Rev. Fac. Med. Hum. July 2019;19(3):35-42.
DOI 10.25176/RFMH.v19i3.2165
ORIGINAL ARTICLE

ISSN Version Online: 2308-0531
Faculty of Human Medicine URP

RISK FACTORS ASSOCIATED WITH EARLY NEONATAL SEPSIS IN PRETERM INFANTS OF THE NATIONAL CHILD MOTHER TEACHING HOSPITAL, 2017

FACTORES DE RIESGO ASOCIADOS A SEPSIS NEONATAL TEMPRANA EN PREMATUROS DE UN HOSPITAL NACIONAL DOCENTE MADRE NIÑO, 2017

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ABSTRACT

Introduction: Neonatal sepsis is one of the most important diseases of our country, it is necessary to know its risk factors in our country. **Objetive:** To determine the risk factors associated with early neonatal sepsis in preterm infants of the National Mother Teaching Hospital San Bartolomé in 2017. **Methods:** Case-control, observational, analytical, cross-sectional and retrospective study. will work with medical records. The dependent variable was early neonatal sepsis. We worked with a sample size of 62 cases and 124 controls (ratio 1: 2). The data was obtained from the medical records. For inferential statistics, bivariate analysis was used to find the Odds Ratio with their respective 95% confidence intervals. Values p <0,05 wereconsidered statistically significant. **Results:** Of the 186 patients studied, 53.8% were female. The factors associated with early neonatal sepsis were: low birth weight -ORa: 4.031 (95% CI: 1.743-9.318); age 35 to over -ORa: 2.729 (95% CI: 1.266-5.88); less than 6 prenatal controls -ORa: 3.315 (IC95%: 1.452-7.567); urinary tract infection (UTI) in the 3rd quarter -ORa: 2.947 (95% CI: 1.063-8.174); meconial fluid -ORa: 5.822 (95% CI: 1.92-17.653) and premature rupture of membranes -ORa: 2.789 (95% CI: 1.035-7.511). **Discussion:** A significant association has been found between early neonatal sepsis and low birth weight, age 35 to more, fewer than 6 prenatal controls, UTI in the third trimester, meconium fluid and premature rupture of membranes.

Keywords: Neonatal Sepsis; Infant; Premature; Infant; Premature; Amniotic Fluid.(source: MeSH NLM)

RESUMEN

Introducción: La sepsis neonatal es una de las enfermedades más importantes de nuestro País, es necesario conocer sus factores de riesgo. **Objetivo:** Determinar los factores asociados a sepsis neonatal temprana en prematuros del Hospital Nacional Docente Madre Niño San Bartolomé en el año 2017. **Métodos:** Estudio de casos y controles, observacional, analítico de corte transversal y retrospectivo. La población consta de 210 recién nacidos prematuros del Hospital Nacional Docente Madre Niño San Bartolomé, año 2017. La variable dependiente fue la sepsis neonatal temprana. Se trabajó con un tamaño muestral de 62 casos y 124 controles (ratio 1:2).Los datos se obtuvieron de las historias clínicas. Para la estadística inferencial se utilizó el análisis bivariado para hallar los Odds Ratio con sus respectivos intervalos de confianza al 95%. Se consideró p<0,05 como estadísticamente significativo. **Resultados:** De los 186 pacientes estudiados, 53,8% fueron del sexo femenino. Los factores asociados a sepsis neonatal temprana fueron: bajo peso al nacer -ORa: 4,031 (IC95%: 1,743-9,318); edad de 35 a más -ORa: 2,729 (IC95%: 1,266-5,88); menos de 6 controles prenatales -ORa: 3,315 (IC95%: 1,452-7,567); infección del tracto urinario en el 3er trimestre -ORa: 2.947 (IC95%: 1,063-8,174); líquido meconial -ORa: 5,822 (IC95%: 1,92-17,653) y ruptura prematura de membranas -ORa: 2.789 (IC95%: 1,035-7,511). **Discusión:** Se ha encontrado una asociación significativa entre sepsis neonatal temprana y bajo peso al nacer, edad de 35 a más, menos de 6 controles prenatales, infección del tracto urinario en el 3er trimestre, líquido meconial y ruptura prematura de membranas.

