

Full Length Research Paper

Clinico-Bacteriological profile of early and late onset sepsis in a tertiary hospital in Nigeria

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Sepsis remains a significant cause of neonatal deaths and its incidence remains unacceptably high in developing countries. Despite diagnostic and therapeutic advances, early and late onset sepsis is associated with substantial morbidity and mortality; thus a high index of suspicion is essential for early diagnosis and prompt treatment. To determine the clinico-bacteriological profile of early and late onset sepsis, its incidence and predisposing factors at the University of Port Harcourt Teaching Hospital. A prospective study of neonate with symptoms/signs, or predisposing factors to sepsis was carried out over 6 months. Blood culture was used as gold standard for diagnosis. 406 neonates were studied; 169(41.6%) had positive blood culture. There were 120(71.0%) neonates with EOS and 49(29.0%) with LOS. The incidence of EOS and LOS was 24.9/1000 and 14.6/1000 live births respectively. Out-born delivery (71.7%) was the commonest predisposing factor to sepsis. Respiratory distress (41.7%) and poor suck (24.2%) were predominant features of EOS while fever (46.9%) and jaundice (32.7%) were observed in LOS. *Klebsiella pneumonia* and *Staphylococcus aureus* were the commonest organisms implicated in both EOS and LOS. The incidence of EOS is high at UPTH. Early diagnosis for prompt intervention is keyed to avoid mortality.

Keywords: Neonatal sepsis, early onset, late onset, Port Harcourt.

INTRODUCTION

Sepsis has remained a major cause of morbidity and mortality in the newborn despite careful hygiene and the use of powerful broad spectrum antibiotics. (Plazek and whitelaw, 1983) The incidence of neonatal sepsis (NNS) remains unacceptably high in developing countries (Dawodu and Alausa, 1980). It varies from 5 to 18.5 per 1000 live births, in contrast to 1- 4 per 1000 live births in developed countries (Airede, 1992; Niger, 1996; Bode-Thomas et al., 2004; Siegel and Cracken, 1981). The incidence of NNS in Nigeria ranges from 6-35 per 1000 live births (Dawodu and Alausa, 1980; Airede, 1992).

Early onset sepsis (EOS) occurs within 72 hours of life (Chako and Sohi, 2005; Al-Zwaini,

2002). It is caused by organisms prevalent in the maternal genital tract or in the labour room and operation theatre (Bellig and Ohning). Eighty-five percent of newborns with EOS present within 24 hours, 5% within 24-48 hours while 10% present between 48-72 hours

(Bellig and Ohning, 2004). Infants with EOS present frequently with pneumonia and less frequently with meningitis and septicaemia (Yadav et al., 2005). Despite diagnostic and therapeutic advances, EOS is associated with substantial morbidity and mortality rate of 15%-50% (Yadav et al., 2005).

On the other hand, late onset sepsis (LOS) occurs after 72 hours of age (Chako and Sohi, 2005; Sankar et al., 2008), usually as nosocomial or community-acquired infections. Neonates with LOS usually present with septicaemia, pneumonia or meningitis (Sankar et al., 2008). Factors that may increase community acquired LOS include poor hygiene, poor cord care, bottle feeding and parenteral fluids (Sankar et al., 2008). The mortality rate of LOS at 15% is lower than that of EOS (Bellig and Ohning).

These high mortality rates of both early and late onset sepsis makes it imperative that predisposing factors be identified and clinico-bacteriological profile highlighted so that early diagnosis and prompt therapy be instituted so as to avoid unnecessary mortality, especially in low income countries where laboratory diagnostic facilities

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Table 1. Characteristics of Neonates with Early (EOS) and Late onset sepsis (LOS).

Characteristics	EOS n=120 No(%)	LOS N=49 No(%)	χ^2	P-value
Sex:				
Male	83(69.2)	37(75.5)	0.68	0.41
Female	37(30.8)	12(24.5)		
Place of birth:				
Inborn	34(28.3)	20(40.8)	2.49	0.11
Out born	86(71.7)	29(59.2)		
GA at birth (weeks)				
Preterm	44(36.7)	39(79.6)	25.65	0.00*
Term/Post term	76(63.3)	10(20.4)		

GA = Gestational age, EOS=Early onset sepsis, LOS=Late onset sepsis,

*=Statistically significant

and personnel may not be readily available. No study on the incidence and clinic-bacteriological profile of EOS and LOS as separate entities has been done at the UPTH which is the main tertiary institution with neonatal services in the south-south Geo-political region of Nigeria and serves as a major referral center and catchment areas for neighbouring regions; thus necessitating this study.

