Original Article

Entering the Post-Antibiotic Era: A Review of 200 Cultures from a Tertiary Care Hospital in Lahore

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ABSTRACT

Objective: To analyse the spectrum of resistance of various pathogens against commonly used antibiotic in a tertiary care hospital, Lahore.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the Lahore General Hospital from January 2017 to April 2018.

Materials and Methods: A total of 200 culture reports, sent from medical and surgical departments including ICUs of the hospital. Cultures of sputum, tracheal secretions, blood, pleural fluid, urine and tip of urinary catheter and CVP line were included.

Results: Out of 200 positive cultures**,** the majority (70%) were of respiratory tract origin. Gram negative bacteria prevailed (92%) as compared to gram positive pathogens which were just (8%). E coli (22%) and Pseudomonas (22%) were the commonest bugs followed by Klebsiella (17%) and Acinetobacter (17%). All gram-negative isolates showed very high rates of resistance against 3rd generation cephalosporins, amoxiclav, ciprofloxacin and gentamycin. Alarming levels of carbapenem resistance was documented in Acinetobacter (55.9%) and Klebsiella (51%) isolates. Ecoli (22%) and pseudomonas (31%) were relatively less resistant to carbapenems. MRSA accounted for 62.5% of staphylococcal samples.

Conclusion: The rapid and exponential rise in antimicrobial resistance is a serious threat for patient in the 21st century. It has reached alarming levels in different parts of world. There is an urgent need to develop and enforce strict controls on antibiotic usage.

Key Words: Antibiotic resistance, culture, pathogens, Bacterial resistance

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INTRODUCTION

Antibiotic resistance varies with time and place.[1] A variety of antibiotics are used to combat common and everyday infections, but due to poor prescription practices, poor application of updated knowledge, antibiotic overuse and extended use of antibiotics in agricultural and animal farming, we are facing a global epidemic of antibiotic resistance.[2]

There is spatio-temporal co-relation with antibiotic usage and resistance patterns.

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At times, certain antibiotics are favoured more in hospitals where they are readily and cheaply available. This overuse eventually leads to resistance patters. Overtime these antibiotics fall out of favour and newer generations are brought into use. This fluctuation is seen in many countries around the world. At the macro level there are plenty of surveillance systems in place, all of which have readily available and high quality data on global trends.[3] By participating in the Global Antimicrobial Surveillance System, the Pakistan National Institute of Health is the custodian of antimicrobial resistance surveillance in Pakistan.[4]

Unfortunately, despite initial planning and significant brain and manpower available there is a lack of funds and willpower to act. According to the WHOs mission report, Pakistan is not completely equipped to detect, act upon and prevent health threats. Despite having large-scale systems in place at the micro level, we are unable to combat resistance. It seems we are close to entering a “Post-Antibiotic” era where all known micro-organisms are developing resistances and all major antibiotics are proving ineffective against them.[5]

In 2014, WHO in collaboration with member states, issued a report “Antimicrobial Resistance, Global Report on Surveillance” which effectively documented high rates of resistance and serious gaps in antibiotic surveillance, standard maintenance and data sharing.[6] The report further documents the multifactorial causes of antibiotic resistance citing misleading advertisements, “quacks”, polypharmacy practices , individual bias towards costly broad spectrum antibiotics, irrational prescription practices and availability of over the counter (OTC) drugs and most importantly poor reporting at the micro level by hospitals and laboratories.

A study was conducted by the Proceedings of the National Academy of Sciences (PNAS) on the use and sale of antibiotics in 76 countries. The results showed that the consumption of antibiotics has tremendously increased from 2000 to 2015, especially in low and middle-income countries.[7] A lack of proper infection control and barrier nursing in hospital environment and in food supply chain where animals are given antibiotics for various reasons, have huge contribution in worsening this situation.[8] Today, bacteria are characterized not only by single drug resistance but also by multi, extremely and pan-antibiotic resistance. Multi-Drug resistant organisms are resistant to most of the antibiotics available.

The World Health Organization has warned about carbapenem, third generation cephalosporin, aminoglycoside and fluoroquinolone resistant bacteria worldwide and have published a list of resistant bugs according to the pathogenicity and priority so that appropriate measures should be taken by countries to combat the situation and to develop new antibiotics.[9] In a developing country like Pakistan its is of utmost importance that we change our prescription practices to and focus on using less broad spectrum antibiotics. Continuous and dedicated monitoring of sensitivity pattern of bacteria in our setups should be mandatory to avoid unnecessary mortality and morbidity and financial burden on governments and patients. Due to isolation and fear of resistant bugs, carbapenem and Colistin like antibiotics are routinely prescribed as empirical treatment even outside ICU which is resulting in emergence of superbugs which are resistant to all major antibiotics.[10]

MATERIALS AND METHODS

We conducted a retrospective audit of 200 positive culture reports, sent from Medical and Surgical Departments including ICUs of the Lahore General Hospital, Lahore which were ordered by pulmonologist from January 2017 to April 2018. Cultures of sputum, tracheal secretions, blood, pleural fluid, urine and tip of urinary catheter and CVP line included. Data was analysed by SPSS version 24.

