Employment of Mapping Technology in Antimicrobial Resistance Reporting in Saudi Arabia

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Abstract

Although Antimicrobial Resistance (AMR) is a worldwide threat, local AMR databases do not exist. Unlike other health disasters, developing containment strategies for AMR cannot be started without a representative, local, updated AMR data. However, Geographical Information Systems (GIS) mapping technology is capable of visualizing AMR data integrated with geographical regions. Due to the absence of AMR databases in Saudi Arabia, we searched Medline and Embase databases from inception until May 28, 2018, including literature that reported AMR data on the most prevalent gram-negative bacterial strains in Saudi Arabia. These data were extracted into Microsoft Excel file and inserted into STATA software, version 13 and ArcMap 10.6 software platform for mapping. We found particularly high levels of AMR in Makkah (Mecca), possibly due to high antibiotic consumption because of the influx of pilgrims, with *Pseudomonas aeruginosa* isolates showing the highest resistance rate against amikacin, aztreonam, cefepime, ceftazidime, ciprolfloxacin, gentamicin, imipenem, meropenem and pipracillin/tazobactam, and *Enterobacteriaceae* isolates against cefuroxime, ciprofloxacin, ampicillin, imipenem and ertapenem. The cause is, however, multifactorial since *Acinetobacter baumannii* isolates showed a variable resistance rate throughout the country. The employment of mapping technology in displaying AMR data extracted from published literature is a practically useful approach, and advanced GIS analyses should help stakeholders create containment strategies and allocate resources to slow down the emergence of AMR.

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Introduction

One of the greatest breakthroughs in the last century was the invention of penicillin by Alexander Fleming, which saved thousands of lives threatened by bacterial infections during the Second World War (Lobanovska and Pilla, 2017). Even though the Second World War ended in 1945, another war started, this time between antibiotics and the bacterial tendency to develop resistance. It has been reported that bacterial resistance to antibiotics has resulted in more than 2 million infections and 23,000 deaths annually in the United States alone, costing 55 billion USD in direct and indirect costs (Slayton *et al*., 2015). Consequently, the US presidential executive order for Combating Antibiotic-Resistant Bacteria was signed in 2014 (Jooma, 2015). The following year saw the launch of the US National Action Plan, which recommends reporting antibiotic use and bacterial resistance to strengthen and monitor the progress of antibiotic stewardship programs in inpatient settings (Slayton *et al*., 2015).

Antimicrobial Resistance (AMR) is a worldwide health problem causing a major threat to global health (Jooma, 2015; Slayton *et al*., 2015). In October 2015, the World Health Organization (WHO) launched the Global Antimicrobial Resistance Surveillance System (GLASS) as a global, collaborative initiative to contain the rapid spread of AMR (WHO, 2016).

In February 2017, the WHO declared a critical need for antibiotics to be developed for a list of 12 resistant bacteria and stated that with this accelerated evolution of bacterial resistance to antibiotics, normal medical procedures would be at risk and potentially jeopardize the life of patients (Shrivastava *et al.*, 2018) Despite the absence of a national database pertaining to antibiotic consumption and AMR in Saudi Arabia, there are many published literature references describing the emergence of AMR, yet, they are inconsistently reported (Al-Obeid *et al.*, 2015; Al-Qadheeb *et al.*, 2010; Al Johani *et al.*, 2010; Baadani *et al.*, 2013; Balkhy *et al.*, 2012; Kader and Kumar, 2004; Khan and Faiz, 2016; Memish *et al.*, 2012; Rotimi *et al.*, 1998; Tawfik *et al.*, 2011; Zowawi *et al.*, 2013). In May 2017, Saudi Arabia enrolled in GLASS and submitted 8,219 isolates from 39 surveillance sites, via the Saudi Center for Disease Control (SCDC) (WHO, 2018). Nevertheless, there are many other difficulties surrounding the estimation of AMR in Saudi Arabia, mainly due to the paucity of data with regard to geographical distribution, prevalence and incidence of AMR, making its burden difficult to measure and hindering the development of strategies for its control (Hay *et al.*, 2018).

