

bacterial strain, number of isolates tested, sensitivity results, location of the study and time of data collection. The data were pooled and summarized using STATA software, version 13 (<https://www.stata.com/>), and the spatial view (mapping) was generated using ArcGIS software platform (ESRI, Redlands, CA, USA). The Excel files were inserted into the GIS platform using the map of the Saudi Arabian administrative regions as base layer (feature class). A number of ArcMap tools and functions such as 'merge', 'dissolve' and 'table join' were used to organize and map the collected datasets. Finally, the maps were presented as a percentage of resistance of each bacterial type in the Saudi Arabian regions.

Results

Enterobacteriaceae

The Antimicrobial Sensitivity Testing (AST) for a total of 11,196 *Enterobacteriaceae* isolates were extracted from the published literature between 1998 and 2015. AST data showed an up-trending pattern with respect to resistance against ciprofloxacin, Trimethoprim/Sulfamethoxazole (TMP/SMX), and amikacin. (Table 1 and Figure 1). Demonstration of the spatial distribution of the AST data showed that most were reported from four of Saudi Arabia's 13 administrative regions: the Eastern Region, Riyadh, Asir and Makkah. AMR in the Makkah region was the highest against ciprofloxacin, imipenem, ertapenem, ampicillin and cefuroxime. In the Riyadh Region it was the highest against gentamicin, while the Eastern Region had the highest AMR against meropenem and in Asir Region the bacterial isolates were particularly resistant against ceftriaxone and TMP/SMX (Figure 2).

Pseudomonas aeruginosa

The AST data for 15,791 *P. aeruginosa* isolates were extracted from the published literature between 1998 and 2015. As can be

seen in Figure 3, an up-trending pattern in resistance against all antimicrobials was shown by the AST data. Demonstration of AST data using mapping techniques showed that the majority of isolates were reported from Riyadh, Makkah, Eastern, Asir and Hail regions. Figure 4 shows that AMR in the Makkah Region was the highest against all reported antimicrobials.

Acinetobacter baumannii

The AST data for 5,312 *Acinetobacter baumannii* isolates were extracted from published literatures between 1998 and 2015. The AST data regarding these isolates showed an up-trending pattern in resistance against all antimicrobials (Figure 5). Demonstration of AST data using mapping techniques showed that most isolates were reported from the Riyadh and Eastern regions. In this case, the AMR data were the highest against amikacin, ciprofloxacin, and imipenem in Madinah region, and against gentamicin and meropenem in Riyadh region (Figure 6).

Discussion

To our knowledge, this is the first study to use mapping techniques to represent AMR data at regional levels in Saudi Arabia. In spite of the inconsistency of the data published, regarding the number of bacterial isolates tested, their regional origin, and the time of their collection, it is very obvious that AMR is a growing trend since the last few years. There was variability in the AMR data among regions, which could indicate differences in resistant strains, practice pattern, and prescribing aptitude of local doctors.

Establishing a national database that reports the prevalence of AMR and antibiotics consumption on a real-time basis at regional levels in Saudi Arabia would be an essential first step to allocate resources, detects outbreaks, and supports antimicrobial stewardship programs. The occurrence of AMR in bacterial pathogens has been illustrated and analysed through maps by agencies like European Centre for Disease Prevention and Control (ECDC) where antimicrobial consumption in thirty European countries are

