Original Article

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Clinical Study of Neonatal Septicemia with Reference to Early Indicators of Sepsis in NICU, PIMS

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Absract

Neonatal septicaemia is a major cause of morbidity and mortality in new born infants. *Back ground and objectives:* to study the incidence, predisposing factors, clinical profile, out come, early indicators of correlation with all clinical aspects and antibiotic sensitivity pattern of neonatal septicaemia. *Materials and Methods*: The 50 neonates who are showing the well documented signs of septicaemia are included in this study. *Results*: culture was bacteriologically positive in 34% cases. Ciprofloxacin had maximum sensitivity 88.2%. Leucopoenia ≤5000/cmm had sensitivity of 47% specificity of 66.67% and ppa of 42.11%,toxic granulation had 70.56% sensitivity, 63.65% specificity and 50% ppa. B/n>0.2 had 88.2% sensitivity 62.4% ppa. m-ESR had sensitivity of 70.56%, specificity of 84.84%, ppa of 70.5%, c-reactive protein had 88.2% sensitivity and 87.8% specificity and 78.95%ppa. Case fatality rate was 28%. *Conclusion:* Clinical features of neonatal septicaemia are non specific and vague. Sepsis screen had good sensitivity, specificity and ppa. combination of tests increase the specificity and ppa. An an individual test c- reactive protein has highest sensitivity.

Keywords: Neonates; Septicaemia; Outcome.

Introduction

Neonatal septicaemia is defined as a bacterial infection documented by a positive blood culture in the first four weeks of life. Systemic bacterial infection during the first month of life have remained a major cause of infant morbidity and mortality.

The early diagnosis of neonatal septicaemia still poses great difficulties. Early clinical symptomatology of neonatal septicaemia is mimicked by lot of other disorders affecting the newborn. It is a major cause of morbidity and mortality and it accounts for half of the neonatal deaths in this country. The overall incidence of neonatal sepsis varies between 1-8 cases/100 live births. Neonatal sepsis can be divided into 2 subtypes depending upon whether the onset of symptoms is during the first 72 hours of life or later. Although the term early onset sepsis had been used to refer to neonatal infection occurring as late as one week of age, it should be restricted to those infections with a perinatal pathogenesis, the usual onset of which occur within 72 hours. Early–onset sepsis is caused by organisms prevalent in genital tract or in the labour room. Ascending infection, transplacental haematogenous spreads are important mechanisms of early onset sepsis.

After the birth the baby is exposed to the environment contaminated with micro organisms, which start setting or colonising at various places. The organisms enter the body through the umbilicus, skin or mucosa. Due to poor immunological defence of the new born, even local infections tend to become generalised. Infections are more commonly met with preterm and low birth weight babies. To prevent serious morbidity and mortality caused by untreated or lately treated neonatal septicaemia, it is important that the diagnosis is made early and the treatment

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started as easily as possible. Even though the positive blood culture is diagnostic of neonatal septicaemia, the technique of blood culture is time consuming that demands a well equipped laboratory and has a success rate of only 40%, therefor the blood culture has its own limitation.

Early tearment with rational antibiotic therapy is possible with the help of certain indirect markers such as leucopenia, toxic granules, band form to neutrophil ratio, micro-esr and c-reactive protein. This investigation excercise is collectively known as sepsis screen. The early diagnosis of neonatal sepsis by clinical examination is vital. In the presence of predisposing factors, early clinical suspicious coupled with sepsis screen will detect neonatal septicemia earlied, which will enable the clinician to treat the infection timely and adequately,which in turn will help to reduce the neonetal morbidity and mortality.

Aims and Objectives

- To study the incidence and predisposing factors of neonatal septicemia.
- To study the clinical profile and outcome of septicemia.
- To study the early indicators and correlation with all clinical aspects neonatal septicemia.
- To study the bacteriology and antibiotic sensitivity pattern of neonatal septicemia.

Material and Methids

This study was conducted in prathima institute of medical sciences, nagunoor. 50 neonates below the age of 28 days with clinical suspicion of neonatal septicemia were included in this study. Neonates admitted in our hospital from out patient depatment and neonates born in same hospital were included in this study group. After admission detailed history was taken and through clinical examination was done. Consent was taken from parents. Institutional ethical commity permission taken. Results were analysed on different parameters.

Results

This study conducted our 50 neonates. Out of 50, males are 33 (66%), females are 17(34%).

Early onset of septicemia was present in 34 (68%) cases, late onset of septicemia was seen in 16 (32%) cases (Table 1). Neonatal risk factors like low birth weight and prematurity were present in 68% and 60% cases respectively. Maternal risk factors observed were prolonged rupture of membranes >18hrs (30%), home delivery 24%, poor maternal health and hygiene of genital (58%). In 86 of cases there was one or more predisposing factor present.

