ORIGINAL ARTICLE

Early Onset Neonatal Septicaemia in a Level II Nursery

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Summary

A prospective study of 486 high risk neonates admitted to a level II nursery in a relatively poor and rural area of Malaysia was carried out to determine the incidence, the spectrum of micro-organisms and predisposing factors in relation to early onset septicaemia. The incidence of proven or probable septicaemia was 57.61 per 1000 high risk newborns over 1.5kg. The case fatality was 10.71 per cent. Coagulase negative staphylococci, *Streptococcus* Group B and *Klebsiella* species were the most commonly isolated organisms. Meconium staining of liquor was the most common risk factor for admission to the nursery, and prematurity was the most significant risk factor for early neonatal infection ($P<0.005$) followed by small for gestational age ($P<0.04$). Although the incidence of septicaemia was quite high in the level II nursery, the mortality rate was comparable to established figures.

Key words: Neonatal septicaemia, Level II nursery, Coagulase negative staphylococci, Prematurity, Small for gestational age.

Introduction

Neonatal septicaemia is a clinical syndrome characterised by systemic signs of infection e.g refusal to take feeds, vomiting, temperature instability, respiratory distress, hepatosplenomegaly, jaundice and bleeding tendency. It is due to invasion of the blood stream by micro-organisms within the first 28 days of life[1]. Based on the age of the infant at the time of onset of illness, neonatal septicaemia is classified as "early onset" (within the first three or seven days of life as defined by different authors)[2-8] and "late onset". Early and late onset neonatal sepsis have different pathogenesis and causative organisms[2]. In early-onset infection (whether ascending or transplacental), sepsis occurs rapidly and babies are often systemically infected at delivery. In late-onset infection, the organism first colonises the baby and only later invades to cause sepsis. The organisms responsible for neonatal sepsis differ between different geographical regions and also in the same area at different times[9-11]. In recent years a number of studies have been performed to analyse neonatal septicaemia with attention focussed on changes in the spectrum of micro-organisms[12-14], predisposing factors[12,13,15], diagnostic studies[16-19] and therapy.

The purpose of the present study was to determine the incidence, the spectrum of micro-organisms, the clinical features, and the predisposing factors in cases of early neonatal sepsis in a level II nursery in Kelantan, Malaysia.

Kelantan is a comparatively poor state of Malaysia and most of its population is rural. Hospital Universiti Sains Malaysia (HUSM) is one of only two referral hospitals for the State of Kelantan with a population of 1.3 million and annual deliveries of 42,000, out of which about 7000 are conducted in this hospital. This study was conducted in the level II nursery of this hospital which cares for non-ventilated babies over 1.5kg birth weight.

Subjects and Methods

Neonates, admitted to the level II nursery of HUSM within 24 hours of their delivery between January 1, 1991 and May 31, 1991 were studied prospectively. The indications for admission to the level II nursery during the period of study were:

- Infants delivered after prolonged rupture of foetal membranes (for >12 hours), prolonged labour (2nd stage lasting for >1hour in primigravida and >1/2 hour in multigravida), instrumentation (e.g. forceps, vacuum extraction) or Caesarean section.
- Premature (<37 weeks but >32 weeks of gestation), small for gestational age with birth weight >1.5kg, or asphyxiated infants.
- Infants of mothers with fever, foul smelling or meconium stained liquor, diabetes, Rhesus negative blood group, bad obstetric history, emergency Caesarean Section, pre-eclampsia or eclampsia, infectious or chronic diseases, positive for hepatitis B surface antigen, or venereal disease research laboratory (VDRL) test.

Neonates having one or more of the following features were managed in the intensive care (level III) nursery and therefore were not included in this study.

1. Birth weight < 1.5 kg.
2. Gestational age < 32 weeks.
3. Requiring assisted ventilation or requiring oxygen inhalation with FiO2 of more than 70 per cent at the time of admission.
4. Multiple congenital abnormalities.

A septic work-up carried out at the time of admission on all the neonates included in the study, consisted of : blood culture and sensitivity, total and differential leukocyte count, platelet count, serum C-reactive protein (CRP), urinalysis and chest X-ray. Skin, ear and umbilical swabs were taken for gram staining and culture when clinically indicated. Cerebrospinal fluid (CSF) examination was done in neonates with suspicion of intracranial infection (irritability, bulging fontanellae, convulsions). The clinical progress of the newborns was monitored carefully. A prescribed proforma was filled during the period of admission and was completed at the time of discharge.

