East African Medical Journal Vol. 93 No. 1 January 2016
ANTI-BACTERIAL SUSCEPTIBILITY PATTERNS OF BLOOD CULTURE ISOLATES AT A REFERRAL HOSPITAL IN KENYA
O. C. Oduor, MBChB, MMed, Department of Internal Medicine, School of Medicine, College of Health Sciences, Moi University, P.O. BOX 4606-30100, Eldoret, Kenya, O. E. Apondi, MBChB, MMed, Department of Child Health and Paediatrics, Moi Teaching and Referral Hospital, Eldoret. Kenya, B. K. Gye, MBChB, MMed, Department of Medical Microbiology and Parasitology, School of Medicine, College of Health Sciences, Moi University, Eldoret, Kenya, W. Siika, MBChB, MMed, FRCA, Department of Anaesthesia and Critical Care, Moi Teaching and Referral Hospital, Eldoret, Kenya and M. K. Kipkoech, BSc, MSc, Kenya Medical Research Institute-Center for Global Health Research, HIV Implementation Science and Services, Kisumu, Kenya

Request for reprint to: Dr. O. C. Oduor, Department of Internal Medicine, School of Medicine, College of Health Sciences,Moi University, P.O.BOX 4606-30100,Eldoret, Kenya

ANTI-BACTERIAL SUSCEPTIBILITY PATTERNS OF BLOOD CULTURE ISOLATES AT A REFERRAL HOSPITAL IN ELDORET

O. C. ODUOR, O. E. APONDI, B. K. GYE, W. SIIKA and M. K. KIPKOECH

ABSTRACT

***Background*: Hospital treatment guidelines are often guided by scientific evidence of efficacy of the anti-microbial agents. In developing countries, most of the treatment guidelines are adopted from the World Health Organisation (WHO). However, local data is often needed to confirm or adjust these guidelines to suit a local situation. In resource limited settings there is scarce data on blood culture isolates and their anti-microbial sensitivity patterns to guide anti-biotic prescription in these settings.**

***Objectives*: To assess the bloodstream bacterial isolates and their anti-biotic sensitivity patterns in patients admitted at a tertiary teaching and referral hospital.**

***Design*: Hospital based laboratory retrospective study**

***Setting*: Moi Teaching and Referral Hospital (MTRH), Eldoret, Kenya.**

***Subjects*: All blood culture specimens received from inpatients at MTRH over a 12 year period from 2002 to 2013.**

***Results*: The median age was 13.4yrs (IQR 0.7-29).Most of the blood samples were from female patients (51.8%). A total of 4046 blood culture samples were analysed of which 29.9% (n=1356) yielded positive growths. Majority of the positive blood cultures were from the New Born Unit (62.4%). *Staph epidermidis* was the most common organism isolated (43.1% n=531) followed by *Klebsiella pneumoniae* (22.8% n=281). Resistance to commonly used anti-biotics (penicillin, cephalosporin) was high among gram positive as well as gram negative organisms. No trend in bacterial isolates was observed over the study period.**

***Conclusions*: *Staph epidermidis* and *Klebsiella pneumoniae* were the most common organisms isolated with higher growth rates occurring in the neonatal and paediatric age groups than in adults. There was no trend in bacterial isolates over the study period. Resistance to commonly used anti-biotics was prevalent.**

INTRODUCTION

Infectious diseases remain the most common reason for hospital visits, hospital admissions and even mortality in sub Saharan Africa (1, 2). Septicemia is one of the leading causes of morbidity and mortality and blood culture is the gold standard in diagnosis (3). In resource poor set ups blood culture and sensitivity testing are not routinely done due to shortage of reagents and the necessary equipment, therefore, empiric anti-biotic treatment is common with poly-pharmacy in an attempt to broaden the anti-biotic cover. These practices compounded by other factors such as self-medication, improper dosing or adherence, contributes to antibiotic drug resistance. Anti-biotic resistance to common organisms has been increasing worldwide with most reports originating from resource rich countries and limited data from sub Saharan Africa (4). Local data on trends of pathogens and their anti-biotic resistance patterns is therefore necessary to inform policy and treatment guidelines aimed at improving antibiotic effectiveness, minimising anti-biotic resistance with resultant improved treatment outcomes. We therefore studied the anti-bacterial susceptibility patterns of blood culture isolates over 12 years at our tertiary

teaching and referral hospital.

