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Bacterial Pathogens and Antibiotic Sensitivity in Neonatal Septicaemia at the Ladoke Akintola University Teaching Hospital, (LTH), Osogbo, Southwestern Nigeria

[1]F.F. Fadero, [2]A.O. Aboderin, [1]M.O. Onigbinde and [3]A.K. Ako-Nai
[1]Department of Paediatrics, Faculty of Clinical Sciences,
Ladoke Akintola University of Technology, Osogbo, Osun State, Nigeria
[2]Department of Medical Microbiology and Parasitology, Faculty of Basic Medical Sciences,
Obafemi Awolowo University, Ile-Ife, Osun State, Nigeria
[3]Department of Microbiology, Faculty of Science, Obafemi Awolowo University,
Ile-Ife, Osun State, Nigeria

Abstract: The objectives of this study were to determine the bacterial pathogens responsible for neonatal septicaemia as well as their antibiotic sensitivity patterns at the Ladoke Akintola University Teaching Hospital, Osogbo, Osun State of Southwestern Nigeria. In this prospective study, blood culture analysis was carried out in every neonate in the study and when a bacterial organism was cultured, its antibiotic sensitivity to a range of antimicrobial was carried out. Results obtained showed that 32 (52.5%) of the 61 neonates studied had neonatal septicaemia; 11 (34.4%) were born in the hospital maternity while the remaining 21 (65.6%) were referred to the hospital. Early onset neonatal septicaemia occurred in 10 (31.3%) and late onset septicaemia occurred in 22 (68.7%). Staphylococcus aureus and Proteus species were the two organisms isolated in 75% of the neonates; the other organisms being Klebsiella, Coagulase Negative Staphylococcus, Bacillus Species and E. Coli. The antibiotics to which most of the organisms were sensitive were Ciprofloxacin, Ceftriaxone and Ceftazidime. Sensitivity to Ampicillin and Cloxacillin were poor. Deaths occurred in 10 (31.3%) neonates with septicaemia and in 8 (27.6%) non-septicaemic neonates. Suggestions for a reduction in neonatal morbidity and mortality from septicaemia include: Infection surveillance unit in the hospital, running water to enhance aseptic technique in the handling of babies in the maternity and the Special Care Baby Units of the hospital.

Key words: Neonatal septicaemia, antibiotic sensitivity, Discharge Against Medical Advice (DAMA)

INTRODUCTION

Neonatal septicaemia refers to systemic infection in the newborn confirmed by a positive blood culture (Mahapatra *et al*., 2002). It remains a major cause of morbidity and mortality amongst newborn especially in developing countries (Lindsay, 1985) where its incidence is higher than in the developed world (Ali *et al*., 1994; Vergnano *et al*., 2005; Onile *et al*., 1985). Apart from the relative immaturity of the immune system of the neonate (Ali *et al*., 1994) risk factors predisposing to neonatal septicaemia in developing countries include prolonged rupture of membranes, prematurity, birth asphyxia, delivery outside a hospital, material used in cutting and dressing the cord and maternal infections during pregnancy (Ali *et al*., 1994; Owa *et al*., 1992). While gram-negative bacteriae dominate the causative organisms in the developing world (Mahapatra *et al*., 2002; Musoke and Revathi, 2000; Tallur *et al*., 2000) the picture is different in Europe and North America where Group B Streptococcus (GBS) is the prominent organism in neonatal infections (Vesikari *et al*., 1985).

The effective management of neonatal septicaemia depends on the understanding of the changing nature of the causative organisms and their patterns of antibiotic sensitivity from time to time even within the same geographical zone. Therefore, the application of results of studies from other centres to a centre where no study on neonatal septicaemia has been carried out may not be fully appropriate in the management of neonatal septicaemia (Al-Zwaini, 2002). Obtaining blood specimens for bacteriological culture and antibiotic sensitivity of isolates are central to effective management of neonatal septicaemia (Mahapatra *et al*., 2002).

Ladoke Akintola University of Technology Teaching Hospital (LTH) Osogbo is a major referral centre in Osun State, Southwestern Nigeria. Since the formal establishment of the Special Care Baby Unit (SCBU) of the

Corresponding Author: F.F. Fadero, Faculty of Clinical Sciences, Ladoke Akintola University of Technology, Osogbo, Osun State, Nigeria

hospital in 2002, any neonate admitted has received antibiotics on the presumption that he/she is infected. This is because of the inability to make a definitive diagnosis of neonatal septicaemia resulting from financial constraints on the part of the parents and the non-availability of materials for blood culture at all times in the hospital. Prescribed antibiotics for the neonates vary, as there are no previous studies from the unit to guide clinicians on the bacteriology and antibiotic sensitivity patterns in neonatal infections.

This study is therefore aimed at determining the common bacterial pathogens isolated in neonatal septicaemia and their antimicrobial susceptibilities at the SCBU of the LTH. The knowledge obtained will be useful in reducing neonatal morbidity and mortality through an informed management of neonatal septicaemia.

