East African Medical Journal Vol. 78 No. 10 October 2001
SEPTICAEMIA IN HIGH RISK NEONATES AT A TEACHING HOSPITAL IN ILE-IFE, NIGERIA
E.A. Adejuyigbe, FMCPaed (Nig), Lecturer, O.O. Adeodu, FWACP, Senior Lecturer, Department of Paediatrics and Child Health, K.A. Ako-Nai, PhD, Professor, Department of Microbiology, O. Taiwo, FRCPaed, Professor and J. A. Owa, FMCPaed, FWACP, Professor, Department of Paediatrics and Child Health, College of Health Sciences, Obafemi Awolowo University, Ile-Ife, Nigeria.

Request for reprints to: Dr. E. A. Adejuyigbe, Department of Paediatrics and Child Health, Obafemi Awolowo University, Ile-Ife, Nigeria.

SEPTICAEMIA IN HIGH RISK NEONATES AT A TEACHING HOSPITAL IN ILE-IFE, NIGERIA

E.A. ADEJUYIGBE, O.O. ADEODU, K.A. AKO-NAI, O. TAIWO and J. A. OWA

ABSTRACT

Objectives: **To determine the incidence, predisposing factors, clinical features, bacteriological pattern and antibiotic sensitivity in septicaemia in high-risk newborns.**
Design: **A prospective study.**
Setting: **Neonatal unit, Ife State Hospital, a unit of the Obafemi Awolowo University Teaching Hospital Complex (OAUTHC), Ile-Ife, Nigeria.**
Subjects: **All newborns admitted with clinical features and/or risk factors suggestive of neonatal septicaemia from February 1994 to March 1995.**
Main outcome measures: **Culture results and mortality rates.**
Results: **The incidence of neonatal septicaemia among new born was 22.9 per 1000 livebirths. The predisposing perinatal factors were low socio-economic status, lack of antenatal care, maternal peripartum pyrexia and congenital malformations. Gram-positive bacteria were found to be the most prevalent causative organisms (59.4%). *Staphylococcus aureus* (36.2%), *Pseudomonas aeruginosa* (18.8%) and Coagulase negative *Staphylococcus* (15.9%) were the commonest causes of septicaemia. Meningitis and UTI were associated diagnoses in 16.7% and 18.2% of the septicaemic babies, respectively. The bacterial isolates showed a high degree of *in-vitro* antimicrobial resistance. However, all the isolates were sensitive to ofloxacin. Amongst the commonly used antibiotics, gentamicin had the lowest resistance. The overall mortality rate was 33.3%.**
Conclusion: **Improvement in the socio-economic status of the populace and availability of affordable antenatal care would reduce the incidence of neonatal septicaemia in Nigeria. Continuous surveillance in every unit, as well as close attention to preventive strategies would be necessary to reduce morbidity and mortality from neonatal septicaemia. We recommend the inclusion of gentamicin in the initial treatment of septicaemia in the neonatal unit of OAUTHC, Ile-Ife, Nigeria.**

INTRODUCTION

Septicaemia accounts for a significant proportion of morbidity and mortality in the newborn and is therefore a major problem in paediatric practice worldwide(1). Recent reports from developing and developed countries indicate an increase in the incidence and changes in the pattern of bacteriologic agents of neonatal septicaemia(1). The incidence is higher in the tropics than in the developed countries because of various reasons, which include the higher incidence of home delivery and the poor environmental hygiene(1,2). Access to sophisticated modern medical technology is limited in developing countries and effective antibiotics are scarce and expensive. Preventive measures would therefore go a long way in reducing the morbidity and mortality from neonatal septicaemia. For this reason we decided to study the predisposing factors so that measures towards prevention can be advocated.

The pattern of bacterial agents implicated in neonatal septicaemia has been shown to vary from place to place and from time to time even in the same institution(1-3). It is therefore recommended that in each unit the incidence, clinical features, the pattern of bacterial agents and their antimicrobial sensitivity profile be studied. In the neonatal unit of the Ife State Hospital (a unit of the OAUTHC), such a study has not been previously carried out. This study was an attempt to fill this gap.

