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Pakistan Antimicrobial Resistance Surveillance System Surveillance Report

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Pakistan Antimicrobial Resistance Surveillance System:

Surveillance Report 2017-18

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Executive Director

Antimicrobial resistance is a global challenge and Pakistan endorsed the Global Action Plan to tackle AMR in the 68th session of the World Health Assembly (WHA) in Geneva during May 2015. The Global Action Plan aims to ensure continuity of successful treatment and prevention of infectious diseases with effective and safe medicines that are quality-assured, used in a responsible way, and accessible to all who need them. In this international movement, support work being coordinated by WHO, FAO, and OIE to develop an integrated and global package of activities to combat AMR, spanning human, animal, agricultural, food and environmental aspects. Global action plan has led to the development of comprehensive National AMR Action plan. The national plan aims to combat antimicrobial resistance by strengthening surveillance and laboratory capacity at the national level following agreed international standards developed in the framework of the Global Action Plan.

National AMR Focal Person

The global emergence of antimicrobial resistance (AMR) is posing a threat to human health. In 2015, WHO launched the Global Antimicrobial Resistance Surveillance System (GLASS) program. Pakistan enrolled in GLASS in 2016 and progressively worked to develop Pakistan AMR surveillance system (PASS) in 2018. This report follows on from the first GLASS Report -2017, and drawing on data from GLASS first and second data call in 2017 and 2018, respectively. The feedback report will help to monitor status of newly developed national AMR surveillance system. The system involves strong commitment from participating laboratories and close collaborations with AMR sentinel lab networks.The increase in enrolment and active participation in a national system to monitor AMR reflects a collective understanding and engagement to support the global effort to control AMR. The support given by WHO Regional Offices, WHO Collaborating Centers, and international partners has been fundamental to the achievements to date.

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Thanks to all focal persons from AMR Surveillance sentinel sites

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List of Abbreviations

AMR	Antimicrobial resistance
AST	Antimicrobial susceptibility testing
GLASS	Global Antimicrobial Resistance Surveillance System
GPs	General Physicians
IHR	International Health Regulation
LIMS	Laboratory information management system
LQMS	Laboratory quality management system
NEQAS	National external quality assurance system
NCC	National Coordination Center
NIH	National Institute of Health
OTC	Over the counter
PASS	Pakistan AMR Surveillance system
UNGA	United Nations General Assembly
WHA	World Health Assembly
WHO	World Health Organization

1 Introduction

1.1 Antimicrobial Resistance

Antimicrobial resistance has led to limited treatment options against infectious diseases. Over the last decade, the problem has become a crisis across the globe. The increasing prevalence of resistance to a broad category of antimicrobials is reported, which significantly threatens human and animal health. The evolution seen in AMR is occurring at an alarming rate and is outpacing the development of new countermeasures capable of thwarting infections in humans. This situation threatens patient care, economic growth, public health, agriculture, economic security, and national security.

The Global Action Plan to tackle AMR was endorsed in the 68th session of the World Health Assembly (WHA) in Geneva during May 2015 by all countries including Pakistan. The Global Action Plan aims to ensure, for as long as possible, continuity of successful treatment and prevention of infectious diseases with effective and safe medicines that are quality-assured, used in a responsible way, and accessible to all who need them. Support work being coordinated by WHO, FAO, and OIE to develop an integrated and global package of activities to combat AMR, spanning human, animal, agricultural, food and environmental aspects (i.e. a one-health approach), including: a) Each country has its own national comprehensive plan to combat antimicrobial resistance; b) Strengthen surveillance and laboratory capacity at the national and international level following agreed international standards developed in the framework of the Global Action Plan, considering existing standards and; c) Improved conservation of existing treatments and collaboration to support the sustainable development of new antibiotics, alternative treatments, preventive measures and rapid, point-of-care diagnostics, including systems to preserve new antibiotics. A significant global step for tackling AMR was achieved during the 71st session of United Nations General Assembly (UNGA) in New York on 21st September 2016 by a declaration on AMR which has been widely hailed as a milestone in the global effort to confront AMR.

1.2 Pakistan Antimicrobial Resistance Surveillance System (PASS)

AMR is one of the major health crises in Pakistan with the overall situation being much more grim than indicated in many studies published over the last two decades. A number of factors have been contributory in this regard. The major challenges and issues identified include unnecessary large number of registered products (approximately 50,000); unjustified or misleading advertisements with only about 15% promotional brochures meeting WHO criteria; self-medication in more than 50% of the population according to different studies/ surveys; and, a high number of quacks in the country. The highest numbers of drugs are prescribed with more than 3 drugs per patient with 70% of patients being are prescribed antibiotics. This irrational and indiscriminate use is more common among General Physicians (GPs) and public sector hospitals with a bias towards costly broad spectrum antibiotics. Availability of over the counter (OTC) without prescription medications, especially antibiotics is a common practice and usage of potent antibiotics for highly resistant infections is also a common phenomenon. These practices have created a vicious cycle with emergence of resistance in common bacteria resulting from antibiotic selection pressure. Only a few institutions have full or partial institutional policies on optimal prescription of antibiotics. However, any impact at country level will be minimal unless majority of the health care institutions and community based general practitioners and physicians are also fully implementing uniform policies.

The Government of Pakistan has recognized AMR as a major threat to the health and development of its population. The National Institute of Health (NIH), as the national focal point for International Health Regulation (IHR) and AMR designated by Ministry of NHSR&C is responsible for implementation of important IHR/GHSA technical areas such as surveillance, response, workforce development, laboratory system and AMR. The Ministry of NHSR&C expressed an interest to join the early implementation of the Global Antimicrobial Resistance Surveillance System (GLASS). The GLASS has been developed to support the Global Action Plan on Antimicrobial Resistance (https://www.who.int/glass/en/). GLASS aims to establish standardized, comparable and validated data collection system on priority AMR pathogens to inform decision-making for local, national and regional actions and to provide evidence base for action and advocacy on AMR. GLASS combines patients, laboratory and epidemiological surveillance data for planning and implementation of AMR activities. In November 2015, a joint WHO/Ministry of NHSR&C team visited selected sites in the country and mapped available capacities for establishing an AMR Surveillance System. Subsequently, an intersectoral core steering committee was formed to oversee the process of developing a national AMR policy. This commitment led to the development of a National AMR Strategic Framework for Containment of Antimicrobial Resistance (2016) and an operational AMR National Action Plan (2017). The Pakistan National AMR Action Plan identifies the establishment of an integrated national AMR surveillance as a major strategic priority and identified the lack of nationwide surveillance to as a principle factor limiting the ability of Pakistan to control the growing threat of AMR. GLASS is adapted by NIH in 2016, and it has led to development of Pakistan AMR Surveillance system in 2018 (PASS).

1.3 AMR surveillance in Pakistan

Goals:

The primary goal of the Pakistan AMR surveillance system is to generate evidence on the burden of antimicrobial drug resistance among priority AMR pathogens isolated from in-patient clinical samples in acute care hospitals throughout Pakistan for informed decision making or for enhancing the response to AMR.

Objectives:

This goal will be met through the following measurable objectives:

1. Conduct routine culture and standardized antimicrobial susceptibility testing (AST) to identify and isolate priority pathogens from specimens of patients with clinical infection at selected surveillance sites

2. Establish regular and systematic communication of all AST results from identified laboratories to clinical providers as described in this document

3. Establish regular and systematic reporting of country defined priority AST results and patient level data from surveillance hospitals to the National AMR Surveillance Coordinating Center (NCC) following the reporting structure described in this document

4. Analyze, interpret, and publicly report annual AMR surveillance data in a written report

1.4 Dataflow system

AMR Surveillance in Pakistan is coordinated by the National Institute of Health acting as the AMR Surveillance National Coordinating Center (NCC). The system is made up of hospital, provincial, federal, and global components with direct engagement of health facilities and laboratories throughout the health system to provide hospital, provincial, and nationally relevant data for informed decision making.

Surveillance sites combine clinical (acute care hospital) and laboratory facilities where lab specimens are routinely collected and tested. Following normal clinical procedures, specimens collected from inpatients is submitted as part of patient care for pathogen identification and antibiotic susceptibility testing (AST). Laboratory results are entered in existing laboratory information management system (LIMS). At set intervals, requested surveillance data elements are exported to an agreed database file (e.g., EXCEL, comma-separated values (CSV)). Exported data is transmitted to the NCC for national collation and analysis. The NCC generate national AMR reports, provide guidance on national AMR/public health policy, and submit aggregated data to the World Health Organization (WHO) Global Antimicrobial Surveillance System (GLASS) completing the global component of the surveillance system (Figure 1).