Common clinical manifestation of neonatal septicemia were refusal of feeds (56%), temperature abnormality (46%), sclerema (44%). jaundice (42%), pallor (36%) not doing well (24%), rash (20%) and convulsion (16%). Culture was bacteriologically positive in 17 (34%) cases, negative in 33(66%) cases. Isolated organism were e.coli 7(42.5%), klebsiella 4(23.5%), staphylo coccus aureus 3(17.6%), pseudomonas 2 (11.7%), proteus 1(5.7%). In this gram negative organism were detected in 14(82.3%) cases, gram positive were in 3 (17.7%) cases (Table 2)

Toxic granulation present in 12 (70.56%) of 17 bacteriologically positive cases (Table 3) Positivity and negativity of combined test shown in Table 4. White blood cell counnt Sensitivity was 47%, specificity was 66.67%. Positive predictive accuracy of the test 42.11% (Table 5). Outcome of the patient with various factor depicted in Table 6.

Table 1: Distribution of cases

Age of onset	Maturity		Total	Birth weight	
	Pretem	Term		≤ 2500gms	> 2500gms
≤7 days	19	34	34	20	14
>7 days	11	16	16	14	2
total	30	50	50	34	16

Table 2: Distribution of isolated organism

Gram Staining	Age of onset		Total	Birth Weight	
	≤7 days	>7 days		≤ 2500gms	> 2500gms
Gram negative	7	1	14	10	4
Gram positive	1	2	3	2	1
total	8	9	17	12	5

Table 3: Different test profile

		Culture		Total
		Bacteriologically positive cases-17	Bacteriologically negative cases-33	
Wbc count	≤ 5000/cmm	8 (47%)	11(33.33%)	19
	>5000/cmm	9(53%)	22(66.67%)	31
Toxic granulation	Present	12(70.56%)	12(36.37%)	24
	Absent	5(29.44%)	21(63.63%)	16
B/N	B/N ≥ 0.2	15 (88.2%)	12(36.37%)	24
	B/N < 0.2	2(11.8%)	21(63.63%)	26
m-ESR	≥ 15mm at the end of 1st hr	12(70.56%)	5(15.16%)	17
	< 15mm at the end of 1st hr	5(27.4%)	28(84.84%)	33
c- reactive protein	Positive	15 (88.2%)	4(12.2%)	19
	negative	2(11.8%)	29(87.8)	31

Table 4: Positivity and negativity of combined tests

		Culture		Total
		Bacteriologically positive-17 cases	Bacteriologically negative-33 cases	
Toxic granulation + c-reactive protein	Positive	10(58.8%)	3(9.11%)	13
	negative	7(41.2%)	30(90.9%)	37
c- reactive protein +m ESR	Positive	11(64.68%)	2(6.07%)	13
	negative	6(35.32%)	31(93.93%)	37
Toxic granulation +m-ESR	Positive	10(58.8%)	4(12.13%)	14
	negative	7(66.7%)	29(87.87%)	36
c- reactive protein + Toxic granulation +m-ESR	Positive	8(47.04%)	2(5.07%)	9
	negative	9(52.96%)	31(93.93%)	41

Table 5: Sensitivity and specificity of different tests

Test	Sensitivity	Specificity	Positive Predictive Accuracy
WBC Count ≤ 5000cmm	47%	66.67%	42.11%
B/N ≥ 0.2	88.2%	63.63%	62.4%
Toxic Granulation	70.56%	63.65%	50%
M-ESR>Mm At The End Of 1st Hr	70.56%	84.84%	70.5%
C-Reactive Protein	88.2%	87.8%	78.95%
C-Reactive Protein+ Toxic Granulation	58.8%	90.9%	76.9%
C-Reactive Protein+ M-ESR	64.68%	93.93%	84.6%
Toxic Granulation+ M-ESR	58.8%	87.87%	71.6%
C-Reactive Protein+ Toxic Granulation+ M-ESR	47.04%	93.93%	88.8%

Table 6: Outcome of the patient with various factor

Factors		Outcome		Total
		Death-14	Survivals-36	
maturity	preterm	9(64.26%)	21(58.5%)	30
	Full term	5(35.74%)	15(41.5%)	20
Age of onset	≤ 7days	10(71.4%)	24	34
	>7days	4(28.6%)	12	16
Birth weight	≤ 2500gm	9(64.26%)	25	34
	>2500gm	5(35.74%)	11	16
culture	Bacteriologically positive	10(71.4%)	8	18
	Bacteriologically positive	4(28.6%)	28	32
Gram staining	Gram negative	9(90%)	5(71.43%)	14
	Gram Positive	1(10%)	2(28.57%)	3

Discusssion

This study was conducted in pims,nagunoor our 50 neonates below the age of 28 days with clinical suspicion of neonatal seticemia were included in this study by considering clinical profile, sepsis screen, outcome of neonatal septicemia.

