Predictive Values of Risk Factors in Neonatal Sepsis

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Summary:

Neonatal sepsis is one of the most important causes of mortality and morbidity especially in developing countries. Management of such cases is difficult, costly and need expert centers in many cases. Therefore, identification of the risk factors and their predictive values may help optimizing its management. With the above idea this case-control study was done to see the effects of maternal and neonatal risk factors and to find their predictive values in the development of neonatal sepsis. Fifty cases and fifty suitably matched controls were enrolled in the study and different maternal, natal and newborn factors were compared. Many risk factors were found to have influence in the development of neonatal sepsis. Among them the maternal intrapartum fever, foul smelling liquor, young mother (< 20 yrs), poor income group, prolonged labor, unclean vaginal examination (UVE) and primi mother were much associated with the occurrence of sepsis. Also the neonatal factors, like prematurity, resuscitation at birth and low APGAR score carried the significant risk of developing sepsis. But when relative influence of these risk factors were analyzed over neonatal sepsis in detecting their predictive values, it was found that irregular antenatal check up, prematurity, resuscitation at birth, and maternal intrapartum fever had influenced most in the development of neonatal sepsis in chronological order.

Key words: Neonatal sepsis, maternal risk factors, neonatal risk factors

(J Bangladesh Coll Phys Surg 2011; 29: 187-195)

Introduction:

Neonatal sepsis or septicemia is the term that have been used to describe the systemic response to infection in newborn infants during the first 28 days of life. There are 2.8 million of neonatal deaths occur annually during the first year of life in the world[1]. Mortality rates vary, ranging from 12-30% in developing countries. [2,3] to 8.3 to 12.5 per 1000 live births in developed countries.[4,5] While infant mortality has been declining all over the world, changes in neonatal mortality rate has been much slower in Bangladesh.[1] The over all incidence of neonatal sepsis varies between 1 and 4 cases per 1000 live births[6] Infection accounts for 70 to 72.7% of neonatal death.[7,8]

The attack rate of neonatal sepsis varies geographically depending on the prevalence of organism in the community. The infection may be mild, moderate or severe and acute, sub acute or chronic or it may be asymptomatic. The absence of clinical signs at the time of the initial physical examination does not preclude infection.

Early manifestations of infection may be subtle and nonspecific.[9] Moreover accurate diagnosis of neonatal sepsis is difficult because there is no definitive diagnostic test; even blood cultures have an unacceptably low sensitivity.

Cause, risk factors and consequences / sequel of sepsis have not been adequately researched and clinical guide lines for detection of sepsis by community health workers have not been evaluated in Bangladesh. Even we are not enriched with all required laboratory facilities and sometimes we cannot bear the cost of all laboratory expenses. Moreover nothing is known about microorganism patterns and their antibiotic sensitivities in community based neonatal sepsis of our country. So, it is important for physicians at periphery to recognize the early features of neonatal sepsis, because late detection and referral, delayed antibiotic therapy and

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Received: 18 June 2008 **Accepted:** 20 September 2011

supportive care may lead to extensive unrecoverable sepsis. Risk approach based identification can help all to detect and treat neonatal sepsis and curb mortality. Therefore detecting all maternal and neonatal risk factors causing neonatal sepsis and relating them with clinical and available laboratory findings neonates can be discharged early from the hospital, stopping the antibiotics, thereby reducing the cost of treatment and anxiety of the family.

Materials and methods:

A total number of 50 cases were enrolled as case having established sepsis and 50 cases were matched as control having no established sepsis. This study was done in Child Health Department of Chittagong Medical College Hospital from 1st October 2002 to 31st March 2003.

Neonates who developed symptomatic sepsis within 28 days of birth irrespective of gestational age and birth weight were included in this study. Those symptomatic neonates who either had positive blood culture or had total WBC count<5000/cmm, IT Ratio e"0.2, CRP e"10mg/dl were regarded as case.[5] Those symptomatic neonates whose blood culture were found negative or those having less than 3 negative screening test were included as control. Cases with neonatal tetanus, TORCH infection, and babies born to hepatitis B virus infected mothers, congenital malformation, perinatal asphyxia; RDS and babies who received antibiotics prior to admission were excluded from this study.