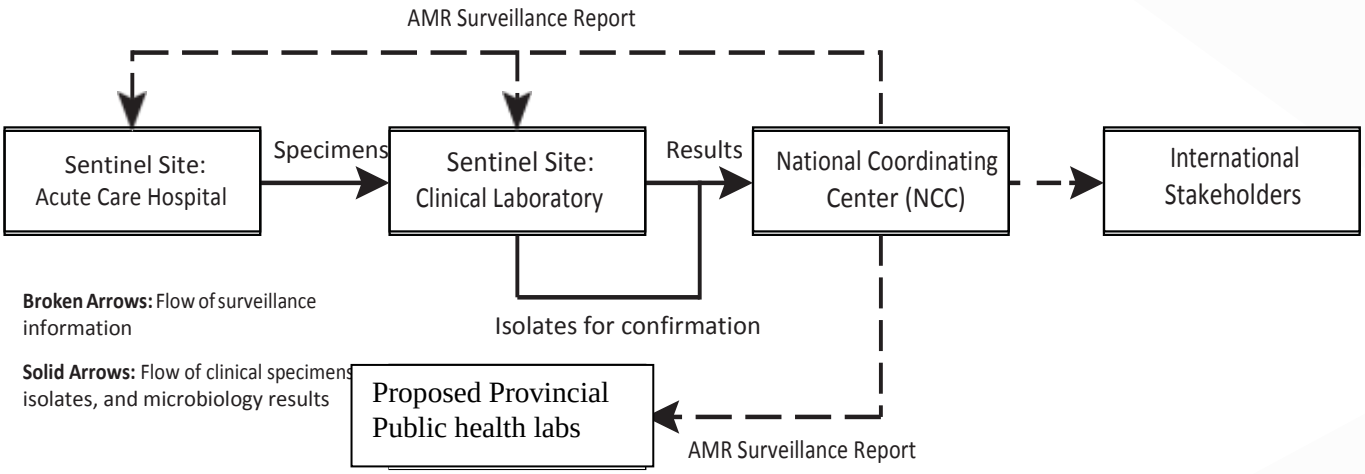


Figure 1: Simplified diagram of clinical specimen, microbiology test results, confirmation isolates, and AMR surveillance report flow in the Pakistan Antimicrobial Resistance Surveillance System

2 Methodology

2.1 Surveillance sites submitting data to NCC

Sr. No.	AMR Surveillance Sites	Location	Province	Bed number
1	Dr Ruth K. M. Pfau Civil Hospital	Karachi	Sindh	1800
2	Jinnah Postgraduate Medical Center (JPMC)	Karachi	Sindh	1800
3	Agha Khan University Hospital (AKU)	Karachi	Sindh	721
4	PNS shifa Karachi	Karachi	Sindh	700
5	Sheikh Zayed Medical Center (SZH)	Lahore	Punjab	1500
6	Shaukat khanum cancer memorial hospital (SKH)	Lahore	Punjab	195
7	Mayo Hospital	Lahore	Punjab	3000
8	Armed Forces Institute of Pathology (AFIP)	Rawalpindi	Punjab	-
9	National Institute of Health (NIH)	Islamabad	Federal	-
10	Rehman Medical Institute	Peshawar	Khyber Pakhtunkhwa	500

Table 1: AMR Surveillance sites their cities and provinces, along with the number of beds in each site

2.2 Data elements submitted

Data was collected from each surveillance site according to a suggested template (attached as Annex A). Variables like patient date of birth, gender, location type, specimen source, name of identified organism, AST susceptibility method and result were collected and analyzed.

2.3 Priority samples/pathogens included in surveillance

Specimen	Basic laboratory case definition	Priority surveillance Pathogens
Blood	Isolation of Pathogens from blood	*Escherchia coli* *Klebsiella pneumoniae* *Acinetobacter baumannii* *Staphylococcus aureus* *Streptococcus pneumoniae* *Salmonella species*
Urine	Significant Growth in urine specimen	*Escherchia coli* *Klebsiella pneumoniae*
Stool	Isolation of *Salmonella spp.* Or *Shigella spp.* from stools	*Salmonella spp.* *Shigella spp*
Urethral and cervical Swab	Isolation of *N. gonorrhoeae*	*Neisseria gonorrhaoeae*

Table 2: list of priority surveillance pathogens in different types of specimens

3 Results

3. RESULTS

National Coordinating Center at NIH started surveillance with five surveillance sentinel sites in 2017 and in subsequent year, the number of sites reporting to NCC is increased to nine. The sites have been selected on fulfillment of following criteria: Agreement to participate in GLASS/ PASS and share requested data, participate in lab assessments, functional laboratory information management system (LIMS) which can export defined data as a flat file database, participation in an accepted external quality assurance (EQA) program for bacteriology including culture, identification, and antimicrobial susceptibility testing (AST), adapt and follow standardized laboratory SOPs for quality assurance.

Overall 7 hospitals and two outpatient laboratories reported AMR data (Jan- Dec 2017, 2018) to NCC for submission in GLASS international platform. The data is analyzed on various parameters including demographic and antimicrobial susceptibility results. In terms of specimen analysis, highest number of isolates being reported from urine (67% and 68% in 2017 and 2018 respectively), followed by blood (31.48% and 30% in 2017 and 2018 respectively, stool (1.5% and 1% in 2017 and 2018 respectively) and cervical/urethral specimens (0.2% and 1% in 2017 and 2018 respectively) collectively from all the sites. The most frequently reported pathogens were *Escherichia coli* (65% and 68.8% in 2017 and 2018 respectively), followed by *Klebsiella pneumoniae* (21% and 8.5% in 2017 and 2018 respectively), *Salmonella typhi* (7.5% and 13.1% in 2017 and 2018 respectively), *Staphylococcus aureus* (4.2% and 6.1% in 2017 and 2018 respectively), *Acinetobacter baumannii* (1.6% and 3.2% in 2017 and 2018 respectively),*Neisseria gonorrhaoeae* (0.2%), *Streptococcus pneumoniae* (0.3%).

Antimicrobial susceptibility testing varied among sites and specimen pathogen antibiotic combination. *Escherichia coli* has been the most frequently reported and isolated pathogen. Regarding its response to cephalosporins varying resistance pattern is seen. Particularly third generation cephalosporin cefixime high resistance is observed in 2018 (94%) as compared to 2017 (18%). Many issues can be linked to seeing this pattern from tertiary care hospitals. The tertiary care hospitals have their central procurement systems and at times, due to high specimen load at a certain period of time, antibiotics testing may not be possible due to unavailability of antibiotic. Resistance to carbapenems has increased from 2017 to 2018; for meropenem from 19% to 20%, for ertapenem 23% to 29% and imipenem from 10% to 15%. The increasing resistance to carbapenems is an alarming finding in *E.coli*.

Multidrug resistance is commonly seen in *A. baumannii*. Resistance to aminoglycosides and quinolones has been observed, and increasing trend from 2017 to 2018. This could be attributed to increase in number of sites from 2017 to 2018. The larger the number of isolates/sample size the lesser are the chances of biasness in the results. Carbapenem resistant *A. baumannii* are reported (45-60%) and this is quite alarming considering the limited therapeutic options available against the said pathogen.

S. aureus remain susceptible to vancomycin in 2017-2018. The resistance to linezolid (0.7%), amikacin(8%) and chloramphenicol(2%) is reported very low. 68% of isolates were resistant to cefoxitin and considered as MRSA. *Salmonella typhi* remains susceptible to azithromycin. XDR typhoid has been reported since 2016 from Sindh region and over the time number of cases reported from various parts of country are increasing. Ceftriaxone resistance is observed as 18% in 2017 and 29.11% in 2018. Resistance to meropenem is observed, 1.1% in 2017 and 0.7% in 2018. Imipenem remains susceptible in 2017 and 2018 against *S. typhi.*

3.1 Year wise distribution of total specimens by type and surveillance site

	No. of isolates from 6 surveillance sites (Jan- Dec 2017)	No. of isolates from 10 surveillance sites (Jan- Dec 2018)
Blood	6021 (31.48%)	12191 (30%)
Urine	12776 (67%)	28166 (68%)
Stool	304 (1.5%)	208 (1%)
Genital	40 (0.2%)	586 (1%)
Total	19141	41151

Table 3: Number of isolates in all specimen types

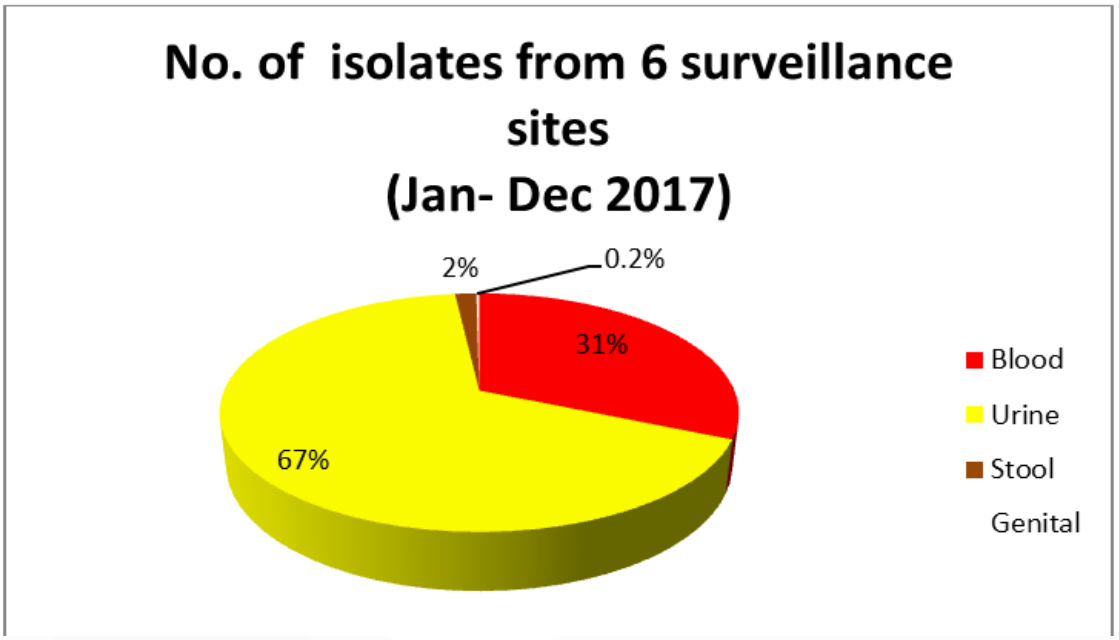


Figure 2: Distribution of number of isolates from each specimen (blood, urine, stool, genital) from 2017

