Risk Factor Analysis of Neonatorum Sepsis in NICU Room Naibonat Hospital, Kupang Regency

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ABSTRACT: Neonatal sepsis is one of the causes of newborn death. Risk factors that can affect neonatal sepsis include maternal risk factors, infectious agent factors, infant risk factors and determinant factors. The purpose of this study was to determine and analyze the factors that influence the incidence of neonatal sepsis in the NICU room at the Naibonat Hospital, Kupang Regency. The design of this study used a case control research design (case control) with a retrospective study approach. The populations in this study were all newborns diagnosed with neonatal sepsis at the Naibonat Hospital, Kupang Regency from January to December 2020 totaling 85 cases. The sample size in this study was taken using a total sampling technique, where the entire population was used as a research sample, namely as many as 85 case samples, with a sample size ratio of 1:1 between cases and controls, so the total sample size was 170 samples. The results showed that maternal risk factors that significantly influenced the incidence of neonatal sepsis were premature rupture of membranes (p=0.020), Inpartum Fever (p=0.001), history of urinary tract infection (p=0.003) and length of parturition (p=0.006). For infectious agent factors that influence is bacteria (p = 0.009). For the baby risk factor that has an effect is the APGAR score (p = 0.000). Simultaneously, the most influential determinants on the incidence of neonatal sepsis were APGAR scores, labor duration and labor fever.

Keywords: Maternal Risk Factors, Infectious Agents, Infant Risk and Determinants.

INTRODUCTION

Neonatal sepsis is one of the leading causes of newborn death in the world. The World Health Organization Statistics report found that the infant mortality rate in the world was 31.7 per 1000 live births (KH), including the neonatal mortality rate of 19.2 per 1000 KH. Africa and the Mediterranean are the regions with the highest neonatal mortality rates, namely 28 per 1000 KH and 26.6 per 1000 KH and the neonatal mortality rate in the Asian region is 24.3 per 1000 KH and places Asia in the third highest number of neonatal deaths after Africa and the Mediterranean [1].

The World Health Organization (2015) reports that Indonesia ranks fifth with the highest neonatal mortality rate, which is 13.5 per 1000 KH. This figure is still far behind compared to neighboring countries. The neonatal mortality rate in Brunei Darussalam is 4.3 per 1000 KH, Malaysia 3.9 per 1000 KH and Singapore 1 per 1000 KH. Neonatal mortality is still a public health problem in the world. Between 1990–2013, around 86 million babies were born in the world with

the most deaths occurring within 28 days of life (WHO 2016). Furthermore, in 2015 it was estimated that there were 2.7 million neonatal deaths worldwide and most of them occurred in developing countries (approximately 98%). Of these deaths, 700,000 neonatal deaths occur in the first 24 hours of life and 2 million neonatal deaths occur in the first 7 days of life [1].

Based on Basic Health Research, it was found that sepsis ranks third in the cause of early neonatal death at 12% and the number one cause for late neonatal death (7-28 days) at 20.5%. WHO report (2015), the death rate caused by sepsis and infectious diseases in Indonesia is 1.8 per 1000 KH. The incidence of neonatal sepsis in several hospitals in Indonesia is around 1.5-3.72% with a mortality rate of 37.09-80%. The infant mortality rate in West Sumatra Province according to the 2015 West Sumatra Provincial Health Service report was 9 per 1000 KH and 69.8% occurred at the neonatal age (0-28 days). The report also showed that sepsis accounted for 1.9% of neonatal deaths. The three districts/cities of West Sumatra Province with the highest infant mortality rates include Mentawai at 28

per 1000 KH, Lima Puluh Kota District at 19 per 1000KH and Solok Regency at 16.9 per 1000 KH [2].

