Factors that may contribute in increasing the prevalence of broad spectrum ß-lactamase producers among Gram-negative bacilli in the Gulf Cooperation Council (GCC) states

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ABSTRACT

Introduction: Broad spectrum β- lactamase producing Gram-negative bacteria are emerging rapidly and spreading widely. Here we review some of the possible unique factors in the GCC states, which may influence bacteria to horizontally acquire resistance mechanisms, increase their prevalence, or spread antimicrobial resistant bacteria within the region.

Methods: We searched MEDLINE for the search terms “antibiotics”, “resistance”, and, “Saudi Arabia”, “UAE”, “Kuwait”, “Oman”, “Bahrain”, or “Qatar”. The word “lactamase” was also combined with the countries’ names to replace the “antibiotics” and “resistance” words. The results were excluded to cover the literature published between 1980 and 2010, concentrating on recent publications. We used the reference lists from articles identified by this strategy as further sources. Finally, we noted the potential factors related to the emergence or spread of ß-lactam resistant Gram-negative bacteria. Our search was restricted to papers published in English.

Results: Due to the socio-economic structure of the GCC states, significant migration activity is prevalent. Beside the high population of temporary foreign workforce, Saudi Arabia is also visited annually by more than 1.5 million pilgrims who might receive health care during their stay. Travel is recognized as a significant contributor to spreading antibiotic resistant bacteria, particularly if hospitalization occurs during travel. The overuse and misuse of antibiotics in the GCC states are not only restricted to the medical setting. The isolation of antibiotic resistant bacteria from agricultural settings may reveal inappropriate use of antimicrobials such as growth promoters with animals. Over-the-counter availability of antibiotics facilitates self-prescribers obtaining drugs, which may lead to overuse. Such overuse might stimulate normal microbial flora to develop antibiotic resistance mechanisms or act as selection pressure for resistant strains. It has been found that a higher rate of conjugation occurs at a temperature of about 30°C. The hot weather in the GCC states might influence bacteria present in the environments such as the Arabian Gulf coast to share transmissible genetic elements encoding antibiotic resistance mechanisms. Other environments such as desert sand could be contaminated with medically important antibiotic resistant bacteria. Since sandstorms are a common incident in the Gulf region, the spreading of resistant bacteria to other sites might be expected, but no data was found to support this.

Conclusions: The spread of antimicrobial agents in the GCC countries seems to be multifactorial. This search has assisted in the identification of many possible factors. However, more studies looking into the relationships of these factors and their true impact on spreading and stimulating emergence of antibiotic resistance mechanisms are needed. Such information would be helpful in future planning of interventional methods.

BACKGROUND

The emergence and increase in antibiotic resistant organisms is a serious concern for modern healthcare practice. In Gram negative bacilli (GNB) an important cause of multi-drug resistance is the production of broad spectrum β-lactamases [1]. This emergence of antimicrobial resistance can negatively affect patients’ outcomes, cause treatment failure and prolong hospital stay, which can be associated with a high morbidity, mortality, recurrent infections and increased healthcare system costs.

The emergence and spread of broad spectrum β-lactamases producing GNB may be due to the high consumption of antibiotics used in hospitalized patients or inadequate infection control, including hand hygiene and environmental cleaning. Here we review some of the possible factors that may influence bacteria to horizontally acquire resistance mechanisms, increase their prevalence, or spread antimicrobial resistant bacteria. Some of the reviewed factors are unique to the GCC states and others exist in different parts of the world including this region.

METHODS

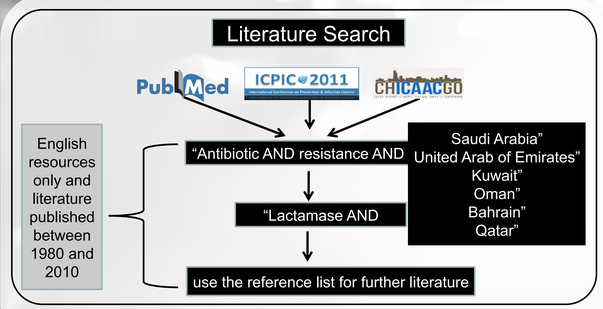

Figure 1. Summary of the methodology used to search for the literature.