MATERIALS AND METHODS

This was a retrospective review of blood culture records from the Microbiology Laboratory at MTRH from January 2002 to December 2013. Laboratory register of all the blood culture requests during the study period was reviewed. Data variables extracted from the register included date of culture request, age and gender, ward of the patient, organism cultured and the anti-biotic sensitivity profile of the isolate. All these variables are routinely captured in the microbiology laboratory record book. Blood specimens were cultured in BACTEC 9120 and BACTEC 9050 (Becton-Dickinson, New Jersey, USA) automated systems. Positive BACTEC blood culture vials were sub-cultured into blood culture plates overnight at 37degrees Celsius. Bacterial identification was done using standard bacteriological techniques such as colony morphology, gram staining and rapid bench tests. Anti-biotic sensitivity was performed by disc diffusion method using modified Kirby-Bauer technique and susceptibility reported based on Clinical and Laboratory Standards Institute (CLSI) susceptibility criteria (5). Our laboratory is certified by the International Organization for Standardisation (ISO 15189) and has internal quality management systems. Data were analysed using SAS version 9.3 (SAS Institute Inc., Cary, NC). Categorical variables are presented as frequencies and percentages while continuous variables are expressed as medians and inter-quartile ranges.

RESULTS

A total of 4552 blood culture samples were received from 2194 (48.2%) males and 2358 (51.8%) females with no repeat samples from the same patient. The median age was 13.4 years (IQR of 0.7- 29.0) with an age range from one day old neonate to 103 year old adult. The ward distribution of the samples is shown in table1.

The overall positivity rate on the samples tested was 29.9 % with the new born unit (NBU) leading with a rate of 62.4%. These summaries are shown in table 2. The N for table 2 is lower than that for table 1 since some samples that were received in the laboratory without a ward designation assigned were excluded from the analysis.

The prevalence of the organisms ranged from moderate to very low. *Staphylococcus epidermidis* and *Klebsiella pneumoniae* were the most common isolates as shown in table 3. The distribution of blood culture isolates by ward of admission is as shown in figure 1. There was no trend in bacterial isolates over the study period as shown in figure 2.

The anti-bacterial resistance patterns of gram positive and gram negative pathogens are shown in table 4 and table 5 respectively.

Table 1
Demographic characteristics and ward distribution of participants

Characteristic	N=4552 n (%)
Age, yrs (median, IQR)	13.4 (0.7-29.0)
Gender	
Male	2194(48.2)
Female	2358 (51.8)
Wards	
Medicine(Adult)	1181(25.9)
Paediatric	1200(26.4)
New Born Unit(NBU)	884(19.4)
Surgical	45(1.0)
Obstetrics/gynaecology	105(2.3)
Intensive Care Unit(ICU)	155(3.4)
Others	657 (14.4)
Missing/Unknown	325 (7.1)

N = total number of blood cultures received

Table 2
Blood culture growth rates by ward of admission

Ward	(N=4046) n (%)
Overall positivity	1356 (29.9)
Ward positivity rates	
Adults	219(18.6)
Paediatric	344(28.7)
New Born Unit (NBU)	551(62.4)
Surgical	13(28.9)
Obstetrics/Gynaecology	24(22.9)
Intensive Care Unit (ICU)	32(20.7)
Others	84(12.8)

N = number of samples that had a ward designation assigned

Table 3
Blood culture bacterial isolates

Organism	n (%) percentage
Staph epidermidis	531 (43.1)
Kleb pneumoniae	281 (22.8)
Enterococcus	115 (9.3)
Staph aureus	112 (9.1)
Salmonella spp	66 (5.4)
Contaminants*	43 (3.5)
E. coli	38 (3.1)
Strep pneumoniae	21 (1.7)
Pseudomonas	11 (0.9)
Strep pyogenes	9 (0.7)
Shigella spp	2 (0.2)
Bacillus spp	2 (0.2)

* Organisms considered contaminants included *Citrobacter spp, Providencia spp, Micrococcus spp* and *Acinetobacter spp*.