RESULTS

A Total of 200 cultures were studied, among which (61) were from sputum, tracheal aspirate (58), urine (22), pleural fluid (21), blood (19), whereas catheter tip and CVP line tip were (11) and (8) respectively (Fig 1). Gram negative bacteria prevailed at (92%) and gram-positive pathogens were just (8%). (Fig 2).Among gram negative bacteria, Escherichia coli and pseudomonas were the most common bugs isolated 45 (22%) each followed by Klebsiella 35 (17.5%), Acinetobacter 34 (17%), Proteus 7 (3%) and Enterococcus 5 (3%).

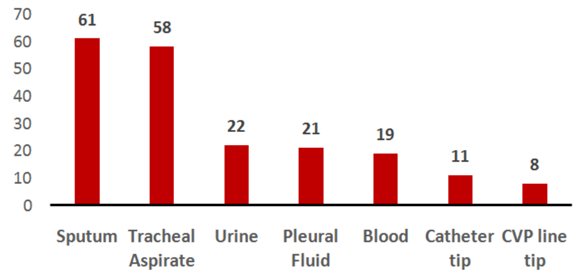

Figure No. 1: Type of samples

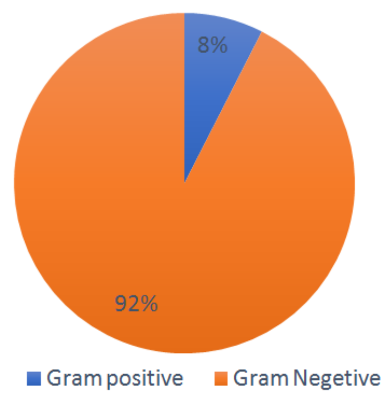

Figure No. 2: Percentage according to Gram staining

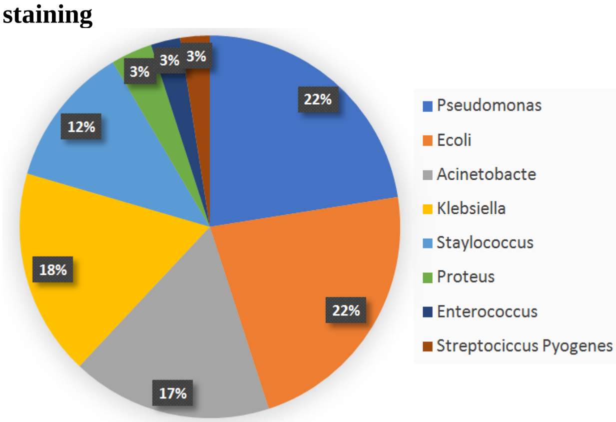

Figure No. 3: Prevalence of bacteria

Among gram positive pathogens, Staphylococcus aureus was 24 (12%) and Streptococcus pyogenes 5 (2.5%) (Fig 3). Overall antibiotic resistance patterns revealed highest rates of resistance against third generation cephalosporins and Amoxicillin-clavulanic acid followed by ciprofloxacin (Fig 4). Over all resistance against ceftriaxone was (85%), cefotaxime

(84%) ceftazidime (77%) whereas Amoxiclav (83.5%) and ciprofloxacin (82%). Among aminoglycosides gentamycin had higher resistance (60%) than amikacin (39%). Overall resistance against meropenem, imipenem and piperacillin-tazobactam was (34.5%, 36% and 39.5%) respectively which is lesser than cefoparazone–salbactam combination (52%). Colistin was least resistant (9%) followed by tigecycline (18%).Resistance patterns of individual bacteria against commonly used antibiotics are shown in (Table 1). Proteus showed 100% resistance against ceftriaoxaone, cefotaxime and ciprofloxacin but remained 100% sensitive to carbapenams, tigacyclin and colistin. Klebsiella and Acinetobacter showed alarming resistance rates against almost all groups of antibiotics and were more resistant than E coli. S. aureus was 62.5% resistant to amoxi-clav and no resistnace was documented against vancomycin and linezolid.

