

Full Length Research Paper

Antimicrobial susceptibility profile of community acquired and nosocomial isolates of *Staphylococcus aureus* and that of coagulase negative staphylococci from clinical blood culture specimens at a Nigerian University Teaching Hospital

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The study was carried out to ascertain the antibiotic susceptibility patterns of *Staphylococcus aureus* and that of Coagulase negative Staphylococci (CONS) recovered from blood culture specimens in Calabar, Nigeria. The study was retrospective in nature and was carried out at University of Calabar Teaching Hospital (UCTH) Calabar; data generated from blood culture specimens over a five year period (February 2004 - February 2009) was compiled, relevant information such as age, sex, organism recovered and antibiotic susceptibility patterns were obtained from patients records. Samples were collected, transported, stored and processed using standard laboratory procedures. Data obtained was analyzed using Epi Info 6 statistical software. *S. aureus* (23%, n = 46) and coagulase negative Staphylococci (CONS) (14%, n = 29) combined were the commonest bacterial isolates. Only ceftriaxone was active against all (100%) the community acquired (CA) and nosocomial (NC) Staphylococcal isolates, while the resistance of the NC compared to the CA isolates of the organisms was significantly higher against several of the antibiotics ($p < 0.05$). The NC Staphylococcal isolates were generally resistant to at least seven antibiotics tested. Local sensitivity patterns of Staphylococci should be generally known while managing their associated blood infections. Also adequate measures should be put in place so as to limit the spread of their hospital acquired strains.

Key words: *Staphylococcus aureus*, coagulase negative staphylococci, sensitivity, blood culture.

INTRODUCTION

Ordinarily isolations of *Staphylococcus aureus* and that of coagulase negative Staphylococci (CONS) in hospital settings should not raise the curiosity of health

personnels appreciably (Kluytmans et al., 1998; Fonsale et al., 2004; Calvo et al., 2000). Besides being normal commensals on human skin with usually no obvious health threat to the host, the organism constitute a significant proportion of bacteria contaminating culture plates in the laboratory (Vandenesch et al., 1993; Ozturkeri et al., 1994; Nur et al., 1997). This makes over 50% of their detection on culture plates especially in

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Microbiology laboratories across Africa being considered contaminants (Ahmed et al., 1998; Johnson et al., 1996; Gakum, 1997). Furthermore, the availability of several antibiotics with spectra of activity well accommodating these organisms, management of infections associated with them should not be a major health challenge (Kluytmans et al., 1995; Kluytmans et al., 1996). Available records presently have however shown the organism to be of serious clinical importance as the resistance of *S. aureus* and that of coagulase negative Staphylococci to available antibiotics has assumed a steady and progressive increase since the mid 70s (Cespedes et al., 2002; Anonymous, 2001; Levy, 1992). The high resistance being documented about these organisms in the new millennium is perhaps believed to have commenced at least a decade earlier than the above date, but with minimal attention or probably no recognition by the health personnel of the time (Moellering, 1995; Gold and Moellering, 1996). And with the emergence of more disturbing strains of the organisms; being resistant to all the available common antibiotics plus the ones reserved as a last result, the patient may apparently be at the mercy of these organisms (Orrett and Land, 2006; Hsuch et al., 2004). With the possibility of these highly resistant staphylococcal strains spreading from hospital settings to the community, the clinical relevance of these organisms become amplified (Kuehnert et al., 2005). As the challenges in the management of staphylococcal infections worldwide deepens due to the varying but increasing resistance pattern of the organisms; the regional and geographic variations in their antimicrobial susceptibility patterns need to be established and probably institutionalized (Montesinos et al., 2003; Hanumanthappa et al., 2003). This would offer formidable guide towards prompt management of its associated infections most especially when recovered from emergency specimens such as blood culture. This study was therefore set up to establish the current antimicrobial susceptibility patterns of Staphylococci so as to offer a guide to clinicians towards prompt management of life threatening infections such as septicemia.

MATERIALS AND METHODS

Setting

The study was carried out at University of Calabar Teaching Hospital (UCTH), which is situated in Calabar city, the capital of Cross Rivers state, south-south Nigeria.

