

Prevalence of Newborn Bacterial Meningitis and Sepsis During the Pregnancy Period for Public Health Care System Participants in Salvador, Bahia, Brazil

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Bacterial meningitis is still a major public health threat inside developing countries. In Brazil, the Department of Public Health estimates that the prevalence of bacterial meningitis is 22 cases per 100,000 persons. During the neonatal period, the bacterial meningitis develops special characteristics that can result in hearing problems and movement loss due to neurological and psychological damages. This study had the aim to analyze the prevalence of bacterial meningitis and sepsis in newborns during the pregnancy period for those using the public health care system in Salvador-Bahia. One of the goal was to describe the risk factors of bacterial meningitis and sepsis in newborns. A second goal was to identify, based on newborn health records, the difficulties to predict issues with the hearing, neurological and psychological problems. This study has a cross-sectional design. The newborns that were included in this study had bacterial meningitis or sepsis within 0-28 days of life. They were admitted in the maternity wards between June-December 2005 at the newborn intensive unit care. We analyzed 72 reports of newborns and only 11 (17%) were bacterial meningitis or sepsis newborn cases. These cases were associated to high intake of ototoxic drugs that can cause oto and nephrotoxicity, and cause serious sequels on the child development. Nervous system infection is one of the 2 major problems in clinical practice, especially during the first month after birth. During this first month, the nervous system infection develops special characteristics, which are different from regular symptoms and it requires treatment due to the increased risk to develop complications. It is strongly recommended to monitor ototoxic drugs use to prevent effects on the hearing system.

Key-Words: Newborn meningitis, sepsis, prevalence, prediction, complications.

The neonatal meningitis is an illness characterized as a result of infection and inflammation of the meninges and it typically happens between birth and the first 28 days of life [1].

The bacterial infection is more common during the first month after birth compared to other stages of newborns. It has an incidence that varies from 0.22 to 2.66/1,000 newborns in different countries and it tends to be more common in developing countries [2].

During the neonatal period, the illness has special characteristics. The etiology, the clinical symptoms and the mortality appear to be different from the observed in older children [3].

The mortality varies based on the treatment, with survival rates of 17% to 29% and with complications rate of 15% to 68%. Among the predictive factors for determining the diagnosis of this condition are the premature birth, newborn weight, type of bacteria, predisposition for the microbial germ, the length of the treatment and complications [4].

Although there have been medical advances of medicines and preventive medicine, the incidence of newborn bacterial meningitis for the last 30 years has been barely affected. This minor change in the incidence can be linked possibly to higher number of pre-term newborns, the effect of the time between the beginning of the condition and the treatment, the type of

bacteria, the sensitivity of microorganisms, and the antibiotic capacity to alleviate the infection site [5].

Typically, the fetus develops in a sterilized environment acquiring bacterial germs only after birth. Various maternal circumstances in the perinatal stages can possibly lead to abnormal colonies and infection [6]. The most common and cited high risk factors are prematurity, low-weight newborn, twins, asphyxia, cardiopulmonary resuscitation (CPR) for neonate, premature rupture of membranes, maternal fever after birth, urinary infections near the ITU, chorioamnionitis, cerebral hemorrhage, hyaline membrane disease, metabolic disturbances, central nervous system (CNS) malformations and insertion ventriculoperitoneal shunt [7].

Near 25% of the risks are associated with development of meningitis in sepsis patients, having both diseases very similar risk factors. A recent study in the Southeast region of Brazil observed these risks factors except for one. This study had 98% of newborns with sepsis showing also risk factors for bacterial meningitis [8].

The infectious agents affect the central nervous system (CNS), usually through haematogenous pathway, and this is the reason why it is associated to newborn sepsis in approximately 75% of the cases. Hence, pathogens causing sepsis are in general the most prevalent and are located in the CNS. Some of these pathogens are *Streptococcus* group B, *Escherichia coli*, *Listeria monocytogenes*, *Staphylococcus epidermidis* and *Staphylococcus aureus*. The last 2 agents listed, along with fungus agents, are associated to specific situations such as mechanical ventilation and premature birth with extended hospital care [9].

Different aspects that are associated to birth and to care during birth are considered significant factors to high risk for severe infections (such as sepsis and meningitis) during neonatal period [10-12].