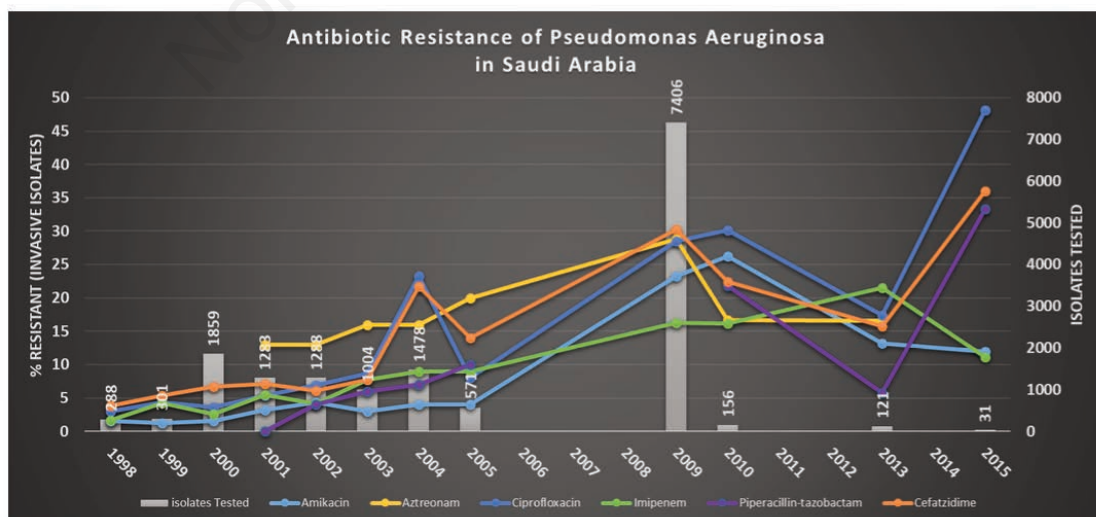


Figure 3. *Pseudomonas aeruginosa* resistance pattern 1998 to 2015 in Saudi Arabia according to literature search. The grey bars indicate time and number of sample collections.

reported on a regular basis (Weist and Högberg, 2016). In another research study, using visual and statistical evidence, Callaghan *et al.* (2009), established the effectiveness of GIS acknowledging that “its unique ability to integrate a large range of datasets in a common framework facilitating in the spatial and non-spatial analysis of disease events adds a different dimension to disease analysis and surveillance”. GIS has also been utilized in other research studies in other regions to investigate methicillin-resistant *Staphylococcus aureus* (Tirabassi *et al.*, 2005), *Streptococcus pneumonia* (Mouro *et al.*, 2011) and *E. coli*.(Kiffer *et al.*, 2011).

This study, the first to investigate antimicrobial resistance trends in Saudi Arabia using GIS, aimed to explore and use GIS

technology applications to gain insight of the extent of AMR in Saudi Arabian regions, and to come up with surveillance and monitoring strategies using GIS derived products (maps, spatial and temporal analyses, etc.) that could help address current and future outbreaks more quickly and efficiently. Although GIS, through the mapping techniques used in this study, presents the best method to visualize the characteristic of AMR in Saudi Arabia, our research did not utilize an advanced GIS analysis due to limitations in the availability of data. Advanced analysis includes, for example, spatial interpolation such as Inverse Distance Weighted (IDW), Kriging, natural neighbour, spline and trend techniques, which may be considered in the future.

