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Full Length Research Paper

Antibiotic resistance profile of staphylococci from clinical sources recovered from infants

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Infants, children and the aged are among the groups most vulnerable to microbial infections more so when these microbial agents become resistant to antimicrobials. The antibiotic resistant profile of *Staphylococcus aureus* and selected coagulase negative staphylococci were determined by standard methods. Of the 178 staphylococcal isolates evaluated, 122 were S. aureus and the rest coagulase negative staphylococci. 68% of S. aureus isolates were resistant to amoxicillin, 69.8% to cloxacillin, 51% to augmentin and 71% to tetracycline. However, only 2.6% of the 116 S aureus isolates tested were resistant to gentamycin making the drug a reliable therapeutic agent in the event of failure of other antimicrobials in treating staphylococcal infections at least in this community. Resistance to the penicillin drugs was mediated by the elaboration of β-lactamase by both pathogenic and non-pathogenic staphylococci. The study shows a high rate of cloxacillin resistance and possibly the existence of methicillin resistance among these strains. 80% of the S aureus strains were multi-resistant with 25% of these resistant to three different antibiotics, 21% to 4 and 6.8% to 6 different drugs. Only 1.2% of these S aureus strains were resistant to 7 different antimicrobials underscoring the need to reduce the high incidence of multi-resistance in this community in the event of an epidemic caused by these strains. The study reveals prevalence of multi-resistance among both pathogenic and non-pathogenic staphylococci in the community.

Key words: Staphylococci, *Staphylococcus aureus*, antibiotics, multi-resistance**.**

INTRODUCTION

Staphylococci are ubiquitous microorganisms important in human and animal infections (Goldmann, Durbin and Freeman, 1981; Dawodu and Alausa, 1980; Ako-Nai et al., 2002). *Staphylococcus aureus*, a major pathogenic strain in man, may occur as the microflora of the anterior nares of 20-40% of Nigerians (Paul et al., 1982; Lamikanra et al., 1985). Nasal carriers of S. aureus are at greater risk of post-operative wound sepsis than non-carriers (Williams et al., 1959; Ako-Nai et al., 1992). Recently reports show high incidences of antibiotic resistance among staphylococcal strains obtained in the Ile Ife community in the neonate and the adolescent (Ako-Nai et al., 2002; Ako-Nai et al., 1999). Resistance to methicillin has also been documented and the phage types characterized (Parker, 1983; Ako-Nai et al., 1991). Non pathogenic strains specifically coagulase negative staphylococci (CONS) often do not cause disease but occasionally, strains of S. saprophyticus have been associated with urinary tract infection (Khawaja et al., 1987; Ako-Nai et al., 1993).

Several studies have demonstrated that the patterns of antibiotic usage may greatly affect the number of resistant organisms which occur in an environment. However, the prevalence of resistant organisms amongst infants who have not used or been exposed to antimicrobials is, therefore, worrisome because of the latter's relatively immature immune system and attendant

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vulnerability to infection early in life. Hence our study is to determine the staphylococci involved in childhood illnesses in our (Ile Ife) community and their antibiotic susceptibility patterns.

MATERIALS AND METHODS

Study population

Infants and children aged 0 - 5 years suspected of suffering from bacterial diseases were recruited from the ambulatory and in-patients that were seen at the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC) Ile-Ife, between March 2001- February 2002. This hospital complex is a major referral tertiary health system that caters for over half a million inhabitants of the ancient city of Ile-Ife, in southwestern Nigeria and neighbouring communities. Criteria of selection of subjects were based on clinical evaluation by the attending pediatrician which included fever, cough, nasal discharge/congestion relating to upper respiratory tract, nausea and vomiting, septicemia, and skin defects that formed pus or crusts. All subjects presented with fever were admitted into the study. Permission for participation was voluntarily obtained from parents or handlers of subjects in accordance with the Institution's ethics committee guideline.