On admission clinical histories were obtained including perinatal history. Through physical examination of the infants were done. All the relevant information was recorded in a pre designed questionnaire and data was compiled at the end of the study.

Results:

Risk factors influencing Neonatal Sepsis have been plotted as Neonatal and Maternal Risk Factors in Table: 1 and Table: 2 respectively. Each risk factor was individually analyzed against sepsis (using 2x2 contingency table I & II), to show their level of significance in producing sepsis and were plotted in Table III and Table IV respectively. Table V show frequency of occurrence of individual risk factor. Table VI and also the Chart: 1.1 and Chart: 1.2 shows the regression slope and also the relative influence of risk factors over neonatal sepsis highlighting predictive values.

Among 50 cases under study 39 were male and 11 were female and among control 31 were male and 19 were female. The frequency rate of sepsis is more in male (55.7%) than female. The difference is, however, statistically not significant (P >0.0810). Male showed 2.173 times greater risk of developing sepsis than female.

Table-I

Distribution of Neonatal Risk Factors

Character		Casen (%)	Controln (%)
Sex of the Baby	Male	39 (55.7)	31(44.3)
	Female	11 (36.7)	19(63.3)
Birth weight (grams)	<2500	24(49)	25(51)
	>2500	26(51)	25(49)
Gestational age in weeks	<37 wks	16(72.7)	6(27.3)
	>37wks	34(43.6)	44(56.4)
APGAR score<5 at 1min	Yes	13(68.4)	6(31.6)
	No	37(45.7)	44(54.3)
APGAR score<7 at 5min	Yes	14(70)	6(30)
	No	36(45)	44(55)
Use of AMBU bag/mouth to mouth breathing	Yes	21(65.6)	11(34.4)
	No	29(42.6)	39(57.4)

Table-II

Distributions of Maternal Risk Factors

Character		Casen (%)	Controln (%)
Age of Mother in years	<20 yrs	30(66.7)	15(33.3)
	>20 yrs	20(36.4)	35(63.6)
Parity	Primipara	40(57.1)	30(42.9)
	Multipara	10(33.3)	20(66.7)
Income group	Poor	25(39.1)	39(60.9)
	Average	25(69.4)	11(30.6)
Antenatal check up	Irregular	36(45)	44(55)
	Regular	14(70)	6(30)
Duration of labor in hours	>24 hrs	37(60.7)	24(39.3)
	< 24 hrs	13(33.3)	26(66.7)
Duration of Rupture of membrane in hours	>24 hrs	30(58.8)	21(41.2)
	< 24 hrs	20(40.8)	29(59.2)
No of Unclean Vaginal examination	>3 times	30(61.2)	19(38.8)
	< 3 times	20(39.2)	31(60.8)
Intrapartum fever	Yes	22(78.6)	6(21.4)
	No	28(38.9)	44(61.1)
Foul smelling liquor	Yes	19(79.2)	5(20.8)
	No	31(40.8)	45(59.2)

Table-III

Analysis of Neonatal Risk Factors influencing neonatal sepsis by level of significance

Character	X^2	df	P	
1	Sex of the Baby	3.048	1	0.081
2	Birth weight (grams)	0.040	1	0.841
3	Gestational age in weeks	5.828	1	0.016
4	APGAR score < 5 at 1 min	3.184	1	0.074
5	APGAR score <7 at 5 min	4.000	1	0.046
6	Use of AMBU /mouth to mouth breathing	4.596	1	0.032

Table-IV

Analysis of Maternal Risk Factors influencing neonatal sepsis by level of significance