Table 4
Anti-bacterial resistance patterns of gram positive pathogens

Anti-biotic group	Pathogens; n/N (%)					
	Staph aureus	*Staph epidermidis*	*Strep pneumoniae*	*Strep pyogenes*	*Enterococcus*	*Bacillus*
Ceftriaxone	18/30 (60.0)	60/116 (51.7)	0/2 (0.0)	1/2 (50.0)	24/35 (68.6)	0/0 (-)
Cefipime	9/22 (40.9)	37/84 (44.0)	1/6 (16.7)	1/1 (100.0)	7/16 (43.8)	0/2 (0.0)
Meropenem	8/16 (50.0)	41/95 (43.2)	0/2 (0.0)	0/1 (0.0)	9/19 (47.4)	0/0 (-)
Imipenem	16/31 (51.6)	67/112 (59.8)	0/2 (0.0)	0/3 (0.0)	13/26 (50.0)	0/0 (-)
Gentamycin	10/28 (35.7)	81/167 (48.5)	2/6 (33.3)	2/3 (66.7)	24/42 (57.1)	1/1 (100.0)
Vancomycin	13/47 (27.7)	30/271 (11.1)	1/9 (11.1)	2/2 (100.0)	10/58 (17.2)	0/0 (-)
Amikacin	17/74 (23.0)	61/292 (20.9)	2/7 (28.6)	2/5 (40.0)	29/61 (47.5)	1/2 (50.0)
Linezolid	1/12 (8.3)	3/43 (7.0)	0/1 (0.0)	0/0 (-)	1/9 (11.1)	0/0 (-)
Tazobactam	7/23 (30.4)	19/63 (30.2)	0/2 (0.0)	0/0 (-)	6/12 (50.0)	0/0 (-)
Piperacillin	17/32 (53.1)	86/134 (64.2)	1/3 (33.3)	0/1 (0.0)	15/22 (68.2)	0/0 (-)
Amoxicillin-Clav. acid	11/25 (44.0)	73/151 (48.3)	2/7 (28.6)	1/3 (33.3)	14/22 (63.6)	0/0 (-)
Ampiclox	1/2 (50.0)	0/6 (0.0)	0/2 (0.0)	0/0 (-)	1/1 (100.0)	0/0 (-)
Floxapen	2/3 (66.7)	6/9 (66.7)	2/2 (100.0)	0/0 (-)	3/3 (100.0)	0/0 (-)
Suprapen-flucloxacillin	1/3 (33.3)	4/9 (44.4)	1/3 (33.3)	0/0 (-)	0/1 (0.0)	0/0 (-)
Cloxacillin	2/9 (22.2)	34/62 (54.8)	1/2 (50.0)	1/2 (50.0)	7/8 (87.5)	0/0 (-)
Penicillin*	26/30 (86.7)	80/90 (88.9)	3/3 (100.0)	1/1 (100.0)	17/19 (89.5)	0/0 (-)
Chloramp-henicol	3/8 (37.5)	16/43 (37.2)	2/2 (100.0)	0/0 (-)	10/17 (58.8)	2/2 (100.0)
Levofloxacin	0/0 (-)	0/4 (0.0)	0/0 (-)	0/0 (-)	0/0 (-)	0/0 (-)
Gatifloxacin	0/0 (-)	0/0 (-)	0/0 (-)	0/0 (-)	0/0 (-)	0/0 (-

Penicillin* (Crystalline, Benzyl and penicillin V)
0/0 (-)*(Not tested for the anti-biotic)

