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PROSPECTIVE OPEN LABEL STUDY, TO DETERMINE THE INCIDENCE OF EARLY ONSET SEPSIS AMONG TERM NEWBORNS IN THE POST NATAL WARD OF TERTIARY CARE HOSPITAL

Paediatrics

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ABSTRACT

Background and Aims: Neonatal sepsis is the commonest cause of neonatal mortality. Sepsis related mortality is largely preventable with early identification, rational antimicrobial therapy and aggressive supportive care

Method: A prospective open label non-randomised study conducted in 1507 live birth.1244(82%) were full term(>37 wks) and 263(18%) were preterm (<37 wks)(excluded from the study).Out of 1244, 37were congenital anomaly, 6-had diabetic mother, 12-HIV positive mother, 87-<1.8Kg, 226 MSL (18.1%) and 163-Birth asphyxia(13.1%), so 531 cases were excluded. 126 cases had risk factors(maternal, clinical, both) for early onset septicaemia(EOS). Out of 126, 26 cases were not included (blood samples not collected).

Result: Among 100 patients,14 patients had proven sepsis (14%) & 34 probable sepsis. Out of 56 vaginal deliveries 9-proven sepsis and 18-probable sepsis. Out of 44 caesarean, 5-proven sepsis and16-probable sepsis. Out of 59 (>2500 grams birth weight) 8-proven sepsis and 19-probable sepsis. Out of 41 (birth weight 1800 -2499 grams), 6-proven sepsis and 15-probable sepsis.24 patients had only maternal, 54 had only clinical and 22 newborns had both (maternal & clinical) risk factors. PROM & Fast breathing-most common maternal and clinical (37.03%) risk factors respectively for EOS. CONS,Ecoli,Klebsiella and Acinetobacter were most common pathogen. Overall, 94% alive and 2% died , 4% - lost to follow up.

Conclusion: PROM (Maternal) and fast breathing (clinical) are strong risk factors for development of EOS.. In the presence of these factors, the neonate should be screened and observed for sepsis and considered for early institution of antibiotics

KEYWORDS

INTRODUCTION

Infections is the single largest cause of neonatal deaths globally. According to National Neonatal Perinatal Database (2002-03), the incidence of neonatal sepsis in India was 30 per 1000 live-births; the two most common organisms klebsiella pneumonia and staphylococcus aureus were isolated. Based on the onset, neonatal sepsis is classified into two major categories: early onset sepsis which usually presents within 72 hours of age and late onset sepsis that usually presents after 72 hours of age. Clinical features of sepsis are non-specific in neonates and therefore a high index of suspicion is required for timely diagnosis.[1]

Sepsis is the commonest cause of neonatal mortality; it is responsible for about 30-50% of the total neonatal deaths in developing countries [1], [2]. It is estimated that up to 20% of neonates develop sepsis and approximately 1% die of sepsis related causes.[2]. Sepsis related mortality is largely preventable with early identification, rational antimicrobial therapy and aggressive supportive al neonates (referred from community/other hospitals), Klebsiella pneumonia was again the commonest organism (27%), followed by Staphylococcus aureus (15%) and Pseudomonas (13%). Although Blood culture is the gold standard for the diagnosis of sepsis, culture reports would be available only after 48-72 hours.

In this study a practical septic screen for the diagnosis of sepsis has been described and some suggestions for rational use of antibiotic have been included.

AIMS AND OBJECTIVE

1. To determine the proportion of term newborns at risk of neonatal sepsis[4].
2. To describe the incidence of early onset sepsis in apparently healthy term newborns at Tertiary care Hospital.