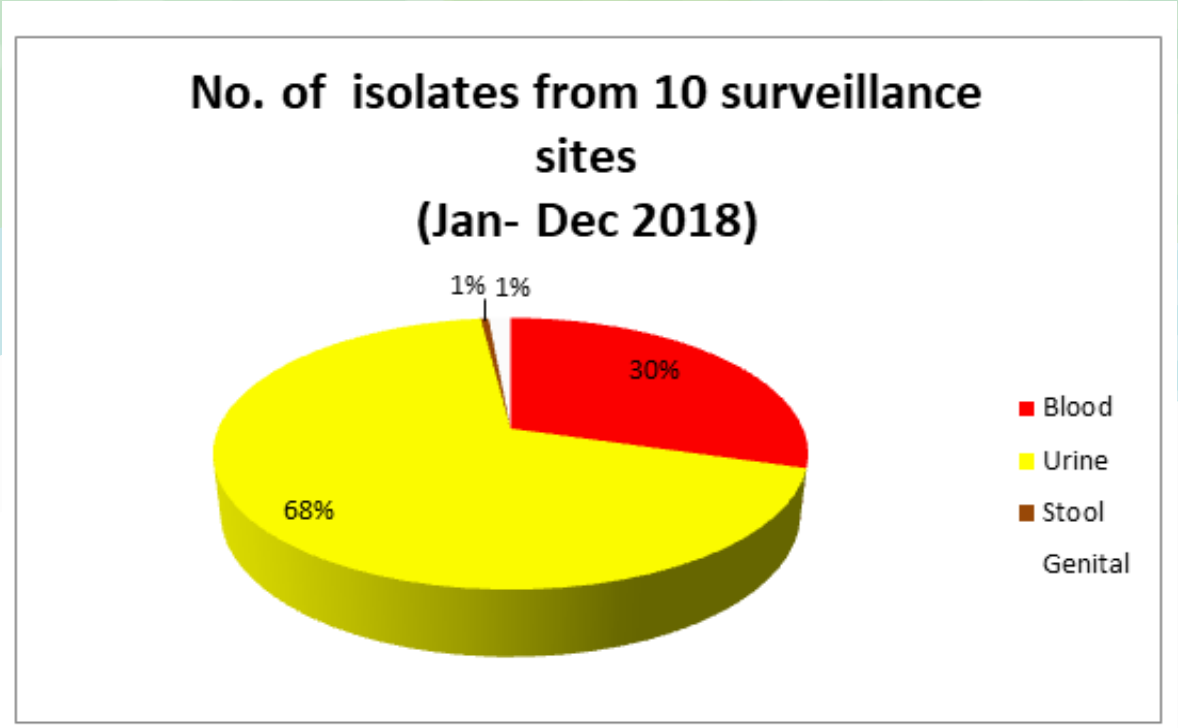
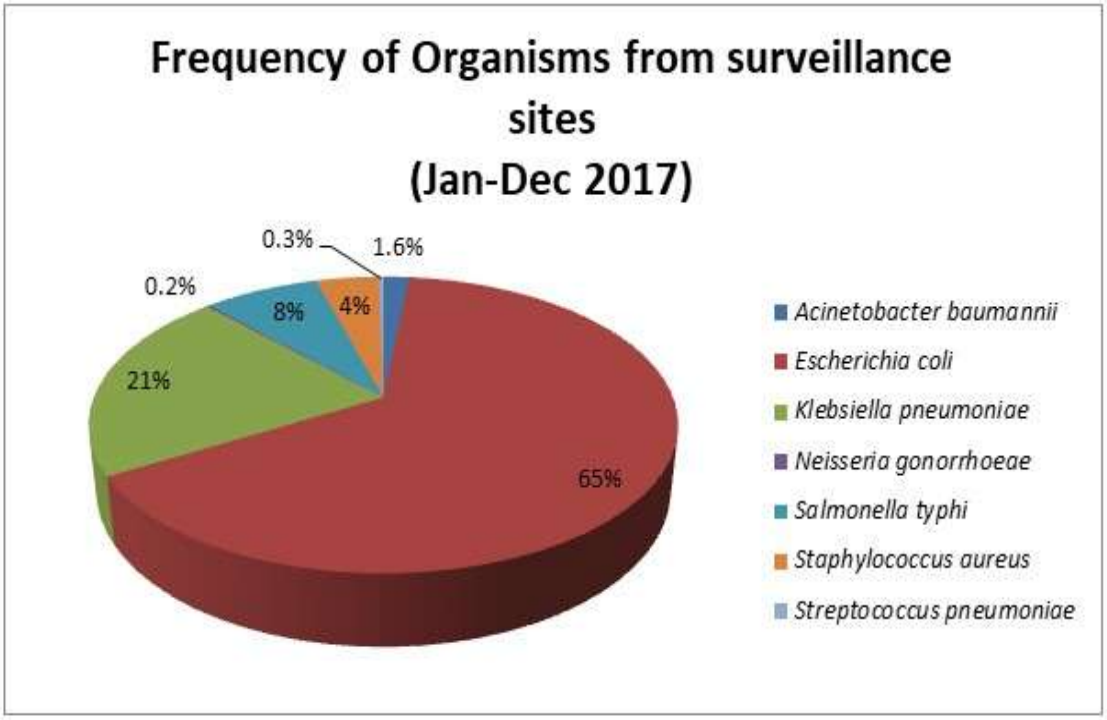


Figure 3: Distribution of number of isolates from each specimen (blood, urine, stool, genital) from 2018

Sr.No	Organism Name	Percentage of Organisms from 6 surveillancesites (Jan- Dec 2017)	Percentage of Organisms from 10 surveillancesites (Jan- Dec 2018)
1	*Acinetobacter baumannii*	1.6	3.2
2	*Escherichia coli*	65	68.8
3	*Klebsiella pneumoniae*	21.2	8.5
4	*Neisseria gonorrhoeae*	0.2	0.1
5	*Salmonella typhi*	7.5	13.1
6	*Staphylococcus aureus*	4.2	6.1
7	*Streptococcus pneumoniae*	0.3	0.2

Table 5: Percentage of organisms from all AMR sites samples in 2017 and 2018



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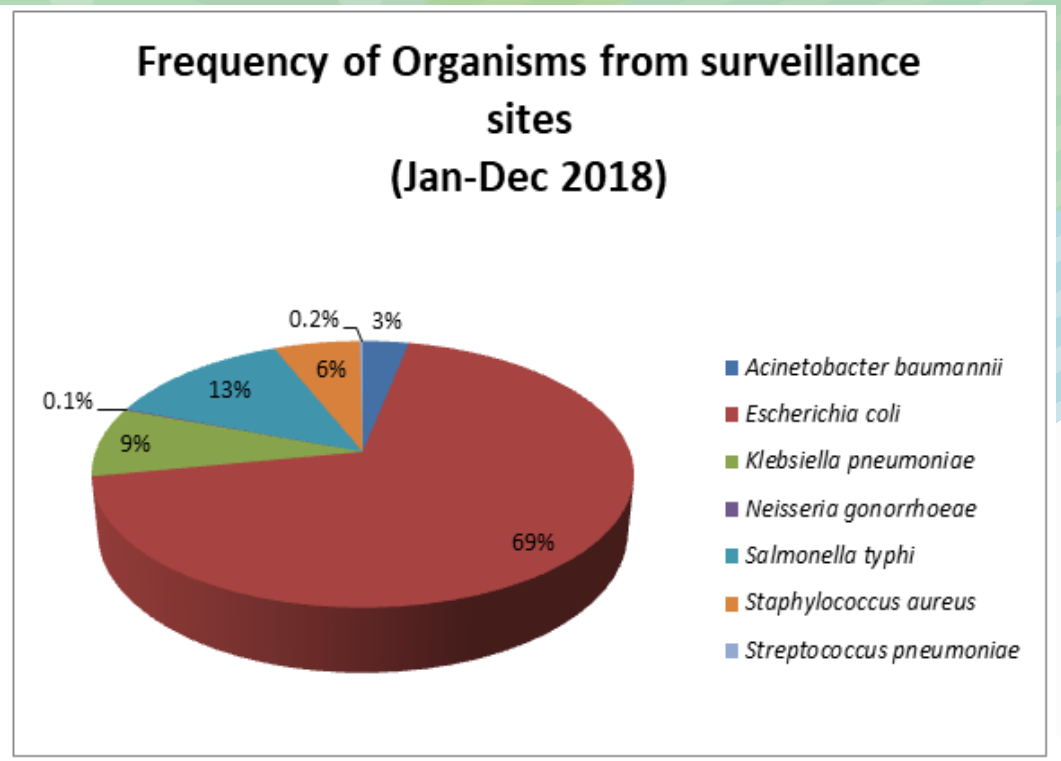


Figure 7: Distribution of organisms from ten surveillance sites monitored from Jan-Dec 2018

Sr.No	Organisms Name	% of Organisms from 6 surveillance sites (Jan- Dec 2017)		% of Organisms from 10 surveillance sites (Jan- Dec 2018)	
		Females	Males	Females	Males
1	*Escherichia coli*	71.02	57.3	77.35	56.6
2	*Acinetobacter baumannii*	1.56	2	2.4	4.2
3	*Klebsiella pneumoniae*	19.45	23.4	6.5	11.2
4	*Neisseria gonorrhoeae*	0	0.5	0	0.3
5	*Salmonella typhi*	5.4	10.2	9.2	19.1
6	*Staphylococcus aureus*	2.5	6.2	4.4	8.26
7	*Streptococcus pneumoniae*	0.2	0.3	0.1	0.3

Table 6: Table showing distribution of organisms from surveillance sentinel sites in 2017 and 2018 among Males and Females

