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Antibiogram Based Antimicrobial Resistance Policy

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A B S T R A C T

Antimicrobial resistance is a current and fore coming worldwide problematic issue. It is more prevalent in healthcare settings; especially in hospital intensive care units. This study aimed to present a simple means of constructing an antibiotic policy from results of cumulative antibiograms for patients' cultures [sputum, urine, blood, wounds] using a battery of narrow and broad spectrum antibiotics. The most commonly isolated pathogens from all samples were *Staphylococcus aureus (S. aureus), Escherichia coli. (E. coli), Klebsiella pneumoniae (K.pneumoniae) and Pseudomonas aeruginosa. E. coli* recorded the highest percentage of resistance in all samples [75.2% for sputum, 74.3%for blood, 65.8%for wounds], while *S.aureus* isolates showed the least resistance [40.0% for sputum, 30.0% for blood]; *K.pneumoniae* revealed the least resistance [19.4% for wounds]. However, all bacterial isolates revealed a similar 40.0% resistance in urine samples. The resistance pattern was recorded and accordingly a sample antibiotic policy was formulated.

Introduction

Antimicrobial resistance has a tremendous impact in health-care settings; where the combination of highly susceptible patients; including the immunocompromised, intensive prolonged antimicrobial use, and cross infection has resulted in hospital acquired infections with highly resistant bacterial pathogens (Santajit and Indrawattana, 2016). The increasing risk for morbidity and mortality associated with such resistant infections, will further attribute to inappropriate, inadequate or delayed therapy and hence to the emergence and spread of resistant organisms to other patients. (WHO, 2011) Lack of compliance to basic standard infection control procedures also contributes to the spread of resistant organisms between patients, medical personnel and the community as a whole further posing a serious public health problem, since future generations may contract infections that are resistant to any treatment (Cecchini *et al*, 2015).

Strategies to prevent the emergence and spread of healthcare associated antimicrobial-

resistant organisms as antimicrobial stewardship and implementation of infection prevention and control measures are therefore, essential. One of the most important criteria in antimicrobial stewardship is establishing a system for monitoring bacterial resistance and practice guidelines or antibiotic policies to control the use of antibiotics, and respond to data from the monitoring system (CDC, 2017).

Hospitals whether large or small, should design their own local antimicrobial policy according to the trend and pattern of resistant organisms within their facility, and hence clinicians must follow such policies (WHO,2015)

This study aimed to assess the antimicrobial resistance pattern of organisms revealed from culture and sensitivity antibiograms for long term inpatients; including intensive care unit [ICU] patients from a public hospital and accordingly present a simple means to construct an antibiotic resistance policy.

Materials and Methods

Culture and sensitivity was performed for all samples (urine, sputum, blood, wounds) using Bauer and Kirby method. The antibiotic discs [Oxoid]represented a combination of narrow and broad spectrum antibiotics as displayed in tables 1, 2 and 3. Inhibition zones were measured. The resistance pattern revealed from antibiograms for all samples was recorded for a 12 months period. Results were tabulated and an antibiotic resistance policy was constructed according to the pattern of resistance (Jorgensen *et al*, 2009 and CLSI,2009)

Results and Discussion

Based on the results of antibiograms the following was revealed:

The primary aim of the hospital antibiotic policy is to minimize themorbidity and mortality due to antimicrobial-resistant infection; and to preserve the effectiveness of antimicrobial agents in the treatment and prevention of communicable diseases. It is essential for prophylaxis, empirical and definitive therapy (WHO 2011).

The most commonly isolated pathogens from all samples were *S. aureus, E.coli, K.pneumoniae and P. aeruginosa. E.coli* recorded the highest percentage of resistance in all samples [75.2% for sputum, 74.3%for blood, 65.8% for wounds], while *S.aureus* isolates showed the least resistance [40.0% for sputum, 30.0% for blood]; *K.pneumoniae* revealed the least resistance [19.4% for wounds]. However, all bacterial isolates revealed a similar 40.0% resistance in urine samples (Figures1, 2, 3, 4 and 4).