Character	X^2	df	P	
1	Age of Mother in years	9.091	1	0.003
2	Parity	4.762	1	0.029
3	Income group	8.507	1	0.004
4	Antenatal check up	4.000	1	0.046
5	Duration of labor in hours	7.104	1	0.008
6	Duration of Rupture of membrane in hours	3.241	1	0.072
7	No of Unclean Vaginal examination	4.842	1	0.028
8	Intrapartum fever	12.698	1	0.000
9	Foul smelling liquor	10.747	1	0.001

Table-V

Individual risk factor for neonatal sepsis by frequency of occurrence

Risk factors		Frequency of occurrence
1	Foul smelling liquor:	(79.2%)
2	Intrapartum fever:	(78.6%)
3	Gestational age <37wks:	(72.7%)
4	APGAR<7at5min:	(70%)
5	APGAR<5at1min:	(68.4%)
6	Age of mother <20yrs:	(66.7%)
7	Resuscitation at birth:	(65.6%)
8	UVE>3:	(61.2%)
9	Duration of labor >24 hrs:	(60.7%)
10	PROM>24 hrs:	(58.8%)
11	Primi Para	(57.1%)
12	Male sex:	(55.7%)
13	Birth weigh<2500gms	49%
14	Irregular ANC:	45%
15	Poor socioeconomic status	39.1%

Table-VI

Relative influence of risk factors over Neonatal sepsis (Multiple regressions)

Risk Factors	B	Significance
Sex (Male)	0.991	0.138
Birth weight (<2500 gms)	-0.861	0.194
Gestational age (<37 wks)	1.772	0.027
APGAR score <5 at 1 min (yes)	0.125	0.906
APGAR score <7 at 5 min (yes)	-0.217	0.843
Resuscitation at birth (yes)	1.578	0.071
Age of mother in years (<20 yrs)	0.995	0.137
Parity (Primi para)	0.498	0.488
Income group (poor)	-0.651	0.275
Antenatal checkup (irregular)	-1.885	0.017
Duration of labour (>24 hrs)	0.826	0.187
Duration of rupture membrane (>24 hrs)	2.651	0.969
Unclean vaginal examination (>3 times)	0.116	0.857
Intrapartum fever (yes)	1.638	0.089
Foul smelling liquor (yes)	0.120	0.904

(B= Beta, which stands for regression slope)

Effects of birth weight on neonatal sepsis showed that 24 neonate among cases and 25 among control had LBW. But statistically LBW showed no significance (P >0.841) in the development of neonatal sepsis.

Sixteen cases and six controls had gestational age < 37 weeks. 72.7 % of these babies developed sepsis, which showed high statistical significance (P<0.016) in the development of neonatal sepsis. They had 3.451 times greater risk of developing sepsis than those having gestational age of >37 weeks. Total 19 babies had an APGAR score of <5 at 1 min of them 13(68.4%) developed sepsis. Though the difference is not statistically significant (P >0.074), they had 2.577 times greater chance of developing sepsis than babies with normal APGAR score. On the other hand 20 babies had an APGAR score <7 at 5 min, of them 14(70%) developed sepsis which is found to be statistically significant (P<0.046) & the development chance of sepsis was 2.852 times greater in this group.