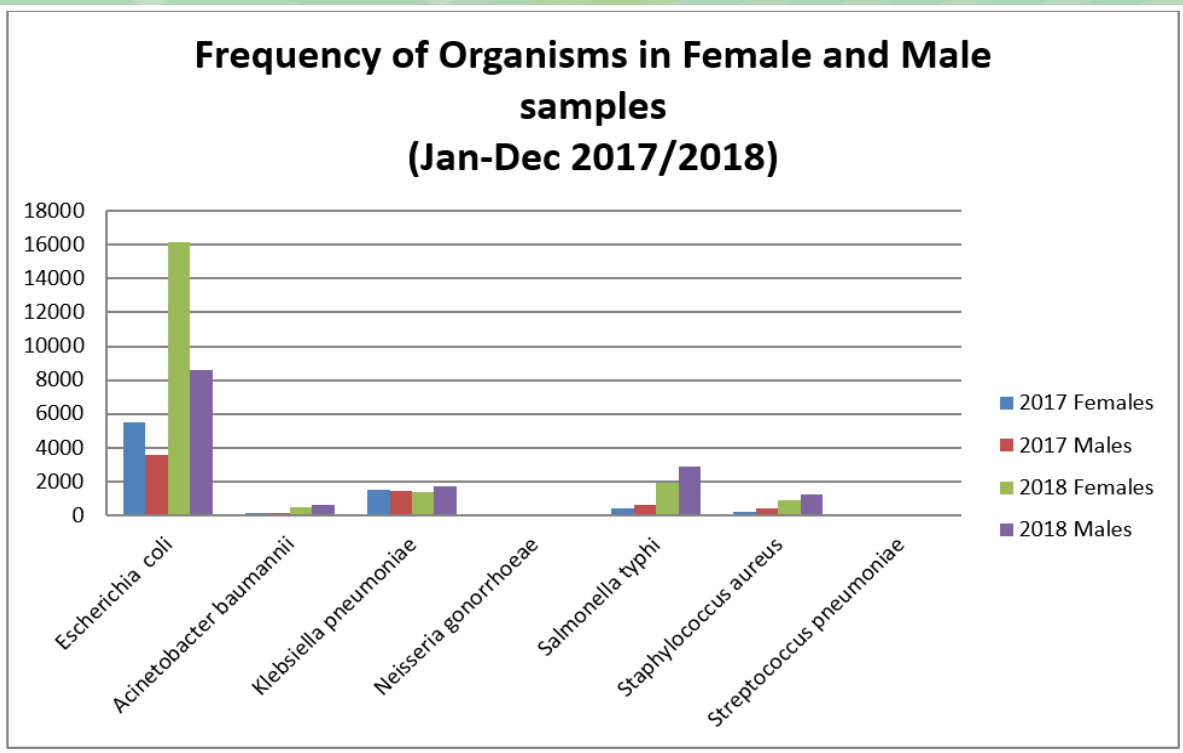


Figure 8: Graph showing distribution of organisms from surveillance sentinel sites in 2017 and 2018 among Males and Females

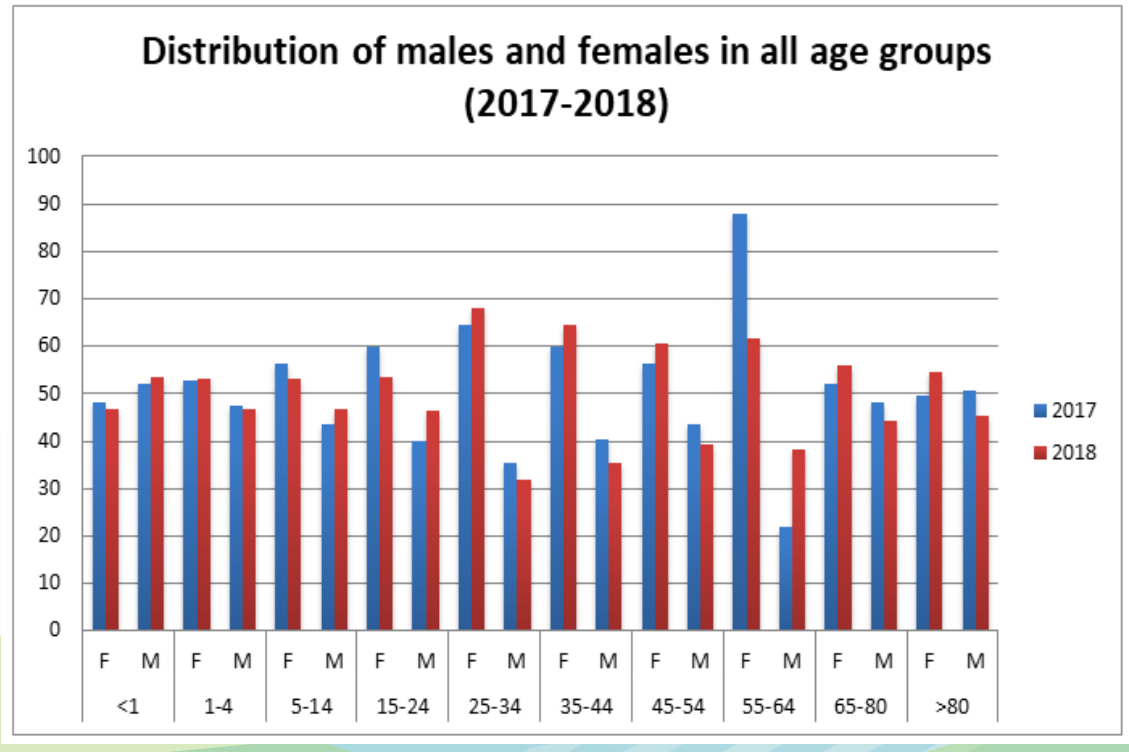


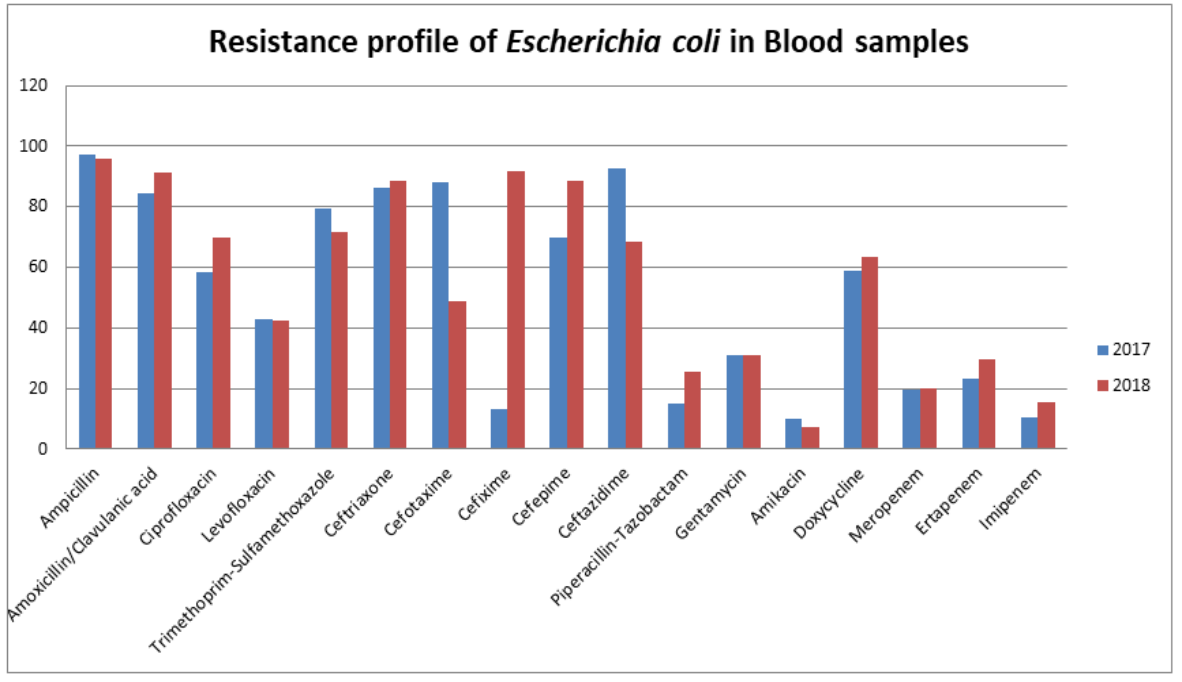
Figure 9: Total submitted data for the year 2017 and 2018 is assessed for distribution of samples among males and females

3.2 Resistance profile of priority GLASS pathogens

Escherichia coli:

Escherichia coli a Gram-negative, facultative anaerobe is responsible for gastroenteritis, urinary tract infections, neonatal meningitis, hemorrhagic colitis. In rare cases, virulent strains are also responsible for bowel necrosis (tissue death) and perforation without progressing to hemolytic-uremic syndrome, peritonitis, mastitis, sepsis, and Gram-negative pneumonia.

About 75% to 95% of urinary tract infections are caused by *E.coli.* Multidrug resistance in *Escherichia coli* has become a worrying issue that is increasingly observed in human worldwide. *E. coli* is intrinsically susceptible to almost all clinically relevant antimicrobial agents, but this bacterial species has a great capacity to accumulate resistance genes, mostly through horizontal gene transfer.
E. coli correspond to the acquisition of genes coding for acquiring resistance to broad spectrum antibiotics. Antibiotic susceptibility profiles of *E.coli* in blood samples from different tertiary care hospitals of Pakistan showed varied pattern against different antibiotics. Highest level of resistance is observed against quinolones (70%) followed by cephalosporins, ampicillin and tetracyclines. Resistance against meropenem and imipenem remains less than 21% against *E.coli* in both years. Ertapenem showed increasing trend of resistance 23% in 2017 and 29.6% in 2018. In urine samples resistance profile of *E.coli* represents increase in resistance against amoxicillin/clavulanic acid, ciprofloxacin, nitrofurantoin, ceftriaxone, and cefixime in year 2018 than 2017.



