

## Mini Review

# How to Deal with Antibiotic Resistance?

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**Abstract**

Antibiotic resistance is the most serious global problem to be addressed. This requires comprehensive surveillance study programs at the level of countries, especially those with high prevalence rates. Therefore, we have tried to point out the missing gaps of Pakistan's antibiotic resistance surveillance study programs in the light of our previously published article. We hope this will help to improve the current situation of antibiotic resistance and the existing surveillance program.

**Keywords:** Pakistan; Antibiotic resistance; Policymakers; Pathogens; Clinical diagnosis

**Introduction**

Antibiotics are chemical substances that kill or inhibit bacterial at various levels having a prominent role in minimizing infectious diseases. However, improper dealing of antibiotics forced the bacteria to develop or acquire resistance and inefficacious antibiotics, known as antibiotic resistance. Antibiotic resistance is now a worldwide grave concern [1]. That is why the world health organization considers antibiotic resistance as a public health emergency that must be managed on a priority basis [2].

South Asia is considered the central region for anticipated antibiotic resistance. A total of 70% of the world's antibiotic resistance has been originated from Asian countries [3]. Being on the list of Asian countries, Pakistan is one of the most important and noteworthy centers for the spread of antibiotic resistance. Studies have shown that 71%, ESBL, 40% carbapenemases producing bacteria, and the clinically most significant resistant genes like *mcr-1*, *bla<sub>KPC-2</sub>*, *bla<sub>NDM-1</sub>*, and many others have been vastly identified from Pakistan [4-7]. Because of its strategically important geographical location, Pakistan's antibiotic resistance is of significant importance to the rest of the world. Pakistan has a shared border with the world's most populous countries like China and India. Similarly, on the southwestern and western northern border, Iran and Afghanistan are located. It is known that resistant bacteria from its cache can disperse to the world's other regions *via* water, animal, and humans [8]. In Pakistan's case, its consequences present the most significant hazard.

The reasons for surging antibiotic resistance in Pakistan have been highlighted through numerous studies, the most common of which are misuse, underuse, and abuse of antibiotics. It is a trifurcated issue involving the apothecary, medical personnel, and patients themselves [9]. The misuse of antibiotics occurs at every level from the officials to the end-users. Irrational prescribing, lack of qualified staff, nonentity of culture sensitivity tests, and self-medication, are among the main reasons for misuse of antibiotics. Incomplete dosage taken by the patients and poverty is the provoking reasons for the underuse of antibiotics. Similarly, the counter sales of drugs, incentives from pharmaceutical companies for overprescribing, and lack of awareness

in the community about antibiotic resistance are the main reasons for the abuse of antibiotics [10].

Actions from governmental and non-governmental organizations like, developing the hospital infrastructures, check and balance on pharmaceutical companies, awareness in the community, training of medical staff, and implementation of culture sensitivity tests are required to combat antibiotic resistance in the region. Besides these, continuous nationwide surveillance studies are needed to depict current situations of antibiotic resistance and quantify the issue to act accordingly [11]. Aiming this, currently, we systematically analyzed original research articles that had presented antibiotic resistance in clinical substantial bacteria in the past decade. Alongside the complete depiction of the antibiotic resistance scenario of Pakistan, we found out gaps in surveillance studies that we think are important to be addressed in upcoming researches [12].

**Gaps in surveillance studies and our recommendations**

Surveillance studies are essential to well-define the scenario of antibiotic resistance. Such studies generate data that help out health officials to understand the depth and degree of the problem. Without proper knowledge about an issue, it is difficult for health officials and policymakers to overcome it. Study characteristics like the location of the study, source of the infection, patient demography, clinical diagnosis, molecular analysis, and bacterial type are some of the key components for surveillance studies in antibiotic resistance [13].

**Location of study**

Evaluating outbreaks by location not only offers evidence about the geographical scope of the issue but also shows clusters or patterns that can provide clues for important etiological causes and their mode of spread [14]. Pakistan consist of three territories i-e Islamabad, Gilgit Baltistan (GB), Azad Jamu Kashmir (AJK) and four provinces, Sindh, Punjab, Khyber Pakhtunkhwa, and Baluchistan. Studies from all the cities and towns of the provinces are required to present a complete scenario of antibiotic resistance in Pakistan. Unfortunately, data from the Baluchistan province about antibiotic resistance is not available. Similarly, most of the studies are from the capitals of the three provinces [12]. Researchers are recommended to focus on

surveillance studies from Baluchistan province and small cities and towns of all the provinces.

