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Antibiotic susceptibility profile of the *Klebsiella pneumoniae* isolated from Africa Inland Church Hospital Kijabe, Kenya

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Keywords

antimicrobial,
resistance,
susceptibility,
profile,
Klebsiella pneumoniae

Abstract

The emergence of antimicrobial resistance is primarily due to excessive and often unnecessary use of antibiotics in humans and animals. A study done in low and middle income countries showed a considerable increasing resistance in Enterobacteriaceae (Ashley et al., 2011). The data revealed that affordable first line agents such as ampicillin and gentamicin are unlikely to be clinically efficacious in a substantial proportion of infections. This results in increasing reliance on the third generation cephalosporins for empirical treatment of serious infections. However, the spread of extended-spectrum beta-lactamase producing strains into the community (Ashley et al., 2011), probably accelerated by this increased consumption, is eroding the usefulness of these drugs. Alternative agents for treating multi-resistant coliform infections, such as the carbapenems, are unaffordable for treatment of community- acquired infections in low-income countries. The clinical specimens which were used included; urine, aspirates, blood, cerebral spinal fluid (CSF), swabs of wound, device swabbing. The design was a prospective observational. Ethical approval was sought from the Kenyatta University ethical review committee and the Ethical committee in AIC Kijabe hospital as attached. antimicrobial susceptibility among the 55 blood samples infected with *K. pneumoniae* showed that 100% was resistant to Ampicillin, 98% was resistant to Ceftadime, 86% was resistant to Ceftriaxone, 83% was resistant to Cefazolin, and none of the isolates was resistant to Meropenem. To test whether the difference in means in relation to antibiotics resistance in Klebsiella pneumoniae isolates was significant, analysis of variance (ANOVA) statistic was used. This parametric test was used to test the hypothesis that there is no antibiotics resistance in *Klebsiella pneumoniae* isolates from AIC Kijabe hospital. The result of analysis indicated that there was statistically significant difference among the means scores 5.547 at 0.05. It was concluded that use of antibiotics has influence on effective management in *Klebsiella pneumoniae* isolates from AIC Kijabe hospital. This study through its findings recommends that; Regular antimicrobial audits and reviews of laboratory data (surveillance) should be done so as to have proper documentation of drug resistance patterns and timely updates of antibiotic formularies. The study focused on AIC Kijabe Hospital Kiambu County only, therefore, the same study can be extended in other hospitals and other counties for comparison purposes

Introduction

Nosocomial infections are responsible for morbidity, mortality and prolonged hospitalization leading to increased hospital cost (Ducel et al, 2012; Inweregbu et al, 2015). Hospital acquired infections are also associated with multi drug resistance especially antibiotics. These are easily transmitted from healthcare workers to patients and vice versa (Ducel et al, 2012).). Nosocomial infections can cause pneumonia, surgical site infections (SSI), Urinary tract infections (UTI) and Catheter-related blood stream infections (BSI) (Corona and Raimondi, 2004). The surgical site infections affect patients after operations causing post-operative morbidity (Edwards et al, 2008). The risk of contracting nosocomial infections in ICU is highest than other wards in any healthcare unit. A study done by Hakan Erbay et al (2004) shows that a higher mortality rate (60.9%) for infected ICU patients. Nosocomial infections are mostly caused by Klebsiella spp especially the pneumonia species. It is estimated that Klebsiella spp causes 8% of all hospital acquired bacterial infections in the United States of America (USA) and Europe. In the USA Klebsiella spp accounts for 3 to 7% of all nosocomial infections placing them among the eight most infectious pathogens in hospitals (Schaberg, 2010).

The emergence of antimicrobial resistance is primarily due to excessive and often unnecessary use of antibiotics in humans and animals. A study done in low and middle income countries showed a considerable increasing resistance in Enterobacteriaceae (Ashley et al., 2011). The data revealed that affordable first line agents such as ampicillin and gentamicin are unlikely to be clinically efficacious in a substantial proportion of infections. This results in increasing reliance on the third generation cephalosporins for empirical treatment of serious infections. However, the spread of extended-spectrum beta-lactamase producing strains into the community (Ashley et al., 2011), probably accelerated by this increased consumption, is eroding the usefulness of these drugs. Alternative agents for treating multi-resistant coliform infections, such as the carbapenems, are unaffordable for treatment of community- acquired infections in low-income countries. In Africa, where Non-Typhoidal Salmonella (NTS) are of greater importance, there have been no clinical trials of fluoroquinolones. As quinolone-resistant salmonellae infections become more common, an alternative oral antimicrobial is required for settings where parenteral ceftriaxone is not a treatment option. Azithromycin is clearly an excellent drug for these infections, but laboratory data to support clinical trial data are lacking (Ashley et al., 2011).

The rising incidence of carbapenemase-producing *Klebsiella pneumoniae* has caused considerable challenge (Patel et al., 2010). Other infectious bacteria producing enzymes identical to the Klebsiella pneumoniae carbapenemases (KPCs) are also emerging rapidly as a cause of multidrug-resistant infections worldwide (Quale, 2011). Carbapenemases other than KPC have also been associated with *Klebsiella pneumoniae.* These associations have been reported from many geographic zones in both Verona Integron-encoded Metallo Beta lactamase (VIM) and New Delhi Metallo Beta lactamase (NDM) and non-metallo KPC and Oxacillinase- 48 (OXA-48) enzyme producing isolates of *Klebsiella pneumoniae* (CDC, 2010). These isolates are capable of hydrolyzing a broad spectrum of βeta-lactam antibiotics including penicillin, cephalosporins, carbapenems and monobactam. Failure to identify individuals colonized with these organisms, difficulty with inoculums preparation, and problems intrinsic to automated systems are some of the reasons associated with this rise (Crichton, 2012).Data on healthcare-associated infections reported to the Centers for Diseases Control and Prevention (CDC) from 2007 indicated that 8% of all Klebsiella spp isolates were carbapenem resistant as compared to a previous report of <1% in 2000 (Srinivasan and Patel, 2008) barely 7 years earlier. This enzyme has recently been isolated in Pseudomonas (Villegas et al., 2013) and Acinetobacter (Rebaudet et al, 2016). organisms outside the Enterobacteriacae family. The mechanisms by which these multi-drug resistant gram negatives spread despite effective infection control measures remains to be elucidated (Quale, 2008). Extended spectrum beta-lactamases (ESBLs) are plasmid mediated, confer multidrug resistance and are detected by in vitro resistance to ceftazidime and aztreonam (Douglas, 2009).

