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ORIGINAL ARTICLE

Bacterial Meningitis in Neonates: A Multicenter Descriptive Study in the City of Medellín, Colombia

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ABSTRACT

Introduction: Bacterial meningitis is a severe infection requiring early empirical therapeutic intervention. In Colombia, there is limited information regarding this disease in the neonatal stage, necessitating up-to-date data to guide timely antibiotic therapy.

Objective: To describe the clinical, microbiological, and epidemiological characteristics of neonatal bacterial meningitis in three hospital centers in the city of Medellín during the years 2010 to 2019.

Methods: A descriptive study was conducted using electronic medical records of newborns treated in three hospitals in Medellín from 2010 to 2019. Clinical records with a discharge diagnosis of bacterial meningitis and corresponding microbiological isolation were reviewed. Data were extracted from SAP® and Servinte Clinical Suite Enterprise® and recorded in a Google® spreadsheet.

Results: A total of 125 records with a diagnosis of neonatal meningitis were reviewed with only 42 cases meeting microbiological isolation criteria. The mean gestational age was 35 weeks, and the most frequently isolated pathogens were *Escherichia coli* (40.5%) and *Streptococcus agalactiae* (40.5%). In 71.4% of cases, the meningitis was classified as late-onset according to age. Primary symptoms included irritability (56.1%) and fever (48.8%).

Conclusions: The most common causative agents identified in this population were *S. agalactiae* and *E. coli*. Principal symptoms were irritability and fever. A significant proportion of neonates did not present suggestive symptoms of central nervous system infection. Additionally, prematurity was predominant in the studied population.

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ARTÍCULO ORIGINAL

Meningitis bacteriana en neonatos: un estudio descriptivo multicéntrico en la ciudad de Medellín, Colombia

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INFORMACIÓN ARTÍCULO

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RESUMEN

Introducción: la meningitis bacteriana es una infección grave que requiere un abordaje terapéutico empírico temprano. En Colombia existe poca información sobre esta enfermedad en la etapa neonatal y es indispensable contar con datos actualizados que orienten la antibioticoterapia de manera oportuna.

Objetivo: describir las características clínicas, microbiológicas y epidemiológicas de la meningitis neonatal bacteriana en tres centros hospitalarios de la ciudad de Medellín durante los años 2010 a 2019.

Métodos: se realizó un estudio descriptivo a partir de todos los registros médicos electrónicos de recién nacidos atendidos en tres hospitales de la ciudad de Medellín desde 2010 hasta 2019. Se revisaron las historias clínicas con diagnóstico de egreso de meningitis bacteriana y que contaran con aislamiento microbiológico. Los datos fueron extraídos de SAP® y Servinte Clinical Suite Enterprise® y registrados en una hoja de cálculo de Google®.

Resultados: se revisaron 125 historias con diagnóstico de meningitis neonatal. Sólo se incluyeron 42 casos con aislamiento microbiológico. La edad gestacional promedio fue 35 semanas, y los patógenos aislados con mayor frecuencia fueron *Escherichia coli* (40,5%) y *Streptococcus agalactiae* (40,5%). En el 71,4% la infección meníngea fue de clasificación tardía según la edad. Los principales síntomas fueron irritabilidad 56,1% y fiebre 48,8%.

Conclusiones: los agentes causales más frecuentes encontrados en esta población fueron *Streptococcus agalactiae* y *Escherichia coli*. Los síntomas principales fueron irritabilidad y fiebre. En un gran porcentaje de neonatos no se evidenciaron síntomas sugestivos de infección del sistema nervioso central. Por otra parte, la prematuridad fue predominante en la población estudiada.

INTRODUCTION

Bacterial meningitis is a severe infection with a high global burden of morbidity and mortality (1). Neonates are particularly susceptible to these infections due to their immature immune system, characterized by deficient humoral and cellular effector responses (2-3). Furthermore, diagnosis is challenging due to the nonspecific clinical manifestations of meningeal involvement (4). Adverse outcomes are common, with high mortality rates (around 40%) and permanent neurological sequelae such as auditory, visual, motor, and language impairments (5-7).