Table 1. Cumulative collection of samples investigated.

Isolate collection (year)	*Enterobacteriaceae* (no.)	*A. baumannii* (no.)	*P. aeruginosa* (no.)
1998	414		288
1999	474		301
2000	350		1859
2001	8,239		1283
2002	374		1288
2003	172		1004
2004			1478
2005		49	571
2006		1,490	
2007		1244	
2008		106	
2009		370	7,406
2010	120	240	156
2011	534	141	
2012		1383	
2013	202	48	121
2014	33	254	
2015	284	17	31
Total	**11,196**	**5,312**	**15,791**

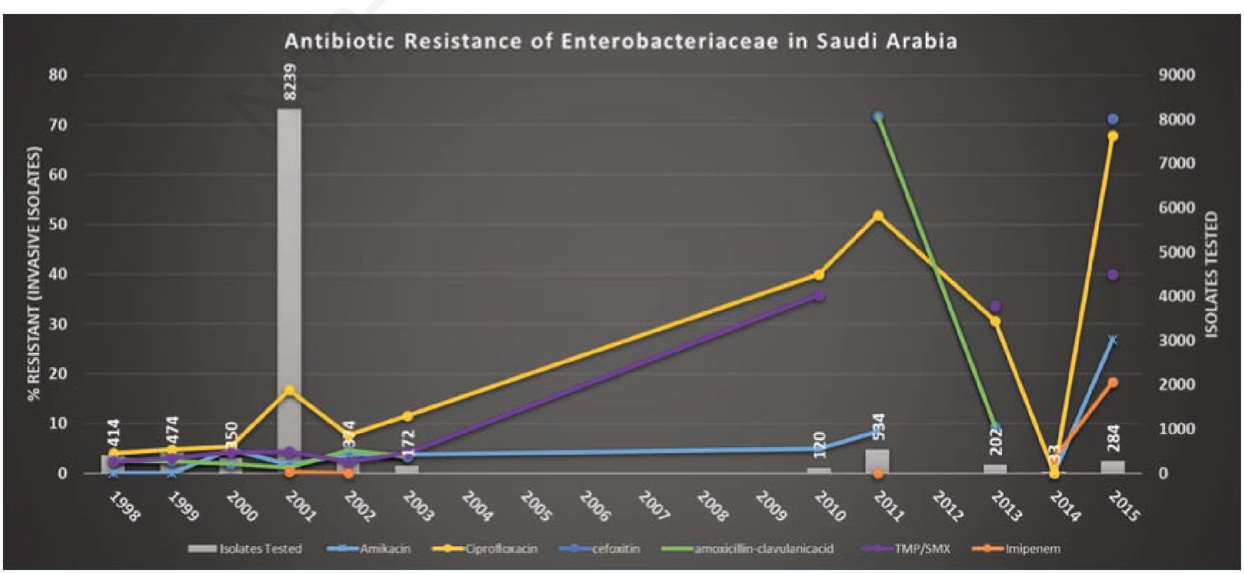

Figure 1. ***Enterobacteriaceae*** **resistance pattern 1998-to 2015 in Saudi Arabia according to literature search. The grey bars indicate time and number of sample collections.**

Geographical Information Systems (GIS) and mapping techniques, powerful tools that can help visualize local, regional and national disease patterns, have been utilized in primary care research in general and in epidemiological studies (Noble *et al.*, 2012; Samarasundera *et al*., 2012). Galvin *et al*. (2013) used GIS to investigate antimicrobial resistance patterns in pathogenic bacteria which highlighted GIS capabilities to visualize epidemiological trends in bacterial pathogens. To the best of our knowledge, GIS has not been used in Saudi Arabia for the purpose of reporting AMR for either public health information or for the management of outbreaks. Thus, this research aims to use the advantage of GIS to map and visualize the characteristic of AMR based on data published in previous research.