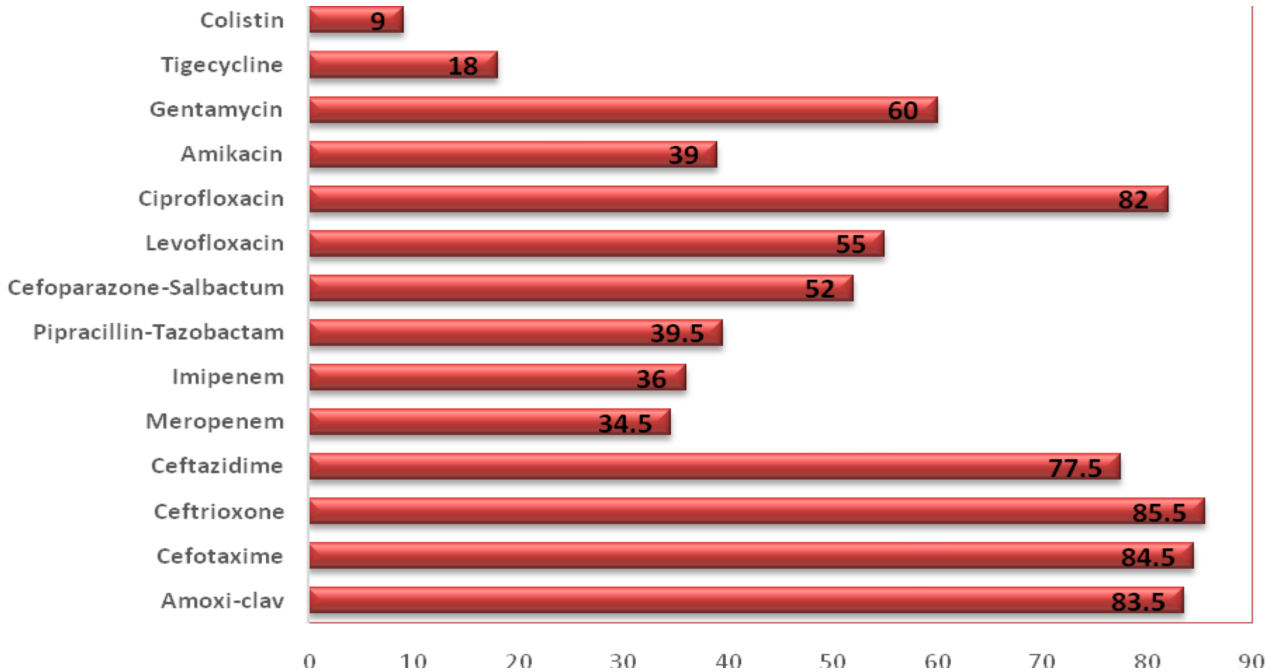

Figure No.4: Overall % resistance of antibiotics

Table No.1: Antibiotic Resistance rates in Bacteria (%)

Organ-isms	Antibiotics															
	AC	**CE**	**CA**	**CT**	**M**	**I**	**PT**	**CS**	**LV**	**Ci**	**AK**	**GN**	**VA**	**LZ**	**TG**	**CO**
Acineto-bacter	94.2	85.3	85.3	82.4	52,9	55.9	50.0	73.5	88.2	97.0	47.0	64.7	-	-	26.2	17.6
E. coli	86.7	86.7	84.5	84.5	22.3	20.0	44.5	42.3	68.9	86.7	26.7	57.8	-	-	33.0	11.2
Entero-coccus	80.0	60.0	80.0	60.0	40.0	40.0	20.0	20.0	20.0	20.0	20.0	40.0	-	-	0	0
Klebsiella spp.	88.6	88.6	88.6	88.6	51.4	51.4	51.4	74.3	77.2	85.7	57.2	71.4	-	-	17.0	17.2
Proteus spp.	71.4	100.0	100.0	42.8	0.0	0.0	0.0	28.6	57.2	100.0	42.8	57.2	-	-	0	0
P. aerugi-nosa	86.7	84.5	84.5	64.5	31.2	35.6	28.9	40.0	60.0	82.3	37.8	64.5	-	-	0	4.5
Strepto-coccus	20.0	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	-	-
S. aureus	62.5	-	-	-	-	-	-	-	-	-	-	-	0.0	0.0	-	-

AC: Amoxi-clav, CE: Cefotaxime, CA: Ceftazidime, CT: Ceftriaxone, M: Meropenem, I: Imipenem, PT: Pipracillin-Tazobactam, CS: Cefoparazone-Salbactum, LV: Levofloxacin, CI: Ciprofloxacin, AK: Amikacin, GN: Gentamycin, VA: Vancomycin, LZ: Linezolid, TG: Tigecycline, CO: colistin