Palabras clave: Sepsis Neonatal; Recien Nacido Prematuro; Enfermedades del Prematuro; Líquido Amniótico. (fuente: DeCS BIREME)

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Cite as: Gretzelle Burga-Montoya, Consuelo Luna-Muñoz, Jhony A. De La Cruz-Vargas. Risk factors associated with early neonatal sepsis in preterm infants of the national child mother teaching hospital, 2017. Rev. Fac. Med. Hum. July 2019; 19(3):35-42. DOI 10.25176/RFMH.v19i3.2165

Journal home page: http://revistas.urp.edu.pe/index.php/RFMH

INTRODUCTION

Sepsis represents a challenge for neonatology services worldwide, as despite advances in antimicrobial therapy, factors related to the development of sepsis with high morbidity and mortality are of great importance[1]. The infection may be bacterial, viral, fungal, or rickettsial[1]. Neonatal sepsis includes several systemic infections of the newborn, such as septicemia, meningitis, pneumonia, arthritis, osteomyelitis, etc.[2].

Depending on the age of onset of the disease, neonatal sepsis is divided into early-onset or late-onset. Early-onset neonatal sepsis (EONS) is mainly due to organisms acquired before and during childbirth (or maternal fetal infection) and late-onset sepsis (LONS) to organisms acquired after childbirth (nosocomial or community sources). However, there is little consensus on which age limits are applied, with an early onset varying from 48 hours to 7 days after childbirth[3].

Over the past two decades, remarkable progress has been shown in reducing maternal and child deaths, and neonatal health is part of the "unfinished agenda." World is experiencing an increase in the proportion of deaths among children under five years of age occurring in the neonatal period4. However, although neonatal deaths are preventable, they are concentrated in the poorest countries of the world4 and 85% of all newborns occurred in low and middle income countries, even though they only house 62% of the world's newborns[4,5].

Overall, 15% of neonatal deaths are caused by neonatal sepsis and is a major concern in low and middle income countries[4].

In addition, it is also associated with increased medical costs, prolonged hospital stays and potentially deficient neurodevelopment outcomes in the long run. Of the surviving newborns, approximately one quarter have significant neurological sequelae as a result of the central nervous system (CNS) septic shock or hypoxemia secondary to severe parenchymatous lung disease despite the early introduction of effective antibiotic treatment. The world is witnessing a steady decline in the number of neonatal deaths due to sepsis. Neonatal mortality from sepsis decreased by only 28%[4-6].

In the American continent, 17% of neonatal deaths in South America are attributed to sepsis neonatal, compared with only 6% of deaths in high income countries. Sepsis neonatal is the main killer of newborns in Peru, accounts for more than one third of neonatal deaths[7]. In the Peruvian jungle, neonatal sepsis is also a major cause of morbidity and neonatal deaths after prematurity and birth asphyxiation[8] is responsible for 24% of the neonatal deaths with such an incidence rate high as 10 per 1000 live newborns[5,7–9].

Many factors contribute to high mortality due to infections caused by delays in the identification and treatment of newborns with infection, specifically; including insufficient recognition of the disease, delays in the seeking care at the household level, delays in the start of treatment and the lack of access to both health care workers trained as to high quality services to manage the sepsis. It is particularly moving that many neonatal deaths occur in the community, without the newborn has contact with the appropriate healthcare services[10,11].

Strategies that can prevent and treat newborns with sepsis are essential to accelerate the progress of newborn survival. However, in many developing countries, the identification and treatment of newborns with infection are unsatisfactory and epidemiological data from developing countries showed differences in incidence, risk factors, patterns and antimicrobial sensitivities of pathogens and mortality in developed countries. Identification of risk factors and early institutionalization of therapy may improve neonatal mortality and morbidity[5,12].

Many centers have studied the common causal agents of neonatal sepsis with their sensitivity patterns, but there are limited studies that tried to verify the risk factors of neonatal sepsis in prematurity in the study area and in the country in general. Therefore, there is a need to carry out an investigation to get to the risk factors of neonatal sepsis in premature infants. This study therefore aimed to determine the risk factors associated with early neonatal sepsis in premature patients of the Madre Niño San Bartolomé National Teaching Hospital: January-December, 2017.

METHODS

A case study and controls were carried out, observational, analytical cross cutting with retrospective data collection.

The population consisted of 210 premature newborns (< 37 weeks of gestation), attended by the neonatology unit of the Madre Niño San Bartolomé National Teaching Hospital during the months of January to December 2017, from which the sample size was calculated.

The case group consisted of premature newborns with early neonatal sepsis and the control group consisted of healthy premature newborns, in both groups the newborns were treated in the neonatology unit of the Madre Niño San Bartolomé National Teaching Hospital, during the months of January to December 2017.

The inclusion criterion was newborn of institutional partum attended at the Madre Niño San Bartolomé National Teaching Hospital and the exclusion criteria were newborns with incomplete clinical histories and illegible letter, perinatal and fetal deaths.

The sample was calculated from a formula to find a sample size for cases and controls taking into account 2 controls for each case (62 cases and 124 controls, ratio 1:2), the estimated prevalence for the proportion of controls exposed was 6,1%.