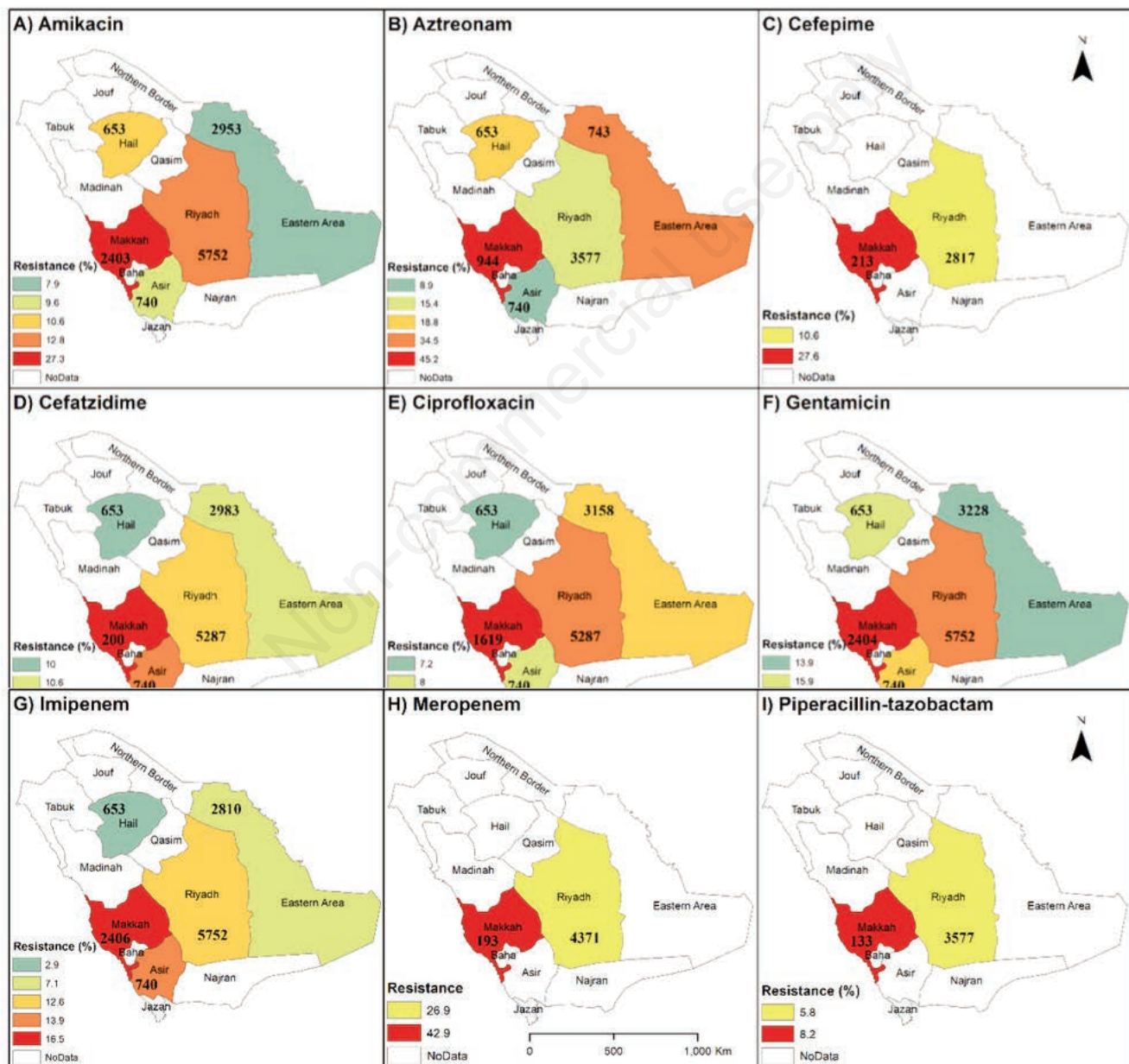


Figure 4. Spatial distribution of the *Pseudomonas aeruginosa* resistance data in Saudi Arabia.

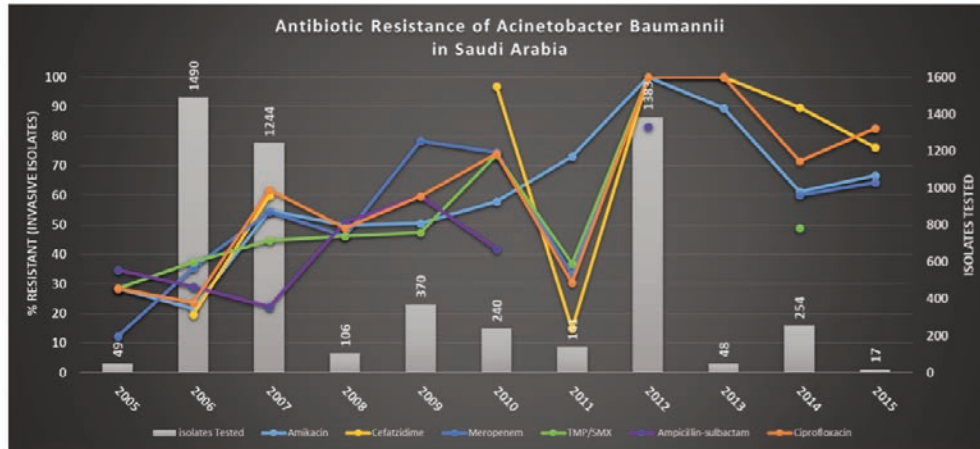


Figure 5. *Acinetobacter baumannii* resistance pattern 1998 to 2015 in Saudi Arabia according to the literature search. The grey bars indicate time and number of sample collections.