The neonatal mortality rate in the Province of East Nusa Tenggara (NTT) is still high, based on the results of the 2012 Indonesian Health Demographic Survey (IDHS), the AKN in NTT Province is 26 per thousand live births. This figure is higher than the national figure of 15 per 1000 KH. Furthermore, the NTT Provincial Health Office reported that there were 796 cases of neonatal death with the cause of death being low birth weight (LBW) of 218 cases, followed by asphyxia neonatorum with 208 cases and sepsis with 25 cases [3]. Attention to efforts to reduce AKN is important because according to the results of the IDHS, neonatal mortality in NTT Province contributes to 58% of infant deaths [4]. The neonatal mortality rate in Kupang Regency in 2018 was 73 cases and in 2019 there were 82 cases, and deaths from neonatal sepsis were 6 cases [5].

The results of the preliminary survey in the medical records section of the Naibonat Hospital in 2018 there were 363 deliveries of which there were 40 newborns diagnosed with neonatal sepsis and in 2019 out of 360 deliveries there were 70 babies diagnosed with neonatal sepsis while in 2020 there were 358 deliveries with 85 diagnoses of neonatal sepsis. The number of deaths due to neonatal sepsis from 2017–2020 was 10 cases. Based on these incidence rates, it appears that the incidence of neonatal sepsis is one of the problems that occur in the Naibonat Hospital, Kupang Regency.

Risk factors that can affect neonatal sepsis obtained from the mother include premature rupture of membranes (KPD), maternal fever, infection without fever, chorioamnionitis, preterm labor, fetal heart sound more than 160x/minute. Neonatal risk factors include low birth weight, male sex, multiple births, certain congenital abnormalities, low APGAR scores and nosocomial factors such as improper hand washing procedures [6].

METHODS
The design of this study used a case control research design (case control) with a retrospective study approach. The research will be carried out at the Naibonat Regional General Hospital, Kupang Regency in June 2021. The population in this study were all newborns diagnosed with Neonatal Sepsis at the Naibonat Hospital, Kupang Regency from January to December 2020 totaling 85 cases. The sample size in this study was taken using a total sampling technique, where the entire population was used as a research sample, namely as many as 85 case samples, with a sample size ratio of 1:1 between cases and controls, so the total sample size was 170 samples. Data collection techniques using questionnaires. Data analysis includes univariate, bivariate with chi square test and multivariate with logistic regression test. Presentation of data in this study in the form of tables and narratives.

RESULTS

Table 1: The Effect of Premature Rupture of Membranes, Inpartum Fever, History of Urinary Tract Infection, Duration of Labor, Bacteria and APGAR Score Incidence of Neonatal Sepsis

Variable	Incident Sepsis Neonatorum				Total		p-value
	Case		Control				
	n	%	n	%	n	%	
Premature Rupture of Membranes							
KPD	43	50,6	28	32,9	71	41,8	
No KPD	42	49,5	57	67,1	99	58,2	0,020
Total	85	100	85	100	170	100	
Inpartum Fever							
Fever	47	55,3	26	30,6	73	42,9	
No Fever	38	44,7	59	69,4	97	57,1	0,001
Total	85	100	85	100	170	100	
History of Urinary Tract Infection							
ISK	42	49,4	23	27,1	65	38,2	
No ISK	43	50,6	62	72,9	105	61,8	0,003
Total	85	100	85	100	170	100	
Duration of Labor							

>24 Jam	15	17,6	1	1,2	16	9,4	
≤24 Jam	70	82,4	84	98,8	154	90,6	0,006
Total	85	100	85	100	170	100	
Bacteria							
There Are	46	54,1	29	34,1	75	44,1	
No There Are	39	45,9	56	65,9	95	55,9	0,009
Total	85	100	85	100	170	100	
APGAR Score							
APGAR < 7	57	67,1	4	4,7	61	35,9	
APGAR ≥ 7	28	32,9	81	95,3	109	64,1	0,000
Total	85	100	85	100	170	100	

Based on Table 1 above, bivariate analysis showed that there was a significant relationship between premature rupture of membranes and the incidence of neonatal sepsis, the p value = 0.020. There is a significant relationship between the inpartum fever variable and the incidence of neonatal sepsis and the p value = 0.001. There is a significant relationship between the variable history of urinary tract infection and the incidence of neonatal sepsis, obtained p value = 0.003. There is a significant relationship between the variable length of parturition and the incidence of sepsis neonatorum obtained p value = 0.006. There is a significant relationship between the bacterial variable and the incidence of neonatal sepsis, the p value = 0.009. There is a significant relationship between the

APGAR value variable and the incidence of neonatal sepsis, the p value = 0.000.