A surveillance study done in two Mexican referral hospitals showed that Klebsiella had high resistance rates to ceftazidime (33.1% compared to 24.0% in P. aeruginosa), but relatively low resistance to fluoroquinolones (≤18.2% vs. >50% in E. coli), more resistance to amikacin (13.1% vs. 0.4% in E. coli), and had similar susceptibility rates to the carbapenems as E. coli, ≥ 98.4%. Acinetobacter was the fourth most common gram negative bacilli isolated. More than 60% of the Acinetobacter isolates were resistant to all antibiotics tested, except imipenem (36.4%

resistance), meropenem (37.4% resistance) and colistin / polymyxin B (1.5% resistance). Enterobacter was the fifth most frequently isolated gram-negative bacilli and had a different resistance pattern than the other gram-negative bacilli tested. All (100.0%) Enterobacter spp. tested were susceptible to imipenem and meropenem. Only 3.7% were resistant to cefepime, 26.1% were resistant to piperacillin/tazobactam, 14.0% were resistant to ciprofloxacin, and 12.6% were resistant to levofloxacin (Morfin-Otero et al., 2012).

During the observation period (2005 to 2010) Klebsiella with an ESBL phenotype increased from 40.5% to 43.8%. Imipenem-non-susceptible Klebsiella phenotype decreased from 8.1% to 2.1%. Ceftazidime-resistant Enterobacter phenotype increased from 32.7% to 46.4%. imipenem-non-susceptible Enterobacter increased from 2.0% to 3.6% and Acinetobacter imipenem resistant phenotype increased from 13.8% to 63.5% ($p<0.001$) (Morfin-Otero et al., 2012).

The study investigated the antibiotic susceptibility on Klebsiella species among patients suspected of UTI in Murtala Muhammad Specialist Hospital, Kano, Nigeria. Two hundred urine specimens of patients comparing of 135(67.5%) outpatients and 65(32.5%) inpatients and classified into 125(62.5%) females and 75(37.5%) males were bacteriologically evaluated. The speciation of Klebsiella species isolated `showed that 14(7.0%) were *Klebsiella pneumoniae* and 2(1.0%) were Klebsiella oxytoca. The antibiotic susceptibility testing for Klebsiella species isolates showed Ofloxacin as the best drug of choice with all the 16 isolates susceptible to Ofloxacin but at the same time all were resistant to ampicillin (Hamza &Abdulhadi , 2016).

A study was conducted to describe the antibiotic resistance pattern of K. pneumonia over a 10 year period in Moi Teaching and Referral Hospital, Eldoret, Kenya. The findings showed that *K. pneumoniae* accounted for 23% of the hospital isolates (231/1356) during the study period; of these, 82.6% were from the New Born Unit. The study Concluded that there was a high prevalence of multidrug resistant *K. pneumoniae* isolates in the hospital, the majority originated from the New Born Unit. Resistance to third generation Cephalosporins and Gentamycin was high while Meropenem and Amikacin had the least resistance. The study further showned that Most of the isolates were multidrug resistant with highest resistance of over 80% to Penicillins, Cephalosporins, Macrolides, Tetracyclines, Sulphonamides, Lincosamides and Chloramphenicol (Table ii). Aminoglycoside and quinolone resistance was at 49.2% and 41.3% respectively. The lowest resistance rates were documented for Carbapenems (23.2 %). An analysis of the resistance levels to individual commonly prescribed antibiotics indicated resistance of over 80% to Ceftriaxone, Cefipime, and Gentamycin (Table iii). Amikacin and Meropenem had least resistance (21% and 7 % respectively) (Ogalo et al., 2016).

Statement of the problem

Hospital-acquired infections (HAI) are a significant hindrance in the delivery of healthcare services. Nosocomial infection prolongs patient's stay in the hospital by 5 - 10 days (Deep , 2014). This is an important preventable cause of increased cost, morbidity and mortality among hospitalized patients. The incidence of HAI increases with the use of invasive devices and with increased duration of hospitalization (Moodley, 2015).

Currently in Kenya there is inadequate information published indicating the prevalence of HAI so that can be of help to know the magnitude of HAIs. The *Klebsiella pneumoniae* have different strains which are widely distributed. There are those which are extended –spectrum Beta –lactamase (ESBL) producer and resistance to most of the antibiotics. The *Klebsiella pneumoniae* can be resistance to one antibiotic for example Amikacin and same species is sensitive to the same antibiotic. This poses a risk of getting a broad spectrum in treatment of *Klebsiella pneumoniae*. Antibiotic susceptibility pattern is an important study so that to determine and understand the antibiotics of choice in case of outbreak in healthcare services. The dealing with microorganism is often cumbersome process which could be as a result of dealing with different strains.

The incidence of HAI varies across intensive care units (ICUs) and with different patient profiles (Tullu , 2010). Patients in hospital facilities offering a higher level of care are at greater risk of developing HAI compared with those facilities offering a lower level of care.