MATERIALS AND METHODS

It was a prospective study carried out in the Special Care Baby Unit (SCBU) of the University of Port Harcourt Teaching Hospital (UPTH) over a period of 6 months from July to December, 2007. The hospital which is located in the South-South geopolitical zone of Nigeria, serves as a major referral and regional neonatal intensive care centre.

All neonates (0-28 days old) with symptoms/signs suggestive of sepsis or predisposing factors to sepsis without prior antibiotic therapy were consecutively recruited into the study. Clinical data sought included age, birth weights, sex, gestational age; place of birth (babies born within the UPTH were referred to as inborn, while those born outside the UPTH were referred to as out-born), and age at onset of symptoms were recorded.

Two milliliter of venous blood for culture was collected from a peripheral vein of all recruited babies after adequate skin preparation and before the commencement of antibiotics. The blood was aseptically introduced into aerobic and anaerobic culture media. The blood culture specimens were processed according to standard protocols in the microbiology laboratory of the UPTH (UPTH, 2007). Inoculated blood culture media were considered negative if there was no growth after continuous incubation for up to seven days, with sub-

cultures being made each day. Antibiotic sensitivity was done using Kirby-Bauer disc diffusion method (UPTH, 2007).

Afterwards, neonates were commenced empirically on intravenous antibiotics (cloxacillin and gentamicin), based on previous antibiotic sensitivity pattern of the hospital. Clinical response was monitored and therapy changed to conform to susceptibility pattern of blood cultures isolates for individual patients, where response was poor or patient was deteriorating. The clinical details and results of laboratory investigations were recorded in a proforma. The results were analyzed using the SPSS version 14.0 and Epi-info version 6.04.

RESULTS

There were 1,368 live births at the UPTH during the study period. A total of Five hundred and eleven neonates were admitted (both inborns and outborns) into the SCBU of which 406 neonates met recruitment criteria and were studied. One hundred and sixty nine neonates had positive blood culture, giving the prevalence rate of blood culture positive sepsis as 33.1% (i.e 169 out of the total admission of 511 neonates). Of these, 54 were inborn while 115 were outborns. One hundred and twenty (42.1%) had EOS while 49 (40.5%) had LOS, ($p= 0.76$).

Characteristics of neonates with EOS and LOS

The characteristics of neonates with EOS and LOS are shown in Table 1. Of the fifty-four inborns with blood culture positive sepsis, 34 (63.0%) had EOS while 20 (37.0%) had LOS, giving the UPTH specific incidence of EOS and LOS as 24.9 per 1000 live births and 14.6 per 1000 live births respectively. Late onset sepsis was signi-

Table 2. Predisposing factors to early onset sepsis and late onset sepsis.

Predisposing Factors	EOS n=120 No (%)	LOS n=49 No (%)	χ^2	P-value
Outborn delivery	86(71.7)	29(59.2)	2.49	0.11
Birth asphyxia	43(35.8)	9(18.4)	4.98	0.03*
Prematurity	28(23.3)	9(18.4)	0.50	0.48
PROM	26(21.7)	4(8.2)	4.35	0.04*
Foul smelling amniotic fluid	12(10.0)	0(0.0)	5.28	0.02*
Peri-partum pyrexia	9(7.5)	2(4.1)	0.67	0.41
Offensive umbilical cord	5(4.2)	1(2.0)	0.46	0.50

PROM=Prolonged rupture of membrane, EOS=Early onset sepsis, LOS=Late onset sepsis, *=Statistically significant