Procedure

The study was retrospective in nature; data generated from the antibiotic susceptibility pattern of bacteria recovered from blood culture specimens were compiled for a period of five years (1st February, 2004 - 31st January, 2009). Specimens were

collected, transported, stored and processed using standard laboratory procedures (Scott, 1989). Briefly, using sterile procedures 2 - 4 mls of blood was collected and introduced into separate blood culture bottles (containing brain heart infusion and thioglycolate broths) and incubated for subsequent subcultures, Gram staining and biochemical methods. Modified Kirby-Bauer's diffusion method was used to carry out susceptibility testing (Baron et al., 1994). Microorganisms recovered were grouped into nosocomial or community acquired based on the epidemiological circumstance of the blood culture specimens.

Nosocomial infection

Micro-organisms recovered from blood culture specimens of patients who have been on admission for more than 24 h for which features of bacterial colonization were not present at the time of initial presentation to the hospital.

Community acquired infection

Micro-organisms recovered from blood culture specimens of patients who were not on admission in the hospital, and from patients within 24 h of admission or patients originally admitted for probable blood related infections. Other relevant information such as: age, sex were obtained from patients records.

Analysis of results

The results were analyzed using Epi Info-6, statistical software, p values ≤ 0.05 were considered significant.

RESULTS

Of the 203 bacterial isolates recovered from the 3,255 blood culture specimens processed in Calabar, *S. aureus* and coagulase negative Staphylococci (CONS) were respectively responsible 23.0% (46/203) and 14.0% (29/203) of the infections; 65.2% (30/46) and 34.8% (16/46) of the *S. aureus* isolates were community acquired (CA) and nosocomial (NC) in origin respectively, while 37.9% (11/29) and 62.1% (18/29) of the CONS were CA and NC isolates respectively. Other bacteria recovered were *Escherichia coli* 15.0% (n = 31), *Proteus* species 11.3% (n = 23), *Klebsiella* species 20.2% (n = 41), *Salmonella typhi/paratyphi* 10.3% (n = 21) and *Citrobacter/Enterobacter* sp. 4.4% (n = 9) (Figure 1).

The age interval for isolation of *S. aureus* was 8 months to 76 years; mean age was 37 years and mode 28 years; 63.0% (29/46) and 37% (17/46) of the patients were of the male and female gender respectively with no significant age difference ($p > 0.05$), but with significantly higher rate infection among males ($p < 0.05$) (Table 1). Also of the 29 isolates of CONS recovered, 38.0% (11/29) and 62.0% (18/29) were from males and females respectively with no significant gender difference ($p > 0.05$). The youngest patient was 3 months old and oldest 78 years; the mean age was 52 years and mode 66 years with no significant age difference ($p > 0.05$) (Table 2).

All the CA isolates of *S. aureus* tested were susceptible

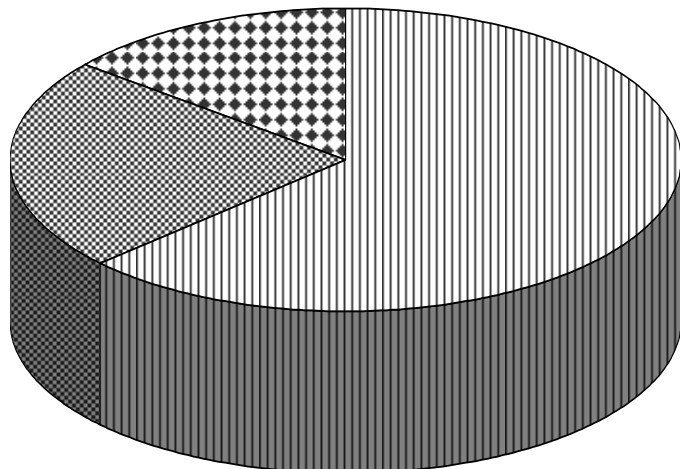


Figure 1. Incidence of isolation of *Staphylococcus aureus* and that of Coagulase negative Staphylococci in relation to other microorganisms from blood culture specimens in Calabar, Nigeria.

to amikacin, Ofloxacin, ciprofloxacin, cefuroxime and rifampicin while only ceftriaxone was active against all (100%) the NC isolates tested. The activity of penicillin G, ampicillin, cloxacillin, amoxicillin, tetracycline, co-trimoxazole, chloramphenicol and erythromycin against both the CA and NC isolates of *S. aureus* was generally below 50% (range 0 - 40%); and the resistance of the NC isolates of the organism were significantly higher ($p < 0.05$) than the CA isolates against ampicillin, cloxacillin, amoxicillin, tetracycline, co-trimoxazole, cefuroxime, chloramphenicol and rifampicin (Figure 2).

