Brief Original Article

Antimicrobial stewardship approach: Prevalence of antimicrobial resistant bacteria at a regional hospital in South Africa

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Abstract

Introduction: Antimicrobial stewardship practices are crucial for the regular surveillance to change the antimicrobial policy. This study was conducted to decide the prevalence of common bacteria and their antibiogram regarding antimicrobial stewardship program within one year, at the regional and district, Stanger hospital in South Africa.

Methodology: It was based the study on clinical data and laboratory records of the patients. It reviewed the clinical and laboratory data. The prevalence/proportion rate was calculated and correlated with the majority of microorganism vs empirical therapy.

Results: The prevalence of MRSA, MRSE, VRSA, ESBL+ *K. pneumoniae*; *E. coli* cultured from the blood was 25%, 49%, 2%, 62% and 27% respectively. Similarly, we analysed for other targeted MDROs organisms (*Acinetobacter* species and *P. aeruginosa, CRE, CPE*) isolated from blood culture and endotracheal aspirate. The prevalence of MDR *Acinetobacter* species exceeded 61%, 33% from the blood and ETA respectively. The prevalence of MDR *P. aeruginosa* was 10% from ETA. The MRSA, MRSE, VRSA, VRE were observed in blood specimen. The majority of the microorganisms cultured from the CSF was *Cryptococcus neoformans* and followed by bacteria: *Streptococcus pneumonia*, *Streptococcus group B* and *Haemorphilus influenza*.

Conclusion: The selection of empirical antimicrobial therapy relates not only the institutions or unit-specific antibiogram but also the site of infection. We can further suggest continuing to do surveillance of antibiogram and prevalence of MDR organisms for infection control as well as for empirical therapy, part of the antimicrobial stewardship program based on yearly records to change the local hospital antibiotic policy.

Key words: prevalence; surveillance; antimicrobial resistant bacteria; empirical therapy; Antimicrobial stewardship program.

Introduction

Antimicrobial stewardship (AMS) practices are crucial for minimise the unnecessary use of antimicrobials and promote the appropriateness of antimicrobial prescribing to improve patient outcomes, cost-effective therapy and reduced adverse consequences of antimicrobial use [1,2]. The prevalence of antimicrobial resistant bacteria from blood and other targeted specimens: cerebrospinal fluid (CSF) and endotracheal aspirate (ETA) in hospital influenced by selective pressure of antimicrobials used in a hospital. Infection control, antibiotics stewardship practices within the hospital, type of hospital and risk factors in a patient are crucial for the regular surveillance to modify the antimicrobial policy [3]. This information is valuable in choosing empirical antimicrobial therapy for serious hospital acquired infections especially for sepsis, meningitis and pneumonia [4] and even for community acquired infections. The mistreatment of antibiotics has also contributed to the growing problem of antibiotic resistance, which has become one of the most serious and growing threats to public health [5]. Unlike other medications, the potential for spread of resistant organisms means that the mistreatment of antibiotics can adversely influence the health of patients who are not even exposed to them. The Centers for Disease Control and Prevention (CDC) estimates more than two million people are infected with antibiotic-resistant organisms, resulting in approximately 23,000 deaths annually [6]

It undertook this study to find the common microorganisms isolated and the prevalence of antimicrobial resistant bacterial isolates from blood,

CSF and ETA specimens at regional and district hospital in Kwa-Dukuza within the ILembe Health District, South Africa. This origin research will aid the infection prevention and control, AMS including modification of antibiotic empirical therapy.

Methodology

We analysed, over a year period (1st April 2016 to 31st March 2017), the antimicrobial resistance profile of cultured bacterial isolates of blood, CSF and ETA specimens, from Stanger hospital, to certain marker antibiotics. Stanger Hospital is a 500-bedded regional and district hospital. The hospital is located in Kwa-Dukuza within the ILembe Health District. The hospital serves an estimated population of 600,000 from the ILembe District (www.kznhealth.gov.za/stangerhospital.htm).