Justification

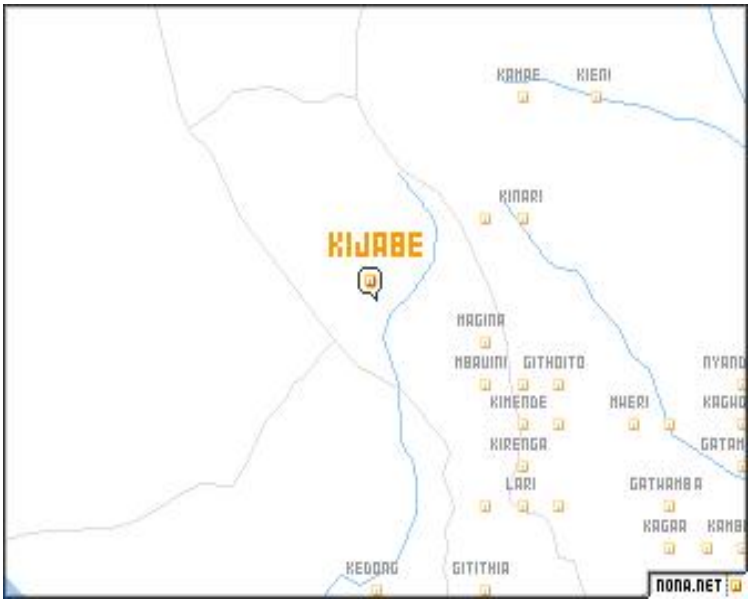
This study is important considering the increase in morbidity and mortality due to hospital acquired infections. The lack of effective infection control

programmes in some hospitals especially in developing countries may be due to poor adherence to safe practices by health workers and also lack of personnel trained in infection control practices. There is need for renewed efforts geared towards education through training and re-training coupled with research to keep nosocomial infections especially with *Klebsiella pneumoniae* in check. The importance of this study is to present an overview of nosocomial infections, identify the major challenges of control in developing countries and make appropriate recommendations aimed at effective control.

Materials and Methods

Study site

The study was carried out at Kijabe Hospital which is sponsored by the African Inland Church (AIC). Kijabe Hospital is situated along Nairobi-Naivasha Highway in Kiambu West District, Kiambu County. Kijabe is a Maasai word which means a place of cold wind. The temperature ranges form 18-22 degree Celsius with a lot of wind mostly at night. It serves all people from different economic status and background.



Research design

The design was a prospective observational whereby, different specimens were collected and analyzed for *Klebsiella pneumoniae*.

Study population

The study population included those in patients who were admitted in the AIC Kijabe hospital.

Variables to be used in the study

They will be mainly: - (i) **Independent:-**
The *Klebsiella pneumoniae* microorganism

(ii) **Dependent:-**
Antibiotics used
Ward/ location in the hospital

Sampling procedure and sample size

Sampling Procedure: was done using the systemic random sampling method. The target sample size was determined using Fischer *et al* (2008) method. This is according to (Fisher *et al*, 2000). The prevalence of 50% (0.5) was considered for there is no documented figure at AIC Kijabe hospital to show the current prevalence.

Sample Size: The formula is as follows;

$N = \frac{Z^2_{\alpha/2pq}}{e^2}$ *$Z^2\alpha/2=Z0.025= 1.96$, $p= 0.5$, $q=1-0.5$, $e=$ error of estimating= 0.05*

$$n= \frac{1.96^2(0.5)(1-0.5)}{0.05^2} = \frac{0.9604}{0.0025} = 384$$

N is portion of population that will be considered for the study.
Z is the Z- Score which has a constant of 1.96.
E is the margin error which is also referred to as confidence interval that will be 95%.
P is the current prevalence of the main study variable.
Q is the 100% of the total population representative which can also be equivalent with one as the whole number.

Inclusive criteria

Inpatients who had bacterial infection symptoms after 48 hours after admission.

The age group from 3 days to 70 years.

Exclusive criteria

The age above 70 years.

Data Management and Analysis

After obtaining ethical approval and permission from the hospital director data were obtained from the Kijabe Hospital microbiology laboratory records. A coded questionnaire was used to abstract the information. Patient's names were left out for the sake of confidentiality. Data were extracted for the time period January 2015- December 2015. All the questionnaires were reviewed by the principle investigator to ensure they are completed appropriately.

The filled questionnaires were in the safe custody of the principal investigator who filed and stored them in a locked cabinet for verification during analysis.

Data collected were entered into an Excel spreadsheet in a password protected computer.Back-up copies were stored in an external hard drive and compact disc which will be in sole custody of principal investigator.

Further cleaning was carried out after entry using frequency distributions and cross-tabulations until no more errors can be detected. The final step in the preparation for analysis was coding of the data and the creation of any composite variables from the cleaned data set. In order to achieve the objectives of the study, descriptive analysis was carried out. This involved frequency distributions for study variables. Variables were presented using bar charts and frequency distribution tables. Descriptive analysis was also used to give an understanding of the characteristics of the findings.

Data analysis was done using Statistical Package for Social Sciences Programme (SPSS) version 20.0.

Dissemination of results

This was carried out by information presentation and thesis write up. The defense of the research expected to done in presence of panel.

Material, methods of sample collection and procedure

Sample collection and preparation:-

The clinical specimens which were used included; urine, aspirates, blood, cerebral spinal fluid (CSF), swabs of wound, device swabbing. Sterile containers and swabs were used in the specimen collection. An autoclave was used to sterilize these containers and where applicable new sterile containers were procured. The morning midstream urine was collected in a sterile container. Blood was collected and aseptically drained in the sterile Bactec bottles which were then entered in the Bactec machine where it gave signal if there was microorganism growth. Aspirates and CSF were collected by clinicians as appropriate and put in sterile bottles. In case of orthopeadic patients sterile swabs were used to swab their wound and placed in staurt transport media.

Procedure

Culture of *Klebsiella pneumoniae*

All the specimens were inoculated on MacConkey and Blood agar Culture media. Inoculated plates were incubated at 37^o C for 18- 24 hours. Lactose fermenters that were non-motile with mucoid colonies, citrate positive and methyl red negative was identified as Klebsiella (Crichton, 2012).