Collectively, *S. aureus* isolates displayed a 65% to a 100% resistance to first and third generation cephalosporins, 71.43% resistance to Meropenem and fortunately only 7.14% for Vancomycin and no resistance to Linezolid (Table 1).

E. coli isolates and *K.pneumoniae* isolates showed a similar range of resistance (65% to 100%) to first, second and third generation cephalosporins, and approximately a 93.0% resistance to Ampicillin- Clavulanic acid. *E. coli* demonstrated a 90.0% résistance to Ampicillin – Sulbactam however, *K. pneumoniae* displayed a lower percentage of resistance(79.0%). The percentage of resistance to fluoroquinolones was much higher for *E. coli* isolates compared to *K.pneumoniae;* namely Ofloxacin 68.18% to 41.67%, Ciprofloxacin 56.25% to 29.63%. (Table 2)

P.aeruginosa isolates were 100% resistant to Ampicillin- Clavulanic acid, Tetracyclin, Rifampicin, and some third and fourth generation cephalosporins, and a range of 80% to 90% resistance to second generation cephalosporins (Table 3).

Table.1 Antibiotic Resistance for *Staphylococcus aureus* isolates in all samples

Antibiotic	Resistance	
	No.	%
Penicillin	4/5	80.00
Ampicillin	6/6	100.0
Oxacillin	6/6	100.0
Flucloxacillin	0/2	0.0
Methicillin	11/13	84.62
Amoxacillin-Clavulanic	8/14	57.14
Ampicillin-Sulbactam	9/15	60.00
Pipracillin-Tazobactam	0/4	0.0
Cefalexin	1/1	100.0
Cefoxitin	3/6	50.00
Cefruxime	2/9	22.22
Cephalocin	1/3	33.33
Ceftriaxone	6/14	42.86
Cefotaxime	4/6	66.67
Cefperazone	8/17	47.06
Cefepime	2/7	28.57
Ceftazidime	1/1	100.0
Cefoperazone-Sulbactam	0/7	0.0
Ofloxacin	0/3	0.0
Ciprofloxacin	1/8	12.50
Norfloxacillin	1/1	100.0
Nitrofurantion	0/1	0.0
Tetracycline	5/5	100.0
Erythromycin	2/7	28.57
Vancomycin	1/14	7.14
Gentamycin	3/7	42.86
Amikacin	4/11	36.36
Chloramphenicol	4/9	44.4
Trimethopim-Sulphamethxazole	4/8	50.00
Imipenem	3/10	30.00
Meropenem	5/7	71.43
Rifampicin	2/13	15.38
Linezolid	0/15	0.0

From Table (1) it is evident that the highest percentage of resistance to *S. aureus* isolates was for Ampicillin, Oxacillin, Cefalexin, Ceftazidime, Norfloxacillin and Tetracycline (100%) followed by Methicillin (84.62%), then Meropenem (71.43%), with the least resistance to Vancomycin (7.14%) and no resistance to Flucloxacillin,Pipracillin-Tazobactam,Cefoperazone-Sulbactam,Ofloxacin,Nitrofurantion and Linezolid (0.0%).

Table.2 Antibiotic resistance for *E.coli and K.pneumoniae* isolates in all samples

Antibiotic	Resistance *E.coli*		*K.pneumoniae*	
	No.	%	No.	%
Flucloxacillin	2/5	40.00	0/5	0.0
Amox/Clavulanic	16/17	94.12	27/29	93.10
Amp/Sulbactam	18/20	90.00	23/29	79.31
Piprac/Tazobactam	3/14	21.43	6/21	28.57
Cefuroxime	7/7	100.0	17/26	65.38
Cefalexin	16/22	72.73	1/1	100.0
Cephalocin	17/23	73.91	9/13	69.23
Ceftriaxone	12/16	75.00	17/9	58.62
Cefotaxime	19/23	82.61	11/17	64.71
Cefoperazone	8/18	44.44	16/24	66.67
Cefepime	15/20	75.00	9/20	45.00
Ceftazidime	2/9	22.22	13/20	65.00
Cefop/Sulbactam	7/9	77.78	5/16	31.25
Ofloxacin	15/22	68.18	5/12	41.67
Ciprofloxacin	9/16	56.25	8/27	29.63
Norfloxacin	1/14	7.14	2/8	25.00
Nitrofurantion	3/8	37.50	2/6	33.33
Tetracycline	1/1	100.0	7/14	50.00
Gentamycin	7/15	46.67	9/15	60.00
Amikacin	5/23	21.74	6/23	26.09
Chloramphenicol	2/7	28.57	2/11	18.18
Trim/Sulphameth	11/15	73.33	6/11	54.55
Imipenem	2/21	9.52	2/24	8.33
Meropenem	5/10	50.00	3/8	37.50
Rifampcin	4/4	100.0	9/9	100.0

