Neonatal sepsis; Prevalence and outcome in a tertiary neonatal unit in Sudan

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Sepsis is one of the most common causes of morbidity and mortality in newborns especially in developing countries. The aim of this study was to determine the prevalence and outcome of neonatal sepsis. This was a prospective study, conducted in the Neonatal Intensive Care Unit at Soba University Hospital, Sudan. A total of 62 babies with the clinical diagnosis of sepsis were included. Chi square test was used to determine the association between C-reactive protein and risk factors for sepsis and also the association between C-reactive protein and blood culture. The prevalence of sepsis was 17.5% and the mortality was 14.5%. Blood culture was positive in 61.3% of babies and C-reactive protein was positive in 44.7% of babies with positive blood culture. There was significant association between C-reactive protein results and blood culture (P=0.019). In conclusion neonatal sepsis remains a major cause of neonatal morbidity and mortality especially in developing countries with low resource settings.

Key words: Neonatal sepsis, C-reactive protein, blood culture, Sudan.

INTRODUCTION

Neonatal sepsis is one of the important causes of neonatal morbidity and mortality particularly in the developing countries (Osiris et al., 2004). Neonatal sepsis is classified into early or late according to the different ages at onset of infection during the neonatal period (Kliegman et al., 2011). The clinical relevance of this distinction is that early-onset disease is often due to organisms acquired during delivery while, late-onset disease is more frequently caused by organisms acquired from nosocomial or community sources (Robinson et al., 2008).

Neonatal sepsis is an important cause of immediate morbidity and mortality (James, 2008). Most of the estimated 4 million neonatal deaths per year occur in low and middle income countries. Case fatality rates for neonatal infections remain high among both hospitalized newborns and those in the community (Qazi and Stoll, 2009).

In developing countries, neonatal mortality defined as deaths in the first 28 days of life per 1000 live births, from all causes is about 34; most of these deaths occur in the first week of life, most on the first day (WHO 2001 Estimates). In contrast, neonatal mortality for developed countries is in the region of five. Neonatal mortality in Asia is about 34, in Africa about 42, and in Latin America and the Caribbean about 17 (Vergnano et al., 2005). Deaths occurring in the neonatal period each year account for 41% (3.6 million) of all deaths in children under 5 years. The majority of these deaths occur in low income countries and almost 1 million of these deaths are attributable to infectious causes including neonatal sepsis, meningitis and pneumonia. Furthermore, neonatal mortality for different African countries ranges from 68 per 1000 live births in Liberia to 11 per 1000 live births in South Africa (Anita et al., 2011).

The diagnosis of infection in neonates is difficult,
because of the non-specific clinical presentation and the lack of reliable diagnostic tests. As a result of this uncertainty, antimicrobial chemotherapy is often commenced on the slightest clinical suspicion of infection (Lam and Ng, 2008). Recently there has been great interest in the potential diagnostic value of a range of hematological and immunological surrogate markers of infection (Ng, 2004).

The aims of this study are to determine the prevalence of neonatal sepsis in a tertiary neonatal unit in Sudan, to identify possible risk factors for neonatal sepsis, to look for correlation between risk factors and occurrence of sepsis and to determine the outcome of neonatal sepsis.

MATERIALS AND METHODS

This was an observational case-finding hospital based study, carried out in the neonatology unit at Soba University hospital in the state of Khartoum, Sudan. This study was conducted during the period from October 2011 to February 2012.

All neonates admitted with proven or suspected sepsis during the study period were included in the study; a total of 62 babies were included in the study. Neonates with major congenital malformations were excluded. The dependent variable was neonatal sepsis and the independent variables were all risk factors for sepsis like prematurity, low birth weight, prolonged rupture of membranes, maternal pyrexia, vaginal discharge and previous sibling with neonatal sepsis.

Data was collected using specifically pre-coded and pre-tested questionnaires from all in-patients diagnosed with neonatal sepsis by positive laboratory tests. Data collected included socio-demographic data such as (age, sex, mode of delivery), risk factors, symptoms and signs and investigation findings.

Newborn babies were classified as having sepsis if they had signs suggestive of sepsis and a positive blood culture. Probable sepsis was diagnosed if they had a negative blood culture with signs suggestive of sepsis and no sepsis if there were no clinical features of sepsis with a negative blood culture. Positive blood culture was considered the gold standard against which C-RP result was compared.

