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Antibiotic Resistance among bacterial Isolates in Neonatal Septicaemia

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Summary

Njokanma OF, Olanrewaju DM and Akesode FA. Antibiotic Resistance among bacterial Isolates in Neonatal Septicaemia. *Nigerian Journal of Paediatrics 1994; 21: 47.* Antibiotic-resistant organisms in septicaemia is reported. This prospective study has revealed an overall rate of septicaemia as being 27.95 per 1000 live births at the Ogun State University Teaching Hospital (OSUTH). The commonest causative organism in the series was Klebsiella species, being responsible for 52.9 percent of the bacterial isolates in both in-born and out-born patients. *Staph aureus* and *E coli* respectively, were the second with 29.4 percent and third with 7.4 percent causative organisms. Klebsiella species was also the commonest resistant isolate with 48 percent resistance in the series. By contrast, 91 percent of other gram-negative organisms were sensitive to gentamicin. The overall 63 percent sensitivity of all the gram-negative organisms to gentamicin in the present series, indicated a declining trend since 1977, from previous findings in different centres in the country. The use of cefotaxime or amikacin as "initial" therapy while awaiting culture results, is recommended.

Introduction

SEPTICAEMIA is one of the causes of high morbidity and mortality in the neonatal period;[1] it often runs a fulminant course necessitating early commencement of treatment, while awaiting results of laboratory investigations.[2]

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The choice of antibiotics for initial therapy depends on the local pattern of pathogens as well as on the prevailing sensitivity to antibiotics. However, significant shifts occur in these patterns from time to time within a given centre or geographical region;[3] it is thus, necessary to constantly review neonatal septicaemia in order to detect these early shifts in pattern. The present study was therefore, undertaken to determine the current pattern of causative bacterial organisms in neonatal septicaemia in the department of Paediatrics, Ogun State University Teaching Hospital (OSUTH), Sagamu.

Patients and Methods

All the babies with a clinical diagnosis of neonatal septicaemia, admitted into the neonatal unit, department of paediatrics, OSUTH, over a period of 20 months (January 1991 - August 1992) were studied. Blood sample was taken under aseptic conditions and was cultured in glucose -broth for aerobic organisms and in thioglycolate broth for anaerobic organisms. Identification of organisms was by standard laboratory techniques,[4] while antibiotic sensitivity was determined by the disc - diffusion method.[5] While awaiting the results of sepsis screening, treatment was commenced with intravenous cloxacillin at 100mg/kg/day in four divided doses and intramuscular gentamicin at 5mg/kg/day in two divided doses, during the first week of life, or 7.5mg/kg/day in three divided doses, thereafter. When there was evidence of clinical and/or *in vitro* resistance, the patient was treated with intravenous cefuroxime at 50 - 75mg/kg/day, in three divided doses, or cefotaxime at 100mg/kg/day in two divided doses. Statistical analysis was carried out, using the Chi-square test to determine significant observations.

Results

There were 68 positive blood cultures obtained from 62 patients, 26 of whom were in-born, while 36 were out-born. The total number of live births in the hospital during the study period was 930; thus, the incidence of neonatal septicaemia was 27.96 per 1000 live births. There were 31 males and 31 females (male : female ratio, 1:1). Over the same 20-month period of the study, there were 86 preterm and 844 term deliveries; the septicaemia rate was 81.4 per thousand pre-term and 22.5 per 1000 term deliveries (X^2 = 9.96, P <0.005). Septicaemia accounted for 62 (10.7 percent) of all 578 neonatal admissions over the same period. Clinical manifestations occurred in 19 (73.1 per cent) of the 26 in-born babies within 48 hours of delivery (early onset), while 15(41.7 percent) of the 36 out-born babies, were admitted with early onset disease (X^2= 6.01, P <0.02).

TABLE I

Clinical Features in 62 Neonates with Septicaemia

Feature	*No of Cases*	*Percent of Total*
Fever (≥ 37.8°C)	32	51.6
Jaundice	18	29.0
Respiratory distress	14	22.6
Poor sucking	10	16.1
Irritability	8	12.9
Hypothermia	6	9.7
Apnoeic attacks	6	9.7
Lethargy	5	8.1
Diarrhoea	4	6.5
Vomiting	4	6.5

Table 1 shows the major presenting clinical features. Fever was the commonest presenting complaint and this feature was also the commonest sign with temperature ≥ 37.8°C. A history of prolonged rupture of fetal membranes was elicited in seven (11.3 percent) of the 62 cases, while in 13 (21 percent), there was a history of moderate or severe birth asphyxia. Associated diseases among the 62 patients included four cases of neonatal tetanus, three cases of pyogenic meningitis, two cases each, of necrotizing

enterocolitis and suppurative otitis media and one case each, of septic arthritis and disseminated intravascular coagulopathy. Isolated organisms in the series are shown in Table II and Klebsiella species was the commonest organism, being 18 (60.0 percent) of the 30 isolates from the in-born and 18 (47.4 percent) of the 38 isolates from out-born patients. There were four (10.5 percent) isolates of *Escherichia coli* (*E coli*) and 11(28.9 percent) of *Staphylococcus aureus* (*Staph aureus*), among 38 out-born babies and one (3.3 percent) isolate of *E coli* and 9 (10.0 percent) isolates of *Staph aureus* among in-born babies. There was no predilection of any organism for early or late onset septicaemia.

