CLINICO-BACTERIOLOGICAL PROFILE OF LATE ONSET SEPTICEMIA IN M. Y. H. NURSERY

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ABSTRACT

BACKGROUND

Septicaemia plays a major role in morbidity and mortality of neonates. This is one of five major causes of death in neonates. Late onset septicaemia remains a significant cause of morbidity and mortality in neonates, more so in developing countries.

AIM OF STUDY

To study the clinical pattern, risk factors, bacteriological profile, antibiotic sensitivity pattern and mortality rate in late onset septicaemia.

STUDY DESIGN

Prospective observational study.

SETTING

Nursery of M.Y. Hospital, MGM Medical College, Indore (M. P.)

PARTICIPANTS

One hundred newborns delivered and admitted in nursery of M.Y. Hospital, Indore, were taken up for study.

METHOD

Cases followed longitudinally regularly till discharge or death. The symptoms and sign closely observed and recorded and risk factors predisposing to late onset sepsis were analysed. Investigation done for sepsis profile, e.g. TLC, DLC, blood culture, CSF routine microscopy and culture and antibiotic sensitivity.

RESULTS

In present study, 78% cases belong to 1-2kg group. Majority of cases (89%) were become culture positive between 3rd-7th day of life. Prematurity at birth was most common indication of admission, 78% of cases followed by respiratory distress in 25%. Neonates show following clinical features, lethargy 89%, refusal to feed 84%, jaundice 60%, hypothermia 63% of the cases; 115 cultures were obtained from 100 patients showed that most common organism isolated was Staph aureus in 48.5% cases followed by E. Coli (30.8%) and Klebsiella pneumoniae (27.9%). Out of 100, 67% cases were discharged and 25% mortality was noted. In the study, maximum deaths were occurred in 5-12 days of life.

CONCLUSION

Pre-term and low birth weight babies are commonly affected, they became septic commonly in first week of life. Lethargy, refusal of feed and hypothermia are the common presentation of septicemia. Staph is the most common pathogen followed by E. coli in our study. Mortality rate in nosocomial septicemia is 25%. Mortality rate is higher in female babies as compared to male babies. Mortality rate is high in LBW babies.

KEYWORDS

Septicemia, Blood Culture, Neonate.

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INTRODUCTION

Septicemia plays a major role in morbidity and mortality of neonates. This is one of five major causes of death in neonates. Late onset sepsis is the nursery acquired septicemia, occurs

usually after 72 hours of life. In late onset infection, the organism first colonizes the baby and only later invades to cause sepsis. Sepsis screen was considered to be positive if at least two tests were positive (Abnormal leucocyte (<5000 - >20,000), I:T ratio >0.12, micro ESR (15mm at 1 hr.) and positive CRP.

Late onset septicemia remains a significant of morbidity and mortality in neonates, more so in developing countries. This may be due to delivery and postnatal followup in an unclean environment and non-adherence to aseptic measures, which increases the chance of contamination with infective organisms. An early diagnosis and appropriate antibiotic therapy leads to better survival rates in septicemia. However,

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antibiotics can be started early if we pick up septicaemia earlier by clinical evaluation. But starting antibiotics without documenting sepsis by blood culture and other haematological profile (Abnormal leucocyte count, thrombocytopenia, elevated micro increased ESR, increased I:T ratio and abnormality in CSF routine microscopy and culture) can result in administration of antibiotics more often babies without septicemia than babies with septicemia. Keeping this thing in mind it is important to study the clinical profile, bacteriological profile and risk factors in detail.

MATERIAL AND METHODS

Type of Study–Prospective observational study.

Source of Data: A total of 100 newborns delivered and admitted in nursery of M. Y. Hospital, Indore, were taken up for study. Newborn should be delivered and admitted in M. Y. Hospital nursery for at least 72 hrs are included in study. Only those cases are selected who develops signs and symptoms of sepsis after 72 hrs of birth.

METHOD

A detailed maternal history was taken followed by examination of the neonate and the cases followed longitudinally regularly till discharge or death. The symptoms and sign closely observed and recorded on case sheet as well as on proforma, specially designed for the purpose. The various symptoms that were inquired were fever, off feed, loose motion, convulsions, respiratory distress, abdominal distension, vomiting, keeping dull.

The various clinical signs looked for were hypothermia, crying, activity, rooting, sucking, cyanosis, pallor, jaundice and bleeding from any site.