The incidence and etiology of neonatal bacterial meningitis (NBM) exhibit heterogeneous behavior concerning socioeconomic conditions, type of delivery, and adherence or access to prenatal care (8-9). Several authors suggest that the etiology differs between high and low-income countries. In the former, *Streptococcus agalactiae* (group B streptococcus) and *Escherichia coli* predominate, while in the latter, bacteria such as *Enterococcus* spp., *Klebsiella* spp., and *Enterobacter* spp. are more common (8,10). In the United States, the majority of cases are attributed to group B streptococci (GBS) followed by *Escherichia coli,* whereas in African countries, other Gram-negative bacilli, such as *Klebsiella pneumoniae,* are predominant (11-12). There are exceptional reports of bacteria like *Streptococcus pneumoniae* and *Haemophilus influenzae* causing neonatal meningitis, primarily in low-income countries; however, these are more significant in children or adults (13).

Globally, there are approximately 126,000 cases of NBM per year with a mortality rate reaching up to 58% in low-income countries, whereas in high-income countries, it decreases to 10% (5,8).

In Colombia, individual reporting of this infection during the neonatal period is not carried out. Instead, cases occurring among these patients are included within the pediatric group (14-15), a practice that obscures the specific profile of bacterial meningitis, whose etiology varies widely according to age. A study in the United States demonstrates that in NBM, the etiological agents and their frequencies of occurrence in children, both inside and outside the neonatal period, exhibit stark differences (12). Identifying these differences is especially important for adjusting empirical antibiotic therapy (16).

Due to the lack of local knowledge on this issue, the aim of this study was to describe the clinical, microbiological, and epidemiological characteristics of neonatal bacterial meningitis in three hospital centers in the city of Medellín from 2010 to 2019.

METHODOLOGY

Electronic records of neonates diagnosed with bacterial meningitis from January 1, 2010 to December 31, 2019 were obtained. These neonates were treated in three reference hospitals: Hospital Universitario San Vicente Fundación, Clínica Universitaria Bolivariana, and Hospital General de Medellín.

Diagnoses were conducted following the codes from the International Classification of Diseases (ICD-10). Patients aged ≤28 days with bacterial isolation in cerebrospinal fluid (CSF), or in blood if there was also an alteration in the former, were included. Cases where no microorganism was isolated or had an additional risk factor for central nervous system infection, such as myelomeningocele, cranial trauma, encephalocele, immunodeficiencies, or central nervous system surgeries, were excluded.

Medical histories and laboratory tests were extracted from the SAP Business Suite® and Servinte Clinical Suite Enterprise® electronic management systems. The information was consolidated into a Google® spreadsheet containing the variables of interest (demographic data, signs and symptoms, diagnoses, microbiological cultures, antibiograms, hemograms, CSF cytology, dates, mother's data, imaging, molecular and serological tests) defined according to relevant literature.

Subsequently, these variables were adjusted through a pilot test conducted with 10 initial medical records to select the definitive ones considering the reporting frequency of each variable. Two researchers searched for and entered the information independently. Data verification was done in Microsoft Excel® v19.0 (contingent and range verification) (17). The statistical analysis was performed using the IBM Statistical Package for the Social Sciences SPSS®26 software.

In cases where microbial isolation was obtained only from blood samples, the CSF cytology had to show at least two of the following criteria to be included: leukocyte count ≥16 and ≥30 cells/mm3 (for full-term and premature patients, respectively), glucose ≤24 mg/dL, proteins ≥128 mg/dL, positive CSF Gram stain, or a positive result in CSF serological or molecular tests (18).

Cases in which an unusual microorganism was identified (such as coagulase-negative staphylococci), were analyzed by a pediatric infectious disease specialist, and only those approved based on clinical and microbiological criteria were included. The protein concentration and leukocyte count in CSF were corrected in case of traumatic lumbar puncture; proportions of 1000 erythrocytes/mm^3 (CSF):1.1 mg/dL protein (CSF) and 1000 erythrocytes/mm^3 (CSF):1 leukocyte/mm^3 (CSF) were used, respectively (19-20).

Based on reports from other studies regarding the elapsed time between symptom onset and diagnosis (21), all symptoms presented by the newborn starting two days before the lumbar puncture were included. The results are presented through tables and descriptive statistics.