Procedures:

DNA Extraction

Deoxyribonucleic acid (DNA) was extracted using the QIAGen DNA extraction kit (Qiagen, Germany) according to the kit manufacturer's instructions. Briefly, 200µl bacterial suspension in 'broth' was mixed with 20µl proteinase K on a 1.5ml Eppendorf tube. Later, the addition of 200µl lysis buffer (AL buffer) was done. This was incubated at 560C for 10 minutes. After incubation, 200µl of molecular grade ethanol was added to the mixture and mixed using a vortex. After the mixing, the Eppendorf tube was briefly centrifuged to remove drops from inside the Eppendorf tube lid. Carefully, 600µl was transfer to a spin column and centrifuged at 8000 rpm for 1 minute. The remaining mixture was added to the spin column and spun at the same conditions as previously described. Later, 500µl of wash 1 buffer (AW1) was added to the spin column and spun at 8000 rpm for 1 minute. The filtrate discarded and add 500µl of wash buffer 2 (AW2) to the spin column. Thereafter spin at 14,000 rpm for 3 minutes. Discard the filtrate and spin again at 14,000 rpm for 1 minute. Later add, 50µl of elution buffer (buffer AE), incubate at room temperature for 15 minutes before spinning at 8000 rpm for 1 min.

PCR Protocols

Two polymerase chain reactions (PCRs) were carried out to determine the presence of resistance genes for extended spectrum beta (β) lactamases (EBSLs) from the bacterial isolates collected. These are the most common plasmid mediated enzymes that confer resistance to these group of antibiotics. One uniplex PCR targeted the TEM while the other was a multiplex PCR targeting the CTX and SHV resistance genes.

TEM PCR Protocol

A uniplex PCR was carried out in order to determine the presence of TEM resistance genes from the bacterial isolates obtained. The primer sequences were obtained from Doosti, et al., 2015. The master mix consisted of 10x buffer (2.5µl), MgCl2 (3µl), dNTPs (1µl), primers forward and reverse (0.5µl each), nuclease free water to make the total master mix volume to 25µl.

The PCR was carried out on an Applied Biosystems 9700 PCR machine with an initial denaturation step at 94oC for 5 min, and then 32 cycles with denaturation at 94oC for 45 sec, primer annealing at 50oC for 40 sec and extension at 72oC for 60 sec. A final extension step at 72oC for 10 min was performed and the products were stored at 4oC. After gel electrophoresis was carried out on a 2% gel stained with ethidium bromide for PCR products visualization.

SHV plus CTX PCR Protocol

A multiplex PCR was carried out in order to determine CTX and SHV resistance genes. The primers were obtained from Ahmed, et al., 2018 targeting a 544bp SHV and 1018bp CTX gene fragments. The master mix consisted of 10x buffer (2.5µl), MgCl2 (3µl), dNTPs (1µl), primers for both CTX and SHV forward and reverse (0.5µl each), nuclease free water to make the total master mix volume to 25µl.

The PCR was carried out on an Applied Biosystems 9700 PCR machine with an initial denaturation step at 94oC for 5 min, and then 30 cycles with denaturation at 94oC for 30 sec, primer annealing at 52oC for 30 sec and extension at 72oC for 50 sec. A final extension step at 72oC for 10 min was performed and the products were stored at 4oC. After gel electrophoresis was carried out on a 2% gel stained with ethidium bromide for PCR products visualization.

3.8.2.2 Identification

Identification was confirmed by using the API method which identifies the species level. The antibiotic susceptibility pattern of these isolates was determined by disc diffusion on Muller Hinton Agar using Kirby-Bauer disc diffusion method (Heathley, 2011).

Picture for API identifying *Klebsiella pneumoniae*

Ethical Consideration

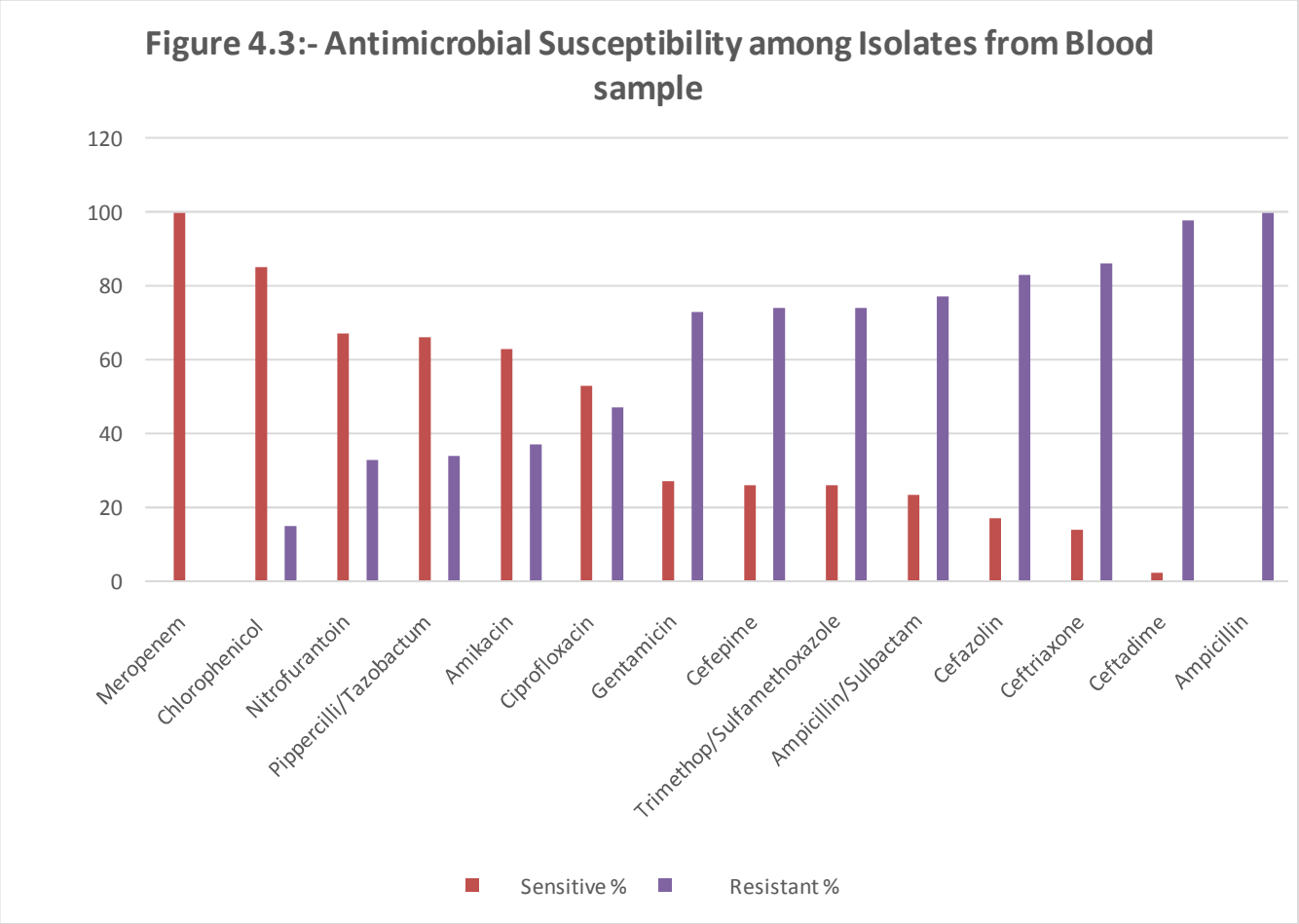
The study complied with International Conference on Harmonization and Good Clinical Practice (ICH GCP) standards on biological research. Ethical approval was sought from the Kenyatta University ethical review committee. Approval was also sought from the Ethical committee in AIC Kijabe hospital as attached. The subjects were informed that information gained was for academic purposes only. No names or any of the identification of subjects was used for example hospital numbers and therefore confidentiality was maintained. The results from the findings were availed to the healthcare providers for the management of the participants. In cases where patients have mixed infections, it was not fully diagnostic to attribute the nosocomial infections to just *Klebsiella pneumoniae* yet this study was only look at *Klebsiella pneumoniae.* Only the consented participants were entered in the study.