The analysis used multivariate with logistic regression method to see the effect of several independent variables at once on one dependent variable which was tested at the same time. Variables that were continued using multivariate were premature rupture of membranes, labor fever, history of urinary tract infection, duration of labor, bacteria and APGAR score. This analysis takes the independent variable which has a p-value <0.05 in bivariate analysis. Table 1 shows that all variables have a p-value > 0.05, meaning that this variable can be continued in multivariate analysis.

Table 2: Multivariat Regresi Logistik Step 1

	B	S.E	Wald	Df	Sig	Exp (B)	95% CI for EXP (B)	
							Lower	Uper
KPD	0.657	0.473	1.930	1	0.165	1.928	0.764	4.869
Demam Inpartu	1.045	0.467	4.999	1	0.025	2.843	1.138	7.104
Riwayat ISK	0.635	0.467	1.845	1	0.174	1.886	0.755	4.714
Lama Partus	2.820	1.140	6.125	1	0.013	16.780	1.798	156.581
Bakteri	0.484	0.465	1.083	1	0.298	1.623	0.652	4.041
APGAR Score	3.760	0.596	39.756	1	0.000	42.955	13.347	138.238

Furthermore, the final modeling of the step 1 multivariate analysis shows that the variables that have a p value > 0.05 in Table 2 are premature rupture of membranes, a history of urinary tract infections and bacteria so that they cannot be included in the final modeling of the next multivariate analysis.

Table 3: Final Modeling of Multivariate Analysis

	B	S.E	Wald	Df	Sig	Exp (B)	95% CI for EXP (B)	
							Lower	Uper
Demam Inpartu	1.255	.451	7.750	1	.005	3.509	1.450	8.493
Lama Partus	3.300	1.126	8.593	1	.003	27.122	2.985	246.399
APGAR Score	3.801	.590	41.512	1	.000	44.746	14.080	142.204

The last result of the multivariate analysis modeling, showed that it still had a significant effect when the variables of labor fever, labor duration and APGAR Score were analyzed together in order of strength of influence from the largest to the smallest labor fever (OR = 8,493), APGAR Score (OR = 142,204) and duration of labor (OR = 246.399). Of the three determinant factors, the most dominant factor that directly influences the incidence of neonatal sepsis is

the length of parturition variable because this factor has the largest odds ratio (OR) value of 246.399.

DISCUSSION

The Effect of Premature Rupture of Membranes on the Incidence of Neonatal Sepsis

Premature rupture of membranes or PROM (premature rupture of membranes) is premature rupture of the membranes without any signs of labor and after 1

hour it is still not followed by a proper delivery process. Premature rupture of membranes (PROM) is an important problem in obstetrics related to complications of premature birth and infectious complications of chorioamnionitis to sepsis, which increases perinatal morbidity and mortality and also causes maternal infection [7].

When the membranes rupture, exposure to bacteria from the vagina will play a greater role in fetal infection. In this situation, bacteria from the genitourinary tract enter the uterine cavity and the baby can be contaminated through the respiratory and gastrointestinal tract. The incidence of bacterial contamination in unborn babies will increase if the membranes have ruptured for more than 18-24 hours. Literature abroad provides a time limit for premature rupture of membranes is 18 hours [7].