From Table (2) it is concluded that the highest percentage of resistance (100%) to *E.coli* isolates was for Cefuroxime and Rifampicin whereas the 100% resistance to *K.pneumoniae* isolates was for Cefalexinand Rifampicin. This was followed by resistance to Ampicillin- Clavulanic acid (94.12%, 93.10%) and Ampicillin – Sulbactam (90.0%,79.0%) respectively. The least percentage of resistance for *E.coli* was7.14% for Norfloxacin whereas *K.pneumoniae* was least resistant to Imipenem (8.33%) and had no resistance to Flucloxacillin (0.0%).

Table.3 Antibiotic Resistance of *Pseudomonas aeruginosa* isolates in all samples

Antibiotic	Resistance	
	No.	%
Ampicillin	1/2	50.00
Flucloxacllin	3/4	75.00
Amoxacillin-Clavulanic Acid	5/5	100.0
Ampicillin-Sulbactam	7/10	70.00
Pipracillin-Tazobactam	1/8	12.50
Cefuroxime	4/4	100.0
Ceftriaxone	8/10	80.00
Cefotaxime	5/6	83.33
Cefoperazone	8/9	88.89
Cefepime	3/3	100.0
Ceftazidime	5/7	71.43
Cefoperazone-Sulbactam	0/4	0.0
Ofloxacin	1/2	50.00
Ciprofloxacin	4/7	57.14
Norfloxacin	1/1	100.0
Tetracycline	4/4	100.0
Gentamycin	6/8	75.00
Amikacin	2/8	25.00
Chloramphenicol	3/5	60.00
Trimethopim-Sulphamethxazole	4/5	80.00
Imipenem	1/7	14.29
Meropenem	4/5	80.00
Rifampcin	1/1	100.0

From Table (3) it is evident that the highest Percentage of resistance to *P. aeruginosa* isolates was to Amoxacillin-Clavulanic acid, Cefipime, Cefuroxime, Norfloxacin, Tetracycline and Rifampicin (100%) followed by Cefoperazone (88.8%) then Cefotaxime (83.3%) then Ceftriaxone (80%). The least percentage of resistance was to Pipracillin-Tazobactam (12.50%), with no resistance to Cefoperazone-Sulbactam (0.0%).

Figure.1 Sputum culture sensitivity pattern for isolated pathogens
S.aureus isolates displayed the least percentage of resistance(40.0%) to all tested antibiotics. On the other hand, *E.coli* isolates revealed the highest percentage of resistance.(75.2%).