MATERIALS AND METHODS

This was a prospective study of patients admitted into the neonatal unit of the Ife State Hospital, OAUTHC, Ile-Ife, over a period of 14 months (February 1, 1994 to March 31, 1995). The Ife State Hospital is a unit of the Teaching Hospital of the Medical School of Obafemi Awolowo University. It serves as the major paediatric referral centre for Osun State and parts of Ondo, Ekiti, Kwara, Kogi and Oyo states in southwestern Nigeria. It is funded by the federal Government of Nigeria but patients

pay fees for hospital services. This is because the hospital has to generate part of its running costs.

Data were entered into a research protocol and the information entered included: name, date of birth, age on admission, place of birth, sex, estimated gestational age as calculated from the first day of the last menstrual period and/or Dubowitz gestational age score. The place of antenatal care, duration of labour, duration of drainage of liquor, mode of delivery, material used in cutting and dressing the cord, and symptoms of illness and its duration were also recorded. Other data included were maternal illness during pregnancy such as pre-eclampsia, eclampsia, jaundice, antepartum haemorrhage, polyhdramnios and diarrhoea, parity of mother, socio-economic class of the parents as calculated from their occupation and educational levels(4). The vital signs and anthropometic data of the baby were also recorded.

The presence of risk factors for and/or clinical features of neonatal septicaemia (NNS) served as inclusion criteria. The risk factors included: prolonged rupture of membranes (PROM), discoloured amniotic fluid, foul smelling amniotic fluid, intrapartum maternal pyrexia, antepartum haemorrhage, obstructed labour, preterm birth, deliveries outside the hospital and neonates who required active resuscitation such as endotracheal intubation and umbilical catheterisation at birth. Clinical features included: fever, hypothermia, lethargy, jitteriness, hypotonia, hypertonia, irritability, poor feeding, diarrhoea and vomiting, unexplained jaundice, tachypnoea, grunting respiration, convulsion and focal lesions. Consecutive neonates admitted with any of the above criteria within the study period were included in the study. Neonates whose mothers were already on antibiotics at the time of birth were excluded from the study.

In all cases of suspected septicaemia, blood, cerebrospinal fluid (CSF), urine and swabs of discharges obtained aseptically, were processed for both aerobic and anaerobic organism. The CSF was also sent for cell count, glucose and protein determination. Based on the Gram stain each sample was inoculated on selective and differential media. Colonies that grew on these media were further studied. Antibiotic sensitivity of the isolates was determined by the method of Ericsson and Sherris(5).

Initial antibiotics used on suspected cases of septicaemia consisted of a combination of intravenous ampicillin and intramuscular gentamicin in appropriate dosages. The response to antibiotic therapy was carefully monitored and therapy was altered if antibiotic sensitivity results indicated otherwise or if there was poor clinical response.

The results were collated and analysed with EPI Info 6 software. Discrete variables between groups were compared with Chi-square test or with the Fisher's exact test where sample size was less than 5. P value < 0.05 was taken as statistically significant.

RESULTS

Two hundred and ninety seven neonates were admitted into the neonatal unit during the study period. One hundred and nineteen (40.1%) of them fulfilled the criteria for inclusion in the study and these were screened. Thirty one (26%) of the 119 neonates studied were inborn while 88 (74%) were out-born. Sixty seven (56.3%) of those screened were males while 52 (43.7%) were females, with a male to female ratio of 1.3:1. The ages of the neonates studied ranged from birth (day 0) to 27 days with a mean of 5.2±5.7 days (median of 3.5 days).

Sixty six (55.5%) of the 119 neonates had culture proven septicaemia. These consisted of 40 males and 26 females with a male to female ratio of 1.5:1. Eighteen (27.3%) of the sixty six neonates with culture proven septicaemia were inborn. There were 787 livebirths in the hospital during the study period. The incidence of neonatal septicaemia among babies delivered at OAUTHC was thus (18/787) 22.9/1000 livebirths (95% confidence interval = 1.24 - 3.33).

Table 1 shows the characteristics of the patients studied and maternal risk factors in relation to septicaemia. The occurrence of maternal peripartum pyrexia, low socio-economic status, lack of antenatal care and major congenital anomalies in the neonate were statistically significantly associated with culture proven septicaemia. There was associated breach of the skin and mucous membrane in five of the seven septicaemic patients with major congenital malformations.