Out of 50 males were 33 female were 17. Nelson [1] stated that males have an approximately 2 fold higher incidence of sepssis than females. H. David [2] wilson

stated that increased incidence of sepsis neonatorum in male infants in probably related to the higher incidence of congenital anomalies of the urinary tract in the the males, resulting primary urinary tract infection and secondary sepsis.

Early onset septicemia is ≤ 7 days was present in 34 cases (68%) and onset septicemia was >7 days was present in 15 cases (32%). In our study the early onset septicemia was more common because of maternal risk factors like prolonged rupture of membranes, home delivery, h/o of intrapartum maternal infection, poor maternal health and hygiiene of genital and neonatal risk factors like prematurity and low birth weight.

According to birth weight low birth weight i.e ≤ 2500 gm was present in cases (68%). These findings were cosistant with other studies. Nellian et. al [3], N mehrotra et al, piyush gupta et. al, agarwal et.al, khatua et al. And koutociby et, al. observedthat low birth weight new born have highter incidence of neonatal septicemia. N.sinha et. al [4] observed that babies with low birth weight predominated (64.9%).

In 50, 30 cases were preterm babies (60%). Anad et. al [5] observed that 62% preterm babies were affected. Khatua et, al [6] observed that out of 92 babies with neonatal septicemia 58 were preterm in 56.52%. Higher incidence of many complication of labour and resuscitation are more common in preterm babies than full term neonates. Preterm babies were relatively immuno- compromissed than immuno inexperienced. These factors predispose them to infection. Common neonatal predisposing factors detected in neonatal septicemia were prematurity (60%) and low birth weight (68%). Nelson [1] and cloherty [7] stated that the prematurity and low birth weight are the most important predisposing factors in neonatal septicemia.Common maternal factors observed were poor maternal health and hygiene of genitals (58%), prolonged rupture of membranes (31%), home delivery (23%) premature rupture of membranes(15%), h/o intrapartum maternal infection (9%). Udani et. al. And kishoret. al have reported high incidence of vertical trasmission and sepsis in babies born to mothers with prolonged rupture of membrane. Anand et. al [5] observed prolonged rupture of membranes in 29.3% of cases. N. mehrotra [8] noted three fold increase in the incidence of sepsis after prolonged rupture of membranes. James C. Overall et. al [9]. Observed that maternal infection, particularly of the uterus and urinary tract also significantly predisposes to neonatal infection. zilliacus and totterman noted a more than 6 fold grater incidence of internal infection in neonates born with mother with urinary tract infection at the time of delivery than in onnes born to mother without such infection.

In our study resuscitation after birth (17%) was observed as one of the important factor in neonatal septicemia. Dawodu et al [10] found that requirement of mechanical ventilation was important risk factor. Agarwal et. al [11] found that birth asphyxia was common predisposing factor. Motor et. al [12] Observed that mechanical ventilation for >5 days was significantly associated with neonatal sepsis. Mucosal abrasions or cutaneous defects associated associated with birth defects, fetal monitoring obstretical manipulation and/or vigorous resuscitation predispose to bacterial invasion and infection. Similarly the use of indwelling catheters. Fanaroff [13] atated that asphyxiated infants requiring resuscitative procedures including mechanical ventilation and catherization are at high risk of developing sepsis.

Commonly observed clinical manifestation were refusal to feeds (56%), temperature abnormality (47%), clerema (45%), jaundice (41%) pallor (36%) not doing well (24%), rash (21%) and convulsions (17%). Khatua et al [6] Observed that refsual of feeds, lethargy,diarrhea, temperature abnormality, abdominal distension, jaundice and vomiting were most common presenting features. Mishra et. al [14] observed that common clinical presentation were jaundice, lethargy, refusal of feeds, vomiting and respiratory distress.The clinical features of neonatal septicemia are non specific and may be clinical features of neonatal septicaemia are non specific and may be clinically indistinguishable from those occurring in non infectious conditions during neonatal period.