Materials and Methods

Due to the absence of AMR databases in Saudi Arabia, we utilized AMR data published in the literature as reference. We conducted a literature search of the Medline and Embase databases from inception until May 28th, 2018. The search terms were AMR and the four most prevalent gram-negative bacterial strains in Saudi Arabia: *Acinetobacter baumannii, Pseudomonas aeruginosa, Escherichia coli* and *Klebsiella pneumoniae* with the two latter here referred to as *Enterobacteriaceae.* The AMR-related data were extracted into Microsoft Excel files, which included type of

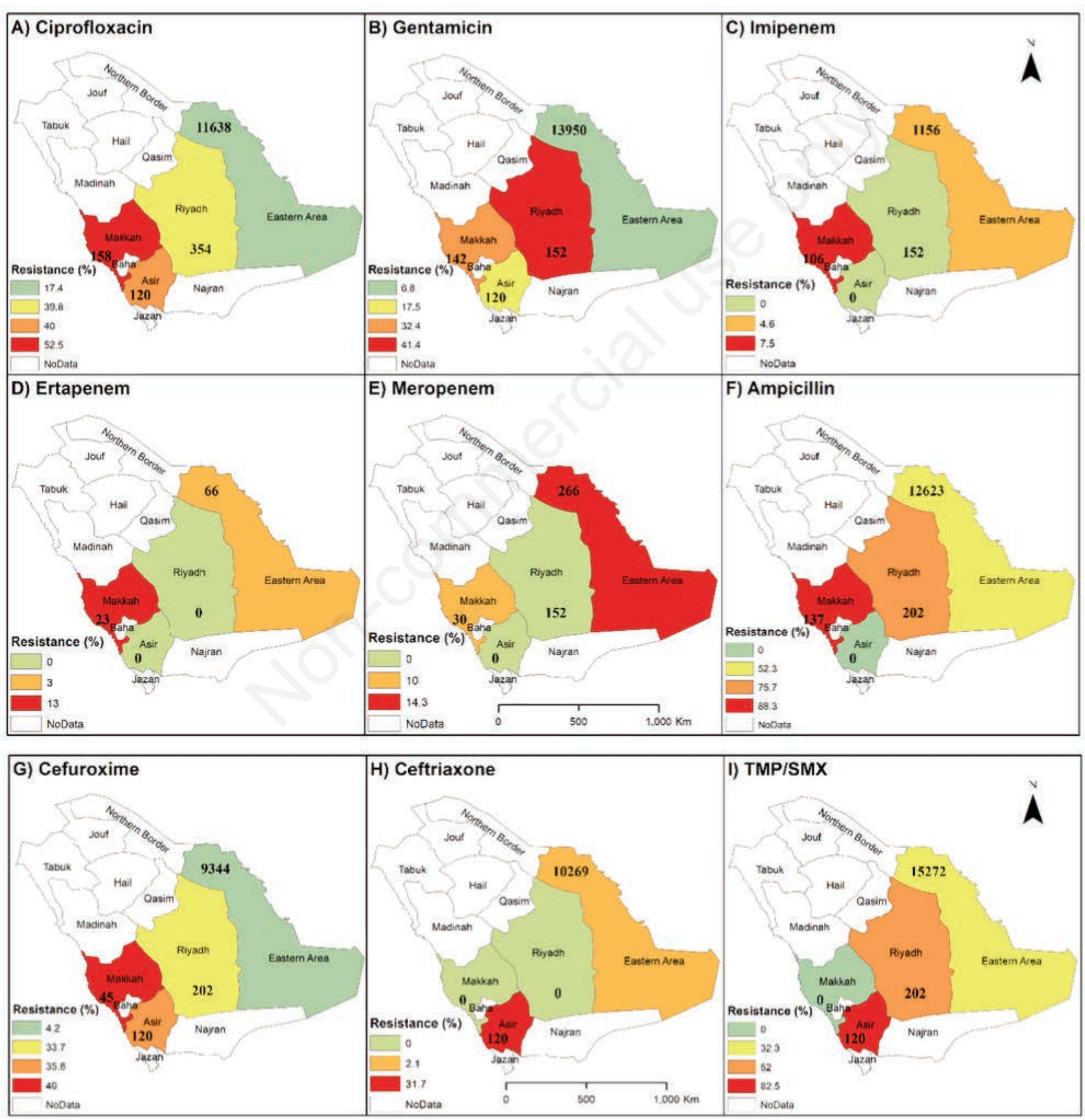

Figure 2. Spatial distribution of the *Enterobacteriaceae* resistance data in Saudi Arabia.