MATERIAL AND METHOD:

A prospective open label non-randomised study was conducted in the post natal ward of Sir Takhatsinhji hospital attached to the Government Medical College, Bhavnagar from March 2015 to July 2015. Total no. of live birth during this 5 month duration was 1507 (42%). Out of them, 1244(82%) were full term >37 wks and 263 (18%) were preterm (<37 wks), so 263 cases were excluded from the study. Out of 1244 full term newborns 37were congenital anomaly (3%), 6 were infants of diabetic mother (0.5%), 12 cases were HIV positive mother (0.98%), 87 had birth weight of <1.8Kg, 226 cases were meconium stained liquor(18.1%) and 163 cases of birth asphyxia(13.1%), so total 531 (42.7%) cases were excluded from my study. Out of 713 (57. 3%) newborns included in this study 126 cases had risk factors (maternal, clinical, both) for early onset neonatal sepsis, so proportion of apparently healthy term newborns at risk for early onset sepsis was 17.7%. Out of 126 newborns, 26 cases were not included in this study as i was not able to collect blood samples for investigations. Out of 100 newborns included in this study, 14 had Proven sepsis* (14%), 34 had Probable sepsis** (34%), 52 had no sepsis (52%). So incidence of proven sepsis was 14% and probable sepsis was 34% in the post natal ward of the hospital. Most common aetiological organism found in this study was coagulase negative staphylococcus aureus in 9/14 (64.3%).[5][6][7]

*Blood culture positive
**ANC and/or CRP positive but blood culture negative

INCLUSION CRITERIA:-

All mother-baby pairs in the postnatal wards who accepted participation in the study

Newborn (birth weight> 1.8 kg) having

- Lethargic
- Refusal to breast feeding
- Vomiting
- Abdominal distension
- Not passed urine(within 24 hours) and stool (within 48 hours)
- Hypothermia(axillary temperature <35.5C)
- Hyperthermia(axillary temperature>37.5C)
- Convulsion
- Tachypnea (RR >60/min)
- Severe chest wall indrawing

Newborns of mother having

- Multiple vaginal examinations(>4)
- Prolonged rupture of membranes(>18 hours)

- Intrapartum fever(>38C)
- Foul smelling liquor

5. Instrumental delivery (forceps, vacuum delivery)

EXCLUSION CRITERIA:-
- Premature infants (gestational age < 37 completed weeks)
- Congenital anomaly
- Infants of diabetic mother
- Infants of HIV positive mother

Consent was taken from all the participants after clear explanation of purpose of the study and involved procedures. Consecutive mother-baby pairs in the postnatal wards were approached for participation in the study and grouped as follows:
1. Term infants with no maternal risk factors and no feature(s) suggestive of neonatal sepsis (group one).
2. Term infants whose mothers had maternal risk factors of neonatal sepsis +/- one or more features of neonatal sepsis in the baby (group two). These were further evaluated.

Mothers were interviewed and clinic cards reviewed (where available) to determine presence of risk factors for early neonatal sepsis. The information was documented in a structured standardized questionnaire. The questionnaire contains biographic details of the participants, antenatal history, perinatal history and postnatal history all to seek newborns at risk of sepsis. [6]

The newborns had their baseline characteristics and examination findings recorded in the newborn assessment form. The first examination was done within 12 hours of delivery and continued daily for three days. Babies who did not have any maternal or neonatal features of possible sepsis were not evaluated further. The newborn baseline characteristics included gestation (in weeks) at delivery, mode of delivery, Apgar score at 5 minutes and sex.

At risk babies (those with maternal risk factors and /or those suggestive features of neonatal sepsis) were further evaluated and investigations like complete blood count, C-reactive protein and blood culture were sent. Then according to case definition baby grouped in one of the three groups (No sepsis, Probable sepsis, proven sepsis).

Case Definition
1. Proven sepsis defined those whose blood culture yielded pathogenic bacteria.
2. Probable sepsis defined those ANC and /or CRP findings were consistent with this diagnosis but cultures were negative.
3. No sepsis defined those with no clinical or CRP findings attributable to sepsis.

All cases of probable and proven sepsis started antibiotics and continued for seven days in probable and fourteen days in proven sepsis according to NICU protocols.[8]

Statistical analysis-
Statistical data were analysed with the chi-square & fisher exact test.

