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## Research Report

### Risk Factors of Neonatal Sepsis: A Preliminary Study in Dr. Soetomo Hospital

Martono Tri Utomo

Department of Child Health Medical School, Airlangga University/Dr. Soetomo Hospital

#### ABSTRACT

The risk factors of developing neonatal sepsis could be caused by maternal and neonatal risk factors. Objective to determine the characteristics and risk factors for neonatal sepsis. Study design was case control study. The data of neonates were taken from the medical record. Neonates who were admitted in neonatal care unit of Dr. Soetomo hospital were included at January 2010 to February 2010, and divided into 2 groups, one group was sepsis cases and other group was non sepsis cases as a control. The risk factors that associated with sepsis were studied. Chi square and logistic regression analysis were used to analyze the data. 97 patients were included and 31 were sepsis cases and non sepsis case were 66. The risk factors that significantly cause sepsis are low birth weight ( $p=0.001$  OR 2.75, 95% CI 1.454–5.200), prematurity ( $p=0.000$ , OR 4.073, 95% CI 2.180–7.609), meconial amniotic fluid ( $p=0.029$ , OR 2.535, 95% CI 1.225–5.245) and C-section ( $p=0.032$ , OR 1.895, 95% CI 1.087–3.303). The significant risk factors of the neonatal sepsis are low birth weight, prematurity, meconial amniotic fluid, and caesarian section

**Key words:** risk factors, neonatal sepsis

#### INTRODUCTION

Newborn infection that is called neonatal sepsis can be very severe disease and lead to the high morbidity and mortality. Neonatal sepsis is clinical syndrome of systemic illness accompanied by bacteremia occurring in the first month of life.<sup>1,2</sup>

The incidence of neonatal sepsis is approximately 7.1 to 38 cases per 1000 live births in Asia, 3.5 to 8.9 per 1000 live birth in South America and the Carribean.<sup>2,3</sup> The incidence rate of neonatal infection in several referral hospitals in Indonesia is approximately 8.76–30.29%, with the mortality rate is 11.56–49.9%.<sup>4</sup> Cipto Mangunkusumo hospital reported at January–September 2005, the incidence of sepsis was 13,68% with the mortality rate 14,18%.<sup>5</sup> Dr Soetomo hospital reported that 49 from 2416 patients showed bacterial positive blood culture (proven bacteremia sepsis).<sup>6</sup>

The clinical manifestation of neonatal sepsis can be varied from the subtle condition until very severe condition. The clinical manifestation of sepsis are hypo- or hyperthermia, lethargy, irritability, or change in tone, mottling, pallor, petechiae, or jaundice, feeding intolerance, vomiting, diarrhea, or abdominal distention, tachypnea,

respiratory distress, apnea, tachycardia, or hipotension, hypo- or hyperglycemia, metabolic acidosis, focal infection.<sup>1,7</sup> The latest criteria to diagnosis sepsis is if we found 1 of the Fetal Inflammatory Response Syndrome (FIRS), i.e. tachypnea, hypo- or hyperthermia, CRT > 3 seconds, WBC < 4.000 or > 34.000, CRP > 10 mg/dl, IL-6 or IL-8 > 70pg/ml, positive 16SrRNA PCR, plus clinical variables.<sup>5,8</sup>

Some conditions had been identified as the risk factors for developing neonatal sepsis. These conditions are:<sup>5</sup>

1. Maternal risk factors are premature rupture of membranes (PROM) especially more than 18 hours, infection and fever of the mother during labor, foul smell of amniotic fluid, turbidity and meconial amniotic fluid, and multiple gestations.
2. Neonatal risk factors are prematurity, low birth weight, asphyxia, resuscitation during delivery, invasive procedure, congenital anomaly, parenteral nutrition, long hospital stay in neonatal intensive care unit.
3. Other risk factors: more frequent found in male than female, in black neonate, and in low social economy neonate.

Attack rate of neonatal sepsis increase significantly in low birth weight infants and the presence of maternal (obstetric)

risk factors especially with sign of chorioamnionitis such as prolonged rupture of membranes, maternal intrapartum fever ( $>37.5^{\circ}\text{C}$ ). The other potential factors are immunity risk factors that associate with male sex, congenital immune defect, congenital anomalies, omphalitis, and twinning; prematurity is a risk factor for both early onset and late onset sepsis.<sup>2,4,5,9,10</sup> In the Collaborative Perinatal Research Study sponsored by the National Institutes of Health in Boston City Hospital at Boston, low birth weight infants acquired sepsis three times more frequent than did term infant who weighed more than 2500 gram.<sup>2</sup>

The purpose of this study is to determine the risk factors for developing neonatal sepsis that associate with maternal or neonatal condition of the patients who were delivered or referred in the neonatal intensive care unit Dr. Soetomo hospital.