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Nonetheless, *Haemophilus influenzae* type B, *S. pneumoniae* and *N. meningitidis* can also occur sometimes in newborns, but this is rare and is in contrast to the higher incidence in infant and toddlers [13].

A previous study in Bahia found high incidence of bacterial meningitis in babies with less than 12 months [14]. A recent study about breastfeeding in Hospital Couto Maia, which is considered a reference center for contagious infections, showed high incidence of bacterial meningitis by *S. pneumoniae* and complications such as hearing impairment in 29% of the sample and neurological complications such as epilepsy, hemiparesis and hydrocephalus [15]. However, there are few available publications about the associated complications for newborn meningitis in Brazil.

Some of these complications are caused by infections central nervous system during the neonatal period and can be detected during the clinical evaluation. However, other complications, in lower degree, can be detected if pain is present and thus can occur some years after having the condition. This makes necessary to have special care on child development [16].

This study had the aim to analyze the prevalence of bacterial meningitis in newborns during the birth, in the city of Salvador, Brazil, in order to describe risk factors of this condition and sepsis. Another goal was to identify, using the clinical records, the potential factors that could become complications and affect the neurological, motor and hearing systems.

Materials and Methods

This is a cross sectional design study. This study includes only newborns with bacterial meningitis or sepsis between 0 to 28 days admitted to the intensive care of maternity wards within June-December 2005. All the participants included had been diagnosed for bacterial meningitis or sepsis. The exclusion criteria consisted of central nervous system malformations, meningitis after cranioencephalic trauma, and viral or fungal meningitis. The data for these participants were obtained by doing a retrospective design of the medical records following a structured survey that indicated the mother's age, gestational age, sex, weight at birth, risk factors, related clinical conditions during the prenatal care and medical visits, drug abuse, infections due to vertical transmission, urinary tract infections, and perinatal characteristics such as amniotic fluid and water breaks. The diagnosis of bacterial meningitis or sepsis is established by the following laboratory criteria: presence of cell >20 leukocytes/mm³, predominance of neutrophil; proteins in cerebrospinal fluid >200 mg/dL; glycorrachia $<50\%$ - 75% of the concomitant glycemia; identification of bacteria in the bacterioscopic examination and/or culture of eliminate cerebrospinal fluid (CSF). The clinical manifestations are inexact during the newborn stage, although there are some that are prominent and helpful for diagnosis, like lethargy, vomiting, convulsions, irritability, refuses to feed, tremors and bulging fontanelles.

The criteria for diagnosis of neonatal sepsis are clinical signs or laboratory findings, and may not have confirmation through hemoculture. Among the most prominent symptoms or related conditions to nervous system are breathing problems, apnea, decreased activity and tone, fever, vomiting, abdominal distention, petechiae and low tissue perfusion. Also, other risk factors evaluated for this infection are low birth weight, prolonged rupture of membranes, maternal fever, purulent amniotic fluid, and mother's urinary infection.

This study used for database creation and data analysis EXCEL and ACCESS. To disseminate the results, a descriptive statistical analysis was done. This study was submitted and approved by the institutional review board of Maternity Climério de Oliveira/Federal University of Bahia CEP/MCO/UFBA and the identification number is 89/2005.

Results

The study analyzed 72 medical records from newborns attended in neonatal intensive care units during June-December 2005. There were only 13 cases that had bacterial meningitis and sepsis. Also, out of those 13 cases, 2 were excluded when they presented conditions affecting the central nervous system. Therefore, only 11 (17.7%) fulfilled the inclusion criteria.

The mother's age varied from 14-30 years old only having 5 (45.5%) less than 20 years old and 6 (54.5%) mothers who participated with 20-31 years old. The data analysis concludes that in terms of medical visits only 5 (45.4%) participants did not do prenatal care, only 2 (18%) did complete neonatal care and 4 (36%) did incomplete prenatal care.

In terms of sex, the majority of newborns were male (63.6%) and all of them presented risk factors to nervous system infection. Some of the many risk factors for nervous system infection were prematurity, observed in 9 (81%), low-birth weight, in 7 (63.6%), mechanical ventilation, in 4 (36.3%), asphyxia perinatal in 2 (18.1%), illegal drug abuse, in 4 (36.3%), convulsions, in 2 (18.1%), water break, in 4 (36.3%), mother's urinary tract infections (ITU), in 5 (45.4%) and purulent amniotic fluid, in 3 (27.2%). Only 2 cases of syphilis were found (18.1%) in terms of presence of congenital infections (Table 1).