Table5
Anti-microbial resistance patterns among gram negative pathogens

	Klebsiella pneumoniae	Pseudomonas	*Salmonella ssp*	*E.Coli*	*Shigella spp*
Ceftriaxone	68/78 (87.2)	1/3 (33.3)	6/16 (37.5)	11/13 (84.6)	0/0 (-)
Cefipime	108/131 (82.4)	2/5 (40.0)	3/13 (23.1)	8/15 (53.3)	0/1 (0.0)
Meropenem	8/115 (7.0)	0/2 (0.0)	1/14 (7.1)	1/14 (7.1)	0/0 (-)
Imipenem	36/75 (48.0)	0/4 (0.0)	6/10 (60.0)	7/10 (70.0)	0/0 (-)
Gentamycin	106/128 (82.8)	4/5 (80.0)	9/37 (24.3)	14/20 (70.0)	1/2 (50.0)
Vancomycin	26/30 (86.7)	0/2 (0.0)	2/2 (100.0)	5/6 (83.3)	0/0 (-)
Amikacin	48/229 (21.0)	3/9 (33.3)	3/49 (6.1)	9/36 (25.0)	1/2 (50.0)
Linezolid	2/3 (66.7)	0/0 (-)	0/0 (-)	1/1 (100.0)	0/0 (-)
Tazobactam	9/28 (32.1)	0/0 (-)	2/5 (40.0)	3/8 (37.5)	0/0 (-)
Piperacillin	65/79 (82.3)	1/2 (50.0)	6/11 (54.5)	11/13 (84.6)	0/0 (-)
Amoxicillin-Clavulanic acid	19/22 (86.4)	1/1 (100.0)	5/14 (35.7)	1/1 (100.0)	1/1 (100.0)
Ampiclox	5/5 (100.0)	0/0 (-)	0/0 (-)	0/0 (-)	0/0 (-)
Floxapen	6/6 (100.0)	0/0 (-)	1/1 (100.0)	1/1 (100.0)	0/0 (-)
Suprapen-flucloxacillin	2/3 (66.7)	0/0 (-)	1/1 (100.0)	0/0 (-)	0/0 (-)
Cloxacillin	13/14 (92.9)	0/0 (-)	3/7 (42.9)	3/3 (100.0)	0/0 (-)
Penicillin*	6/7 (85.7)	0/0 (-)	2/3 (66.7)	0/0 (-)	0/0 (-)
Chloramphenicol	46/49 (93.9)	2/2 (100.0)	9/22 (40.9)	8/13 (61.5)	0/0 (-)
Levofloxacin	0/4 (0.0)	0/0 (-)	0/0 (-)	1/1 (100.0)	0/0 (-)
Gatifloxacin	1/2 (50.0)	0/0 (-)	0/0 (-)	0/0 (-)	0/0 (-)

Penicillin* (Crystalline, Benzyl and penicillin V)
0/0 (-)*(Not tested for the antibiotic)

Figure 1
Blood culture isolates by ward of admission

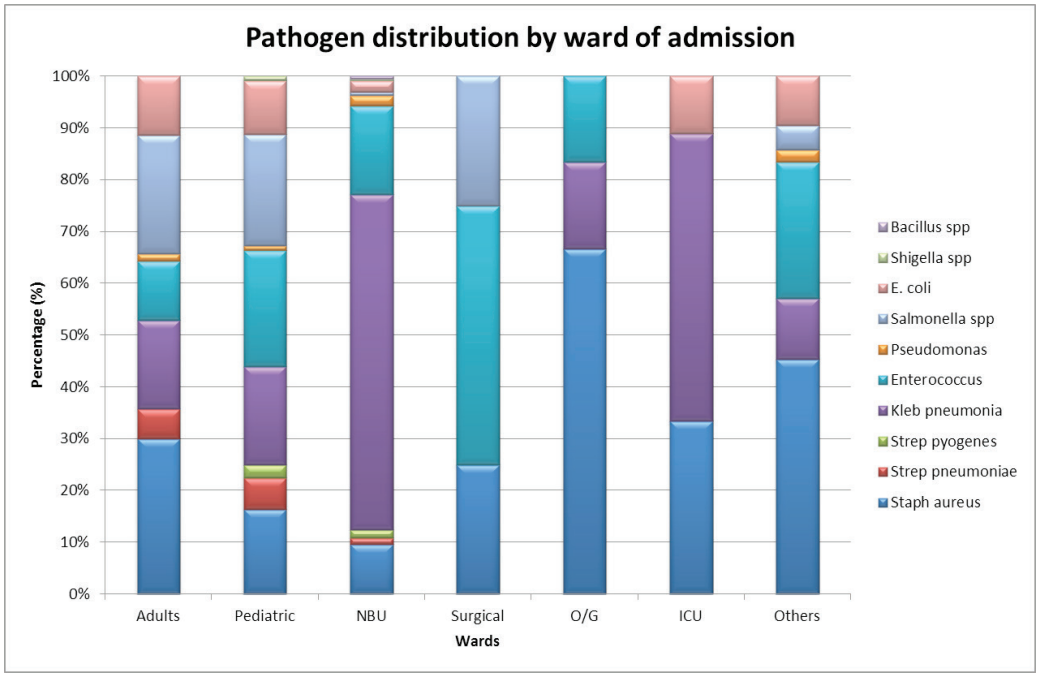
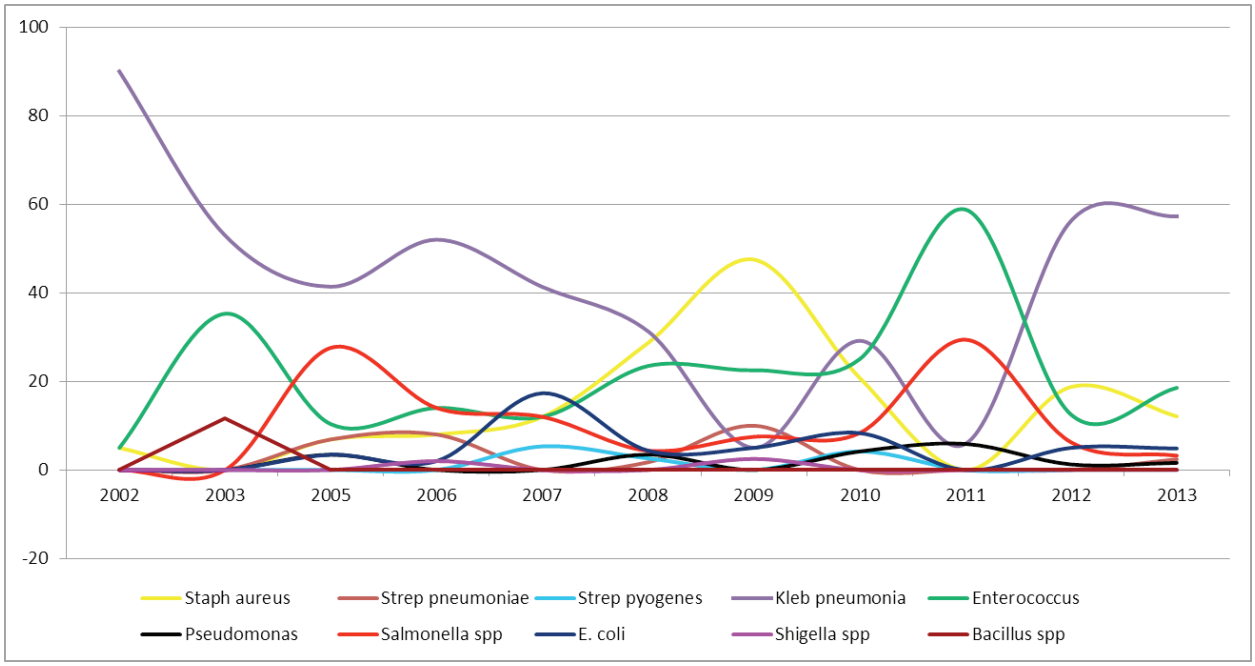