Findings

Antibiotic susceptibility profile of the *Klebsiella pneumoniae*.

Susceptibility among isolates from blood samples

The pattern of antimicrobial susceptibility among the 55 blood samples infected with *K. pneumoniae* showed that 100% was resistant to Ampicillin, 98% was resistant to Ceftadime, 86% was resistant to Ceftriaxone, 83% was resistant to Cefazolin, and none of the isolates was resistant to Meropenem. Additional antimicrobial susceptibility patterns are shown in Figure 4. 3.



Susceptibility among isolates from urine samples

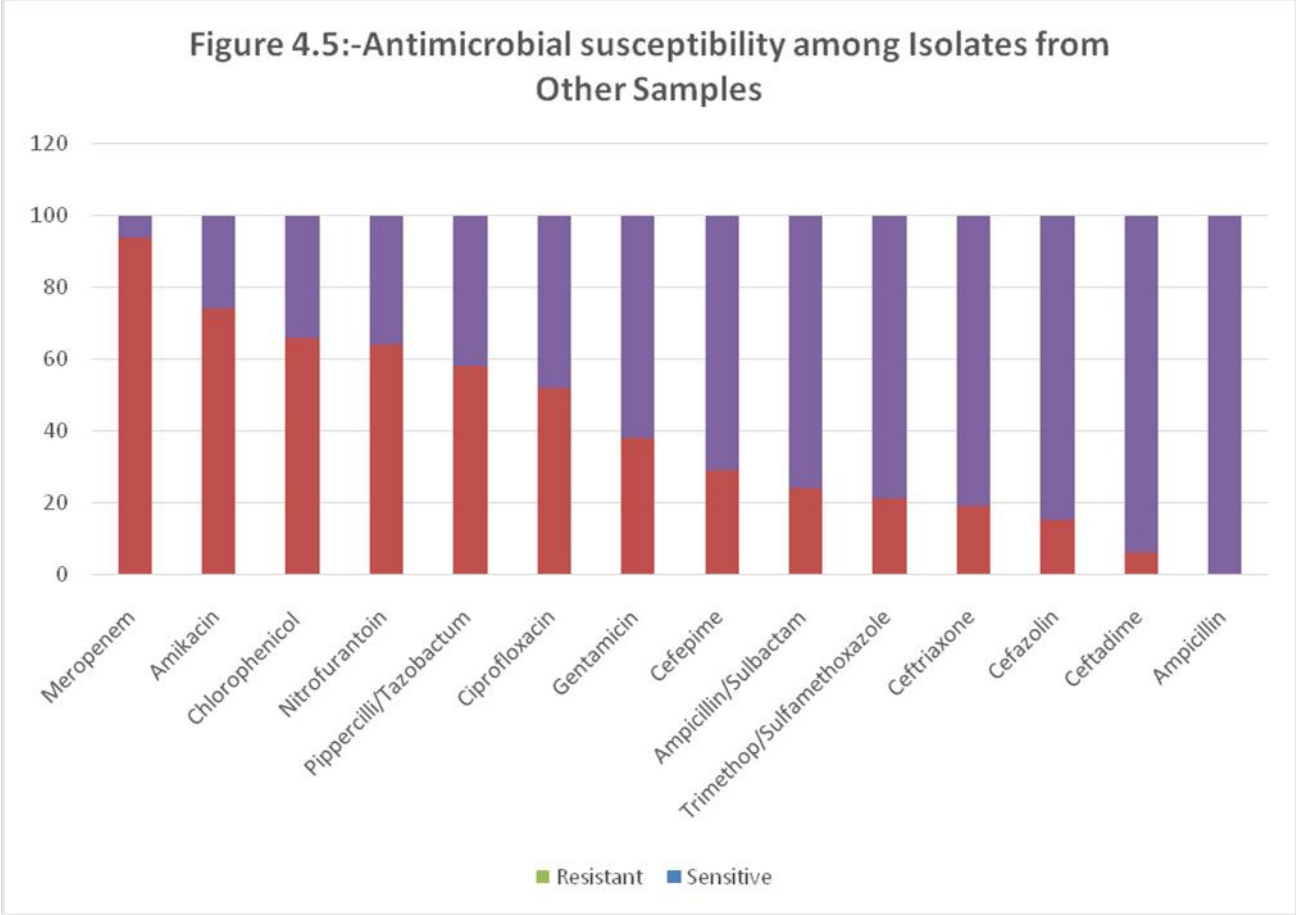
Thirteen antibiotics were tested against the isolated organisms from 78 urine samples. Overall the highest resistance was demonstrated by Ceftadime (90%) and Cefazolin (87%) while Trimethop/Sulfamethoxazole (85%), Ceftriaxone (76%), Ampicillin (72%), Cefepime (70%) and Meropenem (7%) showed the lowest resistance as shown in figure 4.3.