Data were analyzed using Statistical Package for Social Sciences (SPSS) version 17; Chi square test was used to determine the association between C-RP and risk factors for sepsis and also the association between C-RP and blood culture. P value was set on an alpha level at 0.05 and 95% confidence limit. Ethical clearance and approval for conducting this study was obtained from the Ethical Committee of Soba University Hospital. Prior verbal informed consent was obtained from the parents of the babies participating in this study after full explanation of the study.

RESULTS

During the study period a total of 354 neonates were admitted to the neonatal unit, 62 of them fulfilled the criteria of Sepsis. Females were 33 (53.2%) and 29 (46.8%) were males. Twenty five babies (40.3%) weighed between 1500-2500 g; twenty four babies (38.7%) weighed more than 2500 gm. While the remaining thirteen babies (21%) weighed between 1000-1500 g. Cross tabulation between birth weight and the presence of a positive blood culture and C-reactive protein, showed that there was no significant relationship between the birth weight, positive blood culture and C-reactive protein (P - 0.984, 0.696 respectively).

With regards to the gestational age, the majority of the neonates with symptoms of sepsis were full term 23 (37.1%), 21 (33.9%) of gestational age ranging from 28-32 weeks, 16 (25.6%) of 33-36 weeks and 2 (3.2%) post term. Cross tabulation between gestational age and the presence of a positive blood culture and C-reactive protein, showed that there was no significant relationship between the gestational age, positive blood culture and C-reactive protein (P 0.632, 0.701 respectively).

Out of the 62 participants, 100% went through regular antenatal care. Thirty five (56.5%) of maternal delivery were delivered by emergency caesarean section, nineteen (30.6%) were by spontaneous vaginal delivery, and eight (12.9%) were by elective Caesarean section. Forty six (74.2%) of patients mothers did not have prolonged rupture of membranes (PROM), Four (6.5%) had ruptured their membranes for less than 24 h and twelve (19.4%) experienced it for more than 24 h. Cross tabulation between PROM and the presence of a positive blood culture, showed no significant relationship between PROM and a positive blood culture (P 0.600). Whereas cross tabulation between PROM and the presence of a positive C-reactive protein, showed significant relationship between PROM and a positive C-reactive protein (P 0.015).

Only two (3.2%) patients had history of intrapartum fever, antibiotic usage and a history of vaginal discharge. Twenty four (38.7%) of mothers had a history of diseases, of which UTI was found to be most common. None of the mothers had history of previous baby with neonatal sepsis or death due to sepsis. Fifty two (83.9%) babies with neonatal sepsis were symptomatic. The most common clinical presentation of neonatal sepsis was vomiting 6(9.7%), fever and lethargy second common 3 (4.8%), refusal of feeding and poor cry 2(3.2%) and irritability 1 (1.6%). The most common presenting sign of neonatal sepsis was tachypnea 43(69.4%), abdominal distention 12 (19.4%), cyanosis 8(12.9), temperature instability 7(11.3%), apnea and purpura 4 (6.5) each, seizures 3 (4.8%) and poor capillary refill 2 (3.2%) (Tables 1 and 2).

Blood culture was positive in thirty eight (61.3%) of
babies with a diagnosis of sepsis, of which *klebsiella* was the most common aetiological factor twenty seven (71.1%). Other organisms were found to be *Staphylococcus aureus* (15.8%), *E. coli* (5.3%), a gram positive cocci (2.6%) and *Serratia marcescens* (5.3%).

Correlation between blood culture and other risk factors showed that there was no significant relationship between history of vaginal discharge and a positive blood culture (P 0.070), also there was no significant relationship between history of maternal fever and a positive blood culture (P 0.158). However the cross tabulation between blood culture and the presence of a positive C-reactive protein showed that there was significant relationship between the blood culture and a positive C-reactive protein (P 0.019) (Table 3).

C-reactive protein was positive in thirty five (56.5%)
patients. Chest x-ray was done in thirty one (50%) and was found to be normal. Cerebrospinal fluid was tested in three (4.8%) cases and was found to be normal. During the study period 354 babies were admitted to the neonatal unit, among those with neonatal sepsis the mortality rate was found to be nine (14.5%) and out of the total admission the mortality was found to be 3%.