Isolation of staphylococci

Samples of pus, serous, and nasal discharges were collected with sterile cotton-wool applicators (Evepon Nig. Ltd). 2 ml of venous blood was obtained from each subject using sterile 5 ml syringe after cleansing the skin area with 70% acetone/ethanol mixture.

Blood samples obtained from subjects were introduced into Brain Heart Infusion (BHI) broth and monitored for growth at 37^0C initially for 48 h in the presence of 10% CO_2. Each swab obtained from subject was applied onto freshly prepared blood, chocolate and Mannitol salt agar (MSA) plates and streaked for discrete colonies with the aid of flame sterilized inoculating loop. Such plate was thereafter incubated at 37^0C initially for 48 h or longer for evidence of growth. Colonies appearing on MSA were picked and assessed by their Gram reactions. Those appearing as clusters were deemed as staphylococci and were picked and tested for coagulase production by both the slide and tube tests using human pooled plasma. Based on coagulase production, the staphylococci were considered as S. aureus isolates. Those staphylococci that did not ferment mannitol on mannitol salt agar were grouped as coagulase negative staphylococci (CONS). Such isolates were speciated by methods of Schleiffer and Kloos (Schleifer and Kloos, 1975). Other non-significant colonies seen were excluded. The ability of each S. aureus and CONS isolates to elaborate penicillinase was evaluated using method of Odugbemi et al. (1977).

β-lactamase assay

This test was carried out as described by Odugbemi et al. (1977). Strips of starch paper measuring 4 cm by 7 cm were cut and sterilized with 70% ethanol. These strips were then soaked for 10 min in a solution of benzyl penicillin dissolved in phosphate buffer containing 100,000 units. They were spread evenly onto sterile Petri dishes. 18 to 24 h old cultures of test organisms grown on nutrient agar were then inoculated on the surface of the test paper and spread over an area of 2 to 3 mm. Each test paper was then used to test 6 organisms at a time with the inocula placed at least 1.5 cm apart. The Petri dishes were then incubated for 30 min at 37^0C, after which the plate was flooded with Gram iodine solution. This was immediately drained off. This caused the starch paper to turn uniformly black within 30 s of application. Colonies with decolorized zones thereafter were indicative of β-lactamase production. Results were read within 5 min, as black background tends to decolorize, making interpretations more difficult.

Antibiotic sensitivity tests

Antibiotic sensitivity tests of staphylococcal isolates were performed by the disc dilution method (Ericsson and Sherris, 1971). The plating medium was Mueller–Hinton medium and antibiotics used contained amoxicillin (25 mcg), tetracycline (30 mcg), cloxacillin (5 mcg), erythromycin (4 mcg), chloramphenicol (30 mcg), cotrimoxazole (25 mcg), gentamicin (10 mcg), augmentin (30 mcg). Typed culture S. aureus ATCC A25923 was included as control.

RESULTS

Septicemia was diagnosed in 63 of the subjects (32 males and 31 females). Eight subjects each had ophthalmic infections and bronchopneumonia, while 5 wereas diagnosed of tetanus and impetigo. Two neonates had otitis media while another 2 had urinary tract infection. Four subjects had infection in their circumcision sites. Three of the infants had boils and 2 had carbuncles. Ten had wounds on different parts of their body. Ophthalmic infection as well as skin sepsis was recorded in 2 infants while another 2 had impetigo along with urinary tract infection. Urinary tract infection with skin sepsis was recorded in 6 subjects and tetanus occurred along with septicemia in 2 subjects.

Distribution of Staphylococci

Altogether, a total of 178 staphylococcal isolates were cultured from 245 samples averaging 1.37 bacteria per sample. One hundred and twenty-two of these were S. aureus strains and 56 remaining coagulase negative staphylococci (CONS). Six different staphylococcal species were identified: S. aureus predominated (68.5%) out of a total of 178 isolates followed by S. epidermidis (20.2%), S. saprophyticus and S. xylosus (1.7% each) and S. simulans and S. capitis (1.1% each). Of the 122 S. aureus strains recovered, 84 isolates were from the skin, 20 from blood, 9 from wounds, 5 from eye and 4 from nose. The distribution of staphylococci is shown (Table 1).