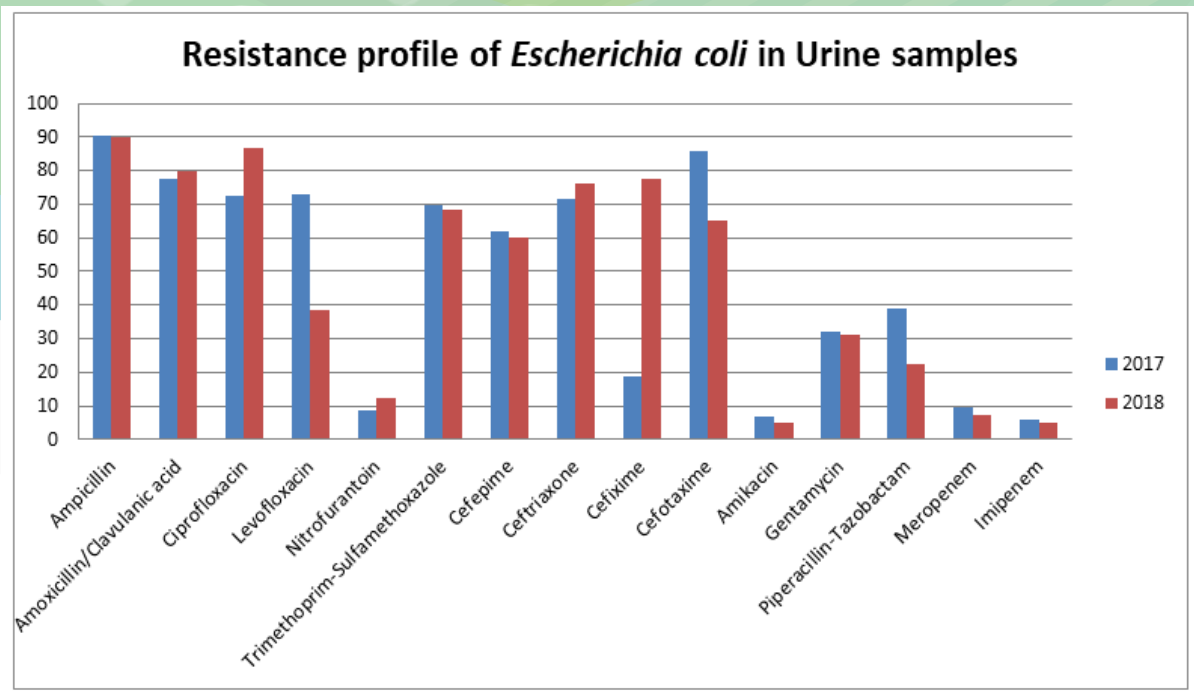


Figure 11: Graph representing resistance profile of *Escherichia coli* in Urine samples

Acinetobacter baumannii:

Acinetobacter baumannii is an opportunistic bacterial pathogen primarily associated with hospital acquired nosocomial infections has a high incidence among immunocompromised individuals. Infections due to *A. baumannii* are frequently found in intensive care units (ICUs) where they are implicated as the cause of ventilator-associated pneumonia (VAP), urinary tract infections, and bacteremia.

Acinetobacter baumannii has become resistant to many classes of antibiotics. *Acinetobacter spp.* has remarkable ability for genetic exchange and is among a unique class of gram negative bacteria that are described as "naturally transformable". *A. baumannii* demonstrate high level resistance to penicillins and extended spectrum cephalosporins, aminoglycosides, quinolones, tetracyclines, colistin. *A. baumannii* also showed the global emergence of resistance to beta lactams.

Antibiotic susceptibility profiles of *A.baumannii* in blood samples from different tertiary care hospitals of Pakistan showed varied pattern against different antibiotics. Resistance against meropenem in blood samples is observed as 73.2% in 2017 and 78.3% in 2018; and imipenem 64.6% resistant in 2017 and 43.8% in 2018. Minocycline resistance increased in *A. baumannii* and showed 13.3% resistance in 2017 and 23.5% in 2018. Amikacin showed high resistance i.e., 68% in 2017 while 37.5% in 2018. Cephalosporins are showing high resistance approximately 80% against *A. baumannii.*

A.baumannii antibiotic susceptibility profile is varied against different antibiotics in urine. Resistance against meropenem is observed as 48.8% in 2017 and 46.9% in 2018; and imipenem 37.1% resistant in 2017 and 40.7% in 2018. Nitrofurantoin resistance increases in *A. baumannii*, it showed 84.9% resistance in 2017 and 93.75% in 2018. Piperacillin-Tazobactam showed highly increasing resistance i.e., 24.1% in 2017; 56.6% in 2018. Ciprofloxacin, Ceftriaxone, Ceftaxime, and Ceftazidime showed high resistance greater than 60% against *A. baumannii.*

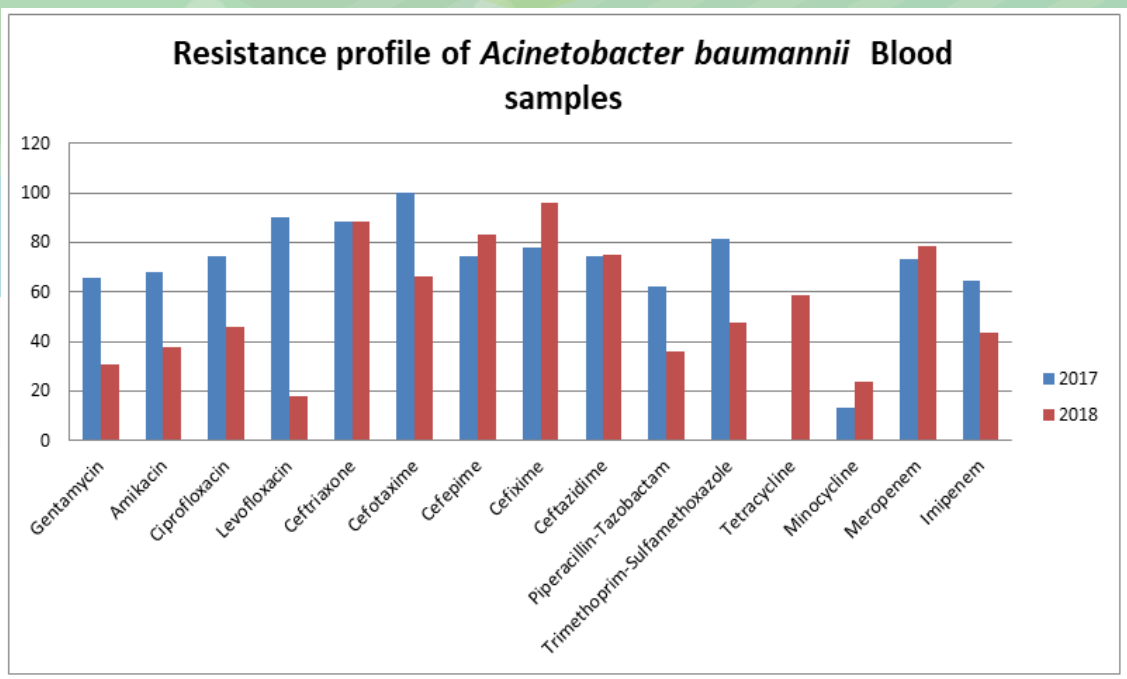


Figure 12: Graph representing resistance profile of *Acinetobacter baumannii* in Blood samples

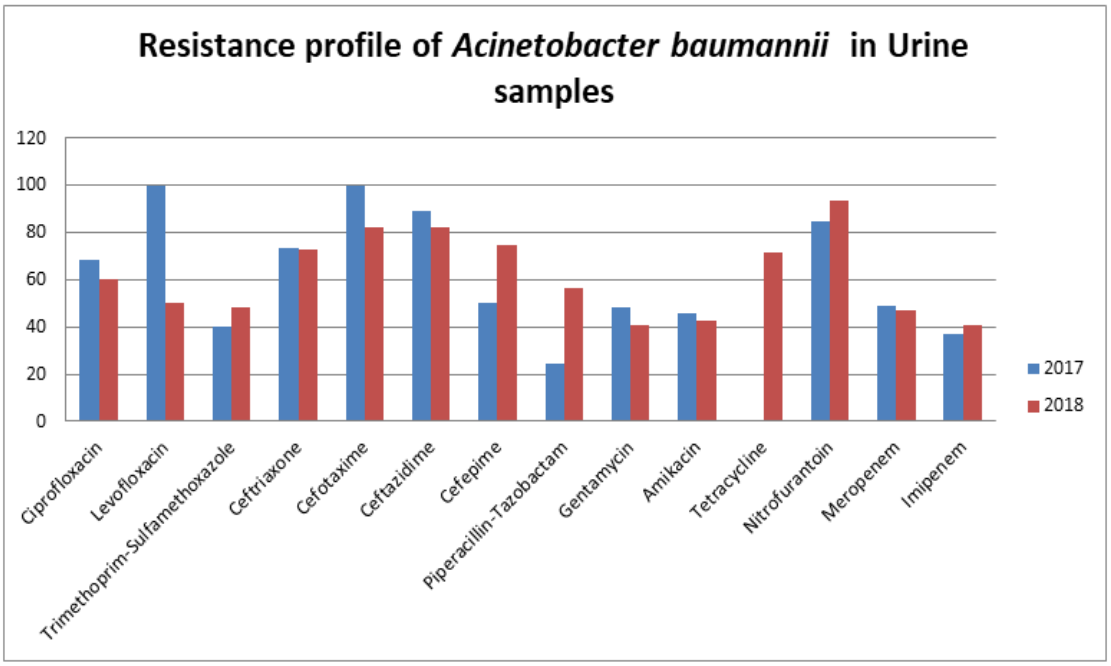


Figure 13: Graph representing resistance profile of *Acinetobacter baumannii* in Urine samples

Klebsiella pneumoniae:

K.pneumoniae infections are particularly a problem among neonates, elderly and immunocompromised individuals within the healthcare setting, but this organism is also responsible for a significant number of community acquired infections including pneumonia and sepsis. *K. pneumoniae* is found in the environment and typically colonizes human mucosal surfaces of the oropharynx and gastrointestinal (GI) tract. *K. pneumoniae* is an important cause of multidrug resistant infections worldwide. Several recent studies highlight the emergence of resistance in multi-drug resistant (MDR) *K. pneumoniae* against third generation cephalosporins, carbapenem and colistin. Resistance in *K. pneumoniae* arises from loss of function due to mutations of the genes or due to acquisition of antibiotic resistance genes.

