Original Article

Our Institutional Antibiogram: The Insight Gained in Selection of Empirical Antibiotics for the Treatment of Burn Wound Infection.

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Abstract

Objective: The aim is to study the prevalence of bacteria involved in burn wound infection and the antibiotic susceptibility patterns of these bacteria.

Methodology: It was a cross-sectional, descriptive, observational study conducted in Burns and Plastic Surgery Center for six months. Sampling was done using a consecutive non-probability method for antibiogram construction. A summary of isolated bacteria's antibiotic susceptibilities to tested antibiotics and the prevalence of isolated species and genera of bacteria in percentages was determined by analyzing wound culture and susceptibility reports of burn wound clinical samples to construct an antibiogram.

Results: Collectively, the gram-negative bacilli (79.13%) and individually Klebsiella pneumonia (P.pneumonia) (23.33%), Pseudomonas aeruginosa (P.aeruginosa) (22.94%) and Staphylococcus aureus (S. Aureus) (14.55%) were most common respectively. The highest susceptibilities by all isolates were shown to carbapenems, piperacillin/tazobactam, and amikacin.

Conclusion: Gram-negative bacteria of Enterobacteriaceae family i.e. K.pneumoniae and Enterobacter spp. along with P.aeruginosa and gram-positive cocci were the most prevalent organisms isolated.

Keywords: Antibiogram, Burn wound infection, Empiric antibiotic treatment

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Introduction

Evidence based antibiotic prescription is essential measure to keep antibiotics effective against bacteria by preventing the development of antibiotic resistance in them, the selection of appropriate empirical antibiotics for the treatment of infections need to be based on cumulative antibiograms.[1] Antibiotic resistance is the decreased susceptibility of bacteria to antibiotics to which it was previously susceptible.[2] Genes that confer resistance to antibiotics have always existed inherently as a defense and survival mechanism in the genomes of bacteria, even before the clinical use of antibiotics was started to treat infections.[3] The deliberate exposure to antibiotics has put the bacteria into a survival challenge. They have started developing resistance at an accelerated pace, either through the activation of already existing genes that were dormant or through new genetic mutations and by acquiring resistance genes from one another through mechanisms present in bacteria. Furthermore, due to the use of antibiotics in humans, there is a selection of antibiotic-resistant bacteria as a result of selection pressure. Thus, the proliferating resistance in bacteria results in antibiotics becoming ineffective against them, rendering bacterial infections difficult to or untreatable, leading to increased suffering, deaths, and risk of further spread along with negative economic consequences.[2,4,5] Non-evidence-based antimicrobial prescribing behavior is one of the major contributors to this phenomenon. Consequently, antibiotic-resistant bacteria, including Multidrug Resistant (MDR), Extensively Drug Resistant (XDR), and pan-resistant bacteria, are on the rise, and there are no limits and boundaries to their proliferation and spread. Few examples are origin of Methicillin Resistant Staph. Aureus (MRSA), Vancomycin intermediate and resistant Staphylococi and resistant enterococci. MDR, XDR gram-negative bacteria of Enterobacteriaceae family like Salmonellatyphi, ESBL, and AmpC-producing Pseudomonas, MDR and XDR-TB, and so on, which are hard to manage.[7] Over 2.8 million antibiotic-resistant infections and 35 000resultant deaths occur every year in the USA.[7] Around 700,000 human deaths worldwide each year occur as a result of drug-resistant infections and may rise to 10 million deaths annually around the globe by the year 2050, and the cost of antibiotic resistance could increase to US$100 trillion.[8,9] The speed with which the bacteria are becoming resistant is more than the speed with which new antibiotics are being developed to tackle the newly evolved more resistant bacteria. The available antibiotics must be kept effective until new ways of tackling infections are discovered; every measure needs to be taken to slow down the development of resistance against antibiotics, or else humans might face a post-antibiotic era comparable to the pre-antibiotic era when deaths would occur from presently trivial looking infections.[10]