RESULT
- There were 52 male (52%) and 48 female (48%) included in the study. There was no significant difference in the number of male and female newborns. This implies uniform distribution of cases in the study group.(Table 1)

TABLE1. Showing sex wise distribution of cases (– 100)

Sex	Cases	Percentage (%)
Male	52	52
Female	48	48

- Out of the 100 newborns at risk, 14 had proven sepsis giving an early onset sepsis prevalence of 14%, 34 had probable sepsis (34%) and 52 (52%) had no sepsis.[9]
- Out of 52 cases of no sepsis 24 were male (48%) and 28 were female (52%). Out of 34 cases of probable sepsis 19were male (55.9%) and 15 were female (44.11%) and
- out of 14 cases of proven sepsis 9 were male (64.3%) and 5 were female (35.7%). In this study, there is no statically significant difference (p value 0.4140, chi-square and D.F.-2) between the incidence of early onset sepsis and sex of the newborn. Hence the present study revealed that the sepsis is independent of the sex of the newborn.[10][11][12][13] (Table-2)

TABLE: 2 Comparison of sex to the three groups (n-100)

Sex	No Sepsis	Probable Sepsis	Proven Sepsis	Total
Male	24	19	09	52
Female	28	15	05	48
Total	52	34	14	100

p=0.4140, chi-square

- Out of 100 newborn studied, 56 were delivered through vagina (56%) and 44 by caesarean section (44%). Out of 56 vaginal deliveries 9 newborn developed proven sepsis (16.07%) and 18 newborn developed probable sepsis (32.14%). Out of 44 caesarean delivery 5 newborn had proven sepsis (11.36%) and 16 had probable sepsis (36.36%). There is no significant association between development of early onset sepsis in the newborn and mode of the delivery. (p value 0.7709, chi-square, D.F.-2). This implies that neonatal sepsis is independent of the mode of delivery. (Table-3)

Table 3: Association between the mode of delivery and the early onset sepsis in the Newborns (N-100)

Mode of Delivery	No Sepsis	Probable Sepsis	Proven Sepsis	Total
Vaginal	29	18	09	56
Caesarean Section	23	16	05	44
Total	52	34	14	100

p =0.7709, chi-square

- Out of 100 newborns included in the study, 59(59%) have birth weight of more than 2500 grams and 41(41%) have birth weight between 1800 to 2499 grams. Out of 59 cases of more than 2500 grams birth weight 8 have proven sepsis (13.6%) and 19 have probable sepsis (32.2%). Out of 41 cases of birth weight between 1800 to 2499 grams 6 have proven sepsis (14.6%) and 15 have probable sepsis (36.6%).Study suggest that there is no significant association (p value0.8628,chi-square,D.F.-2) between the early onset sepsis and birth weight of the full term newborns. This suggests occurrence of early onset sepsis in term newborns is an independent of the birth weight of the newborns.(13)(14)(15) (Table-4)

Table 4: Association between the early onset sepsis and birth weight of the newborn (n-100)

Birth Weight	No Sepsis	Probable Sepsis	Proven Sepsis
>2.5kg	32	19	08
1.8 -2.4kg	20	15	06
Total	52	34	14

p =0.8628, chi-square

Maternal risk factors were compared to sepsis outcome. The study suggests that PROM was the most common risk factor 33.33% identified in those with proven sepsis and 47.82% with probable sepsis but was not unique to this group (p=0.3241, chi-square, D.F.-10). (Table-5)

Table-5: Association of maternal risk factors with three groups (n-100)

Maternal Risk Factors	No Sepsis	Probable Sepsis	Proven Sepsis
PROM	02	11	02
Forceps Delivery	03	0	0
Vaccum Delivery	03	04	01
Foul Smelling Liquor	04	03	01
Intrapartum Fever	05	03	01
PV Examination (>4)	04	02	01
Total	19	23	06

p = 0.3241, chi-square

The study suggests that there is significant association (p -0.0386, chi-square, D.F-14) between factors and incidence of early onset neonatal sepsis. Fast breathing is the most common clinical risk factor present in 42.1% & 36.36% in probable and proven sepsis respectively followed

by convulsion present in 26.32% in probable sepsis and 18.18% in proven sepsis.[16] (Table-6)

TABLE-6: Association of Neonatal risk factors with groups of sepsis (n-100)