The culture was positive in 17 cases (34%). Gupta et al [15]. Observed culture positivity rate of 33%. Although blood culture are normally the basis for a diagnosis of bacterial infection the bacteremic phase of the illness may be missed by poor timing blood sample size so also before drawing blood sample for culture the patient may be treated with some parenteral antibiotic by private practioners or other hospital. Due to this the blood culture have loe sensitivity. Various organisms isolated in 17 culture positive cases were E.coli (42.5%), Klebsiella 4 (23.5%), staphylococcus aureus (17.6%), pseudomonas (11.7%) proteus (5.7%). N. Mehrotra [8] observed that e.coli were the most commonest group of organism isolated. similar observation have been made by Smith et. al [1], pseudomonas, proteus and klebsiella were the other organisms frequently found. In our study gram negative organisms were detected in 14 cases (82.3%). Our findings are consistent with others of Mathur et

al [16]. (66.5%) and khatua et al [6] (76.3%).In this study gram negative organisms were common cause of early onset of septicaemia. Our study consistant with j.n mishra et al study.he observed that early onset of septicaemia was present in 71.7% cases due to gram negative bacteria.In our study gram negative septicaemia was more common in low birth weight babies (83.3%). Our finding are consistant with Mishra et. al [14].

In this study leucopenia had sensitivity of 47% specificity of 66.67% and positive predictive accuracy of 42.11%. This is nearer to Namedo et. al [17] they observed that leucopenia had sensitivity of 44%,specificity of 69% and positive predictive accuracy of 48%. Unfortunately the positive predictive value of an abnormal wbc count is poor. this is not surprising since many non-infectious conditions can be associated with an abnormal neonatal wbc count.thus the initial wbc with differential cell count may not be helpful in the decision to initiate antibiotic therapy for an asymptomatic new born infant with indentified risk factor for sepsis. Nevertheless it is common practice to perform these tests as a part of the immediate post natal assessment of the "at risk" infant. In our study toxic granulation had 70.56%, sensitivity 63.65% specificity and 50% positive predictive accuracy. Our studies are consistant with Namedo et al [17]. They observed that toxic granulation had 80% sensitivity 70 specificity and 69 % positive predictive accuracy.In our study band –total neutrophil ratio had sensitivity (88.2%) specificity (63.63%) and positive predictive accuracy of (62.4%) our observations are consistent with Namedo et al [17]. They observed sensitivity of B/N ratio 82%. In our study micro–ESR test had sensitivity of 70.56%, specificity of 84.84% and positive predictive accuracy of of 70.5%. Our observations consistant with Parida et. al, they observed that m-ESR had 71% sensitivity, 73.3% specificity and 71.4% positive predictive accuracy. In this study C-reactive protein test had 88.2% sensitivity, 87.8% specificity and 78.95% positive predictive accuracy.our study consistant with Singh et. al [18] where 80% sensitivity, 91% specificity and 92% positive predictive accuracy present. In our study it was observed that when two on more tests were combined specificity and positive predictive accuracy were increased while sensitivity was decreased than the individual test.our study observations are consistant with Mishra et. al [17]. where the positive predictive accuracy and specificity of two test combination was higher than individual test at the cost of sensitivity.

In our study case fatality rate was 28%. The mortality was higher in preterm babies.this was due to poor defences against bacterial infections. In this study mortality was higher in early onset septicaemia. Our observations are consistent with Mathur et, al [20]. Where the mortality was 64.5% when the onset of illness was early. In this study mortality was higher in low birth weight babies.

Our observations are consistent with mishra et al [14]. where the mortality was 70%. In this study mortality was higher in gram negative septicemia. Our observations are consistent with khatue et al [6]. where the mortality was 78.5% in gram negative septicemia. one major factor for high mortality rates in gram negative septicaemia is probably the emergence of drug resistant strains.

Conclusion

1. Clinical features of neonatal septicemia are non specific, vague and may be clinically indistinguishable fro those occuring in noninfectious condition during neonatal period.
2. Male, preterm and low birth weight neonates are more prone for septicemia.
3. Early onset septicemia is more common than late onset septicemia.
4. Prolonged rupture of membranes, home delivery, poor maternal health and hygiene of genitals predispose neonatal to infection.
5. Gram negative septicema is more common than gram possitive septicemia
6. Gram negative organisms are common cause of early onset septicemia.
7. Gram negative septicemia is common in low birth weight babies.
8. Sepsis screen has good sensitivity,specificity and positive predictive accuracy and is a valuable aid in early diagnosis of neonatal septicemia.
9. Sepsis screen is simple, cheap, less time consuming and easy to perform even at bedside.
10. As an individual test c-reactive protein has highest sensitivity, specificity and positive predictive accuracy and is a sensitive and responsive indicator of neonatal sepsis.
11. Combination of tests increses the specificity and positive predictive accuracy.
12. Mortality is higher in preterm and low birth weight babies.
13. Mortality is higher in early onset septicemia and gram negative septicemia.

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