

Epidemiological Study of Neonatal Bacterial Meningitis: Moroccan Data

Radouani MA^{1,2}, Kabiri M^{1,2}, Mustapha M^{2,3}, El Hassani A⁴ and Barkat A^{1,2*}

¹Department of Medicine and Neonatal Resuscitation, National Center for Neonatology and Nutrition, Rabat, Morocco

²Research Team on Maternal and Neonatal Nutrition and Health, Faculty of Medicine, University Mohammed V of Rabat, Morocco

³Department of Public Health, Faculty of Medicine, University Mohammed V of Rabat, Morocco

⁴Cheikh zaid Hospital, Morocco

*Corresponding author: Amina Barkat, Department of Medicine and Neonatal Resuscitation, National Center for Neonatology and Nutrition, Children's Hospital, Ibn Sina hospital, Ibn Rushd bd, 10100 Souissi, Rabat, Morocco, Tel: 0661385108; Email: barakatamina@yahoo.fr

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Abstract

Neonatal bacterial meningitis has a mortality rate that exceeds 10% and is responsible for sequelae in 20-50% of cases. The epidemiology of bacterial meningitis is variable depending on the age, areas and periods.

Aim of the study: To study the incidence of neonatal meningitis, know the evolution of bacterial epidemiology and risk factors.

Population and methods: A retrospective study about 60 cases of neonatal meningitis over a period of 3 years (January 2011-December 2013) at the National Reference Centre for Nutrition and Neonatology of the Children's Hospital of Rabat.

Results: The prevalence of neonatal bacterial meningitis was 0.5 per 1000 live births. Parturients were aged between 21 and 35 years in 50% of cases. They were illiterate in 65% of cases. The pregnancies were followed in 60% of cases. Families were from urban environment in 70% of cases. Primiparity was noted in 69% of mothers. We had vaginal delivery in 80% of women. The Apgar was <7 to 20% of newborns. The average age was 4 days with extremes of 2 and 23 days. The sex ratio was 1. Were preterm children in 42% of cases of low birth weight in 93% of cases. The average age at diagnosis was 2 day +/- 1. Neonatal bacterial meningitis were due to *Escherichia coli* in 45% of cases followed by group B streptococcus (GBS), which represents 2% of germs involved. Blood culture was positive in 60% of patients. They were congenital anomalies associated in 13% of cases. Low birth weight, failure monitoring pregnancy and the presence of congenital malformations were risk factors significantly associated with the occurrence of neonatal bacterial meningitis. The death occurred in 8% of cases.

Conclusion: Neonatal bacterial meningitis was significantly related to adverse socio-economic conditions.

Keywords: Neonates; Bacterial; Meningitis; *E. coli*

Introduction

Neonates (≤ 28 days of life) are the most part of population at risk of meningeal infection and neurological complications. Despite progress in their care, neonatal bacterial meningitis remain severe by their high mortality ranging from 8.5 to 15% and neurosensory sequelae observed in 20-58% of survivors [1]. The persistence of neonatal meningitis results from increases in the numbers of infants surviving premature delivery and from limited access to medical resources in developing countries. In addition, the absence of specific clinical findings makes diagnosis of meningitis more difficult in neonates than in older children and adults. Moreover, a wide variety of pathogens are seen in infants as a consequence of the immaturity of their immune systems and intimate exposure to possible infection from their mothers. The aim of our study was to investigate the prevalence of the disease in our context, to determine sociodemographic, obstetric and maternal factors associated, identify risk factors and analyze complications.

Materials and Methods

It is a retrospective descriptive study of 60 cases of neonatal bacterial meningitis observed in the national reference center for neonatology and nutrition of children's Rabat hospital between January 2011 and December 2013. Were included all newborns hospitalized for infection risk and whose maternal-fetal infection was retained on anamnestic and inflammatory positive results, the blood culture wasn't ever positive. All these infants were given a systematic lumbar puncture. Inflammatory balance sheet consisted of a C-reactive protein (CRP) performed 24 hours of life and a complete blood count (CBC). CRP was considered positive when it was greater than or equal to 20 mg/l. Abnormalities of blood count cells have been considered a white blood cell count greater than 25 000/ml or less than 5000/ml and/or a rate of less than 1500 neutrophils/ml. Bacterial meningitis is retained on at least two of the following criteria [1]:

- Cerebrospinal fluid CSF <0.5 g/L and/or report CSF glucose/glucose <0.5 g/L and/or cerebrospinal fluid proteins >1.2 g/L
- Cellular response superior to 20 cells/mm³
- Positive direct examination after Gram staining

- Positive culture or presence of soluble antigens in CSF

The exclusion criterion was a traumatic PL or nosocomial infection.