Pattern of β-lactamase production among Isolates

β-Lactamase enzyme production was tested in all the staphylococcal isolates. Out of all the 178 isolates, 96 (53.9%) staphylococcal isolates were β-lactamase producers, with 70 (72.9%) being S. aureus and 26 (27.1%) being coagulase negative staphylococci (CONS).

Table 1. Distribution of major bacterial isolates from different clinical sources.

ORGANISMS	TOTAL NO	SOURCES				
		SKIN	BLOOD	EYE	WOUND	NOSE
Staphylococcus aureus	122	84	20	5	9	4
Staphylococcus epidermidis	36	24	8	3	1	-
Staphylococcus	3	2	-	1	-	-
saprophyticus	2	2	-	-	-	-
Staphylococcus capitis	2	2	-	-	-	-
Staphylococcus simulans	3	2	-	1	-	-
Staphylococcus xylosus	10	5	3	1	-	1
Other CONS	178	121	31	11	10	5
TOTAL		(68%)	(17.4%)	(6.2%)	(5.6%)	(2.8%)

Table 2: Categorization of *S. aureus* strains.

Source	Total no of strains	No (%) of beta-lactamase positive strains	No (%) of beta-lactamase negative strains
Skin	84	47 (56.0%)	37 (44.0%)
Blood	20	10 (50%)	10 (50%)
Eye	5	5 (100%)	__ (0%)
Wound	9	5 (55.6%)	4 (44.4%)
Nose	4	3 (75%)	1 (25%)
Total	122	70 (57.4%)	52 (42.6%)

Table 3. Categorization of coagulase negative staphylococci

Source	Total no of strains.	No (%) of beta-lactamase positive strains.	No (%) of beta-lactamase negative strains.
Skin.	37	19 (51.4%)	18 (48.6%)
Blood	11	5 (45.5%)	6 (54.5%)
Eye	6	2 (33.3%)	4 (66.7%)
Wound	1	0 (0%)	1 (100%)
Nose	1	0 (0%)	1 (100%)
Total	56	26 (46.4%)	30 (53.6%)

The distribution of the 96 β-lactamase producers is as follows: 66 (68.75%) were obtained skin, 15 (15.62%) from blood and 7 (7.29%) from eye. Also, 5 (5.21%) were obtained from wound and 3 (3.13%) from nose. The distribution of these S. aureus strains are as follows: 47 from skin, 10 from blood, 5 from eye, 5 from wound and 3 from nose (Table 2).

The β-lactamase negative strains were 82 (46.1%); 52 (63.41%) of which were S. aureus and 30 (36.59%) being CONS (Tables 2 and 3).

The distribution of the β-lactamase negative staphylococcal isolates was also evaluated. 55 (67.1%) of them were cultured from skin, 16 (19.5%) from blood, 4 (4.9%) from eye, 5 (6.1%) from would and 21 (2.4%) from nose. All the 4 strains from the eye were all CONS. Out of those that were S. aureus strains, 37 were recovered from skin, 10 from blood, and 4 from wound and only 1 from nose. No β-lactamase producing S. aureus strain was recovered from the eye (Tables 2 and 3).

Pattern of antibiotic resistance among Isolates

Out of the 178 isolates encountered in this study, only 168 (94.4%) of them were tested with various antibiotics.

Table 4. Multiple antibiotic resistance patterns of isolates.