Table 1

Characteristics of newborns with and without septicaemia and their mothers

Characteristic	Neonates with positive blood culture (n=88)	Neonates with negative blood culture (n=53)	P value
Gestational age			
Preterm	21	10	NS
Term	45	43	
Birth weight (kg)			
<2.5	28	22	NS
≥2.5	38	31	
Sex			
Male	40	27	NS
Female	26	26	
Age on admission			
<72 hours	35	23	NS
≥72 hours	31	30	
Tetanus	17	15	NS
Birth asphyxia	5	9	NS
Congenital anomalies	7	1	<0.05
Maternal factors			
*No antenatal care	7	–	0.01
**Socio-economic class*			
I-III	14	22	0.03
IV-V	40	25	
Peripartum pyrexia	11	6	<0.05
**Membrane rupture*			
<24 hours	42		
≥24 hours	19		
**Duration of labour*			
<24 hours	39	38	
≥24 hours	17	7	NS

*Determined only among inborn
**Information was not available in some patients

In general there were no statistically significant differences in the clinical features of the septicaemic and non-septicaemic neonates. However, the neonates with proven septicaemia had a higher occurrence of septic umbilical cord and jaundice. Septic umbilical cord, fever and jaundice were more common in term than in preterm septicaemic neonates. Hypothermia and recurrent apnoea

were however more common in preterm babies. Twenty two (33.3%) of the neonates with proven septicaemia died while eleven (20.6%) of the 53 neonates with negative blood culture died ($\chi 2 = 2.32$, $p = 0.13$).

Table 2

Bacterial isolates in sixty six septicaemic neonates

	Bacterial isolate	No. of isolates (%)
A	Gram positive bacteria	41 (59.4%)
	Staphylococcus aureus	25 (36.2%)
	Coagulase negative *Staphylococcus*	11 (15.9%)
	Listeria monocytogenes	5 (7.2%)
B	Gram-negative bacteria	28 (40.6%)
	Pseudomonas aeruginosa	13 (18.8%)
	Klebsiella pneumoniae	6 (8.7%)
	Escherichia coli	4 (5.8%)
	Enterobacter aerogenes	2 (2.8%)
	Others	3 (4.2%)

The bacterial isolates are as shown in Table 2. There were 69 isolates in 66 patients (three patients had double isolates). Gram-positive bacteria were the commonest isolates and *Staphylococcus aureus* was the predominant organism. Of the Gram-negative isolates, *Pseudomonas aeruginosa* was the commonest isolate. Anaerobic organisms and group B beta haemolytic *Streptococcus* were not isolated in this study. Urinary tract infection was present in twelve (18.2%) of the septicaemic neonates and meningitis was present in eleven (16.7%). Gram-negative organisms were responsible for all the cases of meningitis and UTI. In five cases the same organisms were cultured in the blood, urine and cerebrospinal fluid. The bacteria included *Pseudomonas aeruginosa, Citrobacter freundii, Klebsiella pnuemoniae* and *Escherichia coli.* Thirteen (19.7%) culture proven septicaemic neonates also had positive swabs taken from umbilical cord, skin lesions and eye discharges.

The *in-vitro* sensitivity pattern of the organisms to antibiotic has been reported in an earlier communication(6). All isolates were sensitive to ofloxacin. Less than ten per cent of *Staphylococcus aureus* isolates were sensitive to cloxacillin and erythromycin. About 85% and 75% of *Staphylococcus aureus* isolates were resistant to methicillin and ampicillin, respectively. Amongst the cephalosporin only cefotaxime was tested and 60% of *Staphylococcus aureus,* 60% of the Gram-negative bacteria and 80% of Coagulase negative *Staphylococcus* isolates were resistant to it. Of the commonly used antibiotics, gentamicin had the lowest resistant isolates: 38% of *Staphylococcus aureus,* 27% of *Pseudomonas aeruginosa* and 29% of Coagulase negative *Staphylococcus* isolates were resistant. Clinical response was used in conjunction with antibiotic sensitivity pattern in the treatment of the neonates. On a few occasions we had to change antibiotic treatment to ceftriaxone when the patients' condition was deteriorating.