Figure 2
Trends of bacterial isolates over the study period



DISCUSSION

Our results indicate that there was a low overall yield from blood cultures over the study period with only 29.9% positivity rate. This rate is however higher than the overall rate reported by Kohli R *et al* (5.8%) in a study at Aga Khan University Hospital, Nairobi (6). There were more positive blood cultures realised from the NBU (62.4%) and paediatric wards (28.7%) than from the adult wards. Kohli-Kochhar *et al* reported a blood culture positivity rate of 23% over a ten year period in suspected cases of neonatal sepsis at the Aga Khan University Hospital (7). Other studies in the region have reported rates of 13.5% to 31.9% depending on the risk group studied (2, 8).

Staph epidermidis was the most common bacterial isolate in our study at 43.1%. A similar finding was reported by Kohli-Kochhar *et al* who reported a prevalence of 34% among suspected cases of neonatal sepsis and was the most prevalent isolate (7). Edmond *et al* in a study of nosocomial blood stream infections in US hospitals found *Staph epidermidis* (coagulase negative staph) to be the most common organism isolated at 32%(9).Other studies in the US have also identified *Staph epidermidis* as among the most common causative organism of nosocomial infections (10). *Staph epidermidis* is a normal skin commensal and one of the most common sources of infection associated with indwelling medical devices probably as a result of contamination during insertion. Insufficient aseptic techniques during sample collection may also be responsible for its growth as a contaminant in blood cultures. Its clinical significance remains a dilemma for clinicians as some authors suggest that even a single culture of this organism could have clinical significance and should not be ignored. Growth in patients having various indwelling devices should be considered for treatment especially if the growth occurs within 16 hours of sample collection as well as in cases of two positive growths and in patients whose clinical condition is deteriorating (11-15). Our study however did not characterise the clinical presentations of patients with sepsis to determine whether *Staph epidermidis* was a contaminant or a true pathogen.