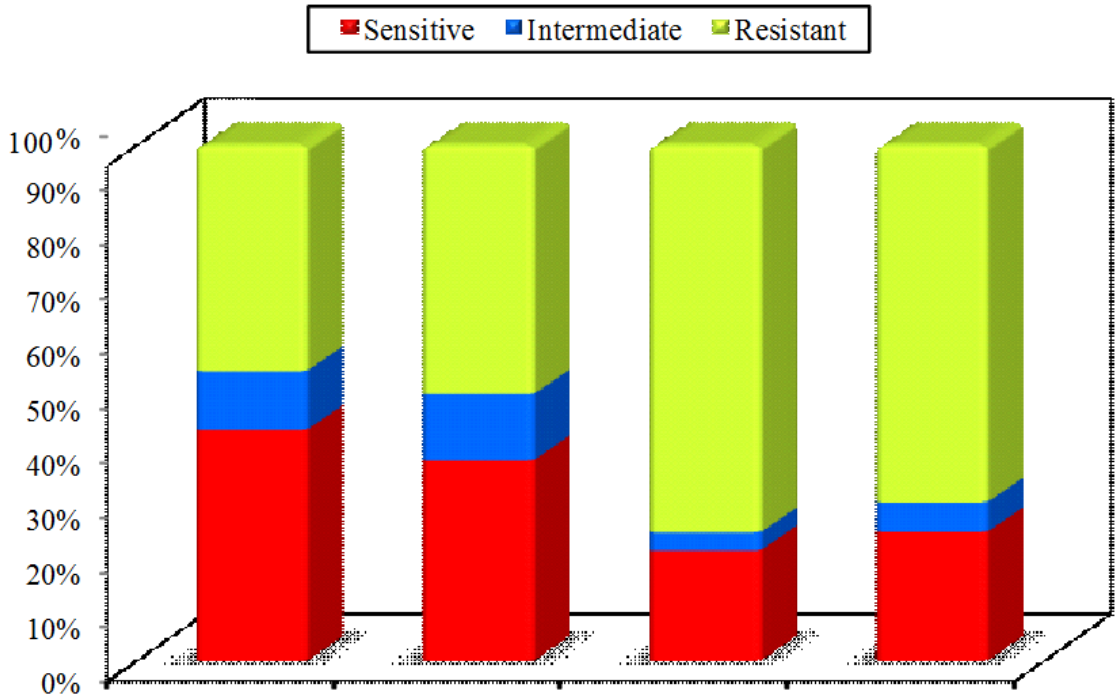


Figure.2 Urine culture sensitivity pattern for isolated pathogens
All pathogens showed an equal percentage of resistance (40.0%) to all tested antibiotics

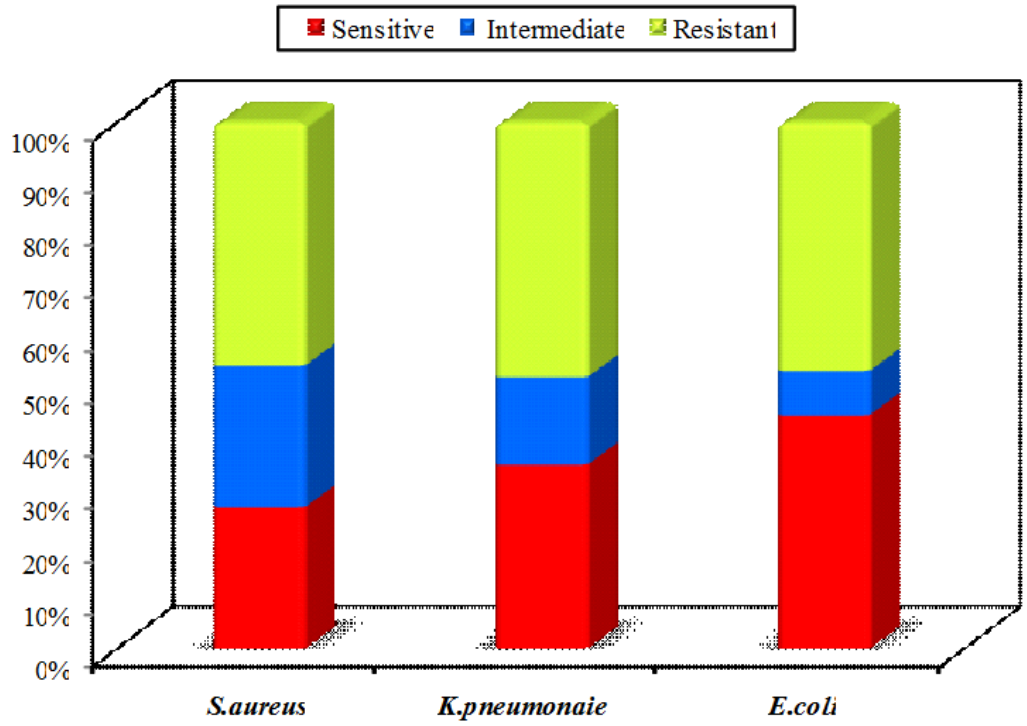


Figure.3 Blood culture sensitivity pattern for isolated pathogens
S.aureus isolates showed the least percentage of resistance (30.0%) to all tested antibiotics, whereas *E.coli* isolates showed the highest percentage of resistance (74.3%).