In the analysis from two years data of blood samples from Pakistan in 2017-2018, *K.pneumoniae* showed high resistance more than 70% to amoxicillin-clavulanic acid, ceftriaxone, cefepime, and ceftazidime. Carbapenems show increasing trend of resistance against MDR *K. pneumoniae*; meropenem showed 46% in 2017 and 56.8% in 2018 imipenem 19.2% in 2017 and 54% in 2018 and ertapenem 31.8% in 2017 and 46% in 2018.

Resistance profile of *K.pneumoniae in* urine samples from Pakistan in 2017-2018 showed high resistance more than 70% to amoxicillin-clavulanate, and ceftazidime. In urine samples carbapenem showed good susceptibility against MDR *K. pneumoniae*; Meropenem showed 29.8% in 2017 and 17% in 2018. Imipenem 16.2% in 2017 and 15.3% in 2018 and ertapenem 16.4% in 2017 and 16.8% in 2018.

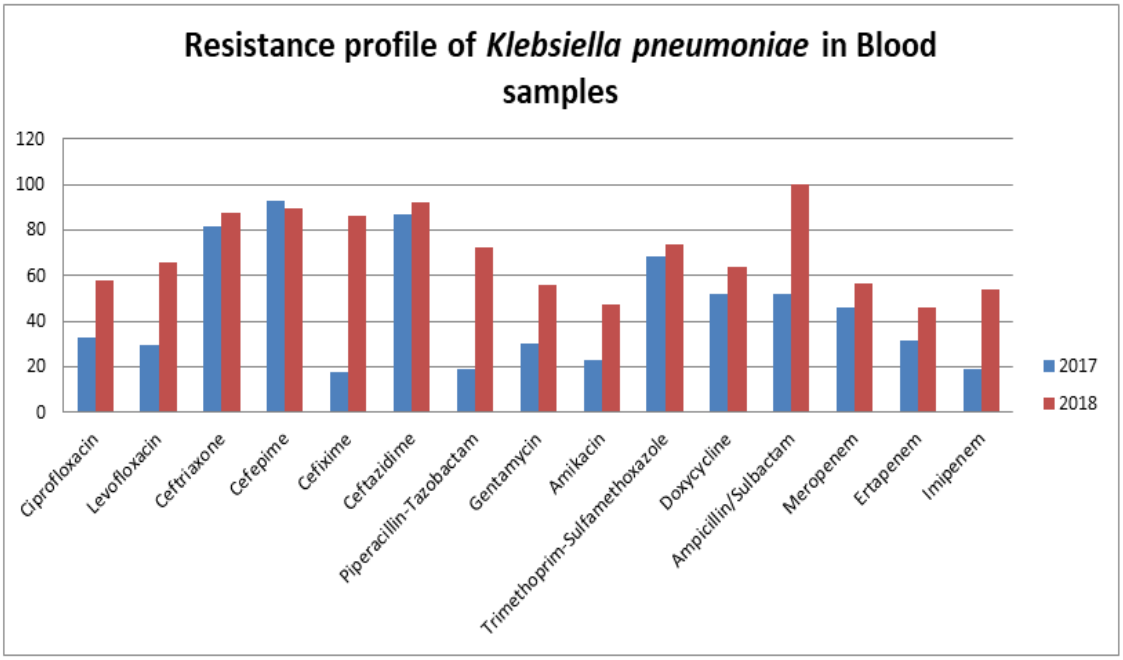


Figure 14: Graph representing resistance profile of *Klebsiella pneumoniae* in Blood samples

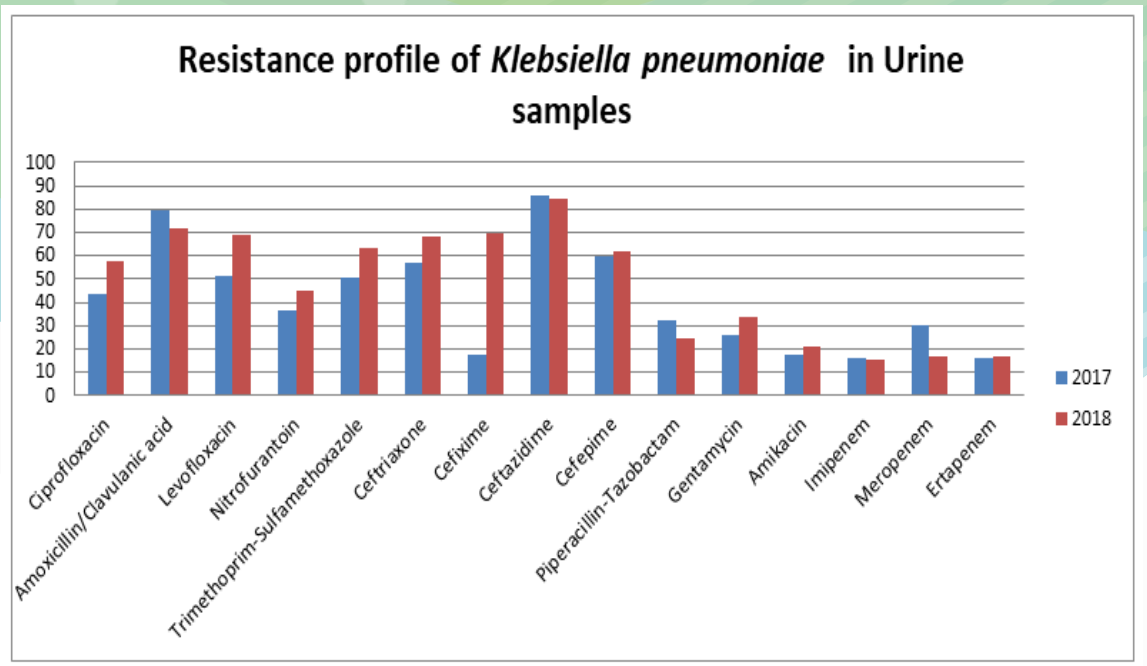


Figure 15: Graph representing resistance profile of *Klebsiella pneumoniae* in Urine samples

Staphylococcus aureus:

Staphylococcus aureus infections are common both in community acquired as well as hospital acquired settings and treatment remains challenging to manage due to the emergence of multi-drug resistant strains such as MRSA (Methicillin-Resistant *Staphylococcus aureus*). *S. aureus* are the causative agents of multiple human infections including bacteremia, infective endocarditis, skin and soft tissue infections (e.g., impetigo, folliculitis, furuncles, carbuncles, cellulitis, scalded skin syndrome, and others), osteomyelitis, septic arthritis, prosthetic device infections, pulmonary infections (e.g., pneumonia and empyema), gastroenteritis, meningitis, toxic shock syndrome and urinary tract infections.

Penicillin resistant strains of *Staphylococcus aureus* emerged shortly after the introduction of the antibiotic in the early 1940s. The mechanistic basis of resistance to methicillin and oxacillin is through acquisition of a resistant gene. The increasing rate of antibiotic resistance reported in *S. aureus* aganist β-lactam antibiotics, daptomycin, vancomycin and other glycopeptides.

In 2017-2018 in Pakistan ampicillin and penicillin remains highly resistant(>80%). The increasing trend in resistance is an alarming finding. Vancomycin remains susceptible against *S.aureus* in 2017 and 2018.

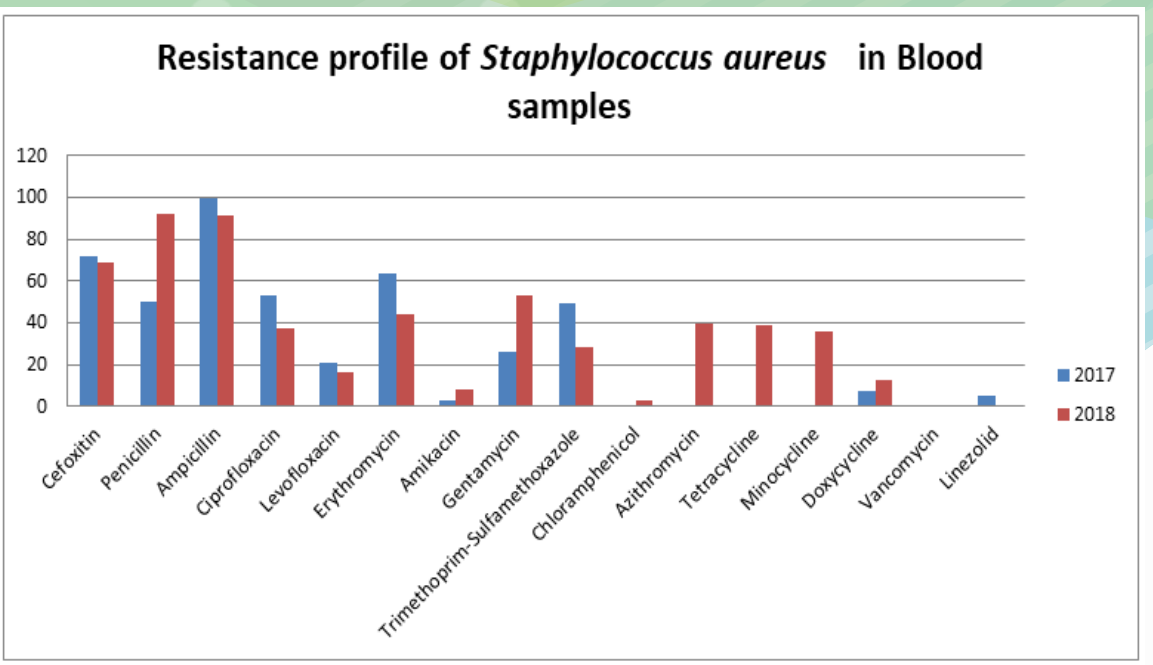


Figure 16: Graph representing resistance profile of *Staphylococcus aureus* in Blood samples