MATERIALS AND METHODS

This prospective study was carried out between May 1, 2004 and April 30, 2005. Since materials for processing blood cultures were not always available during the period of study, only neonates who had blood culture done were enrolled for the study. These patients included those born at the LTH Labour Ward ("Inborn" neonates) and those referred to LTH SCBU ("Outborn" neonates). Relevant information regarding antepartum, intrapartum and postpartum events that could have bearing on the health of each baby in the study was recorded. Each neonate was followed up until discharge, transfer or death.

On admission, approximately 2 mL of blood was collected from a peripheral vein in the upper limb with proper aseptic precautions using a 23-gauge scalp vein needle. The blood taken was inoculated into brain-heart infusion broth and incubated at 37°C. Cultures were inspected daily and held for seven days. Bottles showing signs of growth at any time during the seven days were sub-cultured unto blood agar and McConkey agar plates. The organisms growing on the culture plates were identified by bacteriological techniques, including colony characteristics, Gram staining, and biochemical properties (Cowan, 1993; Finegold *et al.*, 1978). Antibiotic sensitivity patterns of bacterial isolates were determined by the disc diffusion method of Bauer *et al.* (1966).

Following collection of blood samples for culture and other investigations, each neonate was commenced on antibiotics (gentamycin and ampicillin/cloxacillin or ceftriaxone/ceftazidime); duration of antibiotic usage varied between 7 and 14 days depending on the clinical response of the neonate. However, gentamycin and ampicillin/cloxacillin combination is more frequently used empirically due to easy availability and cheaper cost. In some cases, antibiotics were changed when a neonate was considered not to be responding to treatment on clinical grounds.

Results in the study are presented in simple percentages. Chi Square (χ^2) was used to compare differences between proportions with the value of ≤ 0.05 taken as statistically significant.

RESULTS

Sixty-one neonates had blood culture consisting of 21 (34.4%) inborn and 40 (65.6%) outborn neonates. There were 39 males and 22 females giving a Male: Female (M: F) ratio of 1.8: 1.

The indications for admitting the neonates to the SCBU are shown in Table 1. Neonatal jaundice, birth asphyxia, prematurity and respiratory distress were the common indications for admission in both the inborn and outborn neonates.

In 32 (52.5%) of the neonates, investigation by blood culture confirmed neonatal septicaemia: 22 (68.8%) of them were males and 10 (31.2%) were females; the male to female ratio (M: F) among the infected neonates being 2.2: 1. Although the M: F ratio of 2.2: 1 in babies with proven infection was higher than 1.4: 1 in babies without infection, this difference was not statistically significant ($\chi^2 = 0.68$, df = 1, p = 0.41) probably due to small number of patients in each group.

Table 2 shows that outborn neonates constituted 21 (65.6%) of those with septicaemia while the remaining 11 (34.4%) were inborn ($\chi^2 = 0.000$, df = 1, p = 0.99). Ten (31.3%) of the neonates were cases of early onset sepsis (those presenting less than 72 h after birth) and the remaining 22 (68.7%) were cases of late onset septicaemia (those presenting over 72 h after birth). *Staphylococcus aureus* and *Proteus* sp. were the two isolates in 75% of the infected neonates.

Table 1: Indications for admission into the SCBU

	Out-born (n = 40)		Inborn (n = 21)		Total (n = 61)	
Indication	No	%	No	%	No	%
NNJ	17	42.5	5	23.8	22	36.1
Birth asphyxia	8 ()	20	7	33.3	15	24.6
Prematurity	5	12.5	6	28.6	13	21.3
Respiratory distress	5	12.5	3	14.3	8	13.1
Convulsion	4	10	0	0	4	6.6
Fever	3	7.5	1	4.8	4	6.6
Constipation	4	10	0	0	4	6.6
Diarrhea	3	7.5	0	0	3	4.9
Refusal to suck	3	7.5	0	0	3	4.9
Failure to thrive	2	5	1	4.8	3	4.9
Birth trauma	2	5	1	4.8	3	4.9
Skin infection	2	5	0	0	2	3.3
Abdominal distension	2	5	0	0	2	3.3
Vomiting	1	2.5	0	0	1	1.6

Table 2: Shows (1) Bacteriological profile of 32 inborn and outborn neonates with early and late onset sepsis

	Total		Early onset sepsis		Late onset sepsis		Out-born		Inborn	
Organism	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Staphylococcus aureus	18	56.25	7	70	11	50.00	14	66.67	4	36.36
Klebsiella sp.	3	9.38	1	10	2	9.09	1	4.76	2	18.18
CONS*	2	6.25	1	10	1	4.55	1	4.76	1	9.09
Proteus sp.	6	18.75	1	10	5	22.72	2	9.52	4	36.36
Bacillus sp.	1	3.13	0	0	1	4.55	1	4.76	0	0
E. coli	2	6.25	0	0	2	9.09	2	9.52	0	0
Total	32	100	10	100	22	100	21	100	11	100

Note: CONS* = Coagulase Negative Staphylococcus

Table 3: Antibiotic susceptibility Profile: proportions of the bacterial isolates that were susceptible to the antibiotics tested