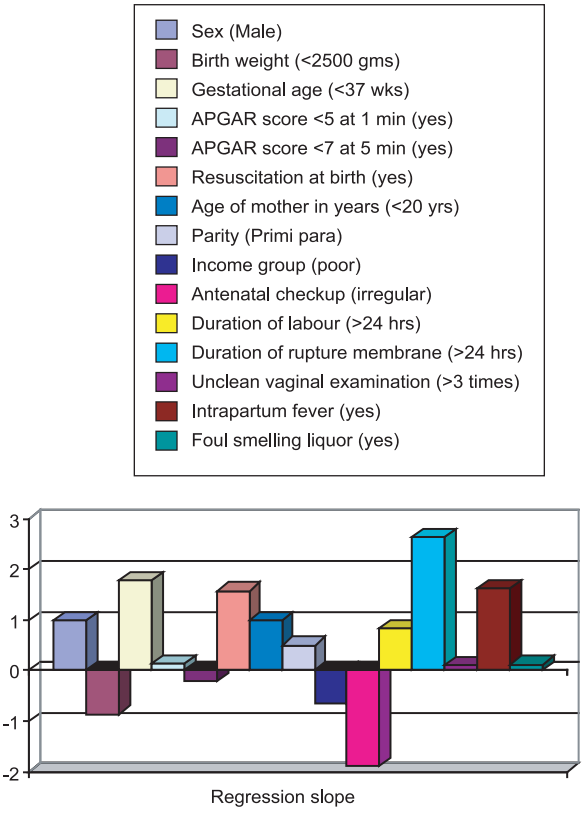

Fig.-1: *Relative influences of risk factors over Neonatal sepsis (Multiple regressions) showing the regression slope.*

Among 50 cases and 50 control 32 patients required resuscitation at birth. 21 (65.6%) of them developed sepsis and carried 2.567 times greater chance to develop sepsis than those who did not require resuscitation procedure. The finding was statistically significant (P<0.032). Out of 50 cases and 50 controls 45 mothers were found to be <20 years of age. Among them 30(66.7%) babies of these mothers had sepsis which is 3.5 times greater than babies born to mother having e" 20 yrs of age. It was also found to be statistically significant (P<0.003). Among 70 babies of total Primi mothers 40(57.1%) had sepsis and carried 2.667 times greater chance of sepsis than babies born to Multipara. It was found to be significant (P<0.029).

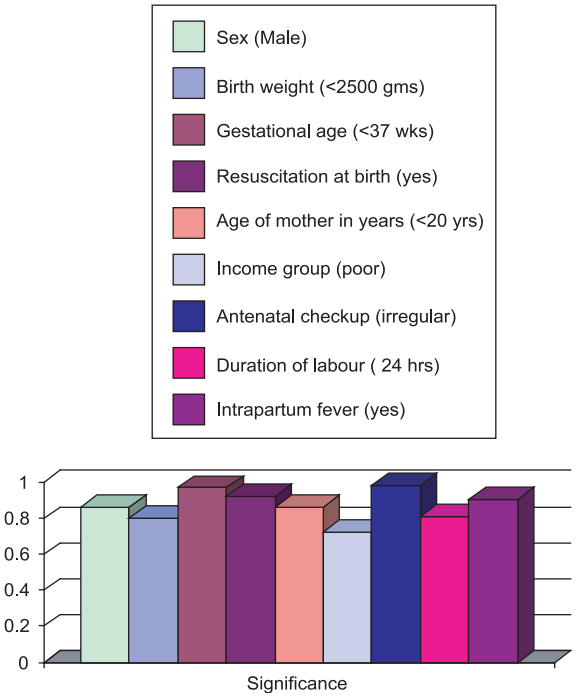

Fig.-2: *Relative influences of risk factors over Neonatal sepsis (Multiple regressions) showing their significance (Predictive value)*

Babies born to poor family was 64, of them 25(39.1%) developed sepsis, so, this poor income group was found significantly (P<0.004) associated with the occurrence of neonatal sepsis. On the other hand 80 mothers had irregular antenatal checkup, 36(45%) of their babies later developed statistically significant (P<0.046) sepsis.

Mothers of 37 infants among cases had prolonged labor of e" 24 hrs as 24 infants among controls. Thus 60.7% of exposed babies ultimately suffered from sepsis with 3.083 time's greater risks than those born after normal duration of labor. This had highly significant (P<0.008) association with the sepsis. PROM >24 hrs was found among 51 mothers, of which 30(58.8%) infants born to them developed sepsis later on. Though PROM carried 2.071 times higher risk of developing sepsis, it was not found statistically significant (P <0.072). History of unclean vaginal examination (UVE) e"3 times was found in 49 mothers. Their 30(61.2%) newborn later had sepsis with 2.447 times greater risk than those born to mothers having <3 UVE. The association of sepsis with UVE was significant (P<0.028).