The recommended treatment in such circumstances is vancomycin since the isolate is often multi-drug resistant including resistance to methicillin (16), however vancomycin resistance has also been reported (17). In our study, *Staph epidermidis* was resistant to most β-lactam antibiotics (>40%) with vancomycin resistance at 11.1% and linezolid 7%.

Klebsiella pneumoniae was the second most prevalent organism isolated constituting 65.5% (205/313) of NBU growths and 50% (5/10) of ICU growths. NBU and ICU have been documented in other studies as the units with highest *K. pneumoniae* burden in both developed and developing countries (18) .It is an opportunistic organism causing severe infections in immuno-compromised patients, patients with prolonged hospital stay and patients with indwelling devices (19, 20). Carbapenem resistant *K. pneumoniae* is considered the most resistant strain and its incidence has been on the rise worldwide (21). The high rate of *K. pneumoniae* isolation could be due to inadequate infection control procedures such as hand washing, disinfection of equipment and congestion. *Enterococcus* was the third most isolated organism

and was the predominant organism isolated from the surgical wards. *Enterococcal* infections are mostly nosocomial and include urinary tract infections, intra-abdominal infections after viscous perforation or surgery and wound infections. Kohli-Kochhar *et al* reported a 12% resistance to gentamycin and 2% resistance to vancomycin which are much lower than rates reported in our study. In India, reported rates of vancomycin resistant *enterococcus* (VRE) range from 0% to 30% (22, 23) .Current treatment options for VRE include linezolid, daptomycin, quinupristin/dalfopristin and tigecycline (24). *Enterococcus* has the ability to transfer drug resistance genes from vancomycin resistant strains (VREs) to *Staphylococcus aureus* thereby promoting cross resistance to antibiotics among pathogens (25).

Staph aureus was most common isolated from the obstetrics/gynaecology wards. We did not characterise *Staph aureus* resistance to methicillin as this is reported in a separate register and is planned for a future analysis. Kohli R *et al* reported methicillin resistance of 21% (6) while Omuse *et al* reported a low prevalence (3.7%) of Methicillin Resistance Staph Aureus(MRSA) in two hospitals in Nairobi, Kenya (26) with no nasal pharyngeal carriage among healthcare workers at Aga Khan University Hospital, Nairobi (7) in contrast to other studies in the region (28, 29). Vancomycin was considered the best alternative for the treatment of MRSA however there are increasing reports of the emergence of vancomycin-resistant Staph aureus (VRSA) strains worldwide (30).We found a VRSA rate of 27.7% contrary to a study by Kohli R *et al* that reported a rate<1% (6). Linezolid and quinupristin/dalfopristin has activity against VRSA and has been approved by Food and Drug Administration (FDA) for the treatment of glycopeptides-resistant Gram positive micro-organisms (31).

Salmonella spp was predominantly isolated from the medical and paediatric wards. There was variable resistance to most common used antibiotics. No organisms were tested for quinolone resistance despite their high use in the treatment of salmonellosis. We did not characterise the *Salmonella spp* into typhoidal and non-typhoidal strains. Various studies have reported resistance of *salmonella spp* to commonly used antibiotics with conflicting results (32-34).

Despite some studies reporting *E. coli* as a common isolate (35, 36), we found a low isolation rate with high resistance to ceftriaxone, vancomycin and gentamycin. *Streptococcus pneumoniae* too was an uncommon isolate with high resistance rates to penicillin. Penicillin resistant *Strep pneumoniae* has been reported with increasing frequency worldwide (37, 38).

Streptococcus pyogens, *Pseudomonas*, *Bacillus spp* and *Shigella ssp* were rare isolates each contributing <1% of total isolates. *Pseudomonas* showed no resistance to carbapenems (meropenem and imipenem). *Pseudomonas* resistance to multiple antibiotics has been described mainly mediated via mutations (39).

Study limitations: Due to low growth rates of some organisms, their antibiotic sensitivity patterns may be unreliable since only a few organisms were subjected to resistance testing.

Due to the retrospective nature of the study design, certain anti-biotics may not have been tested against organisms of interest such as for establishing Extended Spectrum Beta Lactamases (ESBLs).

In conclusion, *Staph epidermidis* and *K. pneumoniae* were the most common organisms isolated with higher growth rates occurring in the neonatal and pediatric age groups than in adults. There was no trend in bacterial isolates over the study period. Gram positive as well as gram negative organisms showed high resistance to crystalline penicillin and ceftriaxone which are most common used antibiotics in our set up.

