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Original Article

Risk Factors and Bacterial Profile of Suspected Neonatal Septicaemia at a Teaching Hospital in Kano, Northwestern, Nigeria

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ABSTRACT

Neonatal septicaemia is a common cause of morbidity and mortality in developing countries and a major health concern. The aim of this study is to evaluate the bacterial profile, antibiotics susceptibility pattern and associated risk factors of suspected septicaemia in neonates in this locality. Five hundred and forty seven consecutive blood samples from neonates admitted in the special baby care unit (SCBU), Aminu Kano Teaching Hospital (AKTH), Kano between January 2007 and December 2008 were cultured aerobically and anaerobically in the Microbiology Department, Aminu Kano Teaching Hospital by standard bacteriological methods. Antibiotic susceptibility pattern was done by disc diffusion methods. One hundred and fifty two (27.8%) positive blood cultures were obtained from the present study. The most frequently isolated organism was *Staphylococcus aureus* (25.0%) followed by *Klebsiella pneumoniae* (21.1%) and *Escherichia coli* (15.0%). Gentamicin, ofloxacin, ceftriaxone and amoxycillin/clavulanate showed higher percentage antibiotic sensitivity pattern while chloramphenicol, cotrimoxazole and ampicillin showed very low percentage antibiotic sensitivity pattern against the various bacterial isolates. The present study showed that *Staphylococcus aureus* is the leading isolate in neonatal septicaemia in Kano. Gentamicin and Ceftriaxone are recommended as first line drugs in the management of neonatal septicaemia in our locality.

Keywords: Antibiotic susceptibility, Bacterial isolates, Neonatal septicaemia, Risk factors

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INTRODUCTION

Infections are frequent and important cause of mortality and morbidity in the neonatal period. New born infants are less capable of responding to infection because of one or more immunologic deficiencies. A wide variety of etiologic agents infect the new born, including bacteria, viruses, fungi, protozoa, and mycoplasma. Neonatal septicaemia is a clinical syndrome resulting from the pathophysiologic effects of local or systemic infections in the first month of life (Stoll, 2004).

In Nigeria, septicaemia is a major cause of death in neonates and children (Dawodu and Alausa, 1980; Antia-Obong, 1992). Absence of urgent intervention can always lead to the death of neonates. Hospital based incidence of neonatal septicaemia is high ranging from 5-25/1000 live births and accounting for 20-25% neonatal mortality (Akindele *et al*.,1992; Omokhodion *et al*.,1993; Ibrahim *et al*., 1996). This high incidence is believed to be related to the prevalence of predisposing factors and lack of basic amenities for optimal hygiene, especially portable water (Omokhodion *et al*., 1993; Ibrahim *et al*., 1996).

Clinical assessments using a combination of symptoms and signs are useful guides to septicaemia. A seven-item weighted clinical score system comprising grunting, abdominal distension, increased pre-feed aspirates, tachycardia, hypothermia, chest retractions and lethargy showed that these criteria were sensitive for identifying neonates with septicaemia (Singh *et al*., 2002). However, prompt diagnosis and effective treatment is necessary to prevent death and complication from septicaemia, hence laboratory diagnosis by culture and antibiotic sensitivity pro-

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cedures are inevitable (Meremikwu *et al*., 2005). Management of newborn with septicaemia will require appropriate antibiotic therapy and supportive care. The choice of antibiotic therapy is best guided by knowledge of the aetiologic agents. Blood culture results could last between 7-10 days, necessitating initial empirical treatment of suspected septicaemia. Thus, it is customary to initiate treatment with an empiric choice of antibiotics that is informed by the epidemiology of causative agents and sensitivity patterns in a given locality (Singh *et al*., 2002). Bacteriology of neonatal septicaemia is required because of the changing pattern of the aetiologic agents even within the same geographic area. Incidentally, antibiotic sensitivity pattern also continues to vary overtime and area (Batisin *et al*., 1981). The aim of this study is to evaluate the bacterial profile, antibiotics susceptibility pattern and associated risk factors for suspected neonatal septicaemia in Kano so as to establish a base line data that could be of relevance to clinicians involved in the management of neonates in this locality.