## METHOD

Study design was case control study. The data were collected from the medical record of neonates who were admitted in neonatal care unit of Dr. Soetomo hospital between January 2010 to February 2010. Technical sampling was purposive sampling. We reviewed data of all neonates who had been diagnosed as sepsis and collected the data of sample characteristic such as sex, gestational age, birth weight, mode of delivery and outcome. The risk factors that associate with sepsis such as sex, gestational age, birth weight, premature rupture of the membrane, turbid and meconal amniotic fluid, asphyxia, and congenital anomaly were studied. The sample was grouped in the sepsis and non sepsis. We compare the risk factors between this two group.

## DEFINITIONS

- Prematurity are liveborn infants delivered before 37 weeks of pregnancy (based on the Ballard score or from first day of the last menstrual period)
- Low birth weight (LBW) neonate is neonate whose birth weight is less than 2,500 gram
- Premature rupture of membrane (PROM) is defined as the time from membrane rupture to onset of delivery was more than 18 hour.
- Meconal amniotic fluid was considered if the amniotic fluid was green in color or mixed with meconal, or appears meconal stained in the baby.
- Congenital anomaly is defined as any abnormality of anatomy and morphology that found during physical examination.
- Asphyxia is defined as Apgar score less than 3 in the five minutes from delivery
- Diagnosis of sepsis neonatorum based on clinical findings and supported by laboratory data (blood cell

examination, value of C reactive protein and microbial blood culture).

- FIRS (Fetal Inflammatory Response Syndrome) defined as 1 of the tachypnea, hypo- or hyperthermia, CRT  $> 3$  seconds, WBC  $< 4.000$  or  $> 34.000$ , CRP  $> 10$  mg/dl, IL-6 or IL-8  $> 70$ pg/ml, positive 16SrRNA PCR is found.

## Statistical analysis

Data are presented in distribution tabulation and data analysis was performed with a computer assisted statistical package (SPSS ver. 12.0). Chi square and logistic regression analysis were used to analyze the data. Risk factors were calculated with odds ratio and 95% Confidence Interval, p values less than 0.05 was considered significant.

## RESULTS

The collected data from 1 January 2010 until 28 February 2010 have been reviewed from all of medical record of the neonates that admitted in NICU ED Dr Soetomo hospital: 97 medical records sample of these neonates were studied, diagnosis sepsis were 31 patients, and no sepsis 66 patients.

The distribution of characteristic samples between sepsis and non sepsis cases i.e., the referral cases is significantly found in sepsis group; the birth weight in sepsis cases were also significantly lower than non sepsis cases, but there were no difference in the mode of delivery between two groups. Mortality rate in the sepsis cases were high (67%) (table 1).

There were no significant difference among sepsis that associated with PROM, turbid amniotic fluid, congenital malformation and asphyxia ( $p>0.05$ ).

Potential risk factors of infection that significantly cause sepsis are low birth weight (LBW), prematurity, meconal amniotic fluid, and caesarian section ( $p=0.001$ ,  $p=0.000$ ,  $p=0.029$ , and  $p=0.032$  respectively). The risk factors which showed significant differences were analyzed by logistic regression analysis showed there were statistically significant association between the incidence of sepsis with prematurity and meconal amniotic fluid ( $p=0.000$ ;  $p=0.001$  respectively).

## DISCUSSION

Neonatal sepsis is still the major problem in developing country that can cause the high morbidity and mortality.<sup>11</sup> The diagnosis of sepsis neonatorum is still difficult, some effort has been developed by using the criteria of FIRS to diagnosis sepsis clinically.<sup>5</sup> Because of the morbidity and mortality of sepsis is high, and the difficult diagnosis, some effort to detect the risk factors for infection has been studied.<sup>11,12,13</sup>

**Table 1.** Characteristics of neonates that admitted in Dr Soetomo hospital January–February 2010

Characteristics of samples	Sepsis (+) n = 31	Sepsis (-) n = 66	p value
Referral case	9	3	0.01*
Sex: Male	21	39	0.413
Female	10	27	
Birth weight (g)	2,091.9	2,720.4	0.00*
Gestational age: Premature	21	12	0.000*
Aterm	10	54	
Mode of delivery:			
- spontaneous	14	14	0,18
- breech delivery	3	3	
- manual aid	1	3	
- vacuum extraction	1	3	
- caesarian section	12	12	
Outcome:			
- live	7	41	0.00*
- death	21	11	
- discharge on request	3	14	