### Source of infections

Source of infections, like hospital-acquired infection and community-acquired infection, are the main terms for analyzing the antibiotic resistance data. Usually, hospital-acquired pathogens are broadly resistant due to more chances of exposure to the antibiotics. Mentioning the sources of infection helps in the easy eradication of pathogens following their source of emergence [15]. About 83% of the studies published from Pakistan did not mention the source of infections, which is needed to be declared in future studies [12].

### Patient demography

The patient demography, especially patient type, occupation, age, and gender records is mandatory for surveillance studies, to know the degree of infections and antibiotic resistance pattern. The demography is needed to describe the case patients and population that is at risk [16]. About 29%, 44%, and 33% of the published research articles on antibiotic resistance did not mention patient type, age, and gender [12]. These aspects of surveillance studies are needed to be addressed in future researches work.

### Clinical diagnosis

Clinical diagnosis is important for defining preventive and control measures for any infectious disease. Proper diagnosis elaborates the pathogenesis, emergence, reemergence, and progression of the diseases. The surveillance systems of clinical diagnosis help out health officials to pick up and eradicate an outbreak at its early stages [17]. Based on our published research, about 45% of the research articles from Pakistan did not declare the clinical diagnosis [12]. Declaring clinical diagnosis is highly recommended to researchers in their future studies.

### Molecular identification

The molecular studies of intrinsic or acquired antibiotic-resistant mechanisms allow researchers to develop alternative or novel medicines for the prevention of infectious diseases. Molecular analysis of the strain type, sequence type, and plasmid type gives in-depth knowledge about the epidemiological sources and root causes of the pathogen. These data help health officials to eliminate the pathogens from their origins and prevent their route of emergence and spread [18]. The trend of molecular studies about antibiotic resistance in Pakistan is overall not satisfactory developed. Only 30% of the studies on this topic performed molecular investigation. Research projects focused on the detection of antibiotic-resistant genes, strains, and plasmids analysis for the understanding of the current situation.

### Pathogens

WHO report (2017) about global priority list of antibiotic-resistant bacteria include carbapenem-resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, carbapenem and third-generation cephalosporin-resistant Enterobacteriaceae (*Klebsiella pneumoniae*, *Escherichia coli*, *Proteus* spp., *Serratia* spp., *Morganella* spp., *Enterobacter* spp., and *Providencia* spp.), vancomycin-resistant *Enterococcus faecium*, methicillin, and vancomycin-resistant *Staphylococcus aureus*, clarithromycin-resistant *Helicobacter pylori*, fluoroquinolone-resistant *Campylobacter*, and *Salmonella* spp., fluoroquinolone and third-generation cephalosporin-resistant

*Neisseria gonorrhoeae*, penicillin-non-susceptible *Streptococcus pneumoniae*, ampicillin-resistant *Haemophilus influenzae*, and fluoroquinolone-resistant *Shigella* spp [19]. Among these, limited data about *Proteus* spp., *Serratia* spp., *Morganella* spp., *Enterobacter* spp., and *Providencia* spp., *E. faecium*, *Campylobacter* spp., *N. gonorrhoeae*, *S. pneumoniae*, and *H. influenzae* are available from Pakistan [12]. Researchers are advised to have a special focus on these strains along with other priority listed antibiotic-resistant bacteria.

### Other activities

Besides the above-mentioned components, study duration, standard bacterial identification methods, morbidity, and mortality rates of the pathogens are needed to be addressed in surveillance studies [20]. The antibiotic susceptibility tests are needed to be performed according to standard antibiotic sensitivity testing guidelines like CLSI or EUCAST using the valid phenotypic detection method to obtain accurate data [21]. As the resistance bacteria can spread *via* the food web and volitionally, so, to trace out the mood of transmission, surveillance studies of environmental and animal pathogen should be followed along with the processing of the clinical samples. [22]. Statistical analysis should be performed to draw a good conclusion. Recommendations and conclusions should be providing from the analyzed data set. Best communication skills are required to present the data set as simple as possible for easy understanding for professionals, health care officials, and policymakers [20].

### Conclusion

This article highlights the importance of basic epidemiological components of surveillance studies on antibiotic resistance based on our previously published systematically analyzed antibiotic resistance data from Pakistan. We enlightened the gaps in surveillance studies and provided recommendations for researchers to follow in their future studies. Following our recommendations, will help the health official and policymakers to combat antibiotic resistance in a better way.

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