The results of this study indicate that there is an influence between premature rupture of membranes on the incidence of neonatal sepsis (p-value = 0.020) < (0.05). Mothers with cases of premature rupture of membranes have a 2,084 times risk of experiencing neonatal sepsis. According to the researchers, this is because PROM can increase pregnancy complications in the mother and baby, especially bacterial infections in the neonatal period. As for the bacterial infection itself is one of the causes of neonatal sepsis. Complications of premature rupture of membranes that most often occur in maternity are infection in childbirth, infection during the puerperium, prolonged labor, postpartum hemorrhage, increasing cases of cesarean section, and increasing maternal morbidity and mortality. While the most common complications in the fetus are prematurity, decreased umbilical cord, hypoxia and asphyxia, fetal deformity syndrome, and increased perinatal morbidity and mortality.

This study is in line with research conducted stating that premature rupture of membranes is associated with the incidence of neonatal sepsis. From the results of the chi-square analysis, the p-value is 0.014 and the OR is 3.66. This shows that there is a relationship between premature rupture of membranes >18 hours with the incidence of neonatal sepsis and premature rupture of membranes >18 hours being a risk factor of 3.66 times for the occurrence of early-onset neonatal sepsis [8].

The Effect of Inpartum Fever on the Incidence of Neonatal Sepsis
Fever is a condition of increasing body temperature to more than 38ºC. Fever indicates the presence of an illness or other condition in the body. Fever generally occurs as a reaction of the immune system against viral, bacterial, fungal, or parasitic infections that cause disease. Some of the diseases that often cause fever are flu, sore throat, and urinary tract infections while impartu is a medical term that refers to the condition of a woman who is in the labor stage.

While labor is a process of expelling the products of conception (fetus or uri) which has been quite a month and allows the fetus to survive outside. So it can be concluded that labor fever is a fever that occurs when a mother is in the labor stage [9].

The results of the analysis of the Simple Logistics Regression test showed that there was an effect of inpartu fever on the incidence of neonatal sepsis (p-value=0.001) < (0.05). Mothers with cases of inpartum fever have 2.807 times the risk of experiencing neonatal sepsis. According to researchers, this is because fever during delivery can indicate the mother's condition is not good, one of which is due to a bacterial infection. This infection by bacteria causes fever in pregnant women. The bacteria that cause this fever include streptococcus, staphylococcus, listeria monocytogenes, Escherichia coli and clostrodium difficile. While bacterial infection itself is one of the causes of neonatal sepsis.

This study is in line with research conducted stating that impartu fever is associated with the incidence of neonatal sepsis. The results of the study showed that only 6 babies were born alive out of a total of 46 babies born to mothers with postpartum fever [10].

The Effect of History of Urinary Tract Infection on the Incidence of Neonatal Sepsis
Urinary tract infection (UTI) is a condition in which germs or microbes grow and multiply in the urinary tract in significant numbers. The term UTI is commonly used to denote the presence of microbial invasion of the urinary tract. UTI is a disease with a condition where there are microorganisms in the urine in very large numbers and can cause infections in the urinary tract [11].

Urinary tract infections are mostly caused by bacteria, viruses and fungi but bacteria are often the cause. The most common causes of UTIs are gram-negative bacteria, including bacteria that normally inhabit the intestines and will ascend to the urinary system, including Escherichia coli, Proteus sp, Klebsiella, Enterobacter. Postoperative infection is also common with Pseudomonas, while Chlamydia and Mycoplasma can occur but are rarely found in UTI patients. In addition to microorganisms, there are other factors that can trigger UTI, namely predisposing factors [11].

The results of this study indicate that there is an influence between a history of UTI on the incidence of neonatal sepsis (p-value = 0.003) < (0.05). Mothers with UTI cases are at 2,633 times risk of experiencing neonatal sepsis. According to the researchers, this is because mothers with a history of UTI during delivery have bacterial colonies that are very likely to infect the baby so that it can cause neonatal sepsis. Regarding

pregnant women with suspected urinary tract infections in this study, it was found in accordance with the theory which states that the risk factors for group B streptococcal infection (GBS) in the mother can occur in the mother's vagina or urine during pregnancy which causes the mother to have intrapartum fever and even KPD. Infection in the mother during childbirth, especially genital tract infection, is an important route of maternal transmission and plays an important role in the incidence of infection in the neonate.