ETHICAL ASPECTS

Proper disposition, handling, and custody of each medical record were ensured during the study and dissemination of its results. The project received approval from the ethics committees of the three hospital institutions and the Faculty of Medicine of the University of Antioquia.

RESULTS

A total of 125 records of patients diagnosed with meningitis, according to the ICD-10, were analyzed. Only 42 met the inclusion criteria, and 83 were excluded for the following reasons: no microbiological isolation (46), incomplete microbiological information (17), isolation of coagulase-negative staphylococci (CoNS) without correlation with an altered CSF (10), congenital diseases (8), and explicit culture contamination throughout its processing, including collection (2). Organized by the institution from which they originated, the sample consisted of 16 records from Hospital Universitario San Vicente Fundación, 13 from Clínica Universitaria Bolivariana, and 13 from Hospital General de Medellín.

Epidemiological Information

50% of the patients were premature; 21% had a gestational age (GA) between 33 and 36 weeks, and 29% had a GA of ≤32 weeks. 42.9% of the cases were children hospitalized from birth. After diagnosis, four neonates died during their stay (total mortality), three of them with a history of prematurity (Table 1).

Table 1. Epidemiological information and other data related to admission

Variable	Categories	n*	Fi (%n)	x̄	SD
Infant Information:					
Gestational Age†	-	42	(100)	35	4
Weight (g)	-	42	(100)	2352.6	833.9
Height (cm)	-	39	(92,8)	44.9	5.2
Gender	Female	42	14 (33.3)	-	-
	Male		28 (66.7)		
Infection Onset (days)	-	42	(100)	11	9
Mother's Information:					
Mother's age (years)	-	36	(85.7)	25	8
Parity	-	37	(88.1)	2	1
Prenatal Check-ups	-	26	(61.9)	6	2
Type of Delivery	Vaginal	41	32 (78)	-	-
	Cesarean		9 (22)		
City of Residence	Medellín	41	18 (43.9)	-	-
	Non-Metropolitan Area§		16 (39)		
About the Disease:					
Hospital Stay (days)	-	42	(100)	34	21
Infection Classification	Early	42	12 (28.6)	-	
	Late‖		30 (71.4)		
Death¶	-	41	4 (9.8)	-	

* Represents valid n. Fi: frequency; x̄: average; SD: standard deviation † Gestational age in weeks
§ FAM: Outside the metropolitan area ‖ ≥ 4 days after birth ¶ Total deaths during hospital stay
Source: own elaboration

Clinical Information

71.4% of the newborns had a late-onset infection, and 28.6% had one that was early-onset. Fevers and irritability were the most prevalent symptoms (Table 2). Muscle tone alteration was observed in 15 children, hypotonia in 12, and hypertonia in 3. Meningeal signs were not evident in any case. Regarding CSF parameters, the most common finding was hyperproteinorrachia (85.7%), followed by pleocytosis at 82.1%. Of these, 46% had counts between 31 and 1000 cells/mm^3, and 20.5% between 1001 and 4000 cells/mm^3. Hypoglycorrhachia (<25 mg/dL) was found in 20 cases (47.6%) (Table 2).

Table 2. Symptoms, laboratory parameters, and invasive interventions

CSF Parameters	n*	Fi (%n)	Median	Q1	Q3
Proteins mg/dL	42†	(100)	310.6	151.4	498.4
Glucose mg/dL	42	(100)	20.3	9.0	46.3
Leukocytes	39	(92.9)	342.0	65.0	2250.0
PMN‡ (%)	36	(85.7)	88.0	69.8	93.6
MON (%)	35	(83.3)	10.0	6.0	32.0
Blood PCR mg/dL	39	(92.9)	7.0	3.2	14.0
Turbid appearance	39	34 (87.2)	-	-	-
Xanthochromic	39	25 (64.1)	-	-	-
Gram stain (positive)	41	16 (39)	-	-	-
Culture (positive)	41	23 (56.1)	-	-	-
Symptoms	**n***			**Fi (%n)**	
Fevers	41			20 (48.8)	
Seizures				12 (29.3)	
Bulging fontanelle				2 (4.9)	
Drowsiness				9 (22)	
Irritability				23 (56.1)	
Inappetence				7 (17.1)	
Sepsis§	42			38 (90.5)	
Invasive Interventions	**n***			**Fi (%n)**	
Urinary catheter	42			16 (38.1)	
Epicutaneous catheter				22 (52.4)	
Mechanical ventilation				13 (31)	
Umbilical catheterization				12 (28.6)	