It based the study on the clinical and laboratory records of the patients at the regional and district hospital. It searched the data from central data warehouse (CDW) analysed by Pathologist. It recorded the data as targeted common potential microorganism, type of specimens and antimicrobial susceptibility results.

It defined study population as patients with suspected infections from specific targeted wards (ICU, Male, Female surgical and medical wards, obstetric gynaecology wards, paediatrics (including neonatal unit) and casualty department) during the study period. Clinicians sent the representative samples of suspected septic patients.

Only one representative isolate from each specimen per patient, regardless of clinical significant isolates, was included in the analysis. The microorganisms isolated from the blood culture, CSF and ETA in the analyses were mainly *Klebsiella pneumoniae*, *E. coli*, *Pseudomonas aeruginosa*, *Acinetobacter* species, and *Staphylococcus aureus*. The selected marker antibiotics were aminoglycosides (gentamicin and amikacin), beta lactams (piperacillin–tazobactam), fluoroquinolone (ciprofloxacin), carbapenems (meropenem) and cloxacillin (methicillin).

Multi-Drug–Resistance (MDR) in the Gram-negative isolates was defined as resistance to three or more first line classes (beta lactams, aminoglycoside, fluoroquinolone) of antibiotics or resistant to carbapenem, ESBL-producing organisms, for that particular isolate [7]. Suspected Carbapenem producing enterobacterecae (CPE) organisms were resistant to the aminoglycosides (gentamicin and amikacin), beta lactams (piperacillin–tazobactam), and fluoroquinolone (ciprofloxacin) although sensitive to the carbapenems in vitro test and some are still sensitive to amikacin and ciprofloxacin [8]. CRE were resistant to carbapenems [9].

Table 1. Percentage (Number) of potential pathogens cultured and resistance profile.

Microorganisms cultured (one year study period)	Specimens		
	Blood %(n)	CSF % (n)	ETA %(n)
MRSA	25 (14/57)		50 (2/4)
MRSE	49 (117/237)		
VRSA	2 (1/57)		
VRE	(1)		
ESBL + *K. pneumoniae*	62 (31/50)		51 (41/81)
CRE- *K. pneumoniae*	0		2 (2/81)
CPE- *K. pneumoniae*	10 (5/50)		9 (7/81)
Ciprofloxacin resistant GNB- *K. pneumoniae*	16 (8/50)		30 (24/81)
Total number of *K. pneumoniae* isolated	**(50)**		**(81)**
ESBL + *E. coli*	27 (11/41)		36 (4/11)
CRE- *E. coli*	0		9 (1/11)
CPE- *E. coli*	10 (4/41)		9 (1/11)
Ciprofloxacin resistant GNB – *E. coli*	34 (14/41)		18 (2/11)
Total number of *E. coli* isolated	**(41)**		**(11)**
MDR *Acinetobacter.* species	61 (11/18)		33 (5/15)
MDR *P. aeruginosa*	0 (0/14)		10 (2/21)
Cryptococcus neoformans		90 (46/51)	
Streptococcus pneumoniae		6 (3/51)	
Strep. Group B		2 (1/51)	
Haemophilus influenzae		2 (1/51)	
Total number of specimen type cultured positive	417	51	132

MRSE: Methicillin resistant *Staphylococcus epidermidis*; VRSA: Vancomycin resistant *S. Aureus*; VRE: Vancomycin resistant *Enterococcus faecalis*; Cip: Ciprofloxacin.

The bacterial isolates were identified using automatic laboratory techniques Vitek® 2 system (bioMérieux, Marcy-l'Etoile, France) and antimicrobial susceptibility was interpreted as recommended by CLSI, USA. Extended beta lactamase production (ESBL), MDR, CPE, CRE and methicillin resistant *Staphylococcus aureus (MRSA)* were detected as well [10] It performed simple data analysis based on laboratory database.

There was total number of specific multidrug resistant isolates in specific specimen for a study time as numerator whereas total number of specific organisms from the specific specimen for a study time as denominator. Prevalence rate is a proportion and can be expressed as a percentage.