For the analysis of the results was carried out comparing the two groups, the infected neonates without meningitis and that of newborns infected with meningitis.

Definition of terms

A full-term newborn is a neonate born between 37 and 41 weeks of gestation

Newborns weighing less than 2500 grams are considered low weight.

Is considered premature birth which born before 37 weeks' gestation (WHO, 1990).

A primipare parturient is any woman that having his first delivery and multiparous that having more than three deliveries.

Fetal asphyxia is a severe impairment of utero-placental gas exchange. The consequences are: encephalopathy; organ failure and neurological sequelae.

We considered meningitis any infection in CSF with a bacteriological confirmation or if at least one positive blood culture was associated with hypercellularity CSF.

Statistical analysis

Statistical analysis was performed through a statistical package SPSS 18.0 for Windows Version. Quantitative variables were expressed as mean +/- standard deviation and those qualitative percentage. Comparisons of continuous data were performed using the Student t test. Comparison of distributions was effected using the Chi² test or Fisher's exact test with significance set at p<0.05. A logistic regression analysis was used to examine the relationship between risk factors and the probable occurrence of meningitis. Parameters with significant correlations were tested by multivariate regression analysis.

Results

Epidemiology

Between January 2011 and December 2013, 1.060 newborns were enrolled. Newborns with bacterial meningitis accounted for 5% of cases (n=60). Comparing groups of infants infected with or without meningitis was made on the basis of antenatal and postnatal factors.

Sociodemographic, maternal and obstetrical features

For the group of newborns infected with meningitis, 60% of them are not monitored pregnancy. Mothers were aged 21-35 years in 50% of cases, 65% were illiterate and 69% primiparous. Seventy percent of families were from urban areas (Table 1).

		Infected neonates with avec meningitis n=60%	Infected neonates without meningitis n=100%	P
Place residence of	Rural	24	9	0.003
	Urban	70	85	

	Periphery	6	8	
Age	≤20 years	37	9	<0.001
	21-35 years	50	80	
	>35 years	13	11	
Parity	Primiparous	69	50	0.002
	Paucipare	20	38	
	Multiparous	11	12	
Pregnancy' monitoring	Yes	40	85	<0.001
	No	60	15	
Mode of delivery	Ceasarean	20	16	0.25
	Vaginal delivery	80	84	

Table 1: Maternal, obstetrical and sociodemographic features

The mode of delivery was vaginal for 80% of newborns with good adaptation to extra-uterine life in 80% of cases.

Neonatal data

Within sixty selected cases of neonatal bacterial meningitis, 47% were certain and 53% were probable. The average prevalence was 0.5 per 1000 live births. There were 32 girls and 28 boys. Children were premature in 42% of cases. The median gestational age was 36 weeks amenorrhea WA with extremes of 32 and 36 weeks. The median birth weight was 2500 g. Low birth weight (<2500 g) was noted in 93% of cases; congenital malformations were observed in 13% of cases. Bacteriological confirmation of meningitis was obtained in 47% of cases. *E. coli* (45%) and group B Streptococcus GBS (2%) accounted for a total of 47% of cases. A positive blood culture associated with cellular response CSF was noted in 13% of cases. Age at diagnosis was 2 days +/-1. The mortality rate was 8%. The average age of death was 7 +/- 2 days. Complications were noted in 13% of cases, hydrocephalus (3%) and brain abscess in 2% of cases (Table 2).

	Infected neonates with meningitis n=60%	Infected neonates without meningitis n=1000%	P
Apgar 5min ≥7	80	99	
	20	1	0.001
Sex M	46	54	
F	54	46	0.35
Weight <1500g	53		
1500-2000g	40		
>2000g	7	100	0.001
Congenital anomalies	13	3	0.002
Deaths in first week	8	1	0.001

Table 2: Neonatal data

Analysis of risk factors for developing bacterial meningitis

Sociodemographic, maternal and obstetrical features: The habitat in rural areas was significantly associated with the occurrence of neonatal bacterial meningitis (24% vs. 9%, $p=0.003$). Mothers aged over 35 years accounted for 13% of cases, this group was statistically more exposed to developing meningitis (13% vs. 11%, $p=0.001$). In univariate analysis, multiparity and not monitored pregnancies were significantly associated with an increased risk of neonatal bacterial meningitis (respectively 11% vs. 12%, $p=0.002$ and 60% vs. 15%, $p<0.001$). We did not observe significant differences in the modes of delivery among newborns infected groups and the control group ($p=0.25$).