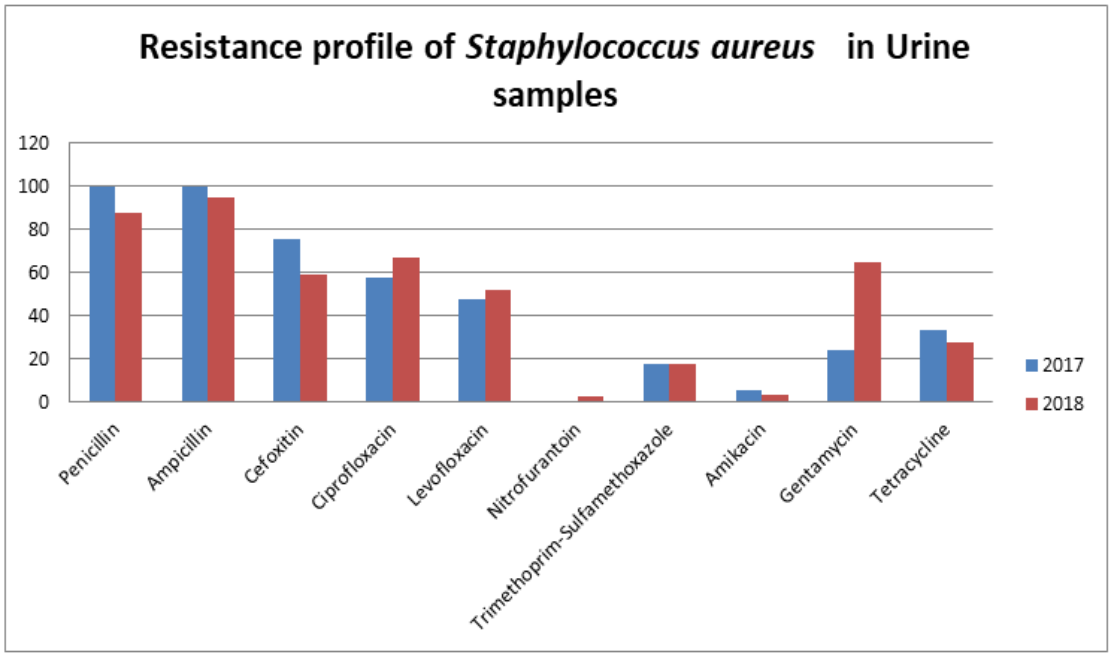


Figure 17: Graph representing resistance profile of *Staphylococcus aureus* in Urine samples

Salmonella typhi:

Salmonella enterica serotype *typhi* is a gram negative bacterium that is responsible for typhoid fever. Typhoid fever is more common in children and young adults and is associated with low income areas in which poor sanitation is prevalent. In 2000, typhoid fever was estimated to cause 21.7 million illnesses and 216,000 deaths globally and the International Vaccine Institute estimated that there were 11.9 million cases of typhoid fever and 129,000 deaths in low to middle income countries in 2010. *Salmonella typhi* is usually contracted by ingestion of contaminated food or water.

The increasing rate of antibiotic resistance in *Salmonella typhi* poses a significant global concern, and an improved understanding of the distribution of antibiotic resistance patterns in *Salmonella typhi* is essential for choosing the suitable antibiotic for the treatment of infections. The most frequently observed (43%) antibiotic resistance patterns found in *Salmonella typhi* were tetra-resistant pattern ASSuT (ampicillin, streptomycin, sulfonamides, and tetracycline) and the penta-resistant pattern ACSSuT (ampicillin, chloramphenicol, streptomycin, sulfonamides, and tetracycline).

In 2017 and 2018 data analysis for *S.typhi*, resistance against the first line antibiotics (ampicillin, chloramphenicol and trimethoprim sulphamethoxazole) has been observed as 60%. Ciprofloxacin resistance pattern in 2017 42% and 66% in 2018. For ceftriaxone increasing resistance trend is observed; 18% in 2017 and 28.5% in 2018. Carbapenems remains a good option against MDR *Salmonella typhi.* Meropenem and Imipenem remains susceptible with 100% susceptibility in both 2017 and 2018 years.

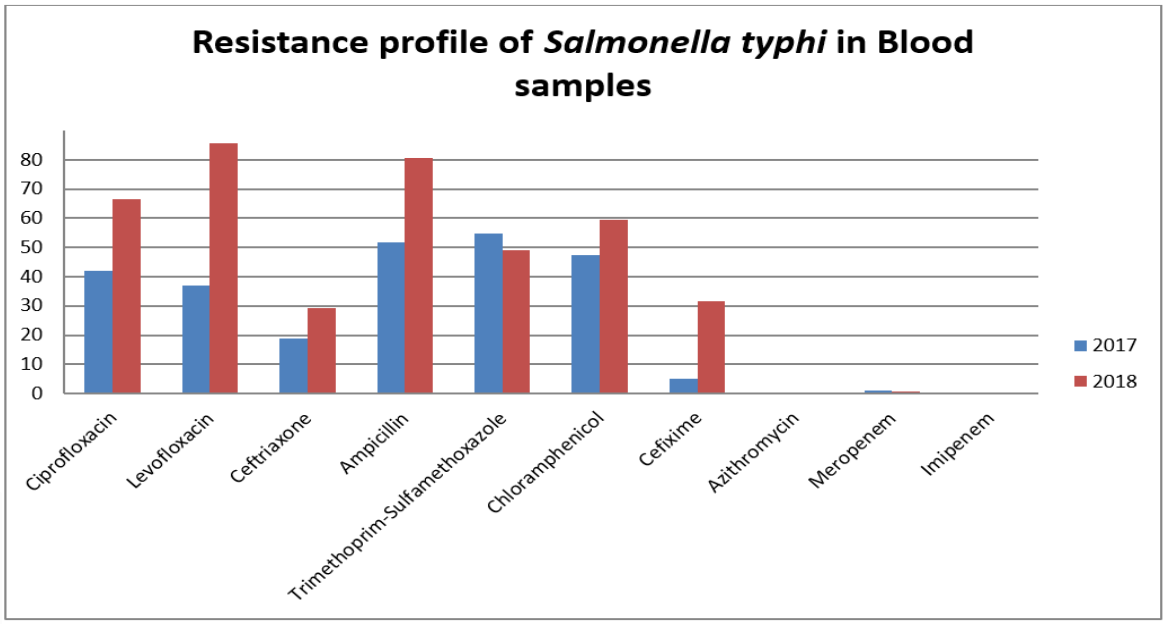


Figure 18: Graph representing resistance profile of *Salmonella typhi* in Blood samples

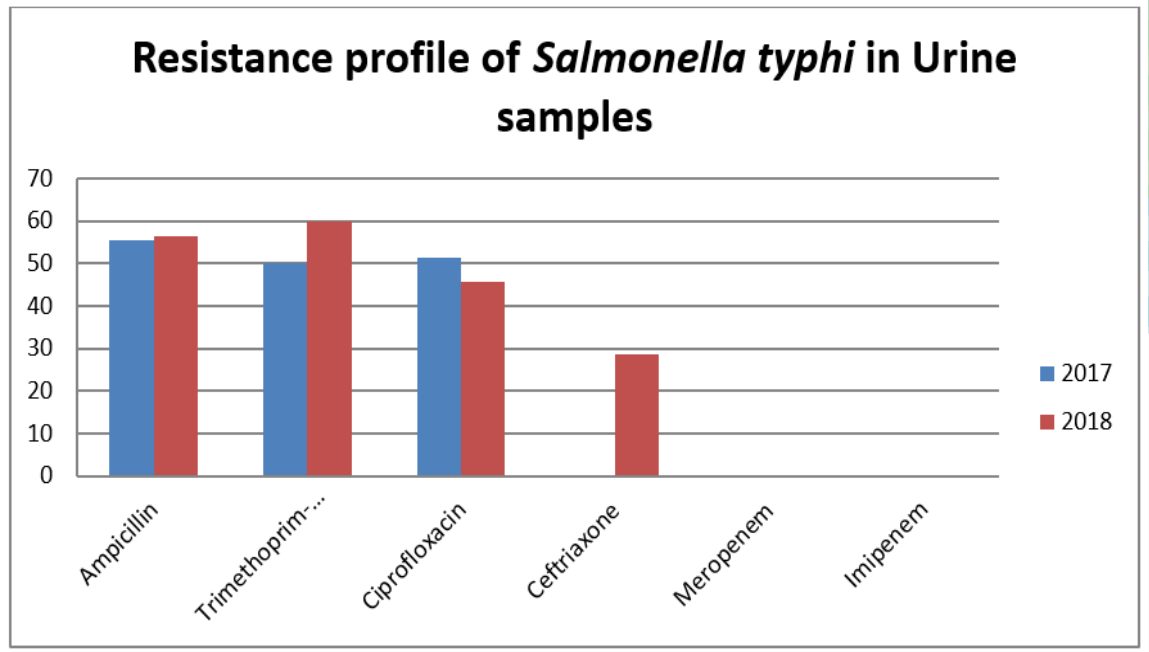


Figure 19: Graph representing resistance profile of *Salmonella typhi* in Urine samples

Streptococcus pneumoniae:

Streptococcus pneumoniae has been the most common pathogen to cause community-acquired pneumonia (CAP) worldwide. *S. pneumoniae* accounts for up to 27% of pneumonia cases worldwide today. *S. pneumoniae* also causes meningitis in children and the elderly, pneumococcal infections and sepsis in those infected with HIV. *S. pneumoniae* can be found in the human upper respiratory system. *S. pneumoniae* isolates are identified to be resistant to clindamycin, macrolide, fluoroquinolone and penicillin-resistant.

In our data, *S.pneumoniae* in blood samples remains susceptible to ceftriaxone (3.6% in 2017 and 3.4% in 2018) over the time. *S.pneumoniae* showed resistance to Penicillin (28% in 2017 and 50% in 2018), and to ampicillin (0% in 2017 and 7% in 2018). *S.pneumoniae* remains susceptible to vancomycin (0% resistance in 2017 and 2018).