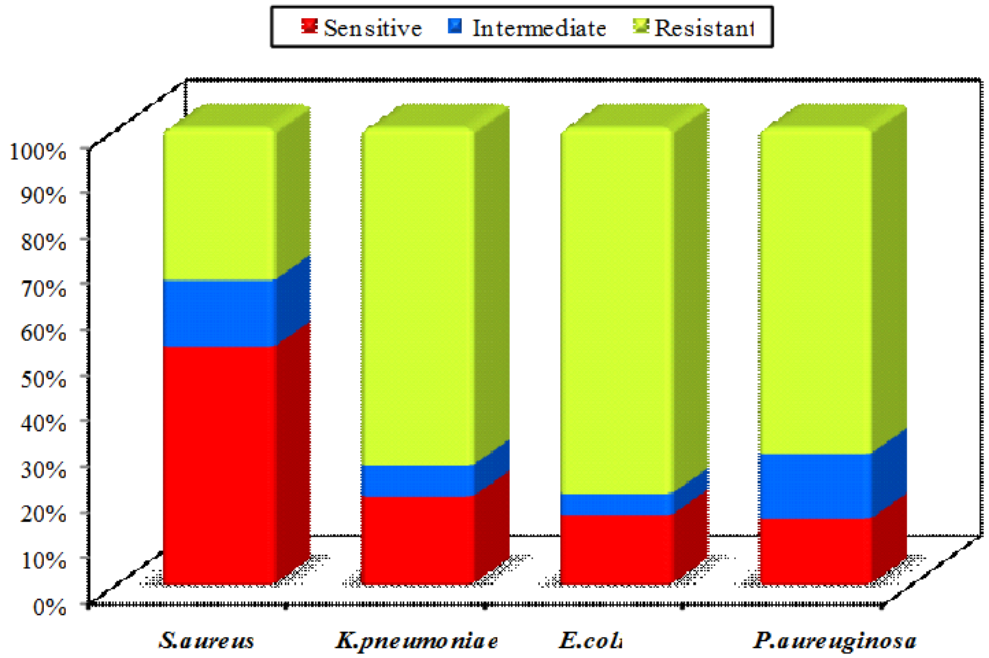
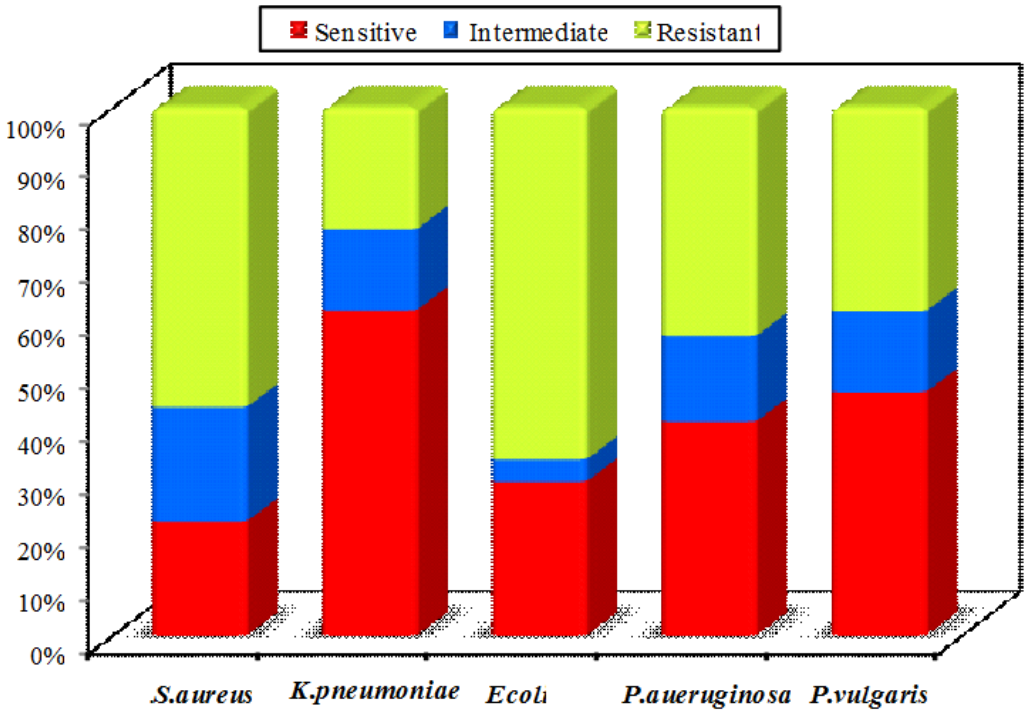