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

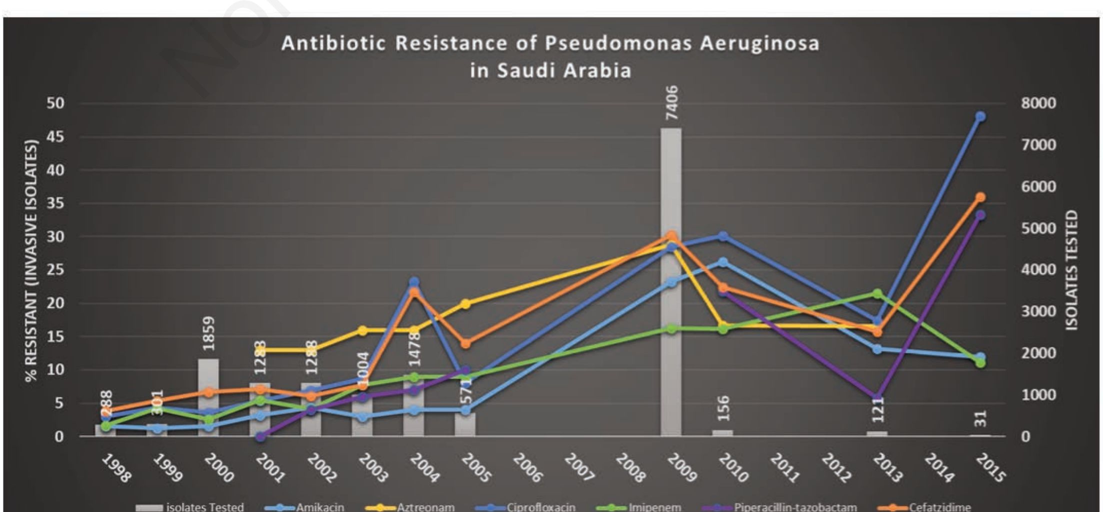

Figure 3. *Pseudomonas aeruginosa* resistance pattern 1998 to 2015 in Saudi Arabia according to literature search. The grey bars indicate time and number of sample collections.

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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.