Bacterial isolate	Total no of isolate	No tested	No of antibiotics to which isolate was resistant								
			0	1	2	3	4	5	6	7	8
S.aureus	122	116	6	9	8	29	25	29	8	2	-
S.epidermidis	36	36	1	3	7	10	7	6	2	-	-
S.saprophyticus	3	3	1	-	-	2	-	-	-	-	-
S. capitis	2	2	-	-	-	-	1	-	1	-	-
S. simulans	2	2	-	-	1	-	-	1	-	-	-
S. xylosus	3	3	-	-	-	1	1	1	-	-	-
Other CONS	10	6	-	2	-	-	1	2	1	-	-
TOTAL	178	168	8(4.8%)	14(8.3%)	16(10%)	42(25%)	35(21%)	39(23%)	12(7%)	2(1%)	-

Table 5. Antibiotic resistance profile of staphylococci.

Bacterial isolate	No of strains	No tested	AMX.	ERY.	TET.	CXC.	GEN.	COT.	CHL.	AUG.
S. aureus	122	118	79(68.1%)	63(54.3)	83(71.6%)	81(69.8%)	3(2.6%)	36(31.0%)	14(12.1%)	60(51.7%
S.epidermidis	36	36	24(66.7%)	11(30.6%)	25(69.4%)	19(52.8%)	0	15(41.7%)	3(8.3%)	20(55.6%)
S.saprophyticus	3	3	0	1(33.3%)	2(66.7%)	2(66.7%)	0	1(33.3%)	0	0
S. capitis	2	2	0	2 (100%)	2(100%)	2(100%)	0	2 100%	1(50%)	1 (50%)
S.simulans	2	2	1 (50%)	1 (50%)	1 (50%)	1 (50%)	0	2 (100%)	0	1 (50%)
S. xylosus	3	3	2 (66.7%)	2(66.7%)	2(66.7%)	3(100%)	0	2(66.7%)	0	1 (33.3%)
Other CONS.	10	6	3 (50%)	2(33.3%)	3 (50%)	5(83.3%)	0	4(66.7%)	1(16.7%)	4 (66.7%)
TOTAL	178	168	109(64.9%)	82(48.8%)	18(70.2%)	113(67.3%)	3(1.8%)	62(36.9%)	19(11.3%)	87(51.8%)

116 (69%) of these were S. aureus and 52 (31%) were CONS strains. 68 (58.6%) of the S. aureus strains were β-lactamase producers and 48 (41.4%) were β-lactamase negative strains, while 26 (50%) of the CONS were β-lactamase producers and the remaining 26 were non-producers.

Most of the staphylococcal isolates were resistant to one or more antibiotics. Only 8 (4.8%) were sensitive to all the antibiotics employed. Of the 8, 5 were β-lactamase producers (3 S. aureus and 2 CONS strains) while the other 3 were β-lactamase negative S. aureus strains. 14 (8.3%) of the isolates tested were resistant to only one antibiotic, 16 (9.5%) to only two while all others were resistant to three or more antibiotics (Table 4).

The patterns of resistance of the isolates recovered different sources were evaluated and are shown in Table 5. 67.3% of the staphylococcal isolates were resistant to cloxacillin, followed by 64.9% to amoxicillin, and 51.8% to augmentin. Resistance to tetracycline was 70.2%, followed by erythromycin (48.8%), cotrimoxazole (36.9%) and chloramphenicol (11.3%). Only 1.85% was resistant to gentamicin.

For the β-lactamase producing strains of S. aureus, resistance to amoxicillin was 86.8%, followed by augmentin (60.3%) and cloxacillin (58.8%) whereas, resistance to tetracycline was 68.2%, cotrimoxazole and erythromycin 38.2% each, and chloramphenicol was 16.2%. Only 2.9% was resistant to gentamicin.

For the S. aureus strains that did not produce the enzyme β-lactamase, 85.4% of them were resistant to cloxacillin, followed by 41.7% to amoxicillin and 39.6% to augmentin. Resistance to tetracycline among this group was 79.2%, while 77% of them were resistant to erythromycin. 20.8% of these were resistant to cotrimoxazole, 6.7 % to chloramphenicol and only 2.1% to gentamicin. The resistance profile of CONS strains was as follows: None of the 52 CONS strains obtained from the various clinical sources and tested was resistant to gentamicin (0% resistance).