The dependent variable was early neonatal sepsis, the independent variables were sex, birth weight, low APGAR, maternal age, prenatal checkups, urinary tract infection (UTI) in 3rd trimester, meconial fluid, delivery route, fetal distress and premature membrane ruptura. With a data collection sheet, designed by the authors, data were collected from the medical records.

The data were statistically processed in order to find the desired associations. For the univariate statistics the frequencies and percentages were found for the qualitative variables and the measures of central tendency and dispersion for the quantitative variables. For the bivariate analysis were found the Ratio odds with their respective 95% confidence intervals. The values $p<0,05$ were considered statistically significant.

As being the present retrospective, the direct participation of patients was not included, therefore it did not require the signature of informed consent. Furthermore, in order to safeguard confidentiality, the names of the patients were not included in the data collection sheet, which made it possible not to identify the patient. In addition, due to retrospective design, there were no physical and/or psychological risks, or potential invasion of privacy, risk of death and/or alteration of the quality of life or damage to others. The custody of the information collected on the data collection sheet was stored for a period of one year in the custody of the equipment, being subsequently removed.

RESULTS

In the univariate analysis we can observe the general characteristics of the population (Table 1) and in the bivariate analysis the factors associated with early-onset neonatal sepsis in the studied population (Table 2).

Table 1. General characteristics of the premature babies of the Madre Niño San Bartolomé National Teaching Hospital in 2017.

	FREQUENCY	PERCENTAGE
Gender		
Male	86	46.2%
Female	100	53.8%
Low birth weight		
Yes	36	19.4%
No	150	80.6%
Low APGAR score		
Yes	4	2.2%
No	182	97.8%
Maternal age		
From 35 years to more	47	25.3%
Under 35 years old	139	74.7%
Prenatal checkups		
Less tan 6	39	21.0%
6 or more	147	79.0%
UTI in the 3rd quarter		
Yes	21	11.3%
No	165	88.7%
Meconial liquid		
Yes	19	10.2%
No	167	89.8%
Cesarean birth		
Yes	61	32.8%
No	125	67.2%
Fetal suffering		
Yes	3	1.6%
No	183	98.4%
Premature membrane rupture		
Yes	22	11.8%
No	164	88.2%

BIVARIATE ANALYSIS

Table 2. Bivariate analysis of the factors associated with early-onset neonatal sepsis the population studied 2017.

Gender	Early-onset neonatal sepsis			Crude OR (IC 95%)	P Value
	Yes	No	Total		
Male	26	60	86	0,77 (0.42-1,42)	0,438
Female	36	64	100		
Low birth weight					
Yes	21	15	36	3,72 (1,75-7,91)	0,001
No	41	109	150		
Low APGAR score					
Yes	3	1	4	6,25 (0,64-61,41)	0,109
No	59	123	182		
Maternal age					
From 35 years to more	23	24	47	2,45 (1,24-4,85)	0,012
Under 35 years old	39	100	139		
Prenatal checkups					
Less tan 6	21	18	39	3,02 (1,46-6,23)	0,004
6 or more	41	106	147		
UTI in the 3er quarter					
Yes	12	9	21	3,07 (1,21-7,74)	0,025
No	50	115	165		
Meconium liquid	62	124	186		
Yes	12	7	19	4,01 (1,49-10,78)	0,008
No	50	117	167		
Cesarean birth	62	124	186		
Yes	20	41	61	0,964 (0,50-1,84)	0,999
No	42	83	125		
Fetal suffering	62	124	186		
Yes	2	1	3	4,1 (0,36-46,11)	0,258
No	60	123	183		
Premature membrane ruptura	62	124	186		
Yes	12	10	22	2,74 (1,11-6,75)	0,031
No	50	114	164		
TOTAL	62	124	186		

MULTIVARIATE ANALYSIS

In Table 3 we can see the multivariate analysis of the factors that were associated in the bivariate analysis, the significance of all is preserved.

Table 3. Multivariate analysis of the factors associated with early neonatal sepsis in premature neonates of the Madre Niño San Bartolomé National Teaching Hospital in 2017.

	Adjusted or	Confidence interval at 95%		P Value
		Lower limit	Upper limit	
Low birth weight	4,031	1,743	9,318	,001
Age 35 and over	2,729	1,266	5,880	,010
Less than 6 prenatal checkups	3,315	1,452	7,567	,004
UTI in the 3rd trimester	2,947	1,063	8,174	,038
Meconial liquid	5,822	1,920	17,653	,002
Premature membrane rupture	2,789	1,035	7,511	,042

DISCUSSION

The results of this study show that there is a relationship between low birth weight and early-onset neonatal sepsis presence; this could be explained by the immune dysfunction and the absence of maternal antibodies acquired transplacently, due to the little development of the neonates.