Table 4.3: General Susceptibility patterns for the Antibiotics used with isolates from urine samples.

	Sensitive		Resistant	
Antibiotic	**n**	**%**	**n**	**%**
Meropenem	73	93	5	7
Amikacin	59	75	19	25
Nitrofurantoin	50	64	28	36
Chlorophenicol	48	61	30	39
Pippercilli/Tazobactum	45	57	33	43
Ciprofloxacin	42	53	36	47
Gentamicin	31	39	47	61
Cefepime	24	30	54	70
Ampicillin/Sulbactam	22	28	56	72
Ceftriaxone	19	24	59	76
Cefazolin	12	15	66	85
Trimethop/Sulfamethoxazole	11	13	67	87
Ceftadime	8	10	70	90

Susceptibility among isolates from other samples

Susceptibility findings among antibiotics tested using isolates from other samples were more less the same as from isolates from urine and blood. Meropenem drugs were very effective with the lowest resistance (6%), followed by Amikacin (26%) and Chlorophenicol drugs at 34%. Ampicillin, Centadime, Cefazolin and Cenftriaxone recorded the highest resistance as 100%, 94%, 85%, and 81% respectively. Additional susceptibility results are tabulated in table 4.4.



H_o: There is no antibiotics resistance in *Klebsiella pneumoniae* isolates from AIC Kijabe hospital

To investigate whether there is no antibiotics resistance in *Klebsiella pneumoniae* isolates from AIC Kijabe hospital, a chi-square test of association was used. The results are presented in table 7.

Table 4.7. Antibiotics resistance in *Klebsiella pneumoniae* isolates

Source of Variation	SS	DF	MS	F
Between (factors)	937.39	K-1 2	468.695	5.547
Within (error)	1563.21	N-K 39	82274	
Total		41		

To test whether the difference in means in relation to antibiotics resistance in *Klebsiella pneumoniae* isolates was significant, analysis of variance (ANOVA) statistic was used. This parametric test was used to test the hypothesis that there is no antibiotics resistance in *Klebsiella pneumoniae* isolates from AIC Kijabe hospital. The result of analysis indicated that there was statistically significant difference among the means scores 5.547 at 0.05. It was concluded that use of antibiotics has influence on effective management in*Klebsiella pneumoniae* isolates from AIC Kijabe hospital.

Discussion

Antimicrobial Susceptibility

Thirteen antibiotics were tested against the isolated organisms from three groups of samples; urine samples, blood samples and other samples. Susceptibility outcome with isolates from blood samples showed that 100% was resistant to Ampicillin, 98% was resistant to Ceftadime, 86% was resistant to Ceftriaxone, 83% was resistant to Cefazolin, and none of the isolates was resistant to Meropenem. Isolates from urine samples revealed that highest resistance was by Ceftadime drugs (90%) and Cefazolin drugs (87%) while Meropenem showed the lowest resistance (7%). With other samples, Meropenem drugs were very effective with the lowest resistance (6%), followed at a distance by Amikacin (26%) and Chlorophenicol drugs at 34%. Ampicillin, Centadime, Cefazolin and Cenftriaxone recorded the highest resistance as 100%, 94%, 85%, and 81% respectively.Overall across the three groups of isolates, the highest sensitivity was demonstrated by Meropenem, Chlorophenicol and Amikacin while Cefazolin, Centadime, and Ampicillin showed the highest resistance.The findings of this study are that MDR and resistance is a developing problem in this hospital. The findings of this study differ from a similar study done in the Medical Intensive Care Unit (MICU) and Critical Care Unit (CCU) of Jawaharlal Institute of Post-Graduate Medical Education and Research, a tertiary care hospital in India from October 2006 to December 2007 to determine the various aetiological agents causing *Klebsiella pneumoniae* and the prevalence of bacterial pathogens in which it was found that thirty-seven (78.7 %) of the 47 *Klebsiella pneumoniae* pathogens were multi-drug resistant (Joseph et al., 2010). The relatively low prevalence of resistant and bacterial pathogens in this study compared to that done in India can be attributed to the finding that most patients were on more than one antimicrobial agent and often the antibiotics were started before specimens for culture were obtained. Rigorous infection control practices were also observed in this hospital. Microbial antibiotic resistance is common among the pathogens responsible for nosocomial infection.

Conclusion

Findings from this study showed that antimicrobial resistance is a problem in resource constrained settings. From this study, Meropenem were found to be more effective than other drugs against the isolated pathogens. However, they are known to be expensive and may not be suitable for use in resource-poor settings. Ampicillin which is readily available perhaps because of its low cost was less effective. To test whether the difference in means in relation to antibiotics resistance in *Klebsiella pneumoniae* isolates was significant, analysis of variance (ANOVA) statistic was used. This parametric test was used to test the hypothesis that there is no antibiotics resistance in *Klebsiella pneumoniae* isolates from AIC Kijabe hospital. The result of analysis indicated that there was statistically significant difference among the means scores FCA 5.547 at 0.05. It was concluded that use of antibiotics has influence on effective management in *Klebsiella pneumoniae* isolates from AIC Kijabe hospital.

The sum of the last column gives ($\chi 2c$) = 22.94 at the 95% confidence level and a degree of freedom of = (2-1) (2-1) = 1, χ 2a=3.841. Since χ 2c is more than χ 2a, we rejected the null hypothesis H_0 `and accept the alternate hypothesis and conclude that there is sufficient evidence to suggest that *Klebsiella pneumoniae* isolated in patients is associated with nosocomial infections in AIC Kijabe hospital.