For the CONS β-lactamase producers, resistance to amoxicillin was 69.2%, followed by 50% of these isolates that were resistant to augmentin, and 38.5% were resistant to cloxacillin. Resistance to tetracycline among these isolates was also high 69.2%, while resistance to cotrimoxazole, erythromycin and chloramphenicol were

Table 6. Profile of antibiotic resistance of beta-lactamase producing *s.aureus* strains.

Source	No of strains	No tested	No tested	ERY.	TET.	CXC.	GEN.	COT.	CHL.	AUG.
Skin	47	45	40(88.9%)	18(40%)	33(73.3%)	28(62.2%)	1(2.2%)	20(44.4%)	7 (15.6%)	30(66.7%)
Blood	10	10	7 (70%)	7 (70%)	7 (70%)	7 (70%)	0 (0%)	2 (20%)	3 (30%)	4(40%)
Eye	5	5	5 (100%)	1 (20%)	1 (20%)	2 (40%)	0 (0%)	1 (20%)	1 (20%)	2(40%)
Wound	5	5	5 (100%)	0 (0%)	2 (40%)	0 (0%)	1(20%)	2 (40%)	0 (0%)	2(40%)
Nose	3	3	3 (100%)	0 (0%)	2(66.7%)	3(100%)	0 (0%)	1(33.3%)	0 (0%)	3(100%)
Total	70	68	59(86.8%)	26(38.2%)	45(66.2%)	40(58.8%)	2(2.9%)	26(38.2%)	11(16.2%)	41(60.3%)

Table 7. Profile of antibiotic resistance of beta-lactamase negative *S.aureus* strains.

Source	No of strains	No tested	AMX.	ERY.	TET.	CXC.	GEN.	COT	CHL.	AUG.
Skin	37	34	13(38.2%)	24(70.6%)	27(79.4%)	28(82.4%)	1 (2.9%)	10(29.4%)	2 (5.9%)	13(38.2%)
Blood	10	9	4(44.4%)	9(100%)	7(77.8%)	9(100%)	0 (0%)	0 (0%)	1(11.1%)	4(44.4%)
Eye	_	__	__	__	__	__	__	__	__	__
Wound	4	4	2(50%)	3 (75%)	3 (75%)	3 (75%)	0 (0%)	0 (0%)	0 (0%)	2 (50%)
Nose	1	1	1(100%)	1(100%)	1(100%)	1(100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total	52	48	20(41.7%)	37(77.0%)	38(79.2%)	41(85.4%)	1 (2.1%)	10(20.8%)	3 (6.3%)	19(39.6%)

Table 8. Profile of antibiotic resistance of beta-lactamase producing (cons) strains.

Source	No of strains	No tested	AMX.	ERY.	TET.	CXC	GEN.	COT.	CHL.	AUG.
Skin	19	19	13(68.%)	2(10.5%)	13(68.4%)	7(36.8%)	0 (0%)	8(42.1%)	1(5.3%)	10(52.6%)
Blood	5	5	3(60%)	1 (20%)	3(60%)	1(20%)	0 (0%)	2 (40%)	0 (0%)	2 (40%)
Eye	2	2	2 (100%)	1(50%)	2 (100%)	2(100%)	0(0%)	2 (100%)	1(50%)	1 (50%)
Wound	__	__	__	__	__	__	__	__	__	__
Nose	__	__	__	__	__	__	__	__	__	__
Total	26	26	18(69.2%)	4(15.4%)	18(69.2%)	10(38.5%)	0 (0%)	12(46.2%)	2(7.7%)	13 (50%)

46.2, 15.4 and 7.7%, respectively. All the isolates were sensitive to gentamicin.