RESULTS

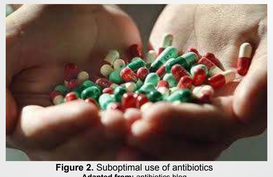

Figure 2. Suboptimal use of antibiotics
Adapted from: antibiotics blog

Suboptimal Use of Antibiotics

- Antibiotics are the most prescribed drugs in Saudi hospitals [2,3].
- Two times higher rate of antimicrobial prescription was used in a paediatric emergency department at a Saudi hospital than recommended by the World Health Organization [4].
- Misprescription of antibiotics:
  - 36.2% of patients with diarrhea in Oman have received antibiotics. However the microbiology laboratory confirmed bacterial gastrointestinitis in 15.2% of the patients [5].
  - Only 25% of patients in HMC, Doha who received antibiotics had ‘microbiologically proven infections’ [6].
  - In a Bahraini study, it was found that most antibiotics were prescribed to treat respiratory tract infections [7].
- Despite the illegal firm to sell antibiotics without prescriptions in Saudi Arabia and other gulf countries :
  - One out of 88 community pharmacists refused to sell antibiotics without a prescription to patients claiming UTI [8].
  - In Riyadh, 77.6% out of 327 community pharmacies dispended antibiotics without prescription to treat scenarios of mostly viral infections [9].
  - In UAE, an investigation on 17 community pharmacies found that 68.4% of total requested antibiotics were sold over-the-counter including injected antibiotics [10].
- Antibiotics misuse in agricultural sittings (e.g. poultry plants) [11, 12].

Figure 3. Hand hygiene compliance
Adapted from: http://www.cdc.gov

Hand Hygiene Compliance (HHC)

- In 2003 at a Saudi hospital, handwashing compliance was 6.7% before patient contact and 23.7% after patient contact [13].
- HHC rates of 50.3% in a Saudi hospital and 33.4% in a Kuwaiti hospital [14, 15].
- Disappointingly, the lowest rates of hand hygiene in one Saudi hospital was amongst intensivists [16].

Figure 4. Water source contaminated with from sewage effluent.
Adapted from: *California Agriculture* 54(5):62-68

Figure 5. Sandstorm in Riyadh.
Adapted from: http://insidethemiddleeast.blogs.cnn.com

Figure 6. Green turtles nesting on the coast of Oman
Adapted from: http://travsatlastravels.blogspot.com

Environmental Contamination with Antibiotic Resistant Bacteria

- Seawater and fish samples collected from Oman where sewage water is dumped were contaminated with antibiotic resistant enteric bacteria including *Klebsiella spp* [17].
- Antibiotic resistant human pathogens have been isolated from the eggshells and oviductal fluid of green turtles in the coast of Oman. [18,19].
- In Bahrain, it was found that sewage water discarded in gulf seawater contain multidrug resistant coliforms [20].
- The spread of antibiotic resistant organisms in water sources indicates the wide spread of antibiotic resistant organisms in the environment.
- Soil and desert sands of the GCC states could also resource antibiotic resistant bacteria, which could be transferred across continents by sandstorms and without the need for patient transmission [21], although definitive data are lacking.
- The high temperature in the GCC states might act as a contributing factor in transmitting the antibiotic resistance genetic elements. It was found that the highest conjugation rate between different GNB species was observed at 30°C [22]. This may raise the suspicion that such activity may also happen in the GCC environments which can get close to this “optimum” temperature.

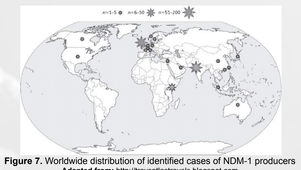

Figure 7. Worldwide distribution of identified cases of NDM-1 producers
Adapted from: http://travsatlastravels.blogspot.com

Figure 8: Annual international travel to Saudi Arabia to perform Hajj
Adapted from: *Lancet* 2006;367:1008-15.

Travel

- Most NDM-1 cases in the GCC have been associated with travel [23, 24].
- High population of foreign workforce living in the GCC states.
- Hospitalization during international travel [25].
- More than 1.5 million pilgrims visit Saudi Arabia annually to do Hajj [26].
- Hajj-related infections is well-known due to mass gathering and other reasons [27].
  - Septicaemia episodes in Makkah increased by 16.5% during Hajj [28].

CONCLUSION

The spread of antimicrobial agents in the GCC countries seems to be multifactorial. The spread of antibiotic resistant organisms in water sources is a concern. This indicates the wide spread of antibiotic resistant organisms. Colonized or infected patients with ESBL or carbapenemase producing GNB may unintentionally spread the antimicrobial resistant organisms to other patients. This search has assisted in the identification of many possible factors. Studies to investigate the relationships of these factors and their true impact on spreading and stimulating emergence of antibiotic resistance mechanisms are needed. Information provided would help in future planning of interventional methods.

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