DISCUSSION

The incidence of neonatal septicaemia of 22.9/1000 livebirths reported in this study is high when compared with that reported by workers in developed countries(7). A previous study(8) from Wesley Guild Hospital, Ilesa, located 40 kilometres from Ife State Hospital, showed an incidence of 17/1000 livebirths, which is lower than the incidence in the present study. This may be due to a rising incidence (since admission policy are the same in the units) probably due to deteriorating socio-economic status of Nigerians in the past ten years. It could also be due to increasing awareness in the populace and/or improvement in the laboratory facilities. It is however in keeping with the rate reported in developing countries and in previous studies from Nigeria(9,10). The high incidence reported from Nigeria, may be due to a high prevalence of predisposing factors such as parental low socio-economic class, as demonstrated among the neonates in this study. Low socio-economic status has been associated with patronage of non-medical facilities like churches for ANC and delivery(10). This is probably due to the inability of this class of people to attend antenatal care in government and private health care facilities because of the relatively high fees charged for services. We consider it significant that our study has also demonstrated that lack of antenatal care was associated with neonatal septicaemia and also that most of the mothers of the neonates studied (56.6%) delivered outside the hospital. The introduction of hospital fees has been shown to be responsible for the low patronage of maternity services in another unit of the OAUTHC(11). The introduction of fees in the Federal Government controlled hospital in Nigeria has come out of the realisation that the Government could no longer provide all funds required by these hospitals. This has been a direct consequence of the declining socio-economic fortune of the country in the last two decades. We, however, suggest that larger number of patients be studied to determine the impact of antenatal care on the incidence of neonatal septicaemia.

The symptoms and signs of neonatal septicaemia have been well documented and found to be vague and non-specific(2), a feature that was evident in this study. Suggestive symptoms and signs were present in 119 screened and sixty six had proven septicaemia. Among the neonates with proven septicaemia, fever was common among term neonates while hypothermia was more common among preterm neonates. This difference in the temperature pattern in term and preterm infants has been attributed to a larger body surface area, smaller muscle mass and low subcutaneous fat in the preterm infant(2).

All the bacteria isolated in this study have been implicated previously in neonatal septicaemia(7). Gram-positive organisms were predominant (59.4%) among the isolates in this study, a finding similar to the reports of other workers(9,12). It was, however, at variance with other reports within Nigeria, which showed a predominance of Gram-negative organisms(2,8,13), *Staphylococcus*

aureus was the commonest isolate in this study as in some other studies(12) within Nigeria.

Coagulase negative *Staphylococcus* accounted for 21.4% of Gram-positive bacteria in this study. Some of the well-documented factors predisposing to Coagulase negative staphylococcal septicaemia such as preterm delivery, and invasive procedures like umbilical catheterisation and endotracheal intubation were present in these neonates(14). There was no case of Group B beta haemolytic streptococcal infection in this study, confirming the observations of others that this organism is not a common cause of neonatal septicaemia in Nigeria(2,8).

In this study, *Listeria monocytogenes* was isolated from the blood of five neonates. This is not a common pathogen from previous reports in the tropics although it is a known cause of neonatal septicaemia in other parts of the world(7). The source of infection in neonatal listeriosis is obscure in most cases, though it could be that the mothers were carriers since many people in the catchment area of the hospital cohabit with animals within the household(15).

One of the striking features of the present study is the high rate of *in-vitro* resistance of the bacterial isolates to commonly used antibiotics. This has been extensively reported elsewhere(5). All isolates in this study were sensitive to ofloxacin while most are already developing resistance to cefotaxime, a third generation cephalosporin. This antibiotic resistance pattern is in conformity to those in recent reports from within and outside Nigeria(10,12). The consequences of this, especially in poor countries where antibiotics play a major part in the treatment of infections, cannot be quantified. Ofloxacin, a quinolone to which all the isolates were sensitive is not currently recommended for use in childhood infections. However, in a small series within Nigeria, it was found to have been very effective in neonates with a similar antimicrobial resistance pattern(13) even though its long-term effect is yet to be determined. We recommend the inclusion of gentamicin in the initial treatment of neonatal septicaemia in our unit because it is cheap, available and the clinical response of its combination with ampicillin was good in this study. We recommend ceftriaxone in combination with amikacin as secondline antibiotics even though its sensitivity pattern was not determined in this study; we obtained good clinical response when we used it.