All the CA and NC isolates of CONS were sensitive to ceftriaxone and rifampicin but only all the CA isolates were sensitive to Ofloxacin, ciprofloxacin and ceftazidime. The activity of augmentin, streptomycin, gentamicin and amikacin was generally in the range of 60 - 80%; the resistance of the NC isolates was significantly higher than the CA isolates of CONS against cloxacillin, amoxicillin, tetracycline, co-trimoxazole, gentamicin, Ofloxacin, ciprofloxacin, cefuroxime, chloramphenicol and erythromycin ($p < 0.05$) (Figure 3).

Comparison of the antimicrobial susceptibility pattern of the isolates of *S. aureus* and that of CONS showed only ceftriaxone to be active against all the isolates (100%); the activity of ampicillin and chloramphenicol was significantly higher against *S. aureus* compared to CONS ($p < 0.05$) while the other antibiotics tested showed no difference in sensitivity profile among the two microorganisms ($p > 0.05$) (Figure 4).

Staphylococci isolates resistant to seven or more antibiotics were 34 (45.3%); 95% (32/34) of these isolates were hospital acquired ($p < 0.05$). Staphylococci resistant to 2 - 3, 4 - 5 and 6 - 7 antibiotics were 8 (10.7%), 24 (32.0%) and 35 (46.7%) while eight of the isolates (10.7%) were resistant to eight or more antibiotic tested (Figure 5).

DISCUSSION

Staphylococci were the commonest bacteria recovered from blood culture specimens while there was no significant difference in susceptibility pattern of *S. aureus* compared to CONS against all the antibiotics tested except ampicillin whose activity was significantly higher against *S. aureus* compared to CONS ($p < 0.05$). This is no doubt not unconnected with the already established regional or geographic variation in susceptibility pattern of individual bacterial strains (Royehoudhury et al., 2001; Daun and Seal, 2001).

Only ceftriaxone was active against all (100%) of the CA and NC of the Staphylococcal isolates from the blood culture specimens; other active drugs (activities 66 - 94%) against both the CA and NC isolates of the organisms were amikacin, Ofloxacin, ciprofloxacin, ceftazidime, cefuroxime and rifampicin. On the other hand the activity of penicillin, ampicillin, cloxacillin, amoxicillin, tetracycline, co-trimoxazole, chloramphenicol and erythromycin against the organisms was generally less than 25% (range 0 - 20%); 60% of the bacteria were resistant to at least six antibiotics. This pattern of resistance has earlier been exhibited by members of Enterobacteriaceae in a similar study in the same locality (Jombo et al., 2009). The fact that methicillin resistance is usually heralded by multiple resistance places several of these bacteria potential candidates for methicillin resistance with the attendant clinical challenges (Gibbons and Udo, 2000; Bukhari et al., 2004; Tarano et al., 2001).

The high resistance documented in the present study has been well corroborated in Germany, where up to 100% resistance by some strains of *S. aureus* to erythromycin, clindamycin, ciprofloxacin, and gentamicin was observed (Von Eiff et al., 2000); a similar sensitivity pattern was documented in Chile, Argentina and Uruguay, where high resistance of *S. aureus* to penicillin, oxacillin, ciprofloxacin, chloramphenicol, clindamycin, erythromycin and gentamicin was recorded (De Sousa et al., 2001); and in Sudan (Ahmed et al., 1998) and Australia (Bell et al., 2002) where *S. aureus* resistance of 100% was recorded against several antibiotics tested. The high resistance of Staphylococci to ciprofloxacin in Germany compared to the relatively low figures recorded in the present study further demonstrate the impact of strain variation on sensitivity profile of bacteria. Local activity profiles of supposedly generally highly active antimicrobials should be known and periodically reviewed so as to positively influence the choice of antibiotic prescriptions in empirical treatments of bacteremia or septicaemia (Topeli et al., 2000; Salgado et al., 2003).

Over 95% of the bacteria resistant to seven and above antibiotics were NC in origin. The sensitivity pattern of CA isolates of CONS was significantly higher than the NC isolates against cloxacillin, ampicillin, tetracycline, co-trimoxazole, gentamicin, Ofloxacin, ciprofloxacin, chloramphenicol and erythromycin ($p < 0.05$). A similar

Table 1. Age* and gender** distribution of *S. aureus* recovered from blood culture specimens in Calabar, Nigeria.