Neonatal features

In univariate analysis, perinatal asphyxia was a risk factor for developing bacterial meningitis in newborns (20% vs. 1%, $p<0.001$). A weight of less than 2000 grams at birth was associated with a higher risk of developing neonatal meningitis ($p<0.001$), as well as congenital defects risk. Multivariate analysis showed that the main risk factors for neonatal bacterial meningitis were: not followed pregnancies (OR=0.1, 95% CI [0.06, 0.18], $p<0.001$), the small birth weight (OR=2.75, 95% CI [1.05, 7.18], $p=0.039$) and the presence of congenital malformations (OR=4.0, 95% CI [1.91; 8.8], $p<0.001$) (Table 3).

Discussion

The decrease of mortality observed in recent years in cases of meningitis can be attributed to better therapeutic efficacy but also to earlier detection. Over the past 20 years, the incidence of neonatal bacterial meningitis has changed not very [1,2]. In our study, the prevalence of meningitis was 0.5 per 1000 live births. The prevalence in industrialized countries varies between 0.22 and 0.3 per 1000 live births. In the UK the last estimated incidence (from mid-1990) was 0.22 per 1000 live births which amounts for about 250 cases/year. The highest numbers are found in the developing countries, varying between 2.4 and 6.1 per 1000 live births [3].

	Odd Ratio	Confidence interval CI 95%	P
Low birth Weight	2.75	1.05-7.18	0.039
Pregnancy' monitoring	0.1	0.06-0.18	<0.001
Congenital malformations	4	1.91-8.8	<0.001

Table 3: Risk factors associated with meningitis in infected group: multivaried analysis

The search for risk factors has a certain interest in the study of bacterial infections. Regarding the presence of risk factors for vertical bacterial meningitis, factors related to childbirth predominate, from 44 to 62% in African series and 39% in European series [4]. The risk factors most often found in all series are: urinary and pelvic infections, cesarean deliveries, and the instrumentation during delivery and the presence of meconium-stained amniotic fluid. In our series, socioeconomic level, primiparity and maternal age greater than 35 years were associated with a high risk of neonatal meningitis. The intellectual level, place of residence and not monitoring pregnancies were also a features correlated with the occurrence of meningeal infections in the newborn, this could be explained by reduced access to

care. The absence of regular monitoring of pregnancies exposed to the occurrence of maternal infections transmitted later to newborns.

In infected newborns with meningitis, perinatal asphyxia was significantly associated, which was mainly explained by the context of meconium amniotic fluid part, as all series of risk factors codified occurrence of neonatal bacterial meningitis [5-7].

Bacterial meningitis is more common in immature newborns because the high permeability of the blood-brain barrier especially at the choroid plexus. The absence of polymorphonuclear cells and immunoglobulin G in the CSF enable faster growth germs. Prematurity and low birth weight is the most perinatal risk factors associated with neonatal bacterial meningitis. This feature was the second element of risk found in our study with a frequency of 53% [8].

Our study confirms the diagnostic difficulties of bacterial meningitis during the neonatal period, firstly, because the signs were nonspecific and, secondly, because the CSF culture was negative in half of the cases.

In UK before 1980, Gram negative (especially *Escherichia coli*) were the leading cause of neonatal meningitis. However, GBS emerged as a cause of neonatal sepsis in many developed countries in the 1970s and 1980s the country became the second cause of neonatal bacterial meningitis. A limited number of bacteria may be associated with meningitis varies according to geographic location and age of onset. In most industrialized countries, the bacteria most frequently isolated in the CSF are group *streptococcus agalactiae* SGB (42-62%), *E. coli* (16-29%) and *Listeria monocytogenes* (1.5 to 5%). In countries developing, Gram-negative are most frequently involved with a predominance of *E. coli* (59-64%) followed by Gram-positive organisms (30-36%). The results of our study are similar to those of the southern countries with a predominance of Gram negative bacteria (at least 45%) [9,10].

Advances in antibiotics and the development of modern methods of neonatal intensive care have greatly improved the prognosis of neonatal bacterial meningitis, but the neurosensory sequelae remain common. Mortality rates are currently estimated between 6.6 and 13% in industrial countries and 27-58% in developing countries, the mortality is related to the severity of meningitis, virulence germs, delay diagnosis, and also to have insufficient means of neonatal resuscitation [11]. However, in the last 10 years, the mortality rate in our neonatal center was reduced from 19 to 8% and the sequelae from 15 to 5%.

Conclusion

Improved means of neonatal care has dramatically improved the prognosis of neonatal bacterial meningitis, this despite the disease continues to be a cause of neonatal mortality and high morbidity. If measures were taken to reduce the risk of maternal-fetal transmission, reflection should be conducted to reduce the risk of neonatal meningitis by emphasizing preventive measures and maternal obstetric, particularly among low birth weight, the most affected population.

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