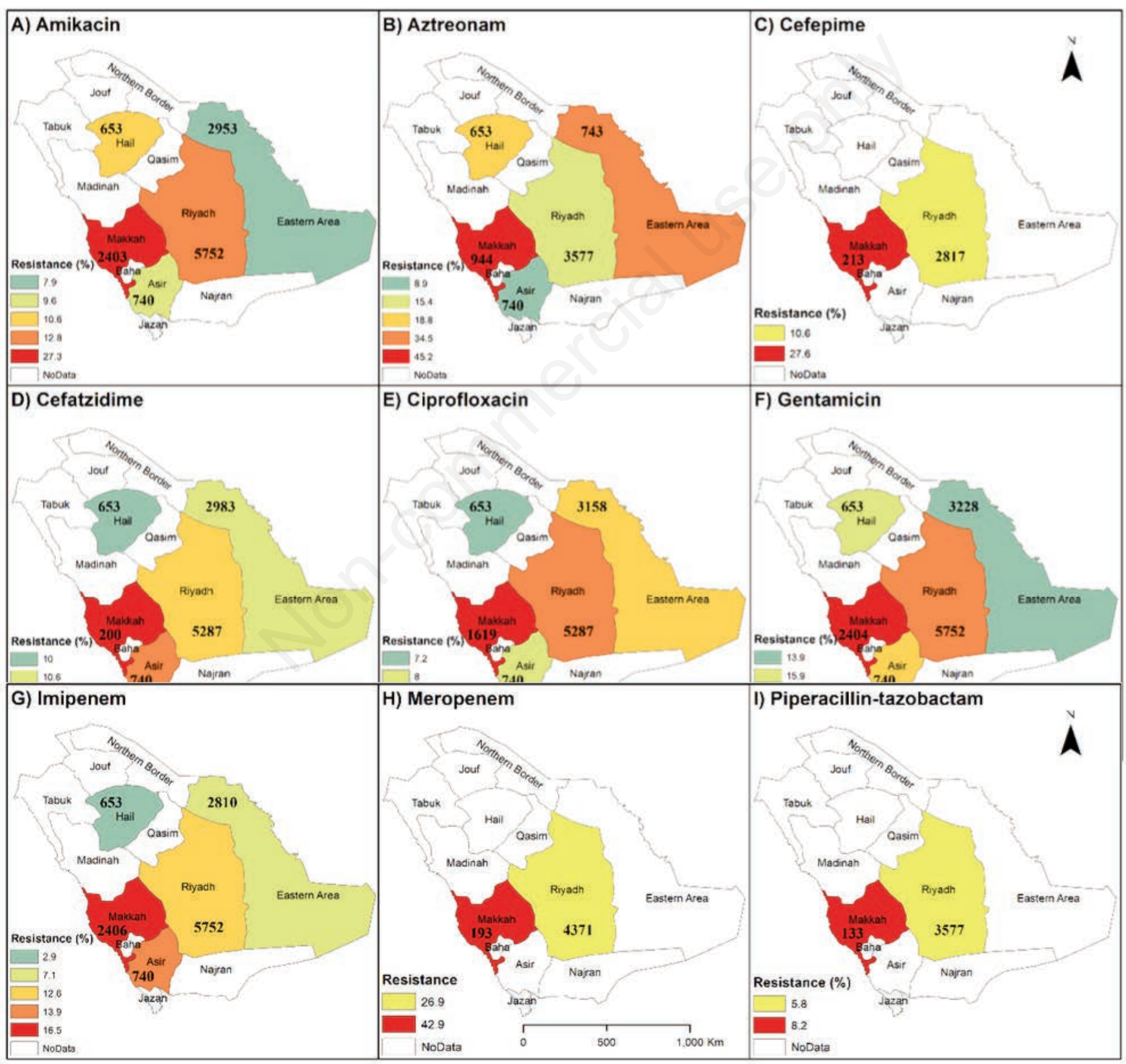

Figure 4. Spatial distribution of the *Pseudomonas aeruginosa* resistance data in Saudi Arabia.

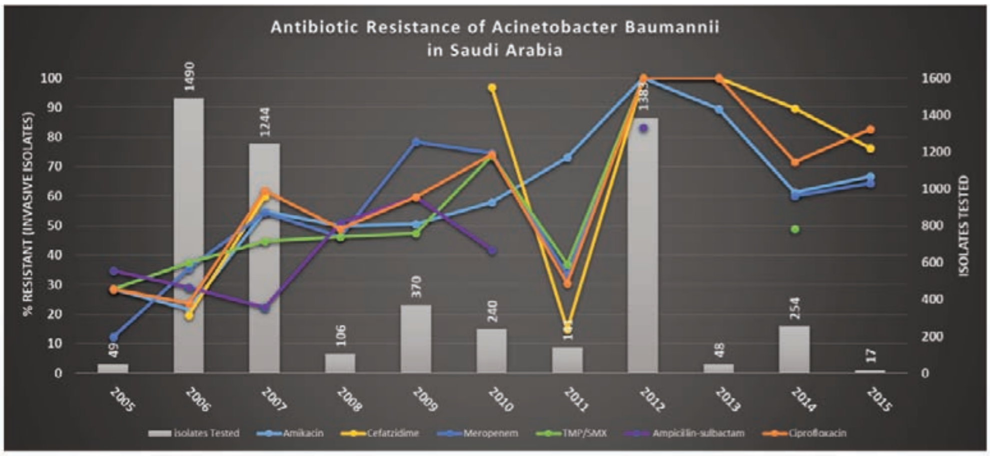

Figure 5. *Acinetobacter baumannii* resistance pattern 1998 to 2015 in Saudi Arabia according to the literature search. The grey bars indicate time and number of sample collections.