Improvement in socio-economic status with provision of affordable antenatal clinics and delivery services will greatly reduce neonatal septicaemia in Nigeria. Indiscriminate use of antibiotics, which promotes development of resistant strains, should be discouraged and the safety of quinolones in neonates should be determined urgently. The synthetic aminoglycosides like amikacin and tobramycin have been recommended for use in situations where there is gentamicin resistance while awaiting blood culture results(16). With the emergence of new organisms and resistant strains to the commonly used antibiotics in neonatal septicaemia, there is need for frequent surveillance in each unit with adjustment of antibiotics and intensification of efforts at prevention or reduction in the incidence and mortality of neonatal septicaemia.

ACKNOWLEDGEMENTS

To the Chairman, Medical Advisory Committee for permission to carry out the study and to publish its findings.

REFERENCES

1. Stoll B.J. The global impact of neonatal infection. *Clin. Perinatol.* 1997; **24**:1-21.
2. Dawodu A.H. and Alausa O.K. Neonatal septicaemia in the tropics. *Afr. J. Med. Sci.* 1980; **9**:1-6.
3. Ohlsson A., Bailey T. and Takieddin F. Changing aetiology and outcome of neonatal septicaemia in Riyadh, Saudi Arabia. *Acta. Paediat. Scand.* 1986; **75**: 540-544.
4. Oyedeji G.A. Socio-economic and cultural background in hospitalised children in Ilesa. *Nig. J. Paediat.* 1985; **12**:111-117.
5. Ericsson H.M. and Sherris J.C. The agar dilution method. *Acta Pathol. Microbiol. Immunol. Scand. (B)* suppl. 1971; **217**:11-12.
6. Ako-Nai A.K., Adejuyigbe E.A., Ajayi F.M. and Onipede A.O. The Bacteriology of Neonatal septicaemia in Ile- Ife, Nigeria. *J. Trop. Pediat.* 1999; **45**:146-151.
7. Vesikari T., Janas M. and Gronroos P. *et al.* Neonatal septicaemia. *Arch. Dis. Child.* 1985; **60**:545-46.
8. Owa J.A. and Olusanya O. Neonatal bacteraemia in Wesley Guild Hospital, Ilesa, Nigeria. *Ann. trop. Paediat.* 1988; **8**:80-85
9. Antia-Obong O.E. and Utsalo S.J. Bacterial agents in neonatal septicaemia in Calabar, Nigeria. *Trop. Doct.* 1991; **21**:169-70.
10. Iroha E.O., Egri-Okwaji M.T.C. and Kesah C.N. Changing patterns of causative organisms of neonatal septicaemia at the Lagos University Teaching Hospital. *Nig. J. Paediat.* 1998; **25**:1-5.
11. Owa J.A., Osinaike A.I. and Makinde O.O. Trends in utilisation of obstetric care at Wesley Guild Hospital, Ilesa, Nigeria. Effects of a depressed economy. *Trop. geogr. Med.* 1995; **47**:86-88.
12. Olusanya O., Olanrewaju D.M., Ogunfowora O.B. and Laditan M.O. Neonatal septicaemia at the Ogun State University Teaching Hospital, Sagamu. *Nig. Med. Pract.* 1991; **22**:39-42.
13. Omokhodion S.I. The use of Ofloxacin in infants with rapidly deteriorating septicaemia and multiple antibiotic resistance. *Nig. J. Paediat.* 1994; **21**:83-84.
14. Munson D.P., Thompson T.R., Johnson D.E., *et al.* Coagulase negative staphylococcus: experience in a newborn intensive care unit. *J. Paediat.* 1982; **101**:602-5.
15. Owa J.A. and Makinde O.O. Hospital survey of neonatal tetanus at Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife. *Niger Med. Pract.* 1995; **30**:56-59.
16. De Louvois J. and Harvey D. Antibiotic therapy of the newborn. *Clin. Perinatol.* 1988; **15**:365-88.