DISCUSSION

Severe neonatal infections are one of the most significant causes of pediatric mortality, resulting in more than 500,000 deaths each year (Black et al., 2010). Ninety-nine percent of these deaths occur in low resource settings (Thaver and Zaidi, 2009). Identifying neonates with severe infections is difficult in high resource settings, and limited laboratory capability in low resource settings makes diagnosis even more challenging. Clinical criteria for the diagnosis of neonatal sepsis have been developed and are included in the WHO Integrated Management of Childhood Illness (IMCI) program (Gove, 1997).

In the present study an attempt has been made to study the prevalence and outcome of neonatal sepsis as neonatal sepsis remains to have a high mortality especially in low resource settings. Our study showed that 62 babies had proven sepsis. During the study period the prevalence was found to be of 17.5%, this is a very high admission rate of neonatal sepsis as expected in developing countries.

We found that 61.3% of neonates had a positive blood culture. This is similar to the finding from a study done in Egypt where it was found that 70% of the neonates had positive blood cultures. In the same study, the identified bacteria included Gram positive cocci, Staphylococcus epidermidis, S. aureus, and Streptococci agalactii as the commonest organisms (Boraey et al., 2012) and this is in contrast to our study where Klebsiella pneumoniae was the commonest bacteria isolated followed by S. aureus and E. coli. This difference might be attributed to the fact that bacterial profile, resistance and the use of intrapartum antibiotics differ from one country to another.

In another study in Tanzania, Positive blood culture was found in 57 (47.1%) and 92(51.4) among neonates with early and late onset neonatal sepsis respectively, which indicates a high percentage of positive blood culture in late onset sepsis. This is probably due to the fact that late cases bacteria are more likely to be evident and active and could result in aetiology of neonatal sepsis (Kayange et al., 2010). CRP was positive in 17 (44.7%) babies with positive blood culture which is different from a study conducted in Poland where 48 babies with a clinical diagnosis of sepsis were recruited, it was found that 18 (58%) out of 31 babies with positive blood culture had increased CRP (Kawczyński and Piotrowski, 2004).

Our results showed that the majority of cases birth weight were between a range of 1500-2500 gm. This is similar to a multicenter study in Italy, which showed that birth weight equal to or less than 2500 g was an independent factor associated with sepsis (Moro et al., 1996).

With regards to the gestational age distribution of the sample, most of the neonates with symptoms of sepsis were of full term 23 (37.1%). This disagrees with a cohort study of 7861 VLBW neonates admitted to the 12 National Institute of Child Health and Human Development (NICHD) during a 32-month period, where results showed that the rate of infection was inversely related to birth weight and gestational age (Stoll et al., 1996). Our study showed that 19.4% of the mothers had PROM > 24 h and there was no significant relationship between PROM and a positive blood culture which disagrees with the research done in Tanzania which suggested that PROM and meconium stained liquor are significantly associated with positive blood culture in both early and late onset disease (Kayange et al., 2010).

Only two (3.2%) patients out of all septic patients had a maternal history of fever or vaginal discharge. There was no significant association between history of fever and vaginal discharge with blood culture and C-RP. This disagrees with the study done in Pakistan, analysis of maternal risk factors revealed a significant association between maternal urinary tract infection (UTI), maternal pyrexia, vaginal discharge with sepsis (Bhutta and Yusuf, 1997). This might be due to the relatively short duration of our study.

Neonatal mortality due to sepsis was found to be (14.5%) of cases which is a significant amount of deaths. A community-based study published from developing countries to estimate the rates of neonatal and young infant infections and infection-specific neonatal mortality showed that infections may be responsible for 8% to 80% of all neonatal deaths and as many as 42% of deaths occur in the first week of life. This data indicated that a significant proportion of neonatal deaths in developing countries are due to infections (Thaver and Zaidi, 2009).

Conclusion

Neonatal sepsis still constitutes a major problem in neonatal units in Sudan leading to significant morbidity and mortality. It is still a leading cause of admission and death in neonatal units in developing countries. Blood culture remains the gold standard for the diagnosis of neonatal sepsis and is positive in the majority of patients.

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REFERENCES