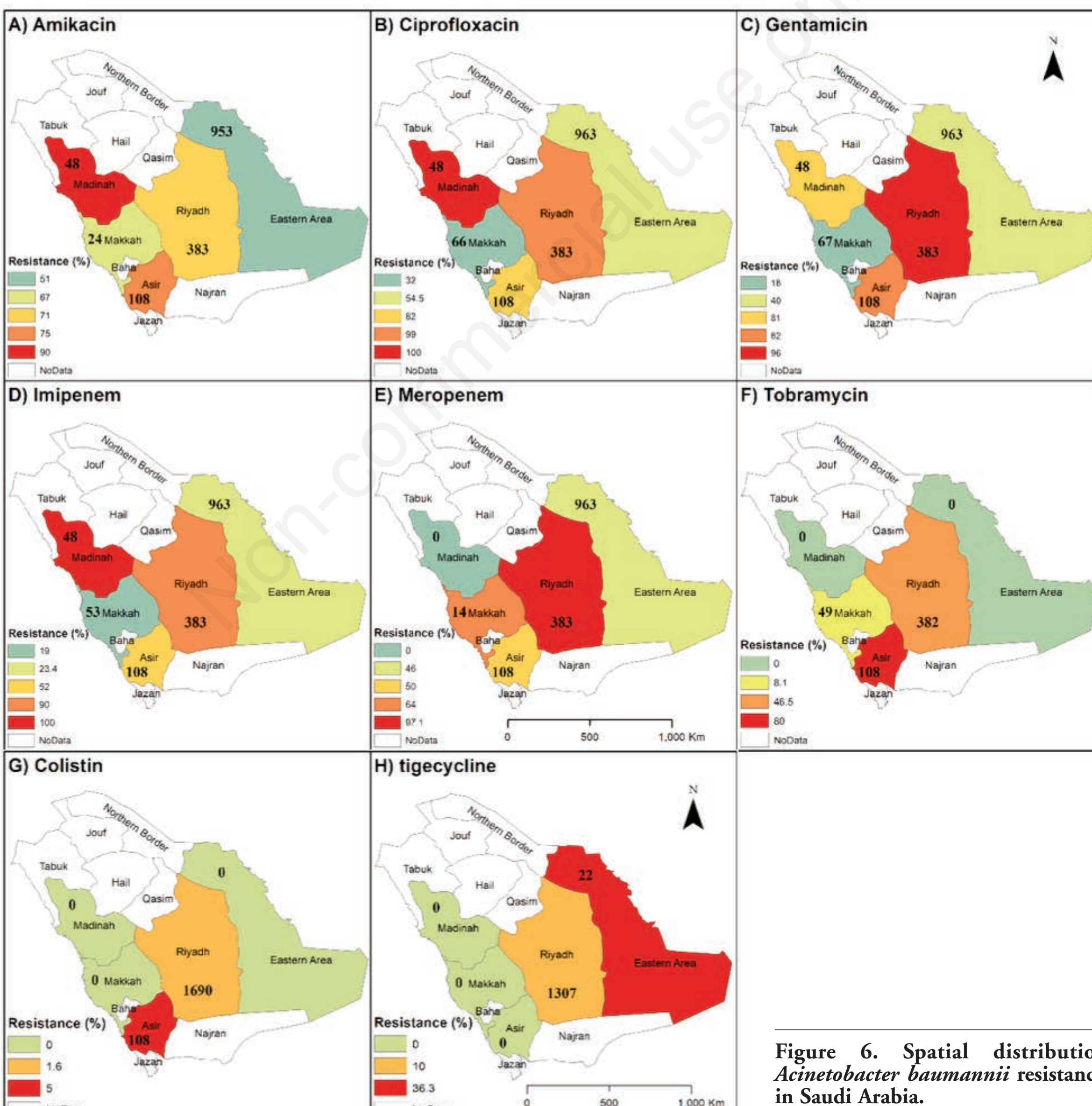

Figure 6. Spatial distribution of *Acinetobacter baumannii* resistance data in Saudi Arabia.

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.

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