Regarding the β-lactamase negative CONS strains, resistance to cloxacillin was 84.6%, augmentin 53.9% and amoxicillin 46.2%. 65.4% of these isolates were also resistant to tetracycline, followed by erythromycin (57.7%), cotrimoxazole (53.9%) and chloramphenicol (11.5%). Similarly (as for the CONS β-lactamase producers), all were sensitive to gentamicin. These values are shown in Tables 6 to 9.

DISCUSSION

The study was undertaken to characterize staphylococci from clinical sources as well as determine the susceptibility patterns of these isolates to commonly used antimicrobials in this community. We found that only 2.6% were resistant gentamicin underscoring the fact that gentamicin may be quite effective in the event of therapeutic failure of other antimicrobials at least in this community. Such observation has been the case in our previous studies with children with acute otitis media (Ako-Nai et al., 2002). The efficacy of gentamicin may due in part to mode of administration (injectable) which does not lend it to ease of abuse by users.

While S. aureus possesses antibiotic resistance genes, metS2 (methionyl-transfer-RNA synthetase) and ileS2 (isoleucyl-transfer-synthetase 2) both of which are on the main chromosome (Baillie and Read, 2000), mupirocin-resistant S. aureus also contains ileRS which can either be plasmid borne or located on the chromosome (Dyke et

Table 9. Profile of antibiotic resistance of beta-lactamase negative (cons) strains.

Source	No of strains	No tested	AMX.	ERY	TET	CXC	GEN	COT	CHL	AUG
Skin	18	16	7 (43.8%)	10(62.5%	11(68.8%)	13 (81.3%)	0 (0%)	6(37.5%	3 (18.8%	9 (56.3%)
Blood	6	5	3(60%)	3(60%)	3 (60%	4 (80%)	0 (0%)	5(100%)	0(0%)	3 (60%)
Eye	4	4	2(50%)	1(25%)	3 (75%)	4 (100%)	0 (0%)	3 (75%)	0(0%)	2 (50%)
Wound	1	1	0 (0%)	1(25%)	0 (0%)	1(100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Nose	1	__	__	__	__	__	__	__	__	__
Total	30	26	12(46.2%)	15(57.7%)	17(65.4%)	22 (84.6%)	0 (0%)	14 (53.9%)	3(11.5%)	14(53.9%)

al., 1991; Gilbart et al., 1993; Hodgson et al., 1994). Occurrence of ileS2 gene in S. aureus is highly strain specific (Brown et al., 2003). Brown et al. (2003) have also observed that horizontal gene transfer is a factor in the occurrence of antibiotic resistance in clinical isolates. Consequently, it has been suggested that the high prevalence of resistance to a particular antibiotic does not always reflect antibiotic consumption as observed by Gaynes and Monnet (1997) in some United States hospitals and by Witte et al. (2000) in Germany hospitals. CONS have been reported to be also resistant to a wide spectrum of antibiotics (Marsik and Brake, 1982). Multi-resistance among S. epidermidis isolates is widespread particularly to penicillin, ampicillin and tetracycline (Ang et al., 1985).

Improvement and strengthening of existing institutional guideline with regard to dispensing and use of antibiotics, establishment of a surveillance group to monitor S. aureus resistance profile, treatment of hospital personnel who are known carriers of multi-resistant S. aureus strains are among steps that could be taken to reduce high incidence of antibiotic resistance. Others have suggested that practice of better personal and environment sanitation in the hospital and the community will assist in no small measure to reduce the incidence of cross infection. It is quite encouraging to know that gentamicin is very effective and can be ready employed in case of treatment failure with some of these antimicrobials.

In conclusion, this study shows prevalence of multi-resistant *S. aureus* strains in the environment and underscores the need to reduce this trend particularly among infants and children who are most vulnerable to bacterial infections. The results obtained here, we hope, will enhance clinicians' capability to better manage these illnesses and reduce possible sequalae.

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