DISCUSSION

Antibiotic resistance is a natural evolutionary mechanism that protects bacteria against antibiotics to which they had been exposed. The most alarming discovery of the recent years is that antimicrobial-resistance genes and their genetic vectors, once evolved in bacteria of any kind anywhere, can spread indirectly through the world's interconnecting commensal, environmental, and pathogenic bacterial populations to other kinds of bacteria anywhere else.[11] Antibiotic consumption is the main driver of antibiotic resistance. Unsupervised and injudicious use of antibiotics in human and animals have favoured the emergence of superbugs. According to a report issued by proceedings of national academy of sciences (PNAS), from 2000 to 2015, there was 65% increases in consumption of antibiotics.[12] The World health organization has issued a list of pathogens that are huge threat for clinicians. Carbapenam resistant Acinetobacter, Pseudomonas, Klebsiella and E.coli and methicilin resistant Staphylococcus aureus are at top of this list.[13] In our study gram negative bacteria were most prevalent, among which E coli and pseudomonas were the commonestbugs isolated (22% each) followed by Klebsiella and Acinetobacter (17% each). It is consistent with many studies done around the world and in Pakistan. Results of studies conducted by Rizvi et al from Pakistan were comparable to our study and revealed E.coli, Klebsiella, and pseudomonas are the most prevalent bugs in hospital infections.[14] Acinetobacter has emerged as another common microorganism known for ventilator associated pneumonia.

In our study, over all high rates of resistance were seen against 3rd generation cephalosporins, co-amoxiclav and ciprofloxacin (85.5%, 83.5%, 82% respectively) while colistin remained the most effective drug with lowest rates of resistance (9%). Among aminoglycosides higher resistance was seen against gentamycin (60%) than amikacin (39%). These results are consistent with the findings of Naeem et al.[15,16] Acinetobacter showed highest resistance rates against Amoxi-clav (94%), cephalosporins (85%), ciprofloxacin (97%) and considerable resistance against carbapenems and pipracillin-tazobactam (55.9% and 50% respectively). It was least resistant to colistin (17%). Klebsiella followed a similar pattern of resistance which is alarming for us.

E. coli and pseudomonas were relatively less resistant to carbapenem (22% and 31% respectively) and against colistin (11.2% and 4.5% respectively) but both pathogens were highly resistant to 3rd generation cephalosporins (86.7% and 84.5% respectively).These results are consistent with findings of Taslima et al.[17] 3rd generation cephalosporins and aminoglycosides, which remained main defence against gram negative bacterial infections are proving ineffective now and we have to rely more on carbapenems and colistin.[18]

In European Centre for Disease Control (ECDC) annual report, a clear gradient from low to high resistance is evident as you move from west to east and north to south Europe. The data for 2017, concerning carbapenem-resistant germs such as Acinetobacter, show the European percentage of resistant strains at 50% in 2015, with Italy alone reporting 78%; Klebsiella at 66% (in Slovakia) while E coli is relatively less resistant and highest is (1.9%) in Greece.[19,20]

In our study, among staphylococcus, (62.5%) were Methicillin resistant (MRSA) and were 100% sensitive to vancomycin and Linezolid. A study conducted my Kakkar et al in India documented MRSA (47%), carbapenem resistant Klebsiella (57%), E coli (13%) and pseudomonas (50%).[21,22] Worrisome resistance rates have been observed in North Korea as well with aAcinetobacter resistance against cefotaxime (84%) and imipenem (85%).[23]

Antimicrobial resistance is worldwide now and a serious threat to public health. For bacterial infections, prompt treatment with effective antimicrobial agents is especially important and is one of the single most effective interventions to reduce the risk of fatal outcome. Emergence of resistant bacterial strains means that standard treatments are no more working and infections are harder to treat with same antibiotics. This would lead to spread of infections, longer hospital stays increased economic and social costs and high mortality. Despite being a resource limited country a recent study suggests that with proper training techniques, mentorship courses, didactic training workshops and adherence to International Health Regulation (IHR) laboratories both private and public can and should lead the line against antiomicrobial resistance.[24]

CONCLUSION

The rapid and exponential rise in antimicrobial resistance is a serious threat for patients in the 21st century. It has reached alarming levels in different parts of world and Pakistan is particularly vulnerable due to multiple reasons identified. There is an urgent need to develop and enforce strict controls on antibiotic usage. Hospitals and private labs must co-operate to provide extensive data to chart resistance patterns or risk a crisis.

Author's Contribution:

Concept & Design of Study:	Aneela Chaudhary
Drafting:	Muhammad Asim Rana
Data Analysis:	Dawar Ayyaz
Revisiting Critically:	Aneela Chaudhary, Khalid Waheed, Muhammad Asim Rana
Final Approval of version:	Aneela Chaudhary

Conflict of Interest: The study has no conflict of interest to declare by any author.

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