The number of mothers who had intrapartum fever of >100.7^{0}F was 28. Babies born to them later developed sepsis, the number of which was 22(78.6%) and showed 5.762 times greater risks of sepsis than those born to mother without intrapartum fever. It was found highly significant(P<0.000). Twenty-four babies born to mother had the history of foul liquor. Out of them 19(79.2%) developed sepsis. It carried 5.516 times greater chance of developing sepsis than babies born to mothers without foul liquor.

Multiple regressions for sepsis were done at the end. There was an overall significant relation of the risk factor for sepsis (F=46.608, P=0.000). The following factors were independently related to sepsis:

Irregular antenatal checkup of mother.

Gestational age <37weeks (Yes).

Resuscitation at birth (Yes).

Maternal intrapartum fever (Yes).

Discussion:

Neonatal septicemia is still a serious condition with high mortality. [2,10] Different risk factors are known to have profound influence on the development of neonatal sepsis. Our study also reflected the same cumulative influence of those risk factors, commonly known as neonatal risk factors and maternal risk factors, in the development of neonatal sepsis. Though, all the risk factors did not show the equal and similar influences as in other previous studies.

Among the neonatal risk factors (T-1 & T-3), Prematurity, APGAR score<7 at 5 min and neonatal resuscitations were significantly found to be associated with neonatal sepsis. But other neonatal risk factors, though found insignificant, are also discussed for comparison with other studies. Sex incidence of neonatal sepsis shows a male preponderance.[11,12,13]

Though our study shows higher frequency rate of sepsis in male(39:11), but it failed to show statistical significance(P<0.081), which is also a similar findings with Raghavan,[14] St. Geme [15] and Buetow et al. [16] Though some studies show nearly equal rate of infection.[17] Birth weight is a well recognized risk factor for sepsis.[18,19, 20, 21,22] As gestational age is not always assessed accurately, and birth weight is taken as a better variable. Though association of low birth weight(LBW) with neonatal sepsis was significantly found in other studies,[13,14,17,21], unfortunately our study showed insignificant result(P<0.841). Many of the LBW neonates included in the study was near to normal birth weight, as well as smaller sample size, might influence our result. Prematurity is a widely accepted risk factor for neonatal sepsis.[22] In our study prematurity (gestational age < 37 weeks) had a significant association (P<0.016) with the development of sepsis, as in other observation [14,17,21,23,24,25] that justified the inverse relationship of sepsis and gestational age. [18, 19]

APGAR score 0-6 [24]or <6 [26] in 1 min. or at 5 min [15,18] is found to be predisposed to neonatal sepsis. In the present study APGAR score <7 at 5 min had significant (P<0.046) influence in the development of sepsis than score <5 at 1 min (P<0.074), like other similar and significant previous observations [14,17,18] Asphyxia causes an immunological insult[27]and resuscitation procedures following birth asphyxia tend to explore them to pathogenic microbes.[14,24] Resuscitation procedures at birth pose greater risk of neonatal sepsis. Many life- supporting procedures such as suctioning and endo-tracheal intubations can lead to transient and persistent bacteremia.[24] Vascular channels[19,28] umbilical catheterization and mechanical ventilatory support, contaminated suction catheters, mouth to mouth breathing predisposed the infants to higher risks of sepsis.[14,18,20,24,29,30] In our study effects of resuscitation was found statistically significant (P<0.032) in the development of sepsis, which is compliant with many previous studies.[14,16]Among the maternal risk factors

(T-2 and T-4) our study shows that the attack rates of sepsis increased significantly with neonates born to mothers <20yrs of age (P<0.003), in Primi (P<0.029), in poor income group family (P<0.004) and those mothers took irregular antenatal checkup (P<0.046). But no previous study could be found to support these factors. Prolonged labor e" 24 hrs is a recognized risk factor for neonatal sepsis. [14,24] We also observed significant (P<0.008) association between this factor and sepsis. Our result compiles with previous researchers. Soman et al [31] and Raghavan et al [14] found significantly higher incidence of neonatal sepsis following prolonged labor but Bhakoo et al [24] and Sing et al [32] described it as a dependent factor, that it needs other factors in association to cause sepsis. Prolonged labor predisposes mothers to frequent handling and also causes fetal compromise and asphyxia. Early rupture invites ascending infection &infected amniotic fluid frequently leads to neonatal sepsis. Prolonged rupture of membrane (PROM) e" 24 hrs has received the maximum attention of investigators, and is an important risk factor,particularly in early onset neonatal sepsis (EONS).[14, 17,25,33,34] It increases the attack rate by more than 10 folds. We found PROM in 58.8% cases though it did not reflect statistical significance (P<0.072).