The gestational age of the participants varied from 26-40 weeks. The use of ototoxic drugs was observed in all newborns that used aminoglycosides (amikacin or gentamicin) associated to therapeutic schemes for this infection (Table 2).

The extended use of nasogastric tube was observed in 72.7% of all newborns, only 25% using the tube during long periods of time resulting in necrosis of newborn nasal septum.

In terms of demographics of newborns and their families, it was observed that 72.7% were single mothers, 45.4% were families with 3 to 4 children, 63.6% were unemployed, 81.8% of the monthly rents were 3 times less than the minimal wages and 36.3% did not have permanent address (Table 3).

Table 1. Risk factors to newborn meningitis and sepsis during the pregnancy periods on public health care system of Salvador- Bahia

Risk factors	N	%
Premature birth	9	81
Low birth weight	7	63.6
Mechanical ventilation	4	36.3
Asphyxia perinatal	2	18
Drug abuse*	4	36.3
Convulsions	2	18
Water Breaks >6 h	4	36.3
Urinary infection (ITU)	5	45.4
Liquid amniotic purulent	3	27.2
Syphilis in the mother	2	18

*Cocaine, crack, tobacco, alcohol.

Table 2. Antibiotic therapy used in 11 newborns with neonatal infection

Antibiotic therapy	N (%)
Gentamicin + oxacillin	1 (9)
Amikacin + gentamicin	1 (9)
Clorofenicol+ oxacillin+ amikacin	2 (18)
Gentamicin+ oxacillin+ penicillin C	3 (27.2)
Ampicillin + gentamicin	4 (36.3)

Table 3. Demographic indicators of newborns and their families

Demographic	N (%)
Single mother	8 (72.7)
Three to four children living in one home	5 (45.4)
Unemployed	7 (63.6)
House rent < three times minimum wage	9 (81.8)
Did not have permanent address	4 (36.3)
Mother's age < 20 years old	5 (45.4)
Mother's age between 20 and 31 years old	6 (54.5%)

Discussion

During the last decades, the gynecology-obstetric care became a binomial formula where mother-child is receiving highest priority and larger attention in particular for prenatal care and labor. Like many developing countries, Brazil is considered to be not providing optimal perinatal care because medical care begins at late stages during pregnancy and the visits are short. These factors are even more extremes in poorer areas of Brazil [17].

One study registered that only 9% of the mothers completed properly the prenatal care, with examples of both populated and poor areas of Brazil. This study exemplifies the typical characteristics during pregnancy. The prenatal care and pregnancy without risks factors are still not considered among Brazilian young mothers.

Today, the nervous system infection is one of the prominent problems, in particular during the first month after birth. During this time, the nervous system infection acquires particular traits that require special care in respect to regular diagnosis and the treatment is difficult since it has higher incidence of developing complications [18].

The diagnosis through CSF was only 18% of the sample and this occurs due to the difficulty for lumbar puncture as it is offered by the state government in Bahia, Brasil. The hospitals controlled by the public government are those with the higher number of infectious-contagious diseases diagnoses. The neonatal meningitis evaluation is still considered a potential factor for the prevalence of this condition among Brazilian newborns. In 2004, Stoll et al. indicated that the lack of lumbar punctures prevents the diagnosis of meningitis [19]. In 2001, Volpe et al suggested that there is a possibility for the relation between the incidence of meningitis and hematoencephalic barrier immaturity [20].

The diagnosis using the etiologic substract is difficult. There are many factors that the literature described as inadequate, such as inadequate collect and storage of materials sent to make exam and early detection and diagnosis of meningitis when the number of bacteria is still small in the liquor [21]. In addition, specialized laboratory tests to detect meningitis or sepsis tend to have an elevated cost and are not available for the sample in this study.

The familiarity about risk factors is a determining factor for diagnosis. The clinical systems are frequently inexact and the neurological symptoms are found only when the infection is in advanced stages. Therefore, the awareness of risk factors is critical for both prevention and diagnosis [4].

There are different aspects during the birth and the pregnancy care that have been indicated as risk factors for severe infections in newborns [22,23].