Although some patients were on prophylactic antibiotics, a large number were either resistance or multi resistant to these antimicrobials, thus limiting their potential benefits in prevention and treatment of nosocomial infection. This may further increase the risk of resistance. There being no gold standard for measuring *Klebsiella pneumoniae*, the measures of *Klebsiella pneumoniae* described in this study were modified from the CDC criteria, but nevertheless derived from published guidelines and relevant literature. The causative pathogens do not appear to relate to the demographics characteristics of the patients and display resistance and multi-drug resistance to the commonly used antimicrobial agents.

5.3 Recommendations

This study through its findings recommends that;

- Regular antimicrobial audits and reviews of laboratory data (surveillance) should be done so as to have proper documentation of drug resistance patterns and timely updates of antibiotic formularies.
- Information about drug resistance should be properly communicated to those prescribing antimicrobials and adequate guidelines regarding the selection of drugs should be availed. Additionally, adequately documented local retrospective data should be availed on the benches of health care providers to guide good antibiotic stewardship.
- Antimicrobial stewardship programs and antibiograms should be developed by healthcare institutions to reduce inappropriate antimicrobial use, improve patient outcomes and reduce adverse consequences of antimicrobial use.
- Antimicrobial research in Kenya should be emphasized and adequately funded.
- As shown in this study, and resources allowing, Meropenem are the choice drugs in treatment of *K. pneumoniae* infections. The government, and other stakeholders, should consider subsidizing the cost of these drugs.

Recommendations for further study

The study recommends further research on molecular characteristics of *K. pneumoniae* to establish whether it is the same strain.

The study focused on AIC Kijabe Hospital Kiambu Countyonly, therefore, the same study can be extended in other hospitals and other counties for comparison purposes.

Acknowledgments

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References

Bates DW, Larizgoitia I, Prasopa-Plaizier N, Jha AK. Global priorities for patient safety research. BMJ 2009; 338: b1775- doi: 10.1136/bmj.b1775.

Bercion R, Gaudeuille A, Mapouka PA, Behounde T, Guetahoun Y. Surgical site infection survey in the orthopaedic surgery department of the "Hôpital communautaire de Bangui," Central African Republic. Bull SocPatholExot 2012; 100: 197-200 pmid: 17824315.

Carmeli Y, S. M. (2010). Carbapenem- resistant Enterobacteriacea a potential threat. *JAMA* , **300**; 290-3.

Cook D. (2011). Nosocomial infection by Klebsiella pneumoniae. Perspectives of the burden of illness. Intensive Care Medicine 26 (13): 1421–1427

CDC. (2014). *Guidance for Control of Infections with Carbapenem-resistant or carbapenemase-producing Enterobacteriaceae in acute care facilities.* Morbidity and Mortality weekly report : PubMed.

Chawla, R. (2012). Epidemiology, etiology and diagnosis of hospital acquired pneumonia and ventilator associated pneumonia in Asian countries. *American Journal infection control* , 36(4):S93-S100.

Chris Rowe Taitt,1,* Tomasz A. Leski,1 Daniel P. Erwin,2 Elizabeth A. Odundo,3 Nancy C. Kipkemoi,3Janet N. Ndonye,3 Ronald K. Kirera,3 Abigael N. Ombogo,3 Judd L. Walson,4,5 Patricia B. Pavlinac,4 Christine Hulseberg,2 and Gary J. Vora1 (2017). Antimicrobial resistance of *Klebsiella pneumoniae* stool isolates circulating in Kenya. Published online 2017 Jun 2. doi: 10.1371/journal.pone.0178880.

Clinical and Laboratory Standards Institute. Supplemental tables. Performance standards for antimicrobial susceptibility testing; fifteenth informational supplement. CLSI Publication M100-S15, M2-A8 and M7-A6.Pennsylvania: CLSI; 2014.

Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Susceptibility Testing*. 21st informational supplement. Wayne, PA: Clinical and Laboratory Standards Institute; 2012. CLSI publication M100-S22.

CLSI. (2013). Performance standards for antimicrobial susceptibility testing. *Twenty third informational Supplement M100-S23; Wayne PA; USA*.

Crichton PB, C. J. (2012). *Practical Medical Microbiology Enterobacteriaceae, Escherichia, Klebsiella, Proteus and other genera.* India: Mackie and McCartney Elsevier.

Carmeli (2009). Klebsiella spp with plasmid-mediated carbapenem resistance. *Antimicrob Agents Chemother*. 2009;46(11):3624-3626.

Center for Disease Control (2018). Metallo Beta lactamase (NDM) and non-metallo KPC and Oxacillinase- 48 (OXA-48) enzyme producing isolates of *Klebsiella pneumoniae*. Journal of *Antimicrob Agents Chemother*. 2009;46(11):3624-3626.

Donnenberg MS. Enterobacteriaceae [Chapter 218]. In: Mandell, Douglas, and Bennett's principles and practice of infectious diseases. 7th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2010:2815–34

Douglas, M. (2009). *Principle and practice of Infectious Disease, 7th Edition.* Churchill livingstone: Elsevier.34 (5): 739–45. doi:10.1128/AAC.34.5.739. PMC171683. PMID 2193616.

Dia NM, Ka R, Dieng C, Diagne R, Dia ML, Fortes L, et al., et al. Prevalence of nosocomial infections in a university hospital (Dakar, Senegal). Med Mal Infect 2013; 38: 270-4 doi: 10.1016/j.medmal.2013.11.001 pmid: 18180124.

Diouf E, Beye MD, DiopNdoye M, Kane O, Seydi AA, Ndiaye PI, et al., et al. Nosocomial ventilator-associated pneumonia in a tropical intensive care unit. Dakar Med 2016; 51: 81-8 pmid: 17632982.

Eriksen HM, Chugulu S, Kondo S, Lingaas E. Surgical-site infections at Kilimanjaro Christian Medical Center. J Hosp Infect 2013; 55: 14-20 doi: 10.1016/S0195-6701(03)00225-1 pmid: 14505604.

Deep (2014). Hospital-acquired infections. . J. Med. 452 (4): 240–91. doi:10.1116.