MATERIALS AND METHODS

Study Design

This is a Prospective cohort study. Consecutive blood samples for culture and sensitivity from 547 neonates admitted at the Special Baby Care Unit (SCBU) of AKTH were analysed at the Microbiology Laboratory Department AKTH between January 2007 and December, 2008. The indication for blood cultures were clinical suspicion of septicaemia (body temp:>37^{o}C). Data recorded on presentation were gestational age, birth weight, age at presentation, sex, place of delivery and presenting signs and symptoms. Risk factors were determined by the attending clinicians through questioning the parents. Two millilitres of blood samples were collected using aseptic technique by the attending clinician into blood culture bottle consisting of 18mls of thioglycolate broth (Oxoid, UK) for anaerobic organism and 18mls of glucose broth for aerobic organism giving a 1:10 dilution. The glucose broth was constituted by adding 0.5% glucose to 100mls of Nutrient broth (Oxoid UK). The cultures were incubated at 37^{o}C for 7days.

Processing of Samples

Processing of blood samples and identifying of various bacterial isolates were carried out using standard bacteriological procedures (Cheesbrough, 1993). Blood cultures were discarded after 7 days of continuous incubation at 37^{o}C. Antibiotic susceptibility pattern was carried out on Mueller-Hinton agar by disc diffusion method (Bauer and Kirby, 1966) and zones of inhibition were determined according to the NCCLS (2001). The antibiotics tested were Amoxycillin/Clavulanate (30µg), Ofloxacin (5µg), Chloramphenicol (25µg), Ceftriaxone (30µg), Cotrimoxazole (25µg), Cloxacillin (10µg), Erythromycin (10µg), Gentamicin (10µg), Ampicillin (25µg) and Cefuroxime (30µg).

Statistical Analysis

Data was analyzed using EPI Info Version 6

RESULTS

Table 1 shows the age and sex distribution of neonates with positive blood cultures. Out of 547 neonates suspected with neonatal septicaemia, 152(27.8%) had positive blood cultures. There were 81 (53.3%) males and 71 (46.7%) females with male female ratio of 1.1:1. The age group with the highest frequency of positive blood cultures was 0-5 days while the least was 26-30 days. The difference was statistically significant (χ^2=18.38, *df* 4, p<0.001). Out of 152 neonates diagnosed as having septicaemia and confirmed with positive blood cultures, 28 neonates died giving a mortality rate of 18.4%. In both early and late Onset, infection was higher in out-born neonates when compared with inborn neonates. This was statistically significant (X^2= 4.05, *df* =1, p< 0.05).

Table 3 shows the clinical characteristics at time of presentation in neonates with suspected septicaemia. In all, 119 (78.0%) were term babies while 33 (22.0%) were preterm. While the highest number of neonates presenting with pyrexia were 29.6 %, followed by neonatal jaundice (18.4%), abdominal distension had the least presentation of 6.6 %. The common risk factors for septicaemia observed in this study were birth asphyxia, prolonged rupture of membranes, prolonged labour, prematurity, poor water supply, poor cord handling and birth outside the hospital with unsupervised antenatal care and delivery. The analyses of bacterial isolates by early and late onset infections among neonates suspected with neonatal septicaemia revealed that early onset infection 0 – 7 days were 40 (26.3%) while late onset infection 8 - 28 days were 112(73.7%)(Table 4).