Age interval (Years)	Male (%)	Female (%)	Total (%)
0 - 9	2 (4.3)	4 (8.7)	6 (13.0)
10 - 19	2 (4.3)	1 (2.2)	3 (6.5)
20 - 29	6 (13.0)	3 (6.5)	9 (19.6)
30 - 39	7 (15.3)	0 (0.0)	7 (15.3)
40 - 49	4 (8.7)	1 (2.2)	5 (10.9)
50 - 59	3 (6.5)	3 (6.5)	6 (13.0)
60 - 69	2 (4.3)	3 (6.5)	5 (10.9)
70 - 79	1 (2.2)	2 (4.3)	3 (6.5)
≥ 80	0 (0.0)	0 (0.0)	0 (0.0)
Unclassified	2 (4.3)	0 (0.0)	2 (4.3)
Total	29 (63.0)	17 (37.0)	46 (100)

* χ^2 (Mantel-Haenszel) = 10.24, OR = 0.39, RR = 0.99, P = 0.001.

** χ^2 (Mantel-Haenszel) = 0.00, OR = 1.00, RR = 1.00, P = 1.00.

Table 2. Age* and gender** distribution of coagulase negative Staphylococci recovered from blood culture specimens in Calabar, Nigeria.

Age interval (Years)	Male (%)	Female (%)	Total (%)
0-9	3 (10.3)	1 (3.4)	4 (13.8)
10-19	0 (0.0)	3 (10.3)	3 (10.3)
20-29	0 (0.0)	1 (3.4)	1 (3.4)
30-39	2 (6.9)	3 (10.3)	5 (17.2)
40-49	1 (3.4)	3 (10.3)	4 (13.8)
50-59	2 (6.9)	1 (3.4)	3 (10.3)
60-69	2 (6.9)	4 (13.8)	6 (20.7)
70-79	1 (3.4)	2 (6.9)	3 (10.3)
≥80	0 (0.0)	0 (0.0)	0 (0.0)
Unclassified	0 (0.0)	0 (0.0)	0 (0.0)
Total	11 (38.0)	18 (62.0)	29 (100)

χ^2 (Mantel-Haenszel) = 0.04, OR = 1.08, RR = 1.00, P = 0.84.

χ^2 (Mantel-Haenszel) = 0.00, OR = 1.00, RR = 1.00, P = 1.00.

sensitivity pattern was recorded by CA isolates of *S. aureus* as compared to the NC counterparts against several of the antibiotics tested ($p < 0.05$). Methods adopted for control of hospital acquired infections should be strengthened to meet internationally accepted best practices and probably surpassed with innovations. These in addition to entrenchment of the basic tenets of personal and environmental hygiene such as hand washing be promoted among both health personnel, patients and their relations (Mayhall, 2003; Falagas et al., 1996). This would help reduce the spread of hospital acquired Staphylococcal isolates which have severally been associated with high profile resistance including methicillin and oxacillin (O'Brien et al., 2004; Blane et al., 2002). In conclusion, the present study has also lend a voice to the already existing body of knowledge that Staphylococci are increasingly becoming resistant to

majority of the available antibiotics in use; hence local sensitivity profile of the organism should be known and the same reviewed periodically. Also in view of the higher resistance demonstrated by the hospital acquired isolates of the bacteria with attendant clinical challenges, control of nosocomial infections should be strengthened and closely monitored so as to reduce the spread of these high profile resistant strains in the hospital environment and beyond. The 21st century offers an opportunity to "roll back" this menace.