Various risk factors predisposing to late onset sepsis were analysed in detail for each baby, e.g. birth weight, resuscitation at birth, gestational age, duration of stay, number of days for which peripheral vascular cannula was placed, etc.

Exclusion Criteria

1. Babies with PROM >12 hours.
2. Maternal fever.
3. Foul smelling liquor.
4. Onset of symptoms within 72 hours of life.

Total Leukocyte Count and Differential Count

Total Leukocyte Count

The sample was taken in EDTA vial and 20 micro lit of sample was taken in pipette with 0.38ml of WBC diluting fluid, after waiting 5-10min Neubauer's was charged. Counting was done in four corner squares of chamber and the number obtained multiplied by 50 to get total leucocyte count.

Differential Count

For differential count a thin slide was prepared, allowed to dry, then staining was done with Leishman stain/Field's stain/Giemsa stain. The counting was done at the junction of tail and body part of the slide. Counting was done in oil immersion power of light microscopy. Counting was done in zig-zag fashion after dividing slides in 10x10 squares.

Counting for neutrophil was done for various forms depending on number of segment of nucleus. Cells were considered as immature when nucleus were seen as bilobed with two segments joining by broadband and more than four

or five segmented nucleus neutrophils considered as mature. A ratio of >0.12 of immature to total cell count was considered as abnormal.

Blood Culture

Cultures were taken with full aseptic precautions. Child was placed in supine position and cleansed the site with 70% ethanol swab in one direction only, approx. 50mm area is cleaned, then finally povidone iodine was applied and dried. The sample was taken by 22-gauge needle; 2-3ml blood was drawn into the container of 25ml of liquid broth (Sodium polyanethol sulphonate), is a good anticoagulant, has added advantage of annulling the natural bacteriological action of blood. Liquid broth incubated at 37°C for 7 days. Blood agar and MacConkey agar incubated aerobically and white chocolate agar incubated anaerobically. Then culture was examined for likely organism by gram staining and specific tests were applied for identification of gram positive and negative bacteria. Whenever no growth seen till 7th day, blood culture was labelled as sterile.

Antibiotic Sensitivity

Organisms were isolated in pure culture and subculture in peptone water. It is kept for 24 hr. in the incubator to multiply. Agar plates were used for study of bacterial sensitivity disc method. Commercially prepared discs of 6mm in diameter were used, antimicrobial content of discs for various antibiotics were ampicillin 10micrgm, cefotaxime 10micrgm, methicillin 5, amikacin 30g, netilmicin 30g, erythromycin 5g, vancomycin 30g, ciprofloxacin 1g. Plates were incubated for overnight in air at 35°C-37°C. The zone of inhibition was measured by millimetre rule. The diameter of clear zone was measured. After measuring the diameter of zone organism was labelled as sensitive, resistant or intermediate by comparing the sizes of zone with control strain. Sensitive labelled when size of zone of the test strain was more than or equal or not smaller than 2mm. Intermediate was labelled when test zone size was equal to 2mm, but it was >3mm, smaller than controls.

CSF Examination: Routine Microscopy

A 3-5ml of CSF was taken in test tube and reported for various features.

Physical appearance: was reported as clear, turbid, haemorrhagic and yellowish. Precipitates were noted by centrifuging the CSF. Glucose determination: were done by glucose oxidase test.

Proteins estimation: were done by spectrophotometers Pandy's test: were done by 2-3ml of phenol with 2-3 drops of CSF in it positive Pandy's were considered when turbidity appears.

Cell count: the count was done in improved Neubauer's chamber by putting 1-2 drops of CSF and 4 drops of CSF diluting fluid in each square. Cell count was done in four corner squares and total count was derived from following formula
No. of cells in 4 square x 25 = total leucocyte count.

RESULTS

Seventy eight clinically septic cases belongs to 1-2Kg weight group, which is 78% of total. Our study shows that 92% cases have birth weight less than 2.5kg; 73% cases were <34 weeks gestation while 98% cases under 37 weeks gestation, which

shows that late onset septicemia is more common in preterm babies. The ratio of male-to-female is nearly 1.2:1.

Majority of cases (89%) became culture positive between 3rd-7th day of life.

Prematurity at birth was most common indication of admission, 78% of cases followed by respiratory distress in 30%, refusal of feed (15%), resuscitation at birth (25%).