Results

The prevalence (proportion) of MRSA, MRSE, VRSA, ESBL produced *K. pneumoniae*; *E. coli* cultured from the blood was 25%, 49%, 2%, 62% and 27% respectively (Table 1). Similarly, we analysed for other targeted MDROs organisms (*Acinetobacter* species and *P. aeruginosa, CRE, CPE*) isolated from blood culture and ETA (Table 1, Figures 1, Supplementary Figure 1).

Although there were high percentage for some organisms, the total number of isolates (denominators) were less than 10. Because of these reasons, Figure 2, Supplementary Figure 1 and 2 showed the number of isolates rather than percentages.

The prevalence/ proportion of MDR *Acinetobacter species* exceeded 61%, 33% from the blood and ETA respectively (Table 1, Supplementary Figure 1). It showed the challenge to choose the appropriate treatment for sepsis patients. The prevalence of MDR *P. aeruginosa* was 10% from ETA and 0% from the blood culture.

Our study also analysed the antibiogram that showed a resistant percentage of drugs for Gram-negative bacteria (GNB) was varied from blood and ETA specimens in all targeted wards (Table 1, Figures 1, Supplementary Figure 1). The MRSA, MRSE, VRSA, VRE were observed in blood specimen (Table 1, Supplementary Figure 2).

Most of the microorganisms cultured from the CSF was 90% (46/51) *Cryptococcus neoformans* and followed by the bacteria 10% (5/51): three *Streptococcus pneumoniae*, one *Strep group B* and one *Haemorphilus influenza* (Table 1, Figure 2). All CSF specimens were received from the female, male medical wards, casualty department and paediatrics units according to the data records. The causative organism causing meningitis was *C. neoformas* mainly for adult patients at casualty department.

The later bacteria (*S. pneumoniae, Streptococcus Group B, H. influenzae*) were isolated from the paediatric wards. It is statistically not acceptable if the denominator was less than 10.

Discussion

Blood culture

It received the blood cultures specimens, for the microscopic examination, culture and susceptibility (MCCS), from the different wards at the district hospital. Interpreting blood culture results will navigate to exclude the primary or secondary bacteraemia part of the septic screen and prepare for proper management of infectious causes of sepsis.

Figure 1. The Prevalence of Resistant *K. pneumoniae* and *E. coli* isolated from Blood and endotracheal aspirate (ETA) specimens.
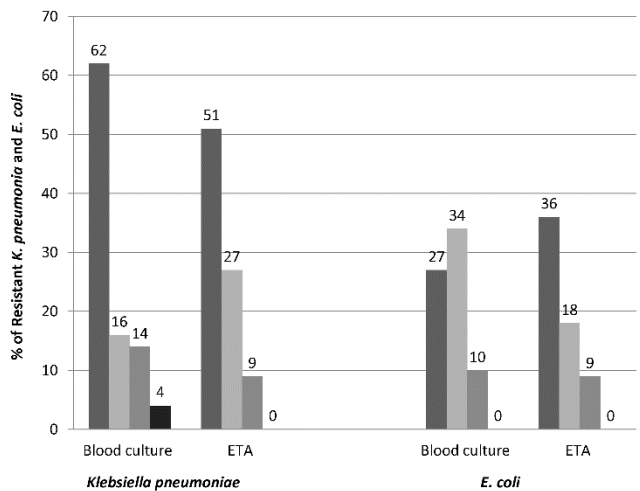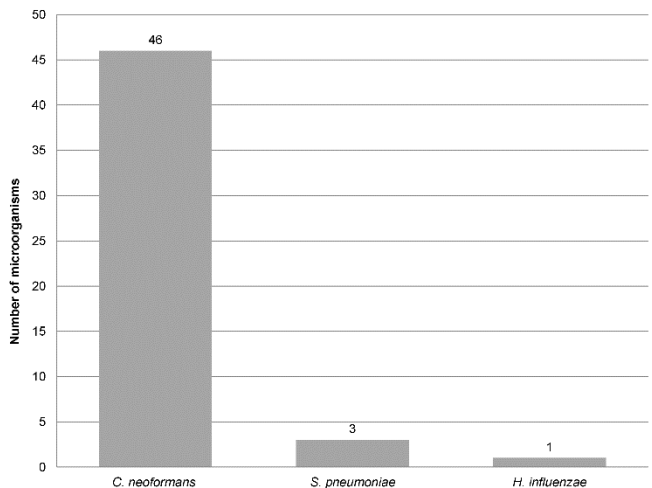

Figure 2. Numbers of Microorganisms cultured from CSF within a year period.