The Anti-biotic Stewardship (ABS) programs optimize the antimicrobial treatment of infections and reduce adverse events associated with antibiotic use as well as development of antimicrobial resistance, through evidence based interventions.[11,12] Cumulative antibiogram of an institution is an essential component of its ABS program. The cumulative antibiogram is a summary of antimicrobial susceptibilities for selected bacterial pathogens and provides comprehensive information about local antimicrobial resistance trends; it is a surveillance of antibiotic resistance and involves the collection of antibiotic susceptibility test results undertaken by microbiology laboratories on bacteria isolated from clinical samples sent for investigation. The development of institution based antibiogram is usually responsibility of microbiology lab, infection control personnel and an input from pharmacist. Cumulative antibiograms are regarded as cost-effective and convenient method of assessment of local susceptibility rates and monitor resistance trends overtime in institutions.[11] In critically ill patients suspected of infection, immediate treatment is usually started empirically as culture and susceptibility test for identification of causative pathogen and its antibiotic susceptibility pattern results may take a few days to be available.[13] For the selection of empirical antibiotic treatment, while the dosing regimen is established on the basis of patient factors, pharmacodynamics and pharmacokinetics and the properties of antimicrobial agents, the cumulative antibiograms give the knowledge of local epidemiology of microorganisms and regional rates of resistance, which need to be considered at the time of empirical antibiotic selection.[12] Although the empirical treatment is given only for a limited time until the targeted antibiotic treatment can be started after culture and susceptibility test results, selecting the most appropriate empirical antibiotic regimen is crucial for favorable patient outcomes and helps mitigate the development of antimicrobial resistance.[14,15]

The aim is to study the prevalence of bacteria involved in burn wound infection and the antibiotic susceptibility patterns of these bacteria.

Methodology

The study was conducted in Burns and Plastic Surgery Center (B&PSC) Hayatabad Peshawar, a tertiary care facility of 120 beds for burns and plastic surgery patients. It was a cross-sectional, descriptive, observational study. The approval of the ethics committee was obtained from Post Graduate Medical Institute Peshawar, KP, Ref No.11322 Dy.REG. /PGMI, dated 05-12-2023. Permission to use laboratory test data for research purposes was obtained from concerned authorities of B&PSC. Antibiogram was prepared for a six month period from 1st April 2023 to 30th September 2023 according to CLSI guidelines M39 A5 2022. For the construction of the antibiogram, we included all the culture and susceptibility test results of the clinical samples of the burn wounds of patients of the hospital, for whom the tests were done at the microbiology laboratory of B&PSC during the study period; the sampling was by nonprobability consecutive method. Where more than one bacterium was isolated from the same diagnostic sample of a patient, they were counted separately. Only those strains of bacteria were included, for which the number of isolates was equal to or greater than 30.

The antibiotic susceptibility test reports from laboratories other than the microbiology department of our institute, surveillance culture, and screening isolates were excluded; strains that show intermediate sensitivity were not counted as sensitive. The culture and susceptibility reports were collected from our hospital's microbiology laboratory records. The total number of each of the isolated genera or species of bacterium was counted individually, and its percent prevalence was determined. Antibiogram was constructed by plotting the number of total susceptible isolates of a particular bacterium as a percentage against the corresponding antibiotic to which it was tested.

Results

For cumulative antibiogram construction a total of 1531 culture and sensitivity test reports of the wounds of burn patients of our hospital were assessed. Growth of bacteria was found in 1088 (71.06 %) and 442 (28.87) had no growth. Antibiogram was developed for 1024 isolates. Among the isolated bacteria 861 (79.13%) bacteria were gram-negative and 163 (14.98%) were gram-positive. The prevalence of different bacteria in numbers and percentage is given in Table 1. The cumulative antibiogram of gram-negative bacteria is shown in Table 2 and of gram-positive bacteria in Table 3. Table 4 shows the key to the abbreviations of names of antibiotics against which sensitivity of bacteria was tested.

To imipenem, meropenem, doripenem, piperacillin/tazobactam every tested bacterium showed susceptibility equal to or greater than 60%.

Discussion

Selection of empiric antibiotic therapy is based on various factors including likely pathogens, antimicrobial resistance patterns on the basis of local epidemiology, and patient characteristics including degree of sickness, infection site and any co-morbidities of the host.[16,17] One variable which is strongly associated with unfavorable outcomes in critically ill patients is ineffective or inadequate empirical antimicrobial regimen.[18,19] Cumulative institutional antibiograms have proved helpful in this regard.[20]

We developed our institution specific antibiogram for bacteria, isolated from the wounds of burn patients, to find out their antibiotic susceptibility patterns and to understand our local trends of resistance. The reason was that the burn patients constitute a unique group of patients and many of these patients acquire infections in hospital, bacteria involved in hospital acquired infections are known to show higher resistance to antibiotics.[21] Patients with burn wounds have specific characteristics, i.e., longer hospital stays, multiple interventions, and sometimes the previous history of antibiotics intake;[22] that is why the organisms isolated may show different susceptibility profiles for the same genera and species of bacteria isolated from the patients of other hospitals. We constructed our antibiogram, in order to be able to recommend suitable empirical antibiotic regimens for our patients, and to avoid suboptimal therapies. The data helped us to see the bigger picture by observing cumulative sensitivities which cannot be understood by seeing individual reports and assisted us in identifying the overuse of inappropriate antibiotics.