One of the risk factors is low birth weight that was present in the majority of newborns. This finding was confirmed in 2001 by Benedict et al. as they analyzed 39 newborns with birth weight below 1,500 g and with bacterial or fungal meningitis, and compared to 25 newborns with low birth weight without meningitis [24]. These authors observed that for those with meningitis the weight and pregnancy stages were different when compared with those in the control group.

The premature aspect is a risk factor for newborn bacterial meningitis as described by various authors that characterized newborns with immature immunology system. Although there have been medical advances in neonatal intensive care and thanks to that even extreme premature newborns can survive, frequently the newborns must stay at intensive care for long periods of time with higher incidence of nosocomial infections [25].

The premature birth and low birth weight are frequently associated with other high risks factors during birth, especially those with meningitis blank during the first 4 days after birth. In addition, meningitis among newborns without low birth weight is associated with the highest risk and potential risk of death [26].

It is evident that newborns from mothers who showed uterus and urinary infections are particularly vulnerable. As a result, if the evaluation of CSF could have been done in this study, it is estimated that the mothers would present a high percentage of bacteria in their CSF cultures. It was observed in this study a rate of ITU of 45.4%. Previous scientific literature confirms that there is 6% of risk of sepsis and meningitis in newborns from mothers with urinary infection that were not receiving medical services [27].

The special characteristics of CNS development indicate a biological vulnerability to ototoxic aggressions, particularly to encephalus. Also, drug abuse could change the shape and the function of encephalus. In 2001, Cunha et al. showed many teratogenic effects related with drug abuse [28]. The use of new toxicological analysis showed that the prevalence of fetus exposition to drug abuse in developing countries is higher than the estimated [29]. This evidence was found in a study conducted at Porto Alegre-Brazil, where the pre-gestational exposition to cocaine was 4.6% [30].

The high incidence of drug abuse (cocaine, cannabis, alcohol, tobacco) by pregnant women with 36.3% demonstrates lack of orientation about pregnancy and lack of receiving medical care (in particular about breastfeeding). This study suggests that support from medical services to provide health information for this sensitive group (drug abusers) can be very helpful and effective to diminish the harmful effects that could affect the newborns.

This study confirmed that ototoxic drugs (aminoglycosides) were used to control infection in all newborn. The use for long periods of time of ototoxic antibiotics can result in irreversible damage to hair cells of Corti's organ in the inner ear, especially the aminoglycosides that can develop into cochlear ototoxicity and, thus, turn into hearing loss with higher manifestation in high frequencies. This hypoacusia, or hearing loss, can be permanent and have several degrees [30].

The general incidence of ototoxicity caused by aminoglycosides antibiotics varies from 5% to 33%, depending on the drug, doses, administration, newborns, individual susceptibility and medical evaluation [31].

The extended use of nasogastric tube can result into various consequences, especially in breastfeeding and respiratory systems of a child. The babies that use the nasogastric tube for long period, without any other stimulation of food intake, typically fail in the coordination between sucking-deglutition-breathing. This condition can turn into dysphagia, ponderal loss, and necrosis of nasal septum. Hence, it is very important that the newborn receive adequate stimulation by a health professional [32].

In terms of family demographics, this study observed a group of poor women, living in suburban and/or metropolitan area in Salvador and with low educational level. A recent study with breastfeeding later meningitis in Papua New Guinea showed the difficulty for medical access to hospitals and clinics, what contributed to inaccurate diagnosis and additional complications after having the illness [33]. One of

the major limitations of this study was the failure to describe the etiology due to the technical difficulty as a result for lack of diagnostic tools such as the analysis of cerebrospinal fluid (CSF).

Conclusion

The nervous system infection is still a major problem when evaluating the first month after birth. During this time, the infection consists of special traits that many times require special medical care and have higher possibility for complications.

Our findings showed the need for neurological and hearing evaluation of all newborns with nervous system infection history, especially in those infected on precocious age, in addition to the assessment through otoacoustic emissions, which is an accessible test and which can be used during intensive care to identify the group with highest risk for late hearing complication.

It is critical the development of educational and preventive programs by health professionals for extended use of ototoxic antibiotics. As consequence, is necessary to monitor the serum levels of these drugs to guarantee that the drugs are effective and reduce renal and hearing problems. The educational components can become a useful tool for preventive care to avoid complications of meningitis and sepsis.

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