Unclean vaginal examination (UVE) is a potential source of bacterial contamination.[35] Multiple UVE (>3) increases the risk of neonatal sepsis.[34, 36]

Our findings (UVE >3) was consistent with other studies [24,37] & it was found to be highly significant (P<0.028).Attack rate of neonatal sepsis increases with rise of maternal intrapartum temperature; a 10 fold is documented when peak temperature rises to 38^0 C or more. Our study also found highly significant (P<0.000) relation of this factor with sepsis. This is consistent with observation of other workers. Knudsen et al [37] found 20% incidence of sepsis & Bhakoo et al found 12.5% incidence in term and 55.5% in pre term babies born to febrile mothers. It has an independent association with neonatal sepsis. [24]

Intrapartum fever is indicative of maternal infections that are frequently transmitted to the baby in utero or during passage through birth canal. [24] Presence of foul smelling liquor has been considered to be indicative of amnionitis by various investigators, [14,38,39] and found to be associated with 10% incidence of sepsis.[40] Our observation was highly significant(P<02.001) and comparable to findings of other researchers. Singh et al [32] described it to be an independent factor. Actually foul smelling liquor is a reliable feature of chorioamnionitis, emitting the smell due to breakdown products of bacterial metabolism, and the infection is easily transmitted to the fetus in utero.[35]

The aim of study was not only to detect sepsis, but also to find out the predictive values of those factors. We have analyzed those factors individually and also found the relative influence of them on neonatal sepsis. Individual analysis of risk factors showed that many factors like prematurity, APGAR score<7 at 5 min and neonatal resuscitations among the neonatal factors (T-1& 3) and all the maternal risk factors (T-2 &4) were significantly found to be associated and influenced the development of sepsis. But when relative influence of those factors was searched by multiple regressions (Table VI & Chart 1.1 & 1.2) to see the predictive values of risk factors, it was found that irregular antenatal checkup of mother (P<0.017) ,prematurity (P<0.027, T-6),resuscitative procedure(P<0.071) & maternalthe risk factors associated with neonatal intrapartum fever (P<0.089); the association of which was near statistical significance. In order to treat all infants with sepsis rapidly and to minimize therapy for those without infection, risk factor analysis by history is important [41,42]. We may correlating them with clinical and laboratory data shall help to recommend intervention strategies designed to reduce incidence and mortality of neonatal sepsis by prompt recognition and effective management of high-risk infants at birth.

Conclusion:

From this study it can be concluded that, maternal intrapartum fever, foul smelling liquor, young mother (< 20 yrs), poor income group, prolonged labor, UVE & Primi mother can be designated as maternal risk factors for neonatal sepsis. Among neonatal factors, prematurity, resuscitation at birth & low APGAR score carried the significant risk of developing sepsis. Relative influence of these risk factors when analyzed over neonatal sepsis in detecting their predictive values, it was found that maternal irregular Antenatal check up, prematurity, resuscitation at birth, and maternal intrapartum fever are the main risk factors in the development of neonatal sepsis in our set up.

Appraisal of these perinatal risk factors for neonatal sepsis could be of great value in identifying the areas requiring attention to improve perinatal care in order to prevent neonatal sepsis in our country. However, small-scale study does not reflect the whole population and definite conclusion is yet to be drawn. Based on the result of our study, a cohort study can be undertaken to obtain additional evidence to refute or support the existence of association between the risk factors and neonatal sepsis.

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