REFERENCES

1. Petit, P. L. and van Ginneken, J. K. Analysis of hospital records in four African countries, with emphasis on infectious diseases. *J Trop Med Hyg.* 1995 **98**: 217-227.
2. Reddy, E. A., Shaw, A. V. and Crump, J. A. Community-acquired bloodstream infections in Africa: a systematic review and meta-analysis. *Lancet Infect Dis.* **10**: 417-432.
3. Diekema, D. J., Beekmann, S. E., Chapin, K. C., *et al*. Epidemiology and outcome of nosocomial and community-onset bloodstream infection. *J Clin Microbiol.* **41**: 3655–3660.
4. Anibal de, J., Sosa, D. K. B., Carlos, F., Amabile-Cuevas, *et al*. Antimicrobial Resistance in Developing Countries. 2010.
5. (CLSI): C.a.L.S.I. Performance Standards for Antimicrobial Susceptibility Testing. *Twenty-First Informational Supplement Clinical and Laboratory Standards Institute* 2011.
6. Kohli, R., Omuse, G. and Revathi, G. Antibacterial Susceptibility Patterns of Bloodstream Isolates in Patients Investigated at the Aga Khan University Hospital, Nairobi. *East Afr. Med. J.* **87**: 74-80.
7. Kohli-Kochhar, Omuse, G. and Revathi, G. Neonatal bloodstream infections. *J Infect Dev Ctries.* **5**: 799-803.
8. Arthur, G., Nduba, V. N., Kariuki, S. M., *et al*. Trends in Bloodstream Infections among Human Immunodeficiency Virus-Infected Adults Admitted to a Hospital in Nairobi, Kenya, during the Last Decade. *Clin Infect Dis.* **33**: 248-256.
9. Edmond, M. B., Wallace, S. E., McClish, D. K., *et al*. Nosocomial Bloodstream Infections in United States Hospitals: A Three-Year Analysis. *Clin Infect Dis.* **29**: 239–244.
10. CDC: National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January