Neonatal risk factors*	No Sepsis	Probable Sepsis	Proven Sepsis
Abdominal Distension	0	0	02
Convulsion**	06	05	02
Fast Breathing**	08	08	04
Hyperthermia	04	01	01
Hypothermia	01	0	0
Lethargic	10	02	01
Not Passing Urine (>24hr)	02	0	0
Not Taking BF Well	17	03	01
Total	48	19	11

*** = newborns presenting with clinical features of sepsis as a risk factor**
****p= 0.0386**

A comparison was done between the different risk factors assessed; 24% of recruited newborns presented with maternal risk factors and about 54% exhibited clinical features suggestive of sepsis. Both maternal and clinical risk factors were found in 22% of the newborns. This study suggest that there is significant association (p value-0.0307) between risk factor (maternal, clinical or both) with the incidence of early onset sepsis.[17][18](Table-7)

TABLE-7 Association of sepsis with Risk factors (Maternal, Clinical and Both)

Risk Factors	No Sepsis	Probable Sepsis	Proven Sepsis
Maternal	10	11	03
Clinical*	35	11	08
Both	07	12	03
Total	52	34	14

p = 0.0307, chi-square, significant

PROM is the most common maternal risk factors for early onset sepsis found in the study. There is significant association (p value-0.0004 & chi-square 15.81, D.F.-2)) between PROM and development of early onset sepsis in the newborns. (Table-8)

TABLE-8: Maternal risk factor (PROM)

Risk Factor PROM	No Sepsis	Probable Sepsis	Proven Sepsis
YES	01	11	02
NO	51	123	12
Total	52	34	14

p = 0.0004, chi-square, significant

Fast breathing is the most common among all the clinical features for early onset neonatal sepsis. Study suggests that there is no significant association (p-0.2320, chi-square.D.F.-2) between fast breathing and early onset sepsis. (Table-9)

Table-9: comparing most common clinical risk factor (Fast breathing) with three groups.

Fast Breathing	No Sepsis	Probable Sepsis	Proven Sepsis
Yes	07	09	04
No	45	25	10
Total	52	34	14

p =0.2320, chi-square not significant

The aetiological pathogens were gram positive bacteria (64.3%) (The gram positive isolate was coagulase negative Staphylococci aureus) and the gram negative bacteria (35.7%) were Escherichia coli, Klebsiella and Acinetobacter isolated. This study suggests that there is no significant difference (p-value 1.000 with fisher exact test) in the aetiology (gram positive and gram negative organisms) of early onset neonatal sepsis.[19][20] (Table-10)

Table-10: ORGANISMS FOR SEPSIS:

Organisms	No.	%
Gram Positive	09	64.3
Gram Negative	05	35.7
Total	14	100

p =1.000, Fisher exact test

The newborns were followed up to the third day of life. Overall, 94% were alive and 2% died (one of whom had probable sepsis and other had proven sepsis). 4% were lost to follow up due to DAMA. (Table11).

TABLE11: Outcome of the newborns at risk of sepsis.

Outcome	No Sepsis No. (%)=52	Probable Sepsis No. (%)=34	Proven Sepsis No.(%)=14
Died	0	1(2.9%)	1(7.1%)
Alive	49(94%)	32(94.1%)	13(92.9%)
DAMA	3 (6%)	1 (2.9%)	0

DISCUSSION

There is a concern about increasing incidence of septicaemia in healthy neonates and it is one of the most common causes for neonatal mortality. The need for early detection of sepsis in the newborns from the hospital is therefore important. Therefore knowledge of the infants at risk for developing sepsis is utmost important. In this present study, we assessed the ability of maternal risk factors and clinical risk factors for early detection of early onset sepsis in newborns[9].

The study revealed that the term newborns admitted to the post natal ward, among them 17.7% were at risk of sepsis and of whom 14% had proven sepsis and 34% had probable sepsis. These findings reveal the need to screen all newborns for sepsis during routine clinical practice. A study done in 2009-2010 at the Muhimbili National Hospital in Dar es Salaam assessing the prevalence of sepsis, among other things, in 330 babies, both term (77%) and preterm (23%), mean age of three days, reported a proven sepsis rate of 22.4% [20]. This higher rate could be explained by the addition of some preterms in the study population who suppose to have a greater risk of having sepsis.