Table 1: **Age and Sex Distribution of Neonates Suspected of Neonatal Septicaemia in Kano**

Age (Days)	No. tested	Number (%)		
		Positive cultures	Male	Female
0-5	395	97(24.6%)	50(51.5%)	47(48.5%)
6-10	105	36(34.3%)	19(52.8%)	17(47.2)
11-15	18	3(16.7%)	1(33.3%)	2(66.7%)
16-20	8	6(75.0%)	4(66.7%)	2(33.3%)
21-25	16	6(37.5%)	6(100%)	-
26-30	5	4(80.0%)	1(25.0%)	3(75.0%)
	547	**152(27.8%)**	**81(53.3%)**	**71(46.7%)**

χ^2=18.38 df=4 P=0.001

Table 2: Onset time of Infection and Place of Delivery among the 152 Neonate with Positive Blood Cultures

Onset time	Total number infected	Number (%)	
		In-born	Out-born
Early onset	40	8(20.0%)	32(80.0%)
Late onset	112	44(39.3%)	68(60.7%)
Total	**152**	**52(34.2%)**	**100(65.8%)**

χ^2=4.05 df=1 p<0.05

Table 3: Clinical Characteristics at Presentation in Neonates with Septicaemia

	Neonates Presenting	Number (%)
Gestation age:		
Preterm	40	26.3
Term	112	73.7
Birth Asphyxia	27	17.8
Neonatal jaundice	28	18.4
Pyrexia	45	29.6
Respiratory distress	15	9.8
Abdominal distension	10	6.6
Seizure	15	9.8
Low birth weight	12	7.8

Table 4: Distribution of Bacterial Isolates by Early and Late Onset Infections among Neonates Suspected with Neonatal Septicaemia

Types of bacterial isolates	No. positive (%)	
	Early onset infection 0-7days	Late Onset infection 8 to 28days
Gram positive *Staphylococcus aureus*	9(23.7%)	29(76.3%)
Staphylococcus epidermidis	0(0)	4(100%)
Enterococcus faecalis	1(14.3%)	6(85.7%)
Streptococcus spp.	3(16.7%)	15(83.3%)
Gram negative *Escherichia coli*	6(25.0%)	18(75.0%)
Klebsiella pneumonia	12(37.5%)	20(62.5%)
Proteus vulgaris	0(0)	2(100%)
Proteus mirabilis	2(50.0%)	2(50.0)
Citrobacter freundii	0(0)	1(100%)
Salmonella spp.	5(33.3%)	10(66.7%)
Pseudomonas aeruginosa	2(28.6%)	5(71.4%)
Total	**40(26.3%)**	**112(73.7%)**

Table 5: Age Distribution among 152 Bacterial Isolates from Blood Cultures of 547 Neonates Suspected of Neonatal Septicaemia in Kano

Types of bacterial isolates	No. of neonates with positive bacterial cultures in age groups Age in days						Sub total
	0-5	6-10	11-15	16-20	21-25	26-30	
Staphylococcus aureus	23	11	0	1	2	1	38(25.0%)
Salmonella spp.	7	7	1	0	0	0	15(9.9%)
Proteus mirabilis	4	0	0	0	0	0	4(2.6%)
Proteus vulgaris	1	1	0	0	0	0	2(1.3%)
Escherichia coli	14	7	1	1	1	0	24(15.8%)
Klebsiella pneumoniae	27	2	0	1	0	2	32(21.1%)
Streptococcus spp.	14	1	1	0	1	1	18(11.8%)
Enterococcus faecalis	3	0	0	2	2	0	7(4.6%)
Citrobacter freundii	0	0	0	1	0	0	1(0.7%)
S. epidermidis	1	3	0	0	0	0	4(2.6%)
Pseudomonas aeruginosa	3	4	0	0	0	0	7(4.6%)
Total	**97**	**36**	**3**	**6**	**6**	**4**	**152**

Table 6: Antibiotic Susceptibility Pattern of Isolates Obtained from Blood Cultures of Neonates with Suspected Neonatal Septicaemia in Kano

