more representative data on the matter in the future, it is crucial to recognize the need for the standardization of microbiological methods and antimicrobial surveillance techniques in this region to accurately reflect the true burden of AMR and guide infection control and stewardship efforts.

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