Table 3. Clinical Features of Sepsis in Neonates Presenting with EOS and LOS

Clinical Features	EOS n=120 No (%)	LOS N=49 No (%)	χ^2	P-value
Respiratory distress	50(41.7)	8(16.3)	9.91	0.00*
Poor suck	29(24.2)	8(16.3)	1.25	0.26
Fever	21(17.5)	23(46.9)	15.6	0.00*
Jaundice	10(8.3)	16(32.7)	15.81	0.00*
Hypothermia	10(8.3)	4(8.2)	0.07	0.79
Vomiting	5(4.2)	3(6.1)	0.02	0.89
Convulsion	4(3.3)	4(8.2)	0.89	0.35
Lethargy	4(3.3)	2(4.1)	0.05	0.83
Abdominal distension	2(1.7)	3(6.1)	1.10	0.29
Irritability	0(0.0)	6(12.2)	11.87	0.00*

EOS=Early onset sepsis, LOS=Late onset sepsis, *=Statistically significant

ificantly more in preterm neonates.

Predisposing factors

Table 2 highlights the predisposing factors to EOS and LOS. Birth asphyxia, Prolong rupture of membrane (PROM) and foul smelling amniotic fluids were significant contributors to early onset sepsis. (p= 0.03, 0.04 and 0.02 respectively)

Clinical features

The clinical features of EOS and LOS are shown in Table 3. Respiratory distress (41.7%) was significantly more in EOS; while fever (46.9%) and jaundice (32.7%) were significant features of LOS.

Causative organisms

The distribution of the organisms isolated from blood

culture by age of onset of illness is illustrated in **Figure 1**. *Klebsiella pneumonia* (65.4%), *Staphylococcus aureus* (15.4%) and *Escherichia coli* (7.7%) were the commonest organisms observed in both EOS and LOS.

Outcome

Of 169 neonates with culture proven sepsis 25 died, giving an overall mortality rate of 15.0%. Of the 120 neonates with EOS, 98 (81.7%) neonates were discharged home, three (2.5%) discharged against medical advice while 19 died; giving a specific mortality rate for EOS of 15.8%.

Of the 49 neonates with LOS, 42 (85.7%) were discharged home, three (6.1%) discharged against medical advice and six died; giving a specific mortality rate of 12.2% for LOS.

DISCUSSION

The study showed that sepsis is a common cause of

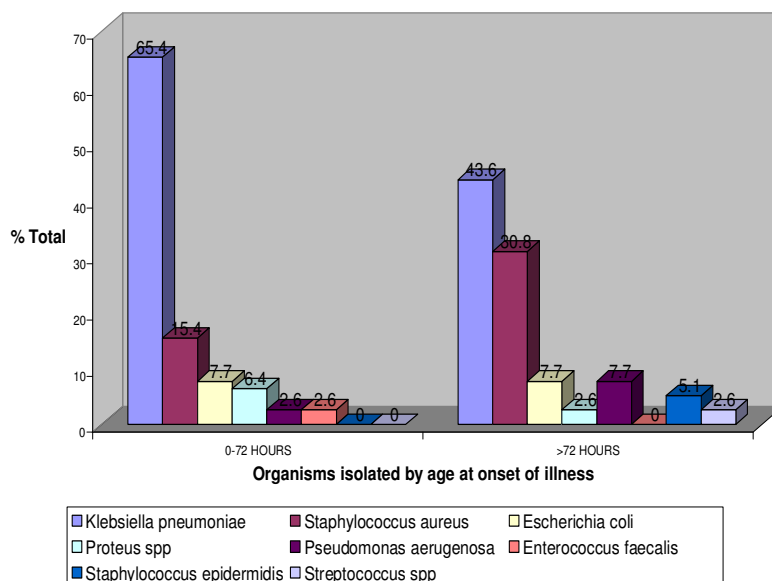


Figure 1. Distribution of Organisms Isolated from Blood Culture by Age at Onset of Illness

morbidity and mortality at the UPTH and that EOS is commoner than LOS. Although comparable with studies done in India (Chako and Sohi, 2005) and Bangladesh (Rasul et al., 2007), it however contrasted with a study done in Iraq (Al-Zwaini, 2002) where LOS was observed to be commoner. The reason for this disparity is not immediately obvious but may be due to differences in methodology. As was observed by Dawodu et al (1997) in Saudi Arabia, both EOS and LOS were significantly more in males than females in the present study. This may be due to the possibility of a sex linked factor in host susceptibility which has been suggested for neonatal sepsis (Schlegel and Bellanti, 1967). Late onset sepsis were observed more in preterm neonates as compared with the term neonate most likely attributable to the increased risk of nosocomial infections in preterms due to their longer stay in the hospital nursery and their increased need for invasive procedures/devices and life support apparatus as compared with term infants. In contrast, studies done in India (Yadav et al., 2005) showed more EOS in preterms. These were however retrospective analysis while the present study is prospective thus making comparison challenging.