Isolates	No. tested	Number(%) sensitive to									
		AMC	CRO	ERY	OFX	COT	CN	CHL	CXC	AMP	CXM
Staphylococcus aureus	38	30(78.9)	34(89.5)	30(78.9)	35(92.1)	5(13.5)	35(92.1)	6(15.7)	18(48.0)	4(10.5)	15(39.5)
Salmonella spp.	15	8(53.3)	12(80.1)	ND	13(86.7)	2(13.3)	12(80.1)	5(33.3)	ND	1(6.6)	6(40.0)
Proteus mirabilis	4	0(0)	3(75.0)	ND	4(100)	0(0)	3(75.0)	1(25.0)	ND	1(25.0)	0(0)
Proteus vulgaris	2	1(50)	2(100)	ND	2(100)	0(0)	2(100)	0(0)	ND	0(0)	2(100)
Escherichia coli	24	18(75.0)	22(91.7)	ND	23(95.8)	6(25.0)	20(83.3)	4(16.6)	ND	4(16.6)	16(66.7)
K. pneumonia	32	24(75.0)	30(93.7)	ND	28(87.5)	6(18.7)	23(71.8)	6(18.7)	ND	0(0)	12(37.8)
Streptococcus spp.	18	16(88.8)	12(66.7)	15(83.3)	14(77.7)	0(0)	12(66.7)	6(33.3)	16(88.8)	0(0)	10(55.5)
Enterococcus faecalis	7	5(71.4)	5(71.4)	6(85.7)	6(85.7)	0(0)	6(85.7)	0(0)	5(71.4)	2(28.5)	2(28.5)
Citrobacter freundii	1	1(100)	0(0)	ND	1(100)	0(0)	1(100)	0(0)	ND	0(0)	1(100)
S. epidermidis	4	2(50.0)	2(50.0)	3(75.0)	2(50.0)	0(0)	3(75.0)	1(25.0)	0(0)	0(0)	0(0)
P. aeruginosa	7	2(28.6)	5(77.4)	ND	6(85.7)	0(0)	5(77.4)	0(0)	ND	0(0)	1(14.2)

Abbreviation: AMC – Amoxycillin/clavulanate, OFX – Ofloxacin, CHL – Chloramphenicol , CRO – Ceftriaxone , COT – Cotrimoxazole, CXC – Cloxacillin , ERY – Erythromycin, CN – Gentamicin, AMP – Ampicillin, CXM, Cefuroxime, ND – Not Done

The predominant organisms in the early onset were gram negative bacilli accounting for 27(67.5%) of the forty isolates identified. *Klebsiella pneumoniae* 12(30.0%) was the most frequently isolated organism in the early onset infection. Fifty four (48.0%) gram positive organisms and 58(52.0%) gram negative organisms were observed in the late onset infections. The age distribution of neonates by bacterial infections is presented on table 5. The age group (0-5) days (63.8%) had the highest number of bacterial isolates while the age group (26-30) days (36.2%) had the lowest. *Staphylococcus aureus* 38(25.0%) was the predominant organism followed by *Klebsiella pneumoniae* 32(21.1%) and *Escherichia coli* 24(15.8%). Chloramphenicol, cotrimoxazole and ampicillin exhibited very low sensitivity against the bacterial pathogens (Table 6).

DISCUSSION

In the present study, an isolation rate of (27.8%) compares favorably with the reports from Ilorin (Mokuolu, 2002) where more males than females were also observed to be affected. However, the reported isolation rates from two other centres, also in Nigeria; Calabar (Antia-Obong *et al*., 1992) and Ile-Ife (Ako-Nai *et al*., 1999), were higher than the findings in the present study. The clinical characteristics observed such as respiratory distress, low birth weight, neonatal jaundice and gestational age were also reported by Tsering *et al.* (2011). Low socioeconomic status and vaginal flora of the mother have been linked to the development of neonatal septicaemia (Ako-Nai *et al*., 1991). This underscores the need to have as many births as possible in the hospital where adequate antenatal care could be provided since prolonged labour, rupture of membrane, frequent vaginal examinations and poor water supply have all been associated with neonatal septicaemia. The reports of mortality rates of 33% and 41% from two tertiary hospitals in the country (Omene, 1979; Adejuyigbe *et al*., 2002) are higher than the mortality rate of 18.4% observed in this present study.