Table 1. The Prevalence of Different Bacteria; Numbers and Percentages

Total Bacteria Isolated	N=1024	%
Klebsiella pneumonia	239	23.33%
Pseudomnasaeruginosa	235	22.94%
Staphylococcus aureus	149	14.55%
Acinitobacterbaumannii	138	13.47%
Proteus spp.	67	06.54%
E.coli	66	06.44%
Enterobacter spp.	60	05.85%
Citrobacter spp.	56	05.46%
Staphylococcus epidermidis	14	01.36%

N=Number, %=Percentage

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Table 2. The Cumulative Antibiogram of Gram -Negative Isolates

Percentage Sensitivity of Gram-Negative Bacteria Isolated from the Samples of Burn Wounds to Tested Antibiotics.																				
	N= 861 %= 79.13%	AM	AMC	TZP	IPM	MEM	DOR	CTX/ CRO	CES	CAZ	SXT	TE	TGC	CN	AK	TOB	CIP	LEV	CT/ PB	TIC	FEB
Klebsiella pneumonia	239 27.75%	00	04	64	69	74	86	13	41	23	05	21	82	31	81	31	25	NT	79	NT	NT
Pseudomna-saeroginosa	235 27.29%	IR	IR	61	62	65	67	NT	32	33	NT	IR	IR	34	54	29	27	14	97	00	02
Acinitobacte-rbaumanii	138 16.02%	IR	IR	60	64	83	86	09	33	18	10	13	88	22	58	26	34	NT	55	NT	NT
Citrobacter spp.	56 06.50%	IR	IR	64	73	86	91	11	41	21	04	07	79	46	59	38	18	NT	77	NT	NT
E.coli	66 07.66%	00	18	74	85	82	87	09	58	21	11	15	88	61	79	47	12	NT	92	NT	NT
Proteus spp.	67 07.78%	IR	00	61	67	88	94	13	37	19	07	IR	IR	19	44	21	19	NT	IR	NT	NT
Enterobacter spp.	60 06.96%	IR	IR	55	62	61	62	05	17	10	03	07	50	08	38	12	17	NT	28	NT	NT

N=number   IR=inherently resistant NT=not tested

Table 3. The Cumulative Antibiogram of Gram-Positive Isolates

Percentage Sensitivity of Gram-Positive Bacteria Isolated from the Samples of Burn Wound to Tested Antibiotics																			
Organism	N=163 14.98%	P	AM	AMC	FOX	TZP	IPM	CN	AK	TE	TG	VA	LNZ	CTX	CES	CIP	E	SXT	LEV
S. aureus	149 91.41%	00	0.6	22	99 67%	61	67	31	60	29	100	99	100	06	43	09	15	08	08

N=number, IR=inherently resistant, NT=not tested, FOX=Cefoxitin, is used as surrogate for oxacillin

Table 4. Key to the Abbreviations of the Names of Antibiotics

Key to the Abbreviations of Names of Antibiotics Against Which Sensitivity of Bacteria was tested.	
AM= ampicillin	TGC=tigecycline
AMC=co-amoxiclav	CN=gentamycine
TZP=piperacillin/tazobactam	AK=amikacin
IPM=imipenem	TOB=tobramycin
MEM=meropenem	CIP=ciprofloxacin
DOR=doripenem	LEV=levofloxacin
CTX/CRO=cefotaxime and /or ceftriaxone	CT/PB=colistin or polymyxin B
CAZ=ceftazedime	TIC=ticarcillin
CES=cefoperazone/sulbactam	FEP=cefepime
TMP/SXT=trimethoprim /sulfamethoxazole	VA=vancomycin
TE=tetracycline	LNZ=linezolid
	E=erythromycin

Our institutional antibiogram also showed the frequency with which different organisms were isolated from burn patients suspected of having infection besides their antibiotic susceptibility pattern, this knowledge of local epidemiology of organisms is also beneficial in selection of empirical antibiotics as our organism were predominantly gram negative but there was substantial number of gram positives so our empirical antibiotic therapy needs to be broad spectrum.