Not surprisingly in our environment, outborn deliveries posed an increased risk of EOS and LOS closely followed by birth asphyxia and prematurity. This is because most cases of outborn deliveries in this environment occurs at home usually tended by traditional birth attendants whose unhygienic methods and sometimes misguided advice on infant cord care and breast feeding practice to the mother poses additional risk (Islam, 2001). This has also been observed by other researchers (Dawodu and Alausa, 1980; Antia-Obong et al., 1992; Iroha et al., 1998).

The clinical features of neonatal sepsis are usually vague and non-specific, thus a high index of suspicion on the part of the doctor is essential. Respiratory distress and poor suck are the commonest clinical features. This is in keeping with studies which have shown that pneumonia which may present with signs of respiratory distress is a common manifestation of EOS (Sankar et al., 2008). This finding has also been documented by other studies in Nigeria by Airede (1992), and Okolo and Omene (1985). As with other studies (Okolo and Omene, 1985; Mustafa et al., 2005; Zeeshan et al, 2005), fever and jaundice were observed to be predominant features of LOS.

The three predominant isolates in our study in both EOS and LOS were *Klebsiella pneumoniae*, *Staphylococcus aureus* and *Escherichia coli*. This compares favourably with other studies done in Nigeria (Dawodu and Alausa, 1980; Antia-Obong et al., 1992; Iroha et al., 1998; Borna and Borna, 2005; Ozigbo et al., 2003) and elsewhere in the world (Al-Zwaini, 2002; Plazek and Whitelaw, 1983; Dawodu et al., 1997; Edwards, 2002). It is interesting to note that in contrast to what obtains in developed countries; Group B Streptococcus (GBS) was not isolated in the present study. This has also been observed in other studies across Nigeria (Bode-Thomas et al., 2002; Omene, 1979; Antia-Obong, 1992; Ozigbo et al., 2003) and Asia (Zeeshan et al., 2005; Misallati et al., 2000; Roy et al., 2002; Manucha et al., 2002). This differences may be explained by environmental factors (MERCK manual, 2004) as women at term in developed countries in Europe and America show invasive GBS colonisation rates of up to 30% thus posing a risk for GBS sepsis in their infants (MERCK manual, 2004). This contrast with the scenario in developing countries where there are fewer colonisation of GBS in pregnant women at term,

and even when colonization occurs, it is usually with the non-invasive species (MERCK manual, 2004).

EOS usually manifest as a fulminant, multisystem infection with a high case fatality rate (Polin et al., 2005) and this was reflected in the high mortality rate of 15.8% for EOS observed in this study. A high index of suspicion for health care workers as well as proper antenatal supervision by qualified health personnel will go a long way to ameliorate the situation. The mortality rate for EOS of 15.8% was higher than that of LOS at 12.2% in the present study. This pattern has been observed by other workers in London (Plazek and Whitelaw, 1983), India (Chako and Sohi, 2005) and Nigeria (Omene, 1979; Amiebenomo et al., 1988) possibly due to the comparatively less fulminant presentation of LOS. Notwithstanding, the rate observed in our study is unacceptable high considering that with proper public enlightenment, the risk factors associated with LOS are easily avoidable and preventable; also, a heightened awareness for prompt intervention amongst health care workers can go a long way to reduce morbidity and mortality.

CONCLUSION

The incidence of EOS and LOS at UPTH are high at 24.6 and 14.6 per 1000 live births respectively, with high mortality rates. Gram negative organisms remain the predominant organisms and predisposing factors are preventable and/or treatable.

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