Ducel *et al*, (2012). Nosocomial infections. *Practical Medical Microbiology of Klebsiella.*7th ed. Philadelphia, PA: Churchill Livingstone Elsevier; 2012:3415–66

Dubois V, Arpin C, Noury P, Quentin C. Clinical strain of *Pseudomonas aeruginosa* carrying a *bla*TEM-21 gene located on a chromosomal interrupted Tn*A*type transposon. *AntimicrobAgents Chemother*. 2012;46(11):3624-3626.

Inweregbu *et al*, (2015). Nosocomial infections in public hospitals. N. Engl. J. Med. 352 (4): 380–91. doi:10.1056.

Emery C. L., Weymouth L. A. (2010). "Detection and clinical significance of extended-spectrum β-lactamases in a tertiary-care medical center". *J. Clin. Microbiol***35** (8): 2061–7. PMC 229903. PMID 9230382.

Eriksen HM, Chugulu S, Kondo S, Lingaas E. (2013). Surgical-site infections at Kilimanjaro Christian Medical Center. J Hosp Infect 2013; 55: 14-20 doi: 10.1016/S0195- 6701(03)00225-1 pmid: 14505604.

Fehr J, Hatz C, Soka I, Kibatala P, Urassa H, Smith T, et al., et al. Risk factors for surgical site infection in a Tanzanian district hospital: a challenge for the traditional National Nosocomial Infections Surveillance system index. Infect Control Hosp Epidemiol 2016; 27: 1401-4 doi: 10.1086/509855 pmid: 17152042.

Forbes *et al*, 2011. Antimicrobial Susceptibility Testing. www.eucast.org/epert_rules. Accessed October 31, 2011.

Friedlander (2012). The etiological factor for the pneumonia seen especially in immunocompromised individuals. Journal of Antimicrob Agents Chemother 2012, 32(2):713–721.

Fischer *et al* (2008). Esxtimating sample size.

Fuchs L., Chronaki C., Park S., Novack V., Baumfeld., Scott D., McLennan S., TalmorD.andCeli. (2012). ICU admission characteristics and mortality rates among elderly and very elderly patients. Intensive Care Medicine 38(10): 1654-1661.

Fehr J, Hatz C, Soka I, Kibatala P, Urassa H, Smith T, et al., et al. Risk factors for surgical site infection in a Tanzanian district hospital: a challenge for the traditional National Nosocomial Infections Surveillance system index. Infect Control Hosp Epidemiol 2016; 27: 1401-4 doi: 10.1086/509855 pmid: 17152042

Giske CG, Monnet DL, Cars O, Carmeli Y: Clinical and economic impact of common multidrug-resistant gram-negative bacilli. Antimicrob Agents Chemother 2012, 52(3):813–821.

Gazin et al., (2012). extended-spectrum cephalosporins. Antimicrob Agents Chemother 2008, 52(3):813–821.

Garrison (2013). Aetiology of hospital acquired infections. Journal of Antimicrob Agents 2008, 42(3):713–721.

Queenan AM, Bush K. Carbapenemases: the versatile _-lactamases. *Clin Microbiol Rev*. 2007;20(3):440-458.

Queenan AM, Bush K. Carbapenemases: the versatile beta-lactamases. Clin Microbiol Rev. 2012;20(3):440–58, table of contents. pmid:17630334

Quale*G.J* (2011). *Klebsiella pneumoniae* carbapenemases emerging rapidly as a cause of multidrug-resistant infections. Journal of *Clin Microbiol Rev*. 2007;20(3):440-458.

Rebaudet *et al*, (2016). Hospital acquired infections have been neglected in Sub-Saharan Africa. Clin Microbiol Rev. 2016;22(3):450-468.

Rosenthal *et al*, (2012). Nosocomial infections studies in Africa countries. Clin Infect Dis 2012; 44:767–78.

Robert (2012). Nosocomial infections prolong duration of hospitalization, increase the cost of health care and multiple antibiotic resistance microorganisms. Journal of Med Int Health. 2012; 17(2): 212–226.

Ryan (2014). Family of Enterobacteriaceae. Journal of Med Int Health. 2014; 17(2): 112–126.

Schaberg *(*2010). *Klebsiella spp in USA. Lancet Infectious Disease* , **5**(2):238-56.

Schwaber (2008). *Klebsiella pneumoniae.* Journal of Med Int Health. 2012; 17(2): 212–226.

Sanou J, Traore SS, Lankoande J, Ouedraogo RM, Sanou A (2010). Survey of nosocomial infection prevalence in the surgery department of the Central National Hospital of Ouagadougou. Dakar Med 2010; 44: 105-8 pmid: 10797997.

Tullu (2010).Hospital-acquired infections. Infectious Diseases Society of America. Journal of Clin Infect Dis 2006; 42:657–68.

Taye M. Wound infection in Tikur Anbessa hospital, surgical department. Ethiop Med J 2015; 43: 167-74 pmid: 16370548.

Villegas MV, Lolans K, Correa A, Kattan JN, Lopez JA, Quinn JP. First identification of *Pseudomonas aeruginosa* isolates producing a KPC-type carbapenem-hydrolyzing _- lactamase. *Antimicrob Agents Chemother*. 2013;51(4):1553-1555.

Vincent J.L., Bihari D.J., Suter P.M., Bruining H.A., White J. and Nicolas Chanoin M.H. (2012). The prevalence of nosocomial infection in intensive care units in Europe. Results of the European prevalence of infection in intensive care (EPIC) Study. Journal of American Medical association 274(8): 639-44.

Vading M, P. Nauclér, M. Kalin, C. G. Giske (2018). Invasive infection caused by *Klebsiella pneumoniae* is a disease affecting patients with high comorbidity and associated with high long-term mortality Published: April 6, 2018 https://doi.org/10.1371/journal.pone.0195258.

WHO, (2017) Prevention of hospital-acquired infections: a practical guide. Geneva: World Health Organization; 2002.

WHO guidelines on hand hygiene in health care. Geneva: World Health Organization; 2017

WHO guidelines on hand hygiene in health care. Geneva: World Health Organization; 2009

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