35% babies stayed in nursery for 10-14 days while 24% babies stay for more than 20 days. More than 79% babies stay in nursery for more than 10 days. Average stay reported during study was 17 days/patient.

Table:1 shows that main clinical features were lethargy 89%, refusal to feed 84%, jaundice 60% and hypothermia 63%.

Table: 2 and 3 shows that maximum number (64%) of values of TLC were within normal limit expected for neonates. While 14% values of TLC were below the normal count and 22% values of TLC were above normal reference value. CSF was done in only 13 babies and was positive in 2 cases (15% of CSF positive).

A total of 115 cultures were obtained from 100 patients (Table: 4). Most common organism isolated was staph aureus (48.5%).

Staphylococcus were most sensitive to vancomycin (69.9%) followed by amikacin 48%, ciprofloxacin, linezolid gentamicin, piperacillin, cefotaxime, co-trimoxazole in decreasing order. E. coli was most sensitive to amikacin followed by netilmicin, ciprofloxacin, Cefotaxime, gentamicin, piperacillin in decreasing order. Klebsiella was most sensitive to amikacin (63.1% cases) followed by netilmicin, ciprofloxacin, piperacillin, co-trimoxazole, cefotaxime, meropenem, gentamycin in decreasing order. Enterococcus were most sensitive to vancomycin (60%) followed by linezolid (50%).

A 67% cases with nosocomial septicemia were discharged while mortality was reported in 25% cases. In the study, maximum deaths were occurred in 5-12 days of life.

DISCUSSION

Out of 100 babies, 55 babies (55%) were male and 45 babies (45%) were female indicating a male predominance. This observation is comparable to results by various authors. M.L. Moro reported no gender association of septicemia. Mortality was high in female neonates. In the present study, it is 44% and 56% for male and female neonates respectively.

Incidence of septicemia is high in low birth weight babies. There is direct correlation between septicemia rate and weight group, as weight decreases rate of septicemia increases. In the present study, 92% babies were below 2.5 Kg. This observation was supported by different authors. Heming et al.¹ found that sepsis was 2.2 times greater in babies with weight <1500gm as compared to >1500gm babies. In the present study there was only 4 cases of <1000gm, because most ELBW babies were certified within 3 days. The mortality was also high in low birth weight babies.

Pre-maturity is associated with increased risk of nosocomial sepsis due to decreased immunoglobulin and opsonophagocytosis as reported by Fanor off AA and Krediet TG et al.² Mortality is also high in pre-terms as compared to term neonates. In the present study, it is 69% in pre-terms. This observation was supported by A. Misallati et al.³ who

reported 8 deaths out of 8 pre-terms with septicemia and one death out of three term babies.

The clinical features of neonatal sepsis are nonspecific and vague. In this study, most common findings were refusal to feed (84%) and lethargy (89%). Refusal to feed as most common feature was also reported by O Batisti.⁴ i.e. 77% cases and 66.25% by Abida Malik et al.⁵ In the present study, jaundice was detected in 63% of cases, but in 77.7% cases jaundice appears to be physiological while 16.67% cases were outside the physiological range and 31% cases of jaundice were of direct hyperbilirubinemia.

Total leucocyte count is highly variable with age and weight of babies, particularly neutrophil count. Total leucocyte count ranges from 5000-20,000. In present study count below 5000 was seen in 14% cases, while counts above 20,000 were seen in 22% cases. Beutew et al.⁶ found leucocyte count of no help in the diagnosis of septicemia in premature infants. Thrombocytopenia is known in neonatal septicemia. In the present study, it was reported in 77% cases. This finding was supported by Easton and Carrigon et al. who reported thrombocytopenia in 47% and 73% cases respectively.

Neonatal sepsis carries a high mortality rate. Two-third deaths in infants are due to neonatal sepsis. In this study, death rate was 25%. This is comparable with observations by other authors (20%-33%). SRS bulletin 2011.⁷ Somanci M.⁸ Mandira Banerjee et al.⁹ 38%, A. K. Pahwa et al.¹⁰ reported 77% deaths with infection and 14% deaths without infection, while O. Battisti.⁴ reported 29% and 64% deaths in 'LOS' and 'EOS' respectively.

Mortality rate also varies with gestational age. In present study, 82% deaths were of pre-terms. This observation was supported by Abida S. Malik et al.⁵ Death rate also varies according to organism. In present study, around 85% deaths are due to gram-negative bacilli. In present series case fatality by E. Coli was very high (23% of total E. Coli septicemia cases).