A diagnosis of proven sepsis was made when both of the following were present.

(a) Bacteria were isolated from specimens of blood and/or CSF, and
(b) The newborn showed signs of septicaemia such as temperature instability, lethargy, respiratory distress, poor sucking, vomiting/excessive aspirate through gastric tube, diarrhoea, recurrent apnoea, abdominal distension, hepatosplenomegaly, jaundice or bleeding tendency.

A diagnosis of probable sepsis was made in newborns with clinical signs of infection without positive culture. In order to qualify for this diagnostic category, newborns had to have at least one of the

above stated clinical signs in the absence of an established alternative explanation, along with at least two of the following haematological findings:

- Total white count > 25000 or < 5000
- CRP >1.0mg per cent
- Presence of toxic granulation in peripheral blood picture
- Platelet count <150000
- Immature to total neutrophil ration >0.2

Sepsis was defined to be early onset when it occurred during the first three days of life[2]. Statistical analysis was performed using Chi square test and Fischer's exact test. Statistical significance was defined as $P<0.05$. It was computed using the program STATCALC in the package EPIINFO.

Results

Patients

A total of 486 neonates admitted to the level II nursery within 24 hours of delivery were enrolled in the study. Table I gives the distribution of these neonates according to the reasons for admission. Meconium staining of liquor was the most common reason for admission, followed by emergency Caesarean section, prolonged leaking of liquor and prematurity. Fifty-six were admitted because of reasons other than risk factors for infection (infants of diabetic mothers, babies of mothers with Rhesus negative blood group, or babies with history of previous neonatal death in siblings). Out of 486 enrolled in the study, 252 were male and 234 were female babies.

Septicaemia

Nineteen neonates (3.90%) had proven early neonatal bacterial sepsis and nine (1.85%) met the criteria for probable bacterial spesis. Therefore, 5.76% of the 486 babies admitted to the level II nursery within 24 hours of delivery had proven or probable early onset bacterial sepsis. One newborn had both blood and cerebrospinal fluid cultures positive. Urine and stool culture was positive in one neonate each. In cases of proven sepsis, the male to female ratio was 2.6:1. Out of these 19 neonates 10 were premature.

Fifteen neonates who had positive blood culture (including mixed growth) but had no associated symptoms and signs or haematological changes of septicaemia were diagnosed as having contaminated cultures rather than true bacterial infection.

Symptoms and signs of septicaemia

Symptoms and signs of early onset septicaemia were as follows. The number of neonates affected is given in parenthesis.

General

- fever (8)
- hypothermia (1)
- bleeding tendency (1)

Gastrointestinal system

- poor feeding (3)
- diarrhoea (3)
- vomiting or excessive gastric aspirate (2)

Abdomen
- abdominal distention (7)
- hepatosplenomegaly (1)

Central Nervous System
- lethargy, irritability (5)
- bulging and tense fontanellae (2)
- seizures (1) -hypotonia (2)

Skin
- umbilical flair and discharge (6)
- pustular lesions (4)

Cardio-Respiratory System
- tachypnoea (11)
- dyspnoea (10)
- apnoea (2)
- grunting (3)
- cyanosis (7)
- mottled skin (2)
- pallor (2)
- hypotension (2)
- arrythemias (2)

Perinatal Risk Factors

The frequency of various perinatal risk factors for early neonatal septicaemia is listed in Table II. All but one septicaemic neonate had one or more perinatal risk factors. The most frequent factor was prematurity. The infection rate of premature infants was 15.5 per cent which was significantly higher than a rate of 3.5 per cent for term infants ($P<0.005$). Others in order of decreasing frequency were small for gestational age ($P<0.04$), prolonged leaking of liquor, meconium staining, emergency Caesarean section, maternal pyrexia and instrumentation during delivery.

Bacteriology of Early Onset Neonatal Septicaemia

The bacteria responsible for septicaemia are listed on Table III.

Coagulase negative staphylococci (CNS) and *Streptococcus* Group B (GBS) appear to be of major importance.The associated risk factors are given in (Table II).

CNS was responsible for septicaemia in nine neonates. The associated risk factors were prematurity, meconium staining of liquor, instrumentation during delivery and small for gestational age.