Our antibiogram showed that, on the whole gram negative bacteria were more commonly isolated from the samples of burn patients. This was also shown by other studies.[23,24] Individually, the most common was K. pneumoniae, followed by P.aerugenosa, gram-positive Staphylococcus aureus was in third place in our study findings.

K.pneumone, P.aeruginosa, and other gram-negative bacteria, which collectively constituted 79.13 % of all isolated bacteria, showed the highest sensitivity to carbapenems, i.e., doripenem, followed by meropenem and imipenem, and penicillin and beta-lactamase inhibitor combination, piperacillin/tazobactam. Gram-positive cocci showed high sensitivity to imipenem and piperacillin/tazobactum among broad-spectrum antibiotics; other carbapenems were not tested against gram positives.

P. aureginosa, A. baumanii, enterobacter spp. and citobacter spp. which collectively made 56.79% of isolated organisms as well as MRSA were among the bacteria that are inherently resistant to co-amoxiclav, and the rest of the isolates also exhibited high resistance to this antibiotic.

In the context of antibiogram susceptibility findings, one of the carbapenem or piperacillin /tazobactam were recommended to be chosen as empirical antibiotic monotherapy, as all tested bacteria showed high cumulative susceptibilities to them, all above 60%. Amikacin may be added if combination therapy is decided for severely ill patients.

Some institutions select a cutoff point of susceptibility as 80% or 90 % susceptible for an antibiotic as a prerequisite, to be selected as empirical antibiotic in monotherapy in managing severe infection. In addition, the clinician may opt to go with the antibiotic that is more likely to cover the bacteria as indicated by the local antibiogram.[21] We took 60 % susceptibility as prerequisite for empirical antibiotic selection for monotherapy to develop recommendations as our isolates were showing high resistance to tested antibiotics. Hence, we took a lower cut off.

The isolated gram-negative bacteria were fairly susceptible to colistin while gram-positive bacteria were to linezolid, vancomycin, and tigecycline, but colistin and linezolid are selective for gram-negative and gram-positive bacteria, respectively,[26,27]

Keeping in view the findings of our antibiogram, we recommended that one of the carbapenems or piperacillin/tazobactum be chosen as the antibiotic of choice for empirical treatment of the patients to get cover for both gram-positive and gram-negative organisms until the definitive report of culture and susceptibility arrive in. Bacteria were also reasonably susceptible to aminoglycoside; amikacin. Aminoglycosides are generally not considered best for treatment as monotherapy in seriously ill patients.[28] However, they may be given in combination with another antibiotic if the physician decides on the basis of patient's condition, since most of isolated organism has shown high susceptibility to it. Formulary of the institution was given recommen-

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dation on the basis of cumulative institutional antibiogram to make the antibiotics suggested, available for prescription as empiric antibiotics.

The limitations of the study were that antibiogram was prepared from manually kept records of antibiotic susceptibilities, software like WHO NET were not available which would be helpful in more efficient antibiogram construction. Antibiogram reflecting cumulative hospital-wide data may have diluted results and masked resistance trends for a particular ward or service e.g., in the ICU, conversely, when ICU data is included in an institution-wide antibiogram the susceptibility patterns can possibly show more resistance than if the ICU data were excluded and reported separately. The resistance pattern was observed on the basis of laboratory culture and susceptibility test results. Repeat samples from patients with prolonged hospital stay may also skew the results.

We recommend that institutional antibiograms should be developed for burn centers and units to have an idea regarding the frequency of bacteria involved in burn wound infection and their antibiotic susceptibility pattern.

Conclusion

Gram-negative bacteria of Enterobacteriaceae family i.e. K.pneumoniae and Enterobacter spp. along with P.aeruginosa and gram-positive cocci were the most prevalent organisms isolated. The isolated organisms showed high resistance to many commonly used antibiotics.

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Authors' Contribution Statement

ZI helped in conception and design, acquisition, analysis and interpretation of data. SB SB drafted the manuscript. ST helped in analysis and interpretation of data. All authors aided in the drafting of the manuscript. All authors are accountable for their work and ensure the accuracy and integrity of the study.

Confilct of Interest

Authors declared no conflict on interest

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Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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