	S. aureus (n = 18)		*Klebsiella* sp. (n = 3)		CONS* (n = 2)		*Proteus* sp. (n = 6)		*Bacillus* sp. (n = 1)		*E. coli* (n = 2)	
Antibiotics	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Ciprofloxacin	15	83.33	2	66.66	1	50	4	66.67	1	100	2	100
Gentamycin	10	55.56	1	33.33	0	0	4	66.67	0	0	2	100
Cloxacillin	1	5.56	0	0	0	0	0	0	0	0	0	0
Ampicillin	1	5.56	1	33.33	1	50	0	0	0	0	0	0
Amoxicillin	1	5.56	0	0	0	0	0	0	0	0	0	0
Ceftazidime	7	38.89	1	33.33	1	50	1	16.67	0	0	2	100
Ceftriaxone	16	88.89	0	0	0	0	0	0	1	100	0	0

Note: CONS* = Coagulase Negative Staphylococcus

Table 4: Outcomes of admission in 61 neonates

	Septicaemic		Non-Septicaemic		Total	
Outcome	No.	(%)	No.	(%)	No.	(%)
Discharged	21	65.62	20	68.96	41	67.21
DAMA	1	3.13	1	3.45	2	3.28
Death	10	31.25	8	27.59	18	29.51
Total	32	100	29	100	61	100

Note: DAMA = Discharge Against Medical Advice

Table 3 illustrates the susceptibilities of the bacterial isolates to different antibiotics; these drugs, apart from ciprofloxacin, are the often-used antibiotics in the unit. Considering the ranges of antibiotic sensitivity and depending on the organism tested, the antibiotics to which most of the isolates were sensitive were ceftriaxone (88.9-100%), ciprofloxacin (50-100%), ceftazidime (38.9-100%) and gentamycin (0-33.3%).

Amongst the 61 neonates studied, there were 18 (29.5%) deaths: 11 (61.1%) of which were outborn and seven (38.89%) were inborn ($\chi^2 = 0.22$, df = 1, p = 0.64). Deaths occurred in 10 (31.3%) of neonates with confirmed infection and 8 (27.6%) of the remaining neonates without infection ($\chi^2 = 0.91$, df = 1, p = 0.76). There were 2 cases (one each in infected and non-infected group) of Discharge Against Medical Advice (DAMA) for financial reasons (Table 4).

DISCUSSION

Although the scope of this study is limited, its prospective design makes it a starting guideline in the management of neonatal septicaemia in this relatively new centre and a reference point for further studies on neonatal sepsis within the centre in the future.

While this study cannot determine the incidence, morbidity and mortality of neonatal sepsis in LTH, a prevalence of 52.5% among the studied patients is high and corroborates results from many other centres in developing countries (Antia *et al*., 1992; Roy *et al*., 2002).

Staphylococcus aureus was the commonest isolate in both inborn and outborn neonates with septicaemia. The prominence of *Staphylococcus aureus* in this study is similar to findings from two nearby referral centres of Ife (Adejuyigbe *et al*., 2001) and Ilorin (Mokuolu *et al*., 2002) both from Nigeria. However, this contrasts with the study from Ibadan in the same Southwestern Nigeria, where Gram-negative enteric bacilli were the most implicated organisms in neonatal septicaemia (Alausa and Onile, 1984). This variation in the microbial pattern of neonatal sepsis is in keeping with the varying nature of bacterial isolates in neonatal septicaemia within the same geographic region. *Staphylococcal aureus* was also the major isolate in inborn neonates with infection. Thus, apart from possible community and nosocomial acquisition of *Staphylococcal aureus* in both inborn and outborn neonates, some of the mothers may harbour the organism in their genital tract as demonstrated in a study from Saudi Arabia (Bilal, 1990).

Ciprofloxacin (a quinolone) is the antibiotic amongst the tested ones to which most of the isolates in the present study were sensitive. However, it is not recommended for children below the age of 5 years (BNF, 2005). Susceptibilities to the third generation Cephalosporins (ceftriaxone and cefotaxime) and gentamycin were lower than that to ciprofloxacin. These third generation Cephalosporins are very expensive in Nigeria where most parents bear the brunt of hospital stay

of these neonates. The isolates demonstrated poor sensitivity to ampicillin and cloxacillin, the commonly affordable and available antibiotics to the populace. The high resistance of the isolates to these commonly used antibiotics may be related to the indiscriminate use of these drugs in the environment as well as lack of antibiotic surveillance in the hospital as suggested in the study conducted by Al-Zwaini (2002) on neonatal infections in Iraq.

Two of the babies studied were Discharged Against Medical Advice (DAMA) at the request of the parents because of inability to continue financing the cost of treatment of the neonates. However, blood culture showed that one of the two babies was not infected.

Early routine blood culture and antimicrobial sensitivity tests in neonates at risk of neonatal septicaemia is a way to cut the costs of management as those who actually needed expensive antibiotics will be easily identified. It is hoped that this will also reduce the number of parents requesting for discharge against medical advice for their wards.

A functioning infection surveillance unit is a necessity in the battle against infections in the newborn unit. Provision of running water at all times and aseptic technique in the delivery at the maternity ward and handling of the babies in the neonatal unit will help in reducing acquisition of infection by inborn neonates.

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