TABLE II

Bacterial Organisms Isolated from In-born and Out-born Patients

Organism	*No of Isolates*		*Total No of Isolates (n-68)*
	In-born (n=30)	*Out-born (n=38)*	
Klebsiella species	18(60.0)	18(47.4)	36(52.9)
E Coli	1(3.3)	4(10.5)	5(7.4)
Proteus species	1(3.3)	2(5.3)	3(4.4)
Pseudomonas species	1(3.3)	1(2.6)	2(2.9)
Atypical coliforms	0(0.0)	2(5.3)	2(2.9)
Staph aureus	9(10,0)	11(28.9)	20(29.4)

Figures in parenthesis represent percent of total isolates.

The *in vitro* sensitivity pattern of the organisms to antibiotics is shown in Table III. Resistance to gentamicin was the commonest with Klebsiella species, being 48 percent of 29 isolates tested against this antibiotic; Klebsiella was followed by *E coli* (20 percent resistance). Resistance was shown by 37 percent of all the 40 gram-negative isolates. Resistance to cefotaxime was commonest with *E coli*, being 33 percent of the isolates. Klebsiella species was sensitive to gentamicin in 52 percent of the isolates and 92 percent for other gram-negative isolates combined. Because of resistance, antibiotics had to be changed to cefuroxime or cefotaxime in 19 (36.6 percent) cases due to Klebsiella species.

TABLE III

Resistance and Sensitivity of bacterial Organisms to Antibiotics

Organism	*Antibiotics*				
	CN	*CTX*	*C*	*PN*	*OB*
Klebsiella species	52(29)	100(11)	20(15)	0(25)	-
E coli	80(5)	67(3)	75(4)	0(4)	-
Proteus species	100(2)	100(2)	0(2)	0(2)	-
Pseudomonas species	100(2)	-	-	50(2)	-
Atypical coliforms	100(2)	-	0(2)	0(2)	-
All gram-negatives	63(40)	94(16)	25(24)	3(34)	-
Staph aureus	100(14)	93(14)	57(14)	7(15)	71(14)

CN =Gentamicin, CTX = Cefotaxime,
OB = Cloxacillin, C = Chloramphenicol,
PN = Ampicillin

Figures in parenthesis represent the numbers of organisms tested against each antibiotic and those outside parenthesis represent the percent of organisms sensitive to the antibiotic.

Six patients (three in-born, three out-born) were discharged by parents against medical advice before completion of therapy. Eight of the remaining 56 patients died, an overall mortality rate of 14.3 percent. Six (30 percent) of the 20 septicaemic babies of low birthweight died, while only two (5.6 percent) of the 36 full term patients died, (X^2 = 4.44, P< 0.05). All eight fatal cases were out-born, a mortality rate of 22.2 percent. Four (13.3 percent) of 30 patients with early-onset septicaemia died, while four (15.4 percent) of 26 neonates with late onset disease died (X^2 = 0.05, P> 0.6). One (5.9 percent) of the 17 patients with gram-positive septicaemia died, in contrast to seven (17.9 percent) of the 39 patients who had gram-negative septicaemia (X^2 = 1.20, P>0.05).

Discussion

The incidence of neonatal septicaemia in our country has reportedly been increasing, rising from five to nine per 1000 before 1985 [2,3,6,7] and to more than 20 per 1000 in recent studies. [5,9] These high incidences are essentially similar to those reported from some other developing countries [10] and they have been associated with an increase in the relative importance of Klebsiella species as an aetiologic agent in neonatal septicaemia. In 1977, Omene [2] reported an incidence of 10.8 percent of Klebsiella isolates in Benin City. In the present study, the incidence of this organism was 53.0 percent, thus confirming the tendency for upward shifts in pattern of bacterial isolates generally.

A striking feature in the present study, was the high rate of *in vitro* resistance of the gram-negative isolates to gentamicin and *Staph aureus* to cloxacillin. Several previous studies in the country have shown a progressive decline in the sensitivity of gram-negative organisms, particularly, Klebsiella species, to gentamicin. [2,3,6,7,11] The implications of this trend are two- fold: first, as Klebsiella species have the ability to transfer antibiotic resistance qualities to other gram-negative organisms, [12] it is therefore, conceivable that other gram-negative isolates may soon acquire resistance to gentamicin. Secondly, antibiotic policy must change to accommodate Klebsiella species, since these organisms constituted as much as 53 percent of all the isolates and 75 percent of gram-negative isolates in the present study. This finding suggests a change to cefotaxime , as the drug of choice for initial therapy, especially as it has good coverage also for staphylococcal isolates. It should be noted that this type of antibiotic policy has been practised to advantage elsewhere and clinical and laboratory trials have confirmed the safety and effectiveness of cefotaxime in neonates. [1] The major limiting factor in its use is the prohibitive high cost. As an alternative to cefotaxime, amikacin, an aminoglycoside, has been recommended as the best drug to use in the face of gentamicin resistance. [1] Whichever policy is adopted must be backed by an attempt to control those factors which might encourage the emergence of resistant strains and such factors include the ease with which antibiotics are purchased and indiscriminately used in our country, often without any prescription from a physician and also the use of inadequate doses which, is believed to be partly responsible for the observed increasing resistance. These factors can be easily controlled by strict enforcement of laws controlling the sale of antibiotics.

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