This study is contrary to previous studies which have stated that a history of urinary tract infections in the mother is not a factor influencing the incidence of neonatal sepsis. The results of the chi-square test obtained p-value $(0.159) > (0.05)$. According to this study, this may be due to the fact that mothers with UTIs are always given antibiotics so that the risk of fetal sepsis decreases [12].

The Effect of Long Parturition on the Incidence of Neonatal Sepsis

Long parturition is a complex process that is when psychological and physiological events are interrelated and cannot be separated. Some mothers experience a longer labor compared to other mothers. Some deliveries are slow because of the large size of the fetus and its unusual location. Prolonged labor is labor that lasts more than 24 hours in primigravida, and more than 18 hours in multigravida. If the progress of labor is not going well during that period, the situation should be assessed immediately, the problem should be identified and resolved before 24 hours [13].

The results of this study indicate that there is an influence between the length of labor on the incidence of neonatal sepsis (p-value = $0.006) < (0.05)$. Mothers with prolonged labor > 24 hours have 18,000 times the risk of developing neonatal sepsis. Based on the data collected, 90.6% of mothers gave birth with a duration of labor < 24 hours and only 9.4% who gave birth > 24 hours. Long parturition, both the active phase is prolonged and the second stage is prolonged, causing effects on both the mother and the fetus. There is an increase in the incidence of uterine atony, bleeding lacerations, infection, maternal fatigue and shock. The high birth rate with the procedure further exacerbates the danger to the mother.

In long labor, the mother experiences fatigue because without eating and drinking which can lead to dehydration, looks sick, pale, sunken eyes, and has cold sweats, pulse increases, blood pressure drops and temperature rises, his stomach starts to weaken and looks bloated. In addition, in the old parturition, the 3P cooperation is not perfect, resulting in a decline in congestion.

This study is in line with research that has been done that mother who experienced labor with prolonged labor experienced more neonatal sepsis, namely 27 (49.1%) while in controls only 16 (29.1%). The results of the chi-square analysis obtained p-value = 0.032 at = 0.05. Because the value of p < means that there is a significant relationship between neonatal sepsis and prolonged labor at Dr. Hospital. H. Moch. Ansari Saleh Banjarmasin. OR value = 2.350 which means that prolonged labor is 2.350 times more at risk for neonatal sepsis than mothers who have not experienced prolonged labor [14].

The Effect of Bacteria on the Incidence of Neonatal Sepsis

Neonatal sepsis is usually defined as a systematic symptom of infection by bacteria, viruses, and fungi in the neonatal period with initial symptoms that vary, from lazy drinking to septic shock. Neonatal sepsis is still a big problem in several countries, especially developing countries like Indonesia. In addition to causing death and illness, it is difficult to establish a definite diagnosis, and the treatment is expensive [15].

The biggest cause of sepsis is gram-negative bacteria (60-70%) cases, which produce various products that can stimulate immune cells. These cells will be stimulated to release inflammatory mediators. The product that plays an important role in sepsis is lipopolysaccharide (LPS). Lipopolysaccharide or endotoxin glycoprotein complex is a major component of the outer membrane of gram-negative bacteria. Lipopolysaccharides stimulate tissue inflammation, fever and shock in infected patients. The structure of lipid A in lipopolysaccharide is responsible for reactions in the patient's body. Staphylococcus, Streptococcus, and other gram-positive bacteria rarely cause sepsis, with an incidence of 20%-40% of all cases [15].

The results of this study indicate that there is an influence between bacteria on the incidence of neonatal sepsis (p-value = $0.009) < (0.05)$. Mothers with cases of bacteria have a risk of 2,278 times the incidence of neonatal sepsis. Based on the data collected, 44.1% of mothers were contaminated with bacteria and 55.9% of mothers were not contaminated by bacteria. This proves that if the mother has bacteria, it is easy to experience cases of neonatal sepsis. Bacterial infections are 5 times more common in newborns weighing less than 2.75 kg and 2 times more common in boys. In more than 50% of cases, sepsis begins within 72 hours of birth. Sepsis that has appeared within 4 days or more is likely due to a nosocomial infection.