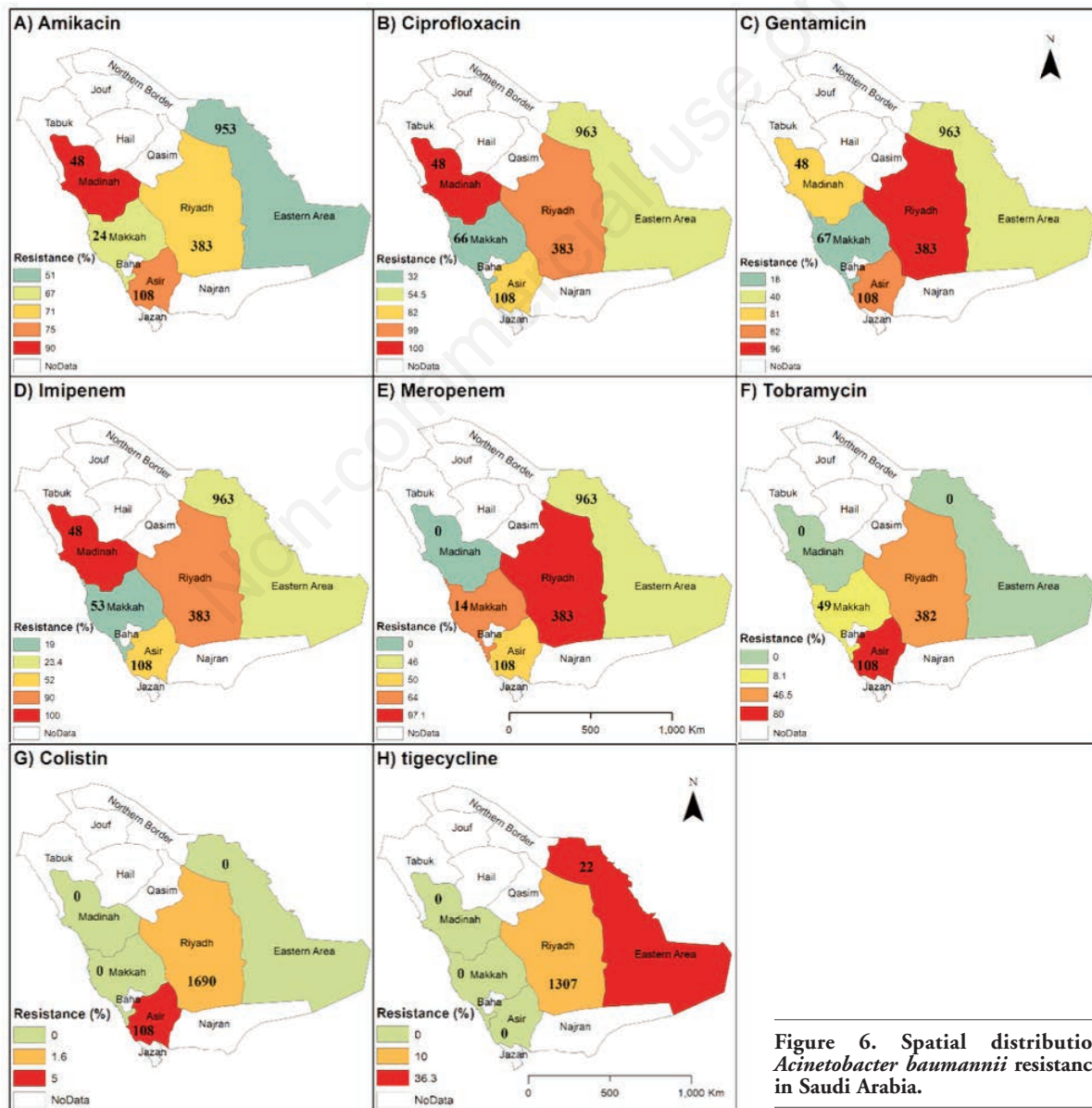


Figure 6. Spatial distribution of *Acinetobacter baumannii* resistance data in Saudi Arabia.