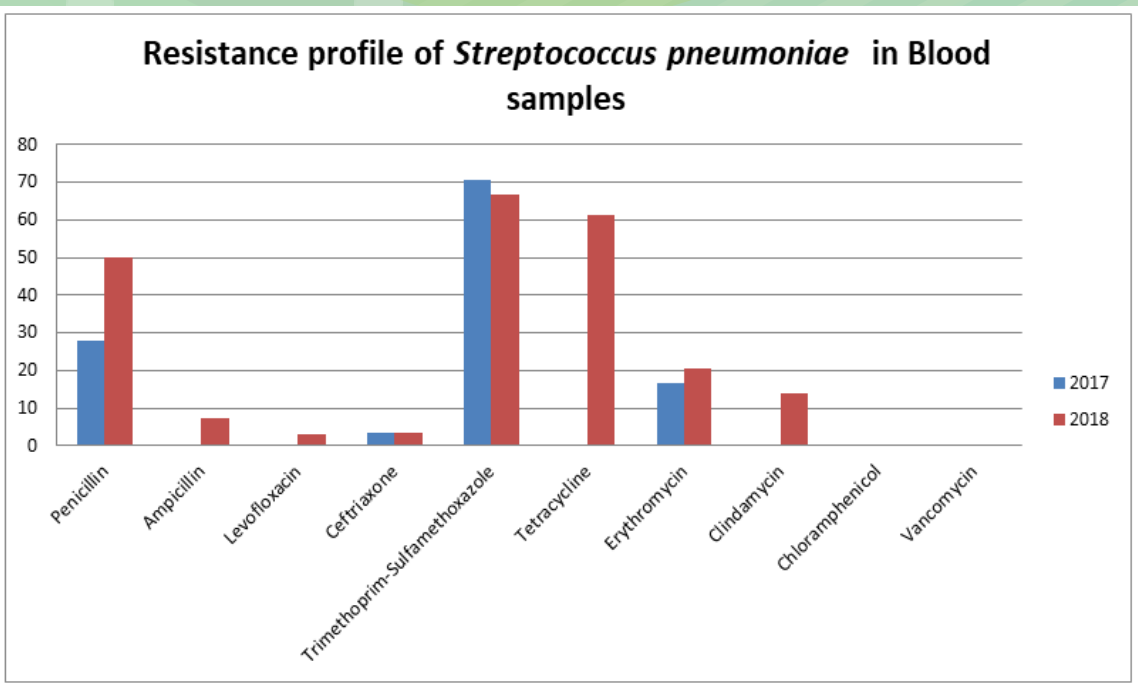


Figure 20: Graph representing resistance profile of *Streptococcus pneumoniae* in Blood samples

Neisseria gonorrhoeae:

Neisseria gonorrhoeae, causes the sexually transmitted genitourinary infection gonorrhea as well as other forms of gonococcal disease including disseminated gonococcemia, septic arthritis, and gonococcal ophthalmia neonatorum. Untreated infection may spread to the rest of the body causes septic arthritis and, in women may cause pelvic inflammatory disease and possible infertility. Antibiotic resistance in *gonorrhea* has been noted beginning in the 1940s. High level resistance to antibiotics including penicillin, ceftriaxone, fluoroquinolones and tetracycline is seen as an emerging public health threat.

In 2017-2018 ciprofloxacin remains highest resistant 93.7% (2017- 2018), followed by penicillin 78% (2017) 50% (2018) tetracycline 45% and azithromycin 8.5% resistant against the said pathogen.

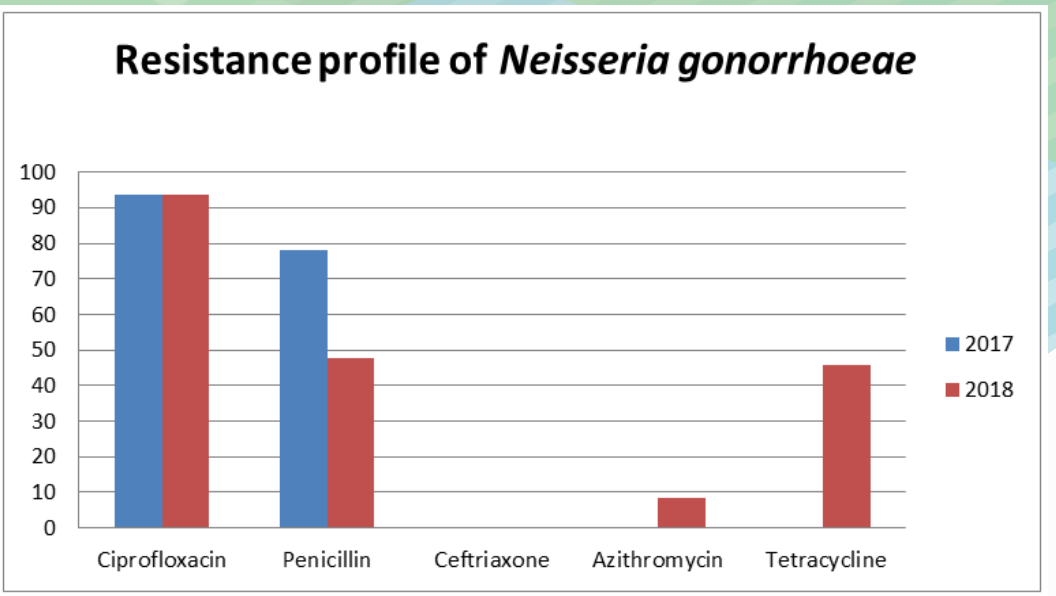


Figure 21: Graph representing resistance profile of *Neisseria gonorrhoeae* in overall samples

4 Recommendations

Recommendations

- The surveillance system focuses on receiving the quality data from the AMR sentinel sites. The need for having skilled IT/ data entry persons is imperative. The effective and user friendly Laboratory Information Management System (LIMS) is critical for being part of surveillance system. The trained IT persons/ Data entry persons at the surveillance sites will help to overcome the problems of software up gradation, backing up of data and data analysis. There are many laboratories in Pakistan which are not using LIMS or Hospital Management Information System, which leads to difficulty in accessing data in systematic way. The surveillance sites need to be trained on rational use of WHONET for data entry/ QC data entry, data analysis and baclink software for data conversion in required formats.

- Expansion of PASS program: More sentinel surveillance sites from the country should be included in PASS program, based on recommendations of criteria mentioned in AMR surveillance plan that includes laboratory assessments, quality data generation and participation in EQA.
- Addition of pathogens in surveillance program: Initially system has started as GLASS, over the time we have shifted to PASS and it aims to receive data from all the pathogens and specimens from all the sites. It is imperative to have a methodical system to understand the pattern of resistant pathogens emerging in the country.
- Quality data Assurance: Quality data need to assured from the participating labs. National External Quality Assurance System (NEQAS) helps in assessing the quality data production of the laboratories. The participating laboratories should be encouraged to participate in NEQAS program as minimal criteria to be part of PASS.
- Laboratory Quality Management System (LQMS) training: AMR surveillance sites should be trained on LQMS; to strengthen all aspects of the laboratory operations, including the organizational structure, processes and procedures in order to assure quality.

Annex A

Sr. No.	Description	Description
1	Patient unique identifier	This is usually the medical record number (MRN). Needed to uniquely identify each patient and for deduplication
2	Patient date of Birth	Patient date of birth in UK date format (dd/mm/yyyy). Needed to calculate age of patient at admission
3	Patient age	Patient age, rounded to full years. If age <5 months = 0 years.
4	Patient gender	Patient gender (male/female/unknown). Please submit if available
5	Patient nationality	If available
6	Date of admission (for inpatients only)	UK date format (dd/mm/yyyy), no time stamp (hh:mm). Mandatory for admitted inpatients, to determine HAI/CAI
7	Date of discharge (for inpatients only)	UK date format (dd/mm/yyyy), no time stamp (hh:mm). For admitted inpatients, to calculate LOS
8	Date of visit (for outpatients only)	UK date format (dd/mm/yyyy), no time stamp (hh:mm). For outpatients
9	Facility Name	Full name of healthcare facility, e.g. 'University Hospital xxx'... etc.
10	Facility identifier	Abbreviated name/code/identifier of healthcare facility, e.g. 'UHS', 'ARPHC', etc.
11	Facility Province or Governorate	Province or Governorate where the facility is located
12	Department/speciality name	Full name of department/specialty
13	Patient location name	Full name of patient location at time when specimen was taken. E.g. 'Surgical ward 5E', 'Diabetes clinic', 'NICU'
14	Location type	E.g. outpatient clinics, standard ward, ICU, CCU, VIP suite, Isolation, HDU, long stay, NICU, PICU, ...
15	Name of Laboratory	Mandatory if microbiology services (culture/AST) are not conducted at the same Facility
16	Microbiological procedure conducted (name)	E.g. Urine culture, wound culture, sputum culture, blood culture, stool culture, …
17	Specimen lab number	As assigned to the specimen by the lab
18	Specimen type/source	E.g. blood, throat swab, wound swab, urine (catheter),
19	Specimen result	Specimen result either positive or negative
20	Name of identified organism	Local organism name, either full species name, (e.g. '*Staphylococcus aureus*'), or '*Staph. spp.*', 'MRSA' etc.
21	AST susceptibility Method	E.g. MIC (Vitek), MIC (Phoenix), E-Test (MIC), Disk diffusion/KB.
22	AST result, categorical	Susceptible (S), intermediate (I), resistant (R)

Sr. No.	Description	Description
23	AST result, numerical	Minimal inhibitory concentration/MIC in ug/ml, or inhibition zone diameter in mm.
24	Antimicrobial agent tested	E.g. Levofloxazine, trimethoprime/sulfamethoxazole, piperacillin/tazobactam, ..
25	Specimen collection date	UK date format (dd/mm/yyyy)
26	Date report finalized	Date when the microbiology report was finalized for each specimen
27	Patient discharge status	E.g. discharged with approval, expired/died, transferred to facility XYZ,..
28	Diagnosis	Principal diagnosis (final main diagnosis).