1992 through June 2004. *Am J Infect Control.* **32**: 470–485.
11. Abdul Rahman, Z., Hamzah, S. H., Hassan, S.A. *et al*: The significance of coagulase-negative staphylococci bacteremia in a low resource setting. *J Infect Dev Ctries.* **7**: 448-452.
12. Beekmann, S. E., Diekema, D. J. and Doern, G.V. Determining the clinical significance of coagulase-negative staphylococci isolated from blood cultures. *Infect Control HospEpidemiol.* **26**: 559-566.
13. García-Vázquez, E., Fernández-Rufete, A., Hernández-Torres, A., *et al*. When is coagulase-negative Staphylococcus bacteraemia clinically significant? *Scand J Infect Dis.* **45**: 664-671.
14. Michael Otto: Staphylococcus epidermidis – the "accidental" pathogen. *Nat Rev Microbiology.* **7**: 555-567.
15. Rogers, K. L., Fey, P. D., and Rupp, M. E. Coagulase-negative staphylococcal infections. *Infect Dis Clin North Am.* **23**: 73–98.
16. Miragaia M.: Molecular characterization of methicillin-resistant Staphylococcus epidermidis clones: evidence of geographic dissemination. *J ClinMicrobiol.* **40**: 430–443.
17. Schwalbe, R. S,. Stapleton, J. T. and Gilligan, P. H. Emergence of vancomycin resistance in coagulase-negative staphylococci. *N Engl J Med.* **316**: 927–931.
18. Savita, J., Rabindranath, M., Nageshawari, G., *et al*. Increasing incidence of multidrug resistance KlebsiellaPneumoniae infections in hospital and community settings. *Int J Microbiol Res.* **253**: 7.
19. Adamski, J., Steggall, M., Yeoh, K. X., *et al*. Outcome of gram negative infection in immunocompromised children. *Pediatr Blood Cancer.* **51**: 499–503.
20. Velasco, E., Byington, R., Martins, C. S. *et al*. Bloodstream infection surveillance in a cancer centre: a prospective look at clinical microbiology aspects. *ClinMicrobiol Infect.* **10**: 542–549.
21. Hirsch, E. B. and Tam, V. H. Detection and treatment options for Klebsiella pneumonia carbapenemases (KPCs): an emerging cause of multidrug-resistant infection. *J Antimicrob Chemother.* **65**: 1119–1125.
22. Agarwal, J., Kalyan, R. and Singh, M. High-level aminoglycoside resistance and beta-lactamase production in Enterococci at a tertiary care hospital in India. *Jpn J Infect Dis.* **62**: 158–159.
23. Fernandes, S. C. and Dhanashree, B. Drug resistance & virulence determinants in clinical isolates of Enterococcus species. *Indian J Med Res.* **137**: 981–985.
24. O'Driscoll, T. and Crank, C. W. Vancomycin-resistant enterococcal infections: epidemiology, clinical manifestations, and optimal management. *Infect Drug Resist.* **8**: 217-230.
25. Noble, W. C., Virani, Z. and Cree, R. G. Co-transfer of vancomycin and other resistance genes from Enterococcus faecalis NCTC 12201 to Staphylococcus aureus. *FEMS Microbiol Lett.* **72**: 195–198.
26. Omuse, G., Kabera, B. and Revathi, G. Low prevalence of methicillin resistant Staphylococcus aureus as determined by an automated identification system in two private hospitals in Nairobi, Kenya: a cross sectional study. *BMC Infectious Diseases.* **14**: 669.
27. Omuse, G., Kariuki, S. and Revathi, G. Unexpected absence of methicillin-resistant Staphylococcus aureus nasal carriage by healthcare workers in a tertiary hospital in Kenya. *J Hosp Infect.* **80**: 71–73.
28. Aiken, A. M., Mutuku, I. M., Sabat, A. J., *et al*. *Antim Resistance and Infect Cont.* **3**: 22.
29. Maina, E. K., Kiiyukia, C., Wamae, C. N., *et al*. Characterization of methicillin-resistant Staphylococcus aureus from skin and soft tissue infections in patients in Nairobi, Kenya. *Int J Infect Dis.* **17**: e115–e119.
30. Benjamin, P. H., John, K. D., Paul, D. R. J., *et al*. Reduced vancomycin susceptibility in Staphylococcus aureus, including vancomycin-intermediate and heterogeneous vancomycin- intermediate strains: Resistance mechanisms, laboratory detection, and clinical implications. *Clin Microbiol Rev.* **23**: 99–139.
31. Schweiger, E. S., Scheinfeld, N. S., Tischler, H. R., *et al*. Linezolid and quinupristin/dalfopristin: novel antibiotics for Gram-positive infections of the skin. *J Drugs Dermatol*. **2**: 378–83.
32. Kariuki, S., Revathi, G., Kiiru, J., *et al*. Typhoid in Kenya is associated with a dominant multidrug-resistant Salmonella entericaserovarTyphi haplotype that is also widespread in Southeast Asia. *J Clin Microbiol.* **48**: 2171-2176.
33. Mengo, D. M., Kariuki, S., Muigai, A., *et al*. Trends in Salmonella enteric serovarTyphi in Nairobi, Kenya from 2004 to 2006. *J Infect Dev Ctries.* **4**: 393-396.
34. Onyango, M. D., Ghebremedhin, B., Waindi, E. N., *et al*. Phenotypic and genotypic analysis of clinical isolates Salmonella serovarTyphimurium in western Kenya. *J Infect Dev Ctries.* **3**: 685-694.
35. Rodríguez-Baño, J., López-Prieto, M. D., Portillo, M. M., *et al*. Epidemiology and clinical features of community-acquired, healthcare-associated and nosocomial bloodstream infections in tertiary-care and community hospitals. *ClinMicrobiol Infect.* **16**: 1408–1413.
36. Valles, J., Palomar, M., Alvárez-Lerma, F., *et al*. Evolution over a 15-year period of clinical characteristics and outcomes of critically ill patients with community-acquired bacteremia. *Crit Care Med.* **41**: 76–83.
37. Alexander, T. Antibiotic Resistance in Streptococcus pneumonia. *Clin Infect Dis.* **24**: S85-88.
38. Whitney, C. G., Farley, M. M. and Hadler, J. Increasing prevalence ofmulti-drug-resistant Streptococcuspneumoniae in the United States. *NEngl J Med.* **343**: 1917-1912.
39. Poole, K. Multidrug efflux pumps and antimicrobial resistance in pseudomonas aureginosa and related organisms. *JMol Microbial Biotechnol.* **3**: 255-264.