Neonatal infection after rupture of membranes is influenced by colonization of group beta streptococci. The duration of rupture of membranes is associated with an increase in bacterial colonies, ascending infection and the number of vaginal touchers. The

frequency of vaginal examinations is associated with an increase in neonatal infections due to increased ascending infection from the vagina to the uterine cavity. The relative risk of septic infection.

This study is in line with research conducted that a total of 72 patients were included in the study, 40 patients with non-extended spectrum beta-lactamase gram-negative bacterial infection and 32 patients with extended spectrum beta-lactamase (ESBL) infection. The most common extended spectrum beta-lactamase bacteria causing sepsis were Escherichia coli, extended spectrum beta-lactamase + and the most common non-extended spectrum beta-lactamase gram negative bacteria causing sepsis was Acinetobacter baumanii. Septic shock is more common in patients with extended spectrum beta-lactamase bacteria [16].

Effect of APGAR Score on the Incidence of Neonatal Sepsis
APGAR is a method for determining the level of a newborn's condition: a number 0, 1 or 2 for each of the five signs, depending on the presence or absence of the sign. Determination of this level is done 1 minute after birth and repeated after 5 minutes. The APGAR score is a simple method used to assess the general condition of the baby immediately after birth. This assessment is necessary to determine whether the baby has asphyxia or not. Assessment is heart rate (heart rate), respiratory effort (respiratory effort), muscle tone (muscle tone), skin color (colour) and reaction to stimuli (response to stimuli), namely by inserting a catheter into the nostril after the airway is cleared [17].

The results of this study indicate that there is a significant effect between the APGAR score on the incidence of neonatal sepsis where the results of the Simple Logistics Regression test analysis show (p-value = 0.000) < (0.05). Mothers with cases of APGAR score < 7 have a 41,223 risk of experiencing neonatal sepsis. Based on the data, the number of cases with APGAR score status at risk was 57 (67.1%) mothers with control sample status not at risk, namely 4 (4.7%) people. This high case makes the APGAR score have a strong influence on the occurrence of neonatal sepsis. This may be due to multifactorial factors such as maternal, fetal and environmental factors that play a role in the occurrence of neonatal sepsis. The close relationship between low APGAR scores and infection could be due to high intervention procedures in these infants from an early age so that they could be infected by germs in the delivery room. Meanwhile, there is a close relationship between the occurrence of sepsis and preterm or premature neonates due to a relative deficiency of immunity.

This study is not in line with research that has been done that the results of the study obtained 50 infants suspected of sepsis. 40 infants with proven sepsis and 10 infants without sepsis. By using the Fisher Exact test and multiple logistic regression analysis, p-value = (0.999) > = 0.05. The conclusion of this study was from the data obtained that infants with neonatal sepsis had the highest percentage of low Apgar scores and low birth weight. With statistical tests, there is no relationship between APGAR score and birth weight with neonatal sepsis [18].

Newborns, also known as neonates, are individuals who are growing and have recently experienced birth trauma and must be able to make adjustments from intrauterine life to extrauterine life. Meanwhile, normal newborns are babies born with a gestational age of 37-42 weeks and birth weight between 2500 ± 4000 grams [18].

CONCLUSIONS & SUGGESTIONS
Maternal risk factors that significantly influence the incidence of neonatal sepsis are premature rupture of membranes, labor fever, history of urinary tract infection and duration of labor. Infectious agent factors that influence the incidence of neonatal sepsis are bacteria. The infant risk factor that influences the incidence of neonatal sepsis is the APGAR score. Determinant factors that influence the incidence of neonatal sepsis are the APGAR value, labor duration and labor fever. Suggestions for Government Agencies to prevent the occurrence of neonatal sepsis in infants, are expected to improve skills in ANC supervision and services as well as conduct intensive education for pregnant women to always check their health and womb in order to detect early risk factors for Neonatal Sepsis so that it can be prevented.

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