Figure.4 Wound culture sensitivity pattern for isolated pathogens
K.pneumoniae isolates displayed the least percentage of resistance (19.4%) to all tested antibiotics, whereas *E.coli* isolates showed the highest percentage of resistance (65.8%).



Laboratories should use standards for reporting quantitative resistance data (e.g. minimal inhibitory concentrations or zone diameters) that will detect decreased susceptibility. This is necessary because antimicrobial test results reported qualitatively (e.g., as susceptible, intermediate, or resistant) may hide an emerging resistance character in microorganisms with a small decrease in susceptibility that may still be classified as susceptible.

A reliable cumulative antibiogram should only include final, verified results of diagnostic species with at least ≥ 30 tested isolates. It should also include the first isolate obtained per patient during the assigned period for analysis, irrespective of the site of specimen collection or the antimicrobial susceptibility pattern. Isolates with intermediate susceptibility should not be included in the calculation of the percentage of isolates that are susceptible (WHO, 2015).

The conclusions of the study are as follows

Antibiotic policy

An antibiotic policy is divided into levels for prescribing antibiotics; first choice antibiotics can be prescribed by all clinicians, while restricted choice and reserve antibiotics can only be prescribed after consulting an infectious disease expert clinician and a clinical microbiologist (Marston *et al.,* 2016, CDC, 2017)

First choice antibiotics for non-restricted use (empirically)

The antimicrobials that showed the least resistance patterns for all pathogens may be prescribed without approval by all clinicians orphysicians. Antibiotics may be written individually by generic name or as a group [eg. second or third generation cephalosporins].

The specimen for the culture and sensitivity testing must be taken before the beginning of the empirical course of antibiotics, which includes the antibiotic disc that represents the empirical antibiotic. If the antibiotic was found to be sensitive according to the results of the antibiogram, then the empirical therapy may be continued; however if found resistant, therapy must be altered to another sensitive antibiotic.

Restricted choice antibiotics

These antibiotics may be more expensive and/or have a wider spectrum of activity and should only be used for specified more serious clinical conditions such as empirical emergency treatment of suspected serious or life-threatening infections pending the result of culture and sensitivity testing.

Reserved antimicrobials

These antibiotics should be reserved for multidrug resistant pathogens causing life-threatening infections[eg. Vancomycin for MRSA].They should only be used when culture and sensitivity testing has indicated resistance to other antibiotics. The intermediate sensitive drugs are only used as an alternative if no sensitive antibiotics were revealed in the antibiogram results, or are commercially.

Recommendations

The most important strategy to decrease antibiotic resistance is to apply an antibiotic stewardship system to change the pattern of prescription and use. This may be achieved by developing policies for appropriate use of antibiotics in each hospital, based on local resistance surveillance data from

antibiograms, and monitoring the compliance and proper implementation of the policy. Moreover, ensuring a quality controlled performance and procedures for microbial identification and antibiotic susceptibility of key pathogens.

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