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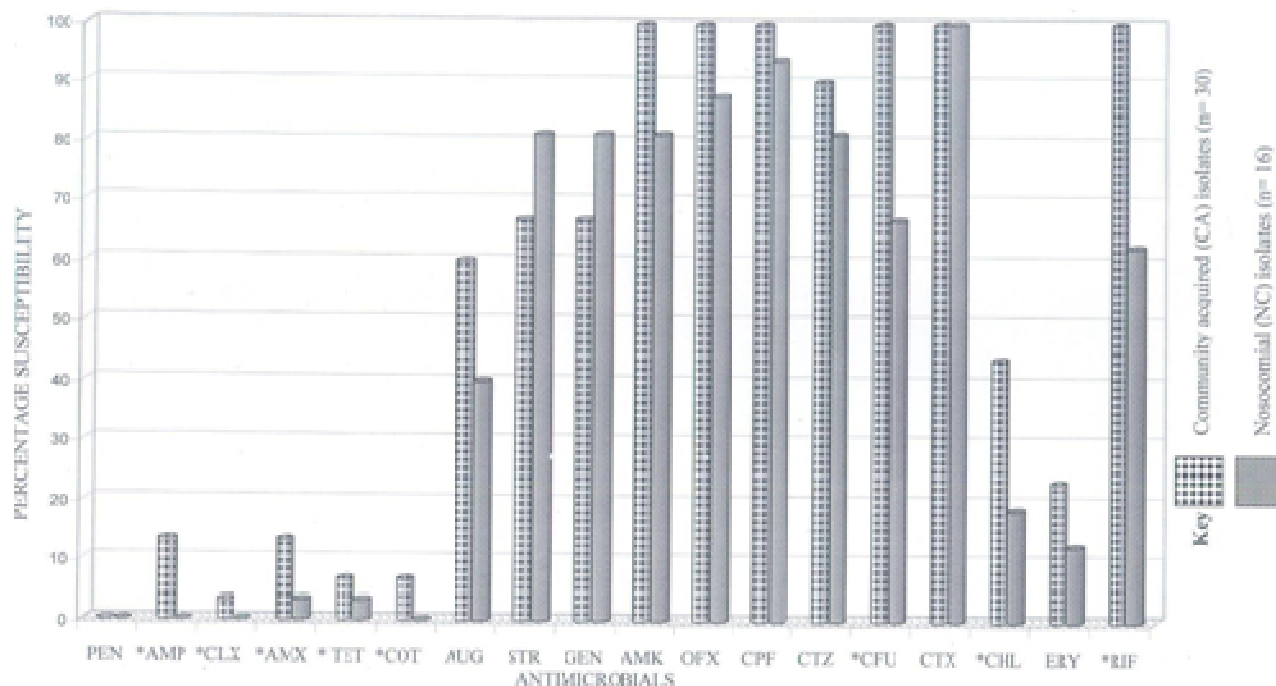


Figure 2. Antimicrobial susceptibility pattern of *S. aureus* recovered from blood culture specimen in Calaba, Nigeria. PEN = Penicillin G, AMP = Ampicillin, CLX = Cloxacillin, AMX = Amoxicillin, TET = Tetracycline, COT = Co-trimoxazole, AUG = Augmentin (clavulanate potentiated amoxicillin), COL = Colistin, STR = Streptomycin, GEN = Gentamicin, AMK = Amikacin, OFX = Ofloxacin, CIP = Ciprofloxacin, CTZ = Ceflazidime, CFU = Cefuroxime, CTX = Ceftriaxone, CHL = Chloramphenicol, ERY = Erythromycin, RIF = Rifampicin, * = $p < 0.005$.