Among the different various wards from the hospital, the targeted bacteria were analysed. The study had discovered that the prevalence of ESBL positive *K. pneumoniae, K. pneumoniae* (62%) was higher than those of *E. coli* (27%). However, Ciprofloxacin resistant prevalence was higher among the Gram-negative bacteria, *E. coli* (34%) than *K. pneumoniae* (16%) during study one-year period. Although the CRE were not cultured from the blood, CPE were determined 10% of both *E. coli* and *K. pneumoniae* based on the antibiogram. It still need to be confirmed by using the molecular method [8].

The study indicated that MRSA (25%), MRSE (49%) were cultured from blood. It is important to exclude whether the MRSE was the skin contaminants or not. It might be skin contaminants especially MRSE and should be advised to do the skin disinfection properly before collection of the blood for culture. The worry part which concerned from our study was emerged 2% VRSA and (n = 1) one VRE from the blood culture.

In addition, MDR *Acinetobacter.*species (61%) from blood culture results gave the challenge of antimicrobial agents even for direct therapy. The interpretation of *Acinetobacter.*species were reported as colonisation if the patients were stable clinically. However, we still advised infection control precautions. Moreover, the blood culture positive with *Acinetobacter* species are usually reported as potential pathogen, skin colonization and common potential outbreak organism [3]. There were (n = 14) *P. aeruginosa* isolated that sensitive to the appropriate antimicrobial agents such as piperacillin + tazobactum, amikacin, ciprofloxacin, ceftazidime, and carbapenem.

Daily microbiological results with interpretation and advice were reported to clinicians, and infection control nurses during study period.

ETA

The respiratory specimens including ETA were received from the patients with suspected pneumonia, respiratory tract infections at the various wards, Stanger hospital to figure the potential pathogens with their susceptibility results. The prevalence of ESBL produced *K. pneumoniae, E. coli* were 51%, 36% respectively from ETA. The prevalence of ciprofloxacin resistance was 30 % (*K. pneumoniae)* and 18% (*E. coli)* regardless of the ESBL producers. Nine percent (9%) of both bacteria were considered as CPE. In fact, CRE were emerged from the ETA specimens; two CRE *K. pneumoniae* and one CRE *E. coli*. The

prevalence of MDR *Acinetobacter* species and *P. aeruginosa* were 33% and 10% correspondingly.

The number of MRSA was insignificant (n = 2), 50% (2/4) from ETA during study one-year period (Table 1). Because of variations of MDR GNB cultured from ETA in the study period, the empirical therapy for the respiratory tract infections was correlated with direct confirmed microbiological results. It is essential for the risk groups of patients in the ICU that the quality management must be included infection control and restriction of antibiotics usage.

CSF

The CSF (via lumber puncture) specimens of patients with suspected meningitis were sent. The common cultured microorganisms were *C. neoformans* (n = 46/51: 90%) from the adults- casualty department and female; male medical wards. There were *S. pneumoniae* (n = 3/51: 6%), *Streptococcus Group B* (n = 1/51:2%) and *H. influenzae* (n = 1/51:2%) from the paediatric unit. Those were sensitive to the appropriate drugs such as penicillin, ampicillin, amoxi-clavulanic acid, 3rd generation cephalosporin, ciprofloxacin and erythromycin. Routinely, the casualty department prescribe the 3rd generation cephalosporin for the symptomatic meningitis patients after collection the CSF specimen. According to the facts, the over prescription of the 3rd generation cephalosporin should be restricted in adult patients especially in casualty department.