The preponderance of late onset septicaemia observed in this study has reported by some other researchers at Lagos (Ako-Nai *et al*., 1999) and Ilorin (Mokuolu, 2002). It is believed that this may be due to unhygienic practices, dirty environments, poor cord handling and exposure of neonates to being carried about by everyone out of joy as it is the tradition in most parts of Africa. However, the main predisposing factors to septicaemia reported in this study were equally reported at Calabar, Nigeria (Antia-Obong *et al*., 1992). This also corresponds with the findings at Ilorin (Mokuolu, 2002) but at variance with their report of gram positive organisms predominating infections in the late onset infections. On the contrary, this study observed a 54(48.0%) gram positive organism and 58(52.0%) gram negative organism in the late onset infections.

The predominant organisms in the early onset were gram negative bacilli. This compares favorably with the findings at Ilorin (Mokuolu, 2002). Generally, the aetiologic agents of neonatal septicaemia varies from place to place and changes with time and unlike other studies (Njokanma *et al*., 1990; Olusanya *et al*., 1991), there appears to be a shift from predominantly gram positive cocci to gram negative bacilli as observed in this study. The predominant isolates in the study were gram negative bacilli. This agrees with the reports published by two separate studies carried out at the University College Hospital (UCH) Ibadan, Nigeria (Dawodu and Alausa, 1980; Alausa and Onde, 1984). However, this contrasts sharply with the observations in other parts of the country where the predominance of gram positive cocci in proven cases of neonatal septicaemia were reported (Ako-Nai *et al*., 1990; Njokanma *et al*., 1990; Antia-Obong and Utsalo, 1991; Olusanya *et al*., 1991). In this present study, *Staphylococcus aureus* (25.0%) was the principal pathogen gram-positive cocci isolated. This is in agreement with the reports of studies that have been carried out in other parts of the country (Adejuyigbe *et al*., 2001; Mokuolu *et al*., 2002; Meremikwu *et al*., 2005; Anah *et al*., 2008).

The *in-vitro* sensitivity tests as observed by the three major isolates in the present study showed resistance to commonly used antibiotic such as ampicillin . The observed antibiotic susceptibility of most of the isolates to ceftriaxone and gentamicin agrees with the reports from Calabar (Meremikwu *et al*., 2005) and Ilorin (Mokuolu, 2002). The high percentage resistance of *S. aureus* to cloxacillin observed in the present study is in agreement with the reports at Ilorin (Mokuolu, 2002). Both studies agree in opinion that this situation is informed by the advent of methicillin resistant strains of *S. aureus*. Susceptibility of *S. aureus* and other gram positive isolates to erythromycin was quite encouraging. Another finding (Meremikwu *et al*., 2005) also confirmed excellent *in vitro* sensitivity results of *S. aureus* to erythromycin. From the results obtained from *in-vitro* antibiotic susceptibility tests in the present study, Ceftriaxone and Gentamicin could be considered as first-line drugs in the treatment of neonatal septicaemia before laboratory results of sensitivity testing are received except in cases involving the central nervous system (CNS) since this drug is not known to penetrate this area. Resistant isolates observed in this study and another study at Ile-Ife (Ako-Nai *et al*., 1999) are of great concern to health care providers because they can increase the morbidity and mortality in this disease. These organisms may have been acquired by neonates through their mothers who could be carriers and may have passively transferred resistant bacteria while feeding their babies (Ako-Nai *et al*., 1999).

CONCLUSION

Gram negative bacilli were the predominant organisms identified in this study. The major isolates in this study were highly susceptible to Ceftriaxone and Gentamicin. These drugs could be used as first-line drugs pending culture and sensitivity results in our locality. However, high standard of hygiene is encouraged around neonates while suspected septicaemia should be treated as an emergency.

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