Other studies show similar results as those developed in Belgium and published in 2015, where 342 neonates who survived the first 72 hours after birth were worked, and who were hospitalized in the Critical Care Unit, it was found that the risk of early-onset neonatal sepsis increases as the birth weight decreases[15].

In a study conducted at the Sergio E. Bernales National Hospital of Lima during 2016, it was reported that a weight less than 2,5 Kg at birth is a risk factor for early-onset neonatal sepsis[16].

Also in the Iquitos Hospital, it was found that a very low birth weight had a higher proportion of neonatal sepsis than controls without neonatal sepsis[17]. In another study conducted in Paita, they find that weighing between 1500 and 2499 grams is a risk factor for early-onset neonatal sepsis. In addition, they report that the maternal age over 35 years of age is a risk factor for early-onset neonatal sepsis, with an adjusted OR of 2,729 probably due to the risk of obstetrics[18]. A similar result was reported in the study conducted at the Sergio E. Bernales National Hospital in Lima, where the risk of early-onset neonatal sepsis increases in the group of mothers at risk age (pregnant women over 35 years of age) and also in teenage pregnant women, as they are at increased risk of obstetrics[16].

Another factor that was statistically significant is the number of prenatal checkups, as is known, the World Health Organization recommends a minimum of 6 prenatal checkups to ensure healthy pregnancy and prevent any complications, such as the detection of other risk factors for perinatal maternal morbidity; an inadequate amount of prenatal checkups, defined as fewer than 6 controls, could put the course of pregnancy at risk. This result was found in the Mercedes de Paita Hospital where one of the risk factors for early-onset neonatal sepsis was having less than 6 prenatal checkups[18]. The same was reported in the Dos de Mayo National Hospital where they worked with 32 cases and 64 controls and having less than prenatal was associated with early-onset neonatal sepsis[19].

Also, Iquitos Hospital also found that less than 6 prenatal checkups in pregnant women is related to a higher prevalence of early-onset neonatal sepsis that in women with 6 prenatal checkups or more[17]. Finally; the same was reported in Sergio E. Bernales National Hospital in Lima[16].

It was found in our study that the urinary infection in the 3er trimester was a risk factor for early-onset neonatal sepsis. This may be explained due to the fact that infections in the last quarter of pregnancy may facilitate canal contamination and exposure of the newborn to bacteria responsable for urinary tract infection, increasing the risk of early infections. A similar result was found at Sergio E. Bernales National Hospital in Lima, in which urinary tract infection in the last trimester was positively associated with early-onset neonatal sepsis[16]. Another similar result was found in the Mercedes Hospital of Paita[18].

Another risk factor associated with early-onset neonatal sepsis was the presence of amniotic meconial fluid. Meconium builds up in the fetal gastrointestinal tract during the ghird trimester of pregnancy and is the first bowel flow to be released withing the first 48 hours after birth. It should be noted that, since meconium and all the contents of the gastrointestinal tract arelocated "extracorporeally," its components are hidden and naturally the fetal immune system does not recognize them. These substances may be excreted early in case the newborn go through some fetal suffering, as it can be from an early infection.

In a study at the Arzobispo Loayza National Hospital, it was found that the presence of amniotic meconial fluid has an association with early-onset neonatal sepsis in premature newborns[20]. The same was reported in the study of cases and checks in Sergio E. Bernales National Hospital where the meconium amniotic fluid resulted being a risk factor for early neonatal sepsis. Also, in India it was reported that the meconial liquid is an indicator of fetal suffering that could be an early indicator of infection by streptococcus[21].

Finally, premature membrane rupture also proved to be a risk factor for early-onset neonatal sepsis. This is because the contaminating membranes of the birth canal, and being rotated prematurely before delivery, may allow for invasion by bacteria of the environment and possible infection of the birth canal, increasing the risk of infection of newborns by increasing their positioning to these germs. A study in the United States found that more time spent with broken membranes increases the risk of early neonatal sepsis[22]. Another study that agrees with these results is that performed at Iquitos Hospital, where the presence of premature membrane rupture increased the risk of early neonatal sepsis[17].

CONCLUSION

There is an association between low birth weight, prenatal checkups, urinary tract infection in the 3rd trimester, maternal age, meconium fluid and early-onset neonatal sepsis in premature babies from the Madre Niño San Bartolomé National Teaching Hospital in year 2017.

Contributions authorship: The authors participated in the generation, drafting and final approval of the original article.

Financing: Self-financed.

Conflict of interest: The authors claim not to have conflict of interest in the publication of this article.

Received: December 2nd 2018.

Approved: May 30th 2019.

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