GBS caused septicaemia in four neonates. One of them was premature. Risk factors included meconium staining of liquor, foetal distress and instrumentation during delivery.

Both the neonates who developed *Enterobacter* and *Acinetobacter* sepsis were prematures. One baby who developed *Pseudomonas* septicaemia was delivered to a febrile mother. *Klebsiella* was responsible in two neonates, one was premature and small for gestational age, and the other had prolonged leaking liquor as risk factor.

Table I
Reasons for admission of 486 neonates in level II nursery

Reasons for Admission	No. of infants*
– Maternal pyrexia	54
– Prolonged leaking of liquor	111
– Foul smelling liquor	8
– Prolonged labour (2nd stage)	19
– Instrumentation during delivery	61
– Caesarean section	142
– Meconium staining of liquor	147
– Prematurity	90
– Small for gestational age	71
– Foetal hypoxia	8
– Others	56

* – *Many neonates had more than one risk factor/reason for admission*

Table II
Perinatal risk factors in 28 neonates with early onset neonatal septicaemia

Risk factors	No. of infants*
– Prematurity	14 **
– Prolonged leaking of liquor	6
– Small for gestational age	8 **
– Meconium staining	6
– Emergency Caesarean section	6
– Maternal pyrexia	3
– Instrumentation during delivery	3
– Others	2

* – *Some of the neonates had more than one risk factor.*
** – *Statistically significant*

CNS and GBS were sensitive to most of the antibiotics whereas *Pseudomonas, Klebsiella* and *Enterobacter* species were resistant to multiple antibiotics and were sensitive only to imipenem and chloramphenicol.

Mortality

Three babies died of septicaemia. Two were premature babies. The causative organisms were GBS, *Acinetobacter* and *Klebsiella.* The case fatality rate of the neonates with early onset septicaemia was 10.71 per cent.

Discussion

Keeping in view the nature of our study population, the high incidence of early onset neonatal septicaemia (5.76%) is expected[2,20]. The risk factors for neonatal septicaemia have been studied quite extensively. Their association with increased risk of sepsis is clear[10,11,13]. In our study all but one neonate had one or more of these perinatal risk factors. Prematurity was the most common perinatal risk factor (P<0.005), followed by small for gestational age (P<0.004), prolonged leaking of liquor and meconium staining of liquor(Table II).

The range of micro-organisms found in this study (Table III) was similar to that found in previous studies[1,2,21,22]. However the relative importance of each organism differs from unit to unit and at different times in the same unit. The major bacteria associated with septicaemia in our study was *Coagulase negative staphylococci* (47.37%). This organism of low pathogenecity has recently been recognised with increasing importance in neonatal sepsis. In UK *Staphylococcus epidermidis* was responsible for late onset neonatal sepsis (>48 hours of life) in 26.13 per cent to 56.25 per cent of cases[2,10]. A recent study in India found this organism in 20.16 per cent of the early onset neonatal sepsis (<7days of life)[24].

Coagulase negative staphylococci obtained from the blood cultures of the "proven septic" babies in this study was most likely not a contaminant because by definition these newborns also had signs or haematological changes highly suggestive of systemic infection. The second most common causative organism responsible for early onset neonatal septicaemia was Group B streptococci, which is a well recognised organism and carries a high mortality[2]. The other organisms seen in this study included *Klebsiella, Pseudomonas* and *Enterobacter* species.

The case fatality rate was low compared to generally quoted figures from developing countries[3]. This is due to selection of population in our study which does not include very sick and very small babies as they are managed in a level III nursery, and also due to the low virulence of *Coagulase negative staphylococci*, the most common cause of sepsis in our nursery.

Table III
Types of organisms isolated in 19 cases of early onset neonatal septicaemia

Organism	Number of Patients	
Coagulase negative staphylococci	9 (5)*	[47.37]**
Streptococcus group B	4 (1)	[21.00]
Enterobacter	1 (1)	[5.26]
Acinetobacter	1 (1)	[5.26]
Pseudomonas aeruginosa	1 (1)	[5.26]
Klebsiella species	2 (1)	[10.52]
E. coli	1 (0)	[5.26]
Total	19 (10)	

* – *number in parenthesis indicate premature babies*
** – *number in brackets indicate the per cent of septicaemia cases*

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