Staphylococcus is the most common organism grown from cultures 33% (33/100). E. Coli being the 2nd most common organism 21% followed by Klebsiella (19%). This is comparable to observation by other workers who showed E. Coli as most common organism, while Choudhary P and Shirivastava G et al.¹¹ reported E. Coli as 10% of total nosocomial septicemia.

Incidence of Klebsiella in this study was 19%. Mandira Banerjee et al.⁹ A. K. Pawa.¹⁰ Adeyemo A. A.¹² P. Choudhary et al.¹¹ reported Klebsiella as most common organism arising as nosocomial sepsis in 70.3%, 68%, 27.8%.

In this study, E. coli most sensitive to amikacin 61% and least sensitive to cotrimoxazole, sensitivity to netilmicin 52.3%, ciprofloxacin 33.3% which were most commonly used prophylactically in babies admitted in our nursery.

Klebsiella was most commonly sensitive to amikacin 63% followed by netilmicin 31.5%, least sensitive to ampicillin and cotrimoxazole each. Mandira Banerjee et al.⁹ recorded Klebsiella sensitivity to various antibiotics as ciprofloxacin 31.5%, piperacillin- tazobact (26%).

Staph was most commonly sensitive to vancomycin (69.9%) followed by amikacin (48%), ciprofloxacin 44.4% and linezolid (42.4%).

CONCLUSION

This study of 100 neonates regarding clinical, bacteriological risk factors profile in late-onset septicemia reveals that,

1. Neonatal septicemia is more common in male babies.
2. Pre-term and low birth weight babies are commonly affected.
3. Most of babies became septic in first week of life.
4. Peripheral intravenous cannulas, IV fluids, LBW, increased duration of stay are significant risk factors for late onset septicemia.
5. Increase duration of stay increases risk of sepsis vice versa septicemia increases the duration of stay.
6. LBW, pre-term, respiratory distress at birth are significant conditions associated with late onset septicemia.
7. Lethargy, refusal of feed, hypothermia, gastric residual, pale, jaundice and bleeding diathesis are the common presentation of septicemia.
8. Leukopenia is commonly associated with septicemia as compared to leukocytosis.
9. Thrombocytopenia is important early marker of septicemia.
10. Staph is the most common pathogen followed by E. coli.
11. Mortality rate in nosocomial septicemia is 25%.
12. Mortality rate is higher in female babies as compared to male babies.
13. Mortality rate is high in LBW babies.
14. E. Coli carries high fatality rate.

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Sl. No.	Clinical Features	No. of Cases (n=100)	Percentage
1.	Lethargy	89	89%
2.	Refusal to feed	84	84%
3.	Hypothermia	63	63%
4.	Jaundice	60	60%
5.	Gastric residual	46	46%
6.	Mottling	42	42%
7.	Generalized pallor	37	37%
8.	Abdominal distension	30	30%
9.	Hyperthermia	22	22%
10.	Seizure episodes	21	21%
11.	Sclerema	19	19%
12.	Bleeding IV/GI/other	15	15%
13.	Apneic episode	15	15%
14.	Bulging fontanelle	2	2%

Table 1: Clinical Features of Neonatal Septicemia

Sl. No.	TLC	No. of Cases (n=100)	Percentage
1.	<4999	14	14%
2.	5000- 9999	34	34%
3.	10000 – 19999	30	30%
4.	>20000	22	22%

Table 2: Showing Distribution of Cases According to TLC

Sl. No.	Thrombocyte Count	No. of Cases	Percentage
1.	<20000	2	2%
2.	20000–49999	18	18%
3.	500000–99999	42	42%
4.	1 Lac- 1.5 Lac	15	15%
5.	> 1.5 Lac	23	23%

Table 3: Showing Distribution of Cases According to Thrombocyte Count

Sl. No.	Organism	No. of Cases (n=100)	Percentage
1.	Staph	33	33%
2.	Sterile	32	32%
3.	E. Coli	21	21%
4.	Klebsiella	19	19%
5.	Enterococcus	5	5%
6.	Pseudomonas	2	2%
7.	Streptococcus	2	2%
8.	Proteus	1	1%

Table 4: Showing Distribution of Cases According to Blood Culture Pattern of Septicemia

Death Distribution According To Weight and Sex