The choice of empirical antimicrobial therapy relates not only the institutions or unit-specific antibiogram but also the site of infection. It had been reported that significant differences exist between the hospital-wide antibiogram and the individual units antibiogram [3].

Our research indicated that the different common isolates cultured from the blood, CSF and ETA. Therefore, it is necessary to practise direct discussion/communication with clinician and microbiologist for appropriate antibiotics based on susceptibility result. We can further indicate going on to conduct surveillance of antibiogram and prevalence of MDR organisms for both infection control and empirical therapy. The result of the study is an essential part of the antimicrobial stewardship program based on annual records to revise the local hospital antibiotic policy.

Conclusion

Our data illustrated that the overall prevalence of antimicrobial resistance to the marker antibiotics was

high in the bacterial isolates (notably in GNB) selected in regional, district hospital.

The prevalence of resistance was diversified among the type of wards, the specimens and the different microorganisms studied. There were CPE; CRE from the ETA and a significant number of *C. neoformans* in CSF which is of major concern. ESBL producing *Klebsiella, E. coli* were commonly isolated from both blood and ETA. Emerging resistance to amikacin, ciprofloxacin and even the carbapenems in the ESBL producing *Klebsiella and E. coli is* of consideration. MDR *Acinetobacter* species exceeded 50% from blood over the study period. Although comparatively less common, the emergence of CPE, CRE, VRE and VRSA is a worrisome aspect. The selection of empirical antimicrobial therapy is based on the institutions, unit-specific antibiogram and the site of infection. We can further indicate going to conduct surveillance. It is imperative part of the antibiotic stewardship program based on annual records to adjust the local hospital antibiotic policy.

Being a regional and district hospital for the province of KZN, it is possible that patients were once colonised/infected at the time of admission with antimicrobial resistant bacteria or community acquired bacteria.

We are evaluating baseline screening at first admission, precise hand asepsis, rational usage of antimicrobials and extended education to ward staff. These measures must be strengthened to prohibit cross infections, to cut down the mortality rate resulting from nosocomial infections.

It is important that the collaboration between clinician and microbiologist for appropriate antibiotics based on the microbiological result interpretation because of different antibiogram of microorganisms cultured from the different specimens.

The usage of third generation cephalosporin as an empirical therapy at casualty unit should have to determine with caution based on the symptoms and clinical relevant history regarding antimicrobials stewardship program in Stanger hospital.

Surveillance of antibiogram and prevalence of MDR organisms will be done continuously not only for infection control but also for empirical therapy modification annually.

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Conflict of interests: No conflict of interests is declared.

Annex – Supplementary Items

Supplementary Figure 1. The number of resistant Gram-negative bacteria from blood culture and endotracheal aspirate (ETA) specimens.
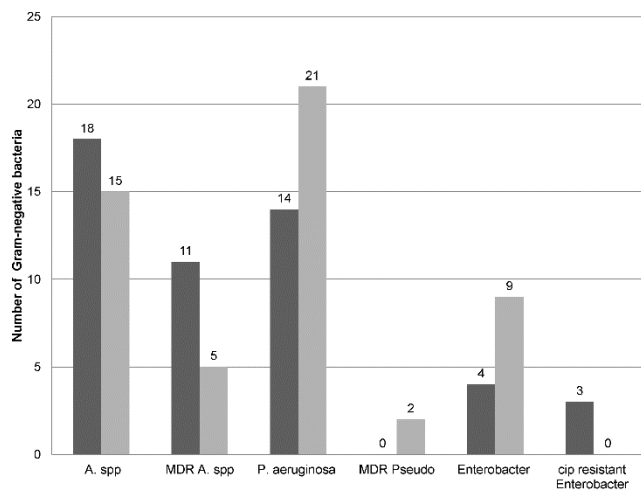
Supplementary Figure 2. The number of Gram-positive bacteria culture from blood culture and endotracheal aspirate (ETA) specimens.