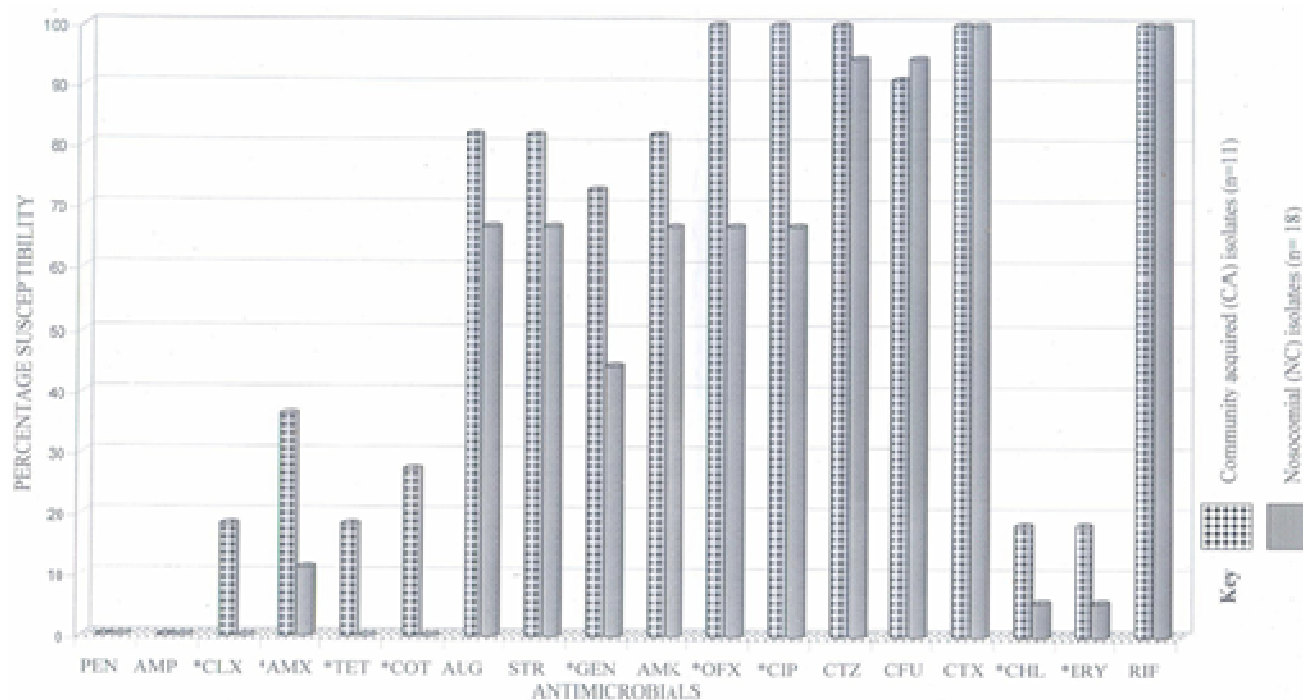


Figure 3. Antimicrobial susceptibility pattern of coagulase negative staphylococci (CONS) recovered from blood culture specimen in Calaba, Nigeria. PEN = Penicillin G, AMP = Ampicillin, CLX = Cloxacillin, AMX = Amoxicillin, TET = Tetracycline, COT = Co-trimoxazole, AUG=Augmentin (clavulanate potentiated amoxicillin), COL = Colistin, STR = Streptomycin, GEN=Gentamicin, AMK = Amikacin, OFX = Ofloxacin, CIP = Ciprofloxacin, CTZ = Ceflazidime, CFU = Cefuroxime, CTX = Ceftriaxone, CHL = Chloramphenicol, ERY = Erythromycin, RIF = Rifampicin, * = $p < 0.005$.