**Table 2.** Risk factors of infection in neonates that admitted in Dr Soetomo hospital January–February 2010

Risk factors of infection	p	OR	95% CI
LBW	0.001*	2.75	1.454 – 5.200
Prematurity	0.000*	4.073	2.180–7.609
ProM > 18 hours	0.274	1.786	0.694–4.596
Turbid amniotic fluid	0,805	0,854	0.237–3.077
Meconal amniotic fluid	0.029*	2.535	1.225–5.245
Congenital malformation	0.983	0.981	0.169–5.707
Caesarian section	0.032*	1.895	1.087–3.303
Asphyxia	0.159	1.688	0.874–3.258

In this study, the determined diagnosis of sepsis based on the FIRS criteria that have been proposed by Haque,<sup>8</sup> beside the other examination such as bacterial blood culture and blood cell laboratory examination. The blood culture sometimes have the problem i.e. the antibiotics already given before the blood culture was taken, the amount of blood that was taken, and disinfectant procedure before collecting the blood. This condition can influence the result of blood culture.<sup>14,15</sup>

Risk factors that can lead to sepsis have been identified i.e.: maternal risk factors are premature rupture of membranes, infection and fever of the mother during labor, foul smell of amniotic fluid, turbidity and meconal amniotic fluid, and multiple gestations; neonatal risk factors are prematurity, low birth weight, asphyxia, resuscitation during delivery, invasive procedure, congenital anomaly, parenteral nutrition, long hospital stay in neonatal intensive care unit. Other risk factors were more frequently found in male than female, in black neonate, and in low social economy neonate.<sup>5,11,13</sup> The other study add the risk factors such as mode of delivery especially caesarian section.<sup>12</sup>

The risk factors that had been analyzed in this study were as follow: LBW, premature, PROM > 18 hours, turbid amniotic fluid, meconal amniotic fluid, congenital malformation, caesarian section and asphyxia. But the

significant risk factors were LBW, premature delivery, meconal amniotic fluid and caesarian section.

In this study the LBW have the significant risk for the sepsis condition. The LBW babies have the risk to become sepsis 2.75 higher than non LBW babies. This result is similar to the other study by Shah 200.<sup>11</sup> Preterm delivery is also contributed to sepsis. In this study the premature delivery had risk of 4 times higher than fullterm babies. The results this study was similar with the other study by Shah and Ladfors.<sup>11,12</sup> The relatively immunodeficiency condition in the premature and LBW infant predisposed to the sepsis condition. These premature and LBW infants were also got some invasive procedure and monitoring leading to nosocomial infections.<sup>11</sup>

Premature rupture of the membrane and prolonged leakage of the amniotic fluid can increase the risk of infection because of ascending bacterial from the urinary tract.<sup>9,11,12</sup> In this study we didn't find the correlation of premature rupture of the membrane and sepsis, some factors may contribute to this finding, such as history taking of the patient such as patient didn't remember when the membrane had been ruptured. This condition is also indicated that post delivery antibiotic that was always given in the PROM neonate as a standard procedure can decrease the risk of neonatal sepsis.<sup>1</sup>

The meconal stained amniotic fluid can be caused by some infection in the uterine, prolonged fetal hypoxia in uterine and other stress condition of fetal in uterine. The choriamnionitis can produce the meconal stained and foul smelling amniotic fluid because of inflammation reaction of the infection.<sup>1,9</sup> In this study we found the significant risk factors of meconal stained amniotic fluid to become sepsis with the risk of 2.5 times higher than non meconal stained amniotic fluid. This finding is similar with the other study.<sup>11,12</sup>

The baby born from caesarian section have a risk 1,89 times higher than non caesarian section to become a sepsis. This finding is similar with the previous study<sup>12</sup> Caesarian section may contribute the changes of normal flora in infant. The caesarian section infant have lower isolation rate of bifidobacteria and a much lower incidence of *Bacteroides* spp.<sup>16</sup> But from the other study showed there was no significant difference in the bowel flora between mode of delivery and feeding method in the seven day postnatally.<sup>17</sup> The normal flora in infants have a role in the immunity system of the infant so the changes in the normal flora normal may lead to risk of sepsis condition. The understanding of the risk factors is important to determine the policy for the high risk babies with the risk factors to sepsis especially on the prevention.

## SUMMARY

The risk factors of sepsis neonatorum in dr. Soetomo hospital at January–February 2010 i.e. Low Birth Weight, prematurity, meconal amniotic fluid and caesarian section.

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