Using such techniques would be worthwhile to improve our understanding regarding spatial trends and pattern recognition of AMR levels in Saudi Arabia. Incorporating different environmental and anthropogenic variables such as wastewater, landfill locations, population number and density, distance from roads and distance from healthcare locations into GIS platform may also be valuable to understand the cause and effect of AMR in Saudi Arabia. Once such data can be obtained, these ideas will be targeted in future research. Nevertheless, the results presented in this research have indicated an effective approach by clearly showing the distribution of AMR in the Saudi Arabian regions between 1998 and 2015.

Conclusion

The employment of mapping technology in displaying AMR data extracted from published literature shows a high resistance rate in Makkah, which could be attributed to the high antibiotic consumption due to multiple factors, including the high influx of pilgrims. Advanced GIS analyses are expected to help stakeholders create containment strategies and allocate resources to slow down the emergence of AMR.

References

- Al-Obeid S, Jabri L, Al-Agamy M, Al-Omari A, Shibl A, 2015. Epidemiology of extensive drug resistant *Acinetobacter baumannii* (XDRAB) at Security Forces Hospital (SFH) in Kingdom of Saudi Arabia (KSA). *J Chemother* 27:156-62. doi:10.1179/1973947815y.0000000019
- Al-Qadheeb NS, Althawadi S, Alkhalaf A, Hosaini S, Alrajhi AA, 2010. Evolution of tigecycline resistance in *Klebsiella pneumoniae* in a single patient. *Ann Saudi Med* 30:404-7. doi:10.4103/0256-4947.67087
- Al Johani SM, Akhter J, Balkhy H, El-Saed A, Younan M, Memish Z, 2010. Prevalence of antimicrobial resistance among gram-negative isolates in an adult intensive care unit at a tertiary care center in Saudi Arabia. *Ann Saudi Med* 30:364-9. doi:10.4103/0256-4947.67073
- Baadani AM, Thawadi SI, El-Khizzi NA, Omrani AS, 2013. Prevalence of colistin and tigecycline resistance in *Acinetobacter baumannii* clinical isolates from 2 hospitals in Riyadh Region over a 2-year period. *Saudi Med J* 34:248-53.
- Balkhy HH, El-Saed A, Al Johani SM, Francis C, Al-Qahtani AA, Al-Ahdal MN, et al., 2012. The epidemiology of the first described carbapenem-resistant *Klebsiella pneumoniae* outbreak in a tertiary care hospital in Saudi Arabia: how far do we go? *Eur J Clin Microbiol Infect Dis* 31:1901-9. doi:10.1007/s10096-011-1519-0.
- Hay SI, Rao PC, Dolecek C, Day NPJ, Stergachis A, Lopez AD, Murray CJL, 2018. Measuring and mapping the global burden of antimicrobial resistance. *BMC Med* 16:78. doi:10.1186/s12916-018-1073-z.
- Jooma S, 2015. Executive action to combat the rise of drug-resistant bacteria: is agricultural antibiotic use sufficiently addressed? *Journal of Law and the Biosciences* 2:129-38. doi:10.1093/jlb/lsv005.
- Kader AA, and Kumar AK, 2004. Prevalence of extended spectrum beta-lactamase among multidrug resistant gram-negative isolates from a general hospital in Saudi Arabia. *Saudi Med J* 25:570-4.
- Khan MA, Faiz A, 2016. Antimicrobial resistance patterns of *Pseudomonas aeruginosa* in tertiary care hospitals of Makkah and Jeddah. *Ann Saudi Med* 36:23-8. doi:10.5144/0256-4947.2016.23