Not taking BF well and fast breathing were the most common clinical features found in this study which were associated with proven sepsis. Kumar similarly found feed intolerance as the most common clinical finding in those found to have sepsis, in addition to lethargy and irritability [21]However, this is in contrast to the Muhimbili study whose participants with fever and hypothermia were noted to have higher frequency of sepsis [20]. This difference could be due to the variation in the population or missed opportunities in the wards of identifying fever/hypothermia (at night, primi-parous women who may not be clear on what fever is). Patient education about newborn health should therefore be re-emphasized in our day to day patient management. Of note is that this study was limited to only three day follow up of the newborns. A longer follow period of the babies and face to face interviews with the mother may have revealed more clinical features associated with proven sepsis. In addition, newborns in the proven and probable sepsis groups were started on antibiotics empirically and this may have altered identified clinical features of sepsis.

PROM was the most common maternal risk factor found in those with proven sepsis in this study. The study shows there is significant association between PROM (maternal risk factor for sepsis) and early onset neonatal sepsis (p 000.4, chi-square).PROM present in 2 cases of proven sepsis (14%) and 11 cases of probable sepsis (78.58%) out of total 14 cases of proven and 34 cases of probable sepsis respectively. Similar observations were also reported by other workers. However, this was not unique to the proven sepsis group as it was present in the probable and no sepsis groups. This is in contrast to a multi-center study done by Puopolo et al that estimated the probability of neonatal early onset infection based on maternal risk factors. Post-term delivery, maternal fever, and PROM were strong individual predictors of infection[22] Notably, the greatest percentage of post-term delivery was in the proven sepsis group.

This study revealed the most common aetiological pathogens were gram positive bacteria (64.3%) (The gram positive isolate was coagulase negative Staphylococci aureus) followed by the gram negative bacteria (35.7%) were Escherichia coli, Klebsiella and Acinetobacter isolated. Our findings differ from other studies which show Escherichia coli and Group B streptococci as the commonest cause of early onset neonatal sepsis worldwide [23][24][25].Kumar et al found CONS responsible for 4.5% of the proven infections in the

newborn unit of KNH though the majority was by Enterobacter agglomerans. The 2009-2010 Muhimbili study revealed Staphylococcus aureus as the commonest isolate, though, predominantly from pus swabs [26],[27]. Similarly, a ten year review study (2000-2009) done at Aga Khan University Hospital in one hundred and thirty two neonates revealed gram-positive organisms were the predominant cause of both early and late onset sepsis; their common isolates were staphylococcus epidermidis (34%) and staphylococcus aureus (27%).There were no isolates of group B streptococcus [28][29]. Almost 50% of the newborns were doing well by day 3. Unfortunately some were lost to follow up after discharge. Notably, all the 2% who died were from the probable sepsis group.

From the rising trend of sepsis rates from previous studies and findings from this study, keener clinical practice by clinicians is necessary for early diagnosis of sepsis.

SUMMERY AND CONCLUSION

- The study revealed proportion of apparently healthy term newborns at risk of early onset sepsis was 17.7%. Out of 100 newborns included, incidence of proven sepsis was 14% and probable sepsis was 34%. Most common aetiological organism found in the study was coagulase negative staphylococcus aureus.
- The study identifies PROM (Maternal) and fast breathing (clinical) as strong risk factors for development of early onset neonatal sepsis. In the presence of these factors, the neonate should be screened and observed for sepsis and considered for early institution of antibiotics.
- Sex, mode of delivery and Birth weight is not associated with early onset neonatal sepsis in full term newborn.
- There is a significant number of well appearing term newborns with sepsis in the post natal ward and as such require routine screening prior to discharge.

RECOMMENDATIONS

- Regular screening for sepsis of all newborns admitted to the post natal ward by the paediatricians including assessment of maternal risk factors.
- A follow up study is necessary to further evaluate the group with probable sepsis who formed the majority in the postnatal wards.

What is already known?

PROM is the most common maternal risk factor associated with early onset neonatal sepsis in the newborn.

What does my study add?

My study supports the above findings.

Fast breathing is the most common clinical feature found with early onset sepsis in the study

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