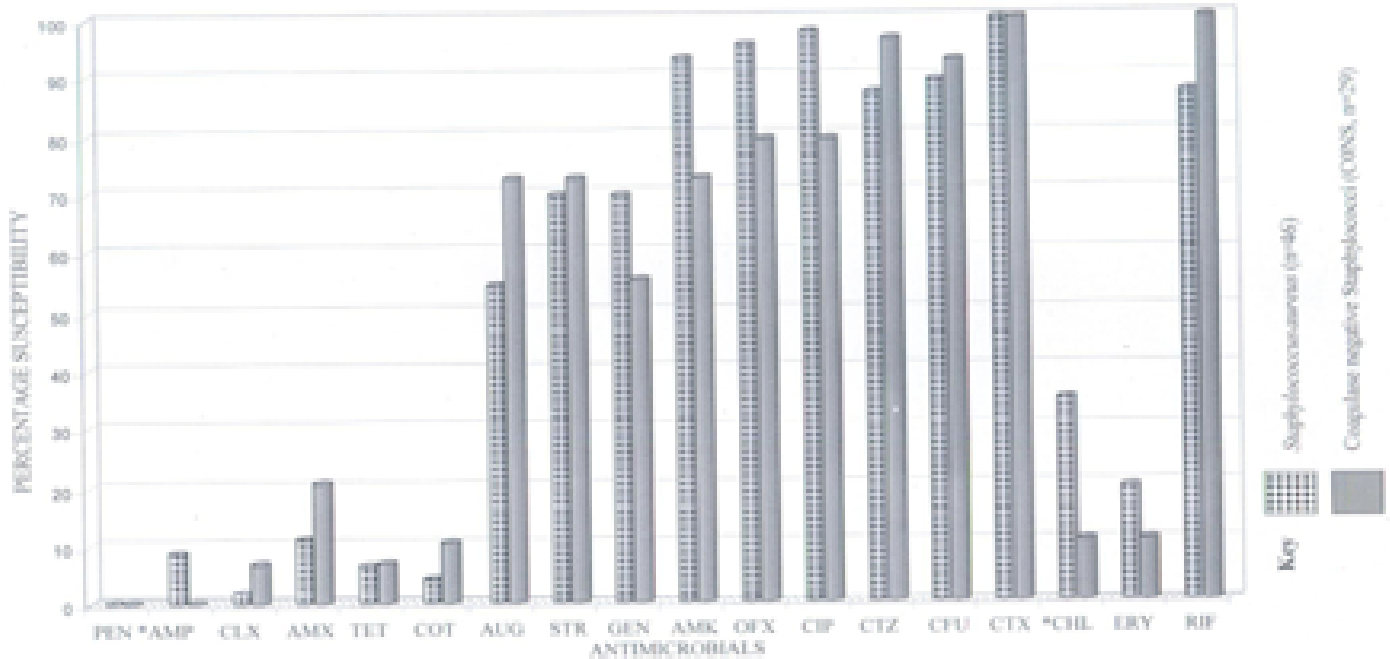


Figure 4. Combined antimicrobial susceptibility pattern of community (CA) acquired and nosocomial (NC) isolates of *S. aureus* compared to that of coagulase negative Staphylococci (CONS) recovered from blood culture specimen in Calaba, Nigeria. PEN = Penicillin G, AMP = Ampicillin, CLX = Cloxacillin, AMX = Amoxicillin, TET = Tetracycline, COT = Co-trimoxazole, AUG = Augmentin (clavulanate potentiated amoxicillin), COL = Colistin, STR = Streptomycin, GEN = Gentamicin, AMK = Amikacin, OFX = Ofloxacin, CIP = Ciprofloxacin, CTZ = Ceflazidime, CFU = Cefuroxime, CTX = Ceftriaxone, CHL = Chloramphenicol, ERY = Erythromycin, RIF = Rifampicin, * = $p < 0.005$.

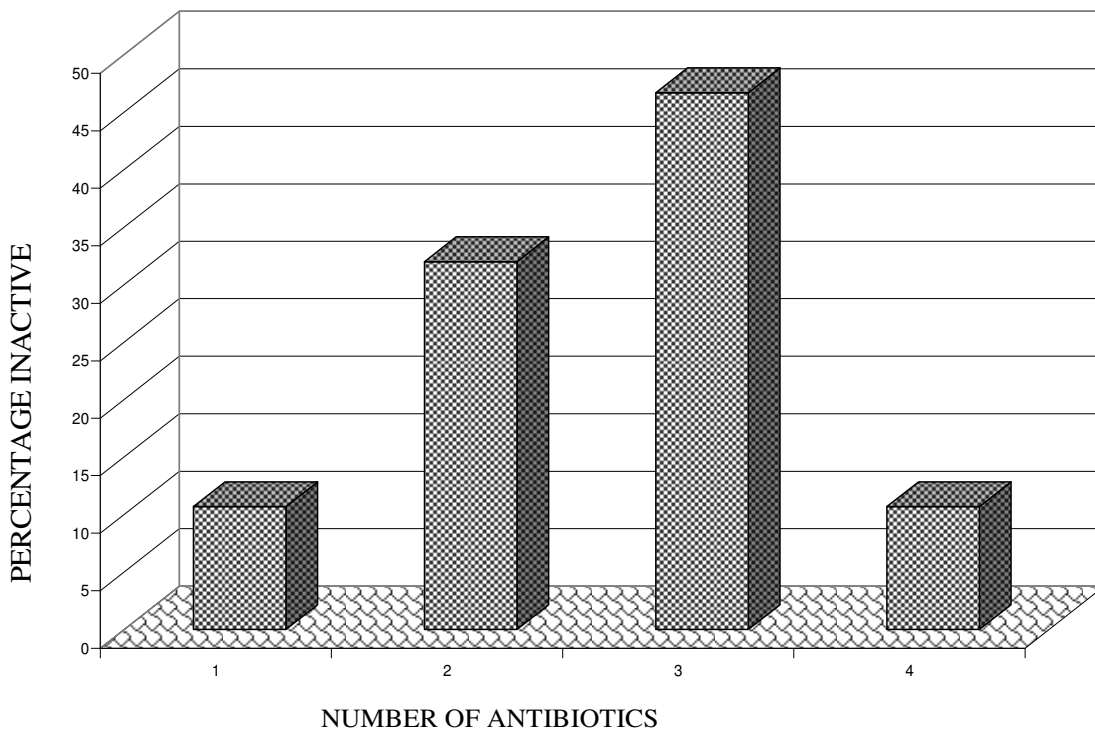


Figure 5. Patterns of multiple resistance to antibiotics by Staphylococcal isolates from blood culture specimens in Calabar, Nigeria. NB: n= number of bacterial isolates.

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