- Kiffer CR, Camargo EC, Shimakura SE, Ribeiro PJ, Jr., Bailey TC, Pignatari AC, Monteiro AM, 2011. A spatial approach for the epidemiology of antibiotic use and resistance in community-based studies: the emergence of urban clusters of *Escherichia coli* quinolone resistance in Sao Paulo, Brasil. *Int J Health Geogr* 10:17. doi:10.1186/1476-072X-10-17
- Lobanovska M, Pilla G, 2017. Penicillin's Discovery and Antibiotic Resistance: Lessons for the Future? *Yale J Biol Med* 90:135-45.
- Memish ZA, Shibl AM, Kambal AM, Ohaly YA, Ishaq A, Livermore DM, 2012. Antimicrobial resistance among non-fermenting Gram-negative bacteria in Saudi Arabia. *J Antimicrob Chemother* 67:1701-5. doi:10.1093/jac/dks091.
- Mouro AK, Koga PC; Monteiro AM; Camargo EC, Pignatari AC, 2011. Spatial exploration of *Streptococcus pneumoniae* clonal clustering in Sao Paulo, Brazil. *Braz J Infect Dis* 15:462-6.
- Noble D, Smith D, Mathur R, Robson J, Greenhalgh T, 2012. Feasibility study of geospatial mapping of chronic disease risk to inform public health commissioning. *BMJ Open* 2:e000711. doi:10.1136/bmjopen-2011-000711
- Rotimi VO, al-Sweih NA, Feteih J, 1998. The prevalence and antibiotic susceptibility pattern of gram-negative bacterial isolates in two ICUs in Saudi Arabia and Kuwait. *Diagn Microbiol Infect Dis* 30:53-9.
- Samarasundera E, Walsh T, Cheng T, Koenig A, Jattansingh K, Dawe A, Soljak M, 2012. Methods and tools for geographical mapping and analysis in primary health care. *Prim Health Care Res Dev* 13:10-21. doi:10.1017/S1463423611000417.
- Shrivastava SR, Shrivastava PS, & Ramasamy J. 2018. World health organization releases global priority list of antibiotic-resistant bacteria to guide research, discovery, and development of new antibiotics. *J Med Soc* 32:76.
- Slayton RB, Toth D, Lee BY, Tanner W, Bartsch SM, Khader K, et al., 2015. Vital Signs: Estimated Effects of a Coordinated Approach for Action to Reduce Antibiotic-Resistant Infections in Health Care Facilities - United States. *MMWR. Morbidity and Mortality Weekly Rep* 64:826-31. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/26247436>
- Tawfik AF, Alswailem AM, Shibl AM, and Al-Agamy MH. 2011. Prevalence and genetic characteristics of TEM, SHV, and CTX-M in clinical *Klebsiella pneumoniae* isolates from Saudi Arabia. *Microb Drug Resist*, 17(3), 383-388. doi:10.1089/mdr.2011.0011
- Tirabassi MV, Wadie G, Moriarty KP, Garb J, Konefal SH, Courtney RA, ... Wait R. 2005. Geographic information system localization of community-acquired MRSA soft tissue abscesses. *J Pediatr Surg*, 40(6), 962-965; discussion 965-966. doi:10.1016/j.jpedsurg.2005.03.010
- Weist K, and Högberg LD. 2016. ECDC publishes 2015 surveillance data on antimicrobial resistance and antimicrobial consumption in Europe. *Eurosurveillance*, 21(46).
- WHO, 2016. National antimicrobial resistance surveillance systems and participation in the Global Antimicrobial Resistance Surveillance System (GLASS): a guide to planning, implementation, and monitoring and evaluation. Available from: <https://apps.who.int/iris/handle/10665/251554>
- WHO, 2018. Global antimicrobial resistance surveillance system (GLASS) report-early implementation 2016-2017. Available from:<https://www.who.int/glass/resources/publications/early-implementation-report/en/>
- Zowawi HM, Balkhy HH, Walsh TR, and Paterson DL. 2013. beta-Lactamase production in key gram-negative pathogen isolates from the Arabian Peninsula. *Clin Microbiol Rev*, 26(3), 361-380. doi:10.1128/cmr.00096-12