* Represents valid n. Fi: frequency; Median; Q1: quartile 1; Q3: quartile 3
† Numbers in bold represent the absolute frequency for each variable
‡ PMN: polymorphonuclear; MON: monocytes; PCR: C-reactive protein
§ Diagnosis concurrent with or prior to meningitis

Source: own elaboration

Regarding the blood count, 70% of the cases were in the range of 5 to 23 x10^3 cells/µL for leukocyte count, and 26.2% had leukopenia (<5 x 10^3 cells/µL). The average was 11.8 x 10^3 cells/µL (SD 7.9). The mean relative value was 52.1% for neutrophils, 32.7% for lymphocytes, and 11.4% for monocytes. 39% (16 of 41) of the patients had thrombocytopenia (platelet count <150,000/µL).

Microbiological Information

The most frequent isolates were *Escherichia coli*, present in 17 cases (40.5%), whose susceptibility profile showed resistance to several cephalosporins, including cefepime; moreover, in two of these isolates, extended-spectrum beta-lactamases (ESBL) were expressed. *Streptococcus agalactiae* was also present in 17 patients. The sensitivity of this microorganism to penicillin was 100% (Table 3).

Table 3. Bacteria isolated in neonates with bacterial meningitis and antibiotic susceptibility

Etiologic agent	Fi (n%)	PEN	AMP	OXA	SAM	TZP	FOX	CTX	CAZ	CRO	FEP	ATM	IPM	MEM	ETP	AMK	GEN	CIP	LVX	LZD	VAN	SXT	Isolates Blood	Isolates CSF
Escherichia Coli	17 (40,5)	_	_	_	*6/16 (37,5)	14/14 (100)	10/10 (80)	_	5/7 (71,4)	3/4 (75)	14/16 (87,5)	6/6 (100)	8/8 (100)	7/7 (100)	7/7 (100)	17/17 (100)	*11/13 (84,6)	9/17 (52,9)	_	_	_	0/2 (0)	9	8
Klebsiella pneumoniae	1 (2,4)	_	_	_	1/1 (100)	_	_	_	_	_	1/1 (100)	_	_	_	_	1/1 (100)	1/1 (100)	1/1 (100)	_	_	_	_	1	
Pseudomonas aeruginosa	2 (4,8)	_	_	_	_	1/1 (100)	_	_	1/1 (100)	_	2/2 (100)	1/1 (100)	2/2 (100)	2/2 (100)	_	2/2 (100)	1/1 (100)	1/1 (100)	1/1 (100)	_	_	_	1	1
Pseudomonas fluorescens	1 (2,4)	_	_	_	_	1/1 (100)	0/1 (0)	_		_	1/1 (100)		_	*0/1 (0)	_	1/1 (100)	1/1 (100)	1/1 (100)	_	_	_	_	1	
Streptococcus agalactiae	17 (40,5)	3/3 (100)	16/16 (100)	_	_	_	_	2/2 (100)	_	2/2 (100)	_	_	_	_	_	_	_	_	1/1 (100)	6/6 (100)	5/5 (100)	4/4 (100)	6	8
Staphylococcus epidermidis	1 (2,4)	_	_	0/1 (0)	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	1	
Staphylococcus aureus	1 (2,4)	_	_	1/1 (100)	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	1	1
Staphylococcus hominis	1 (2,4)	_	_	0/1 (0)	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	1/1 (100)	1/1 (100)	1/1 (100)	1	1
Staphylococcus warneri	1 (2,4)	_	_	0/1 (0)	_	_	_	_	_	_	_	_	_	_	_	_	_	_	_	1/1 (100)	1/1 (100)	0/1 (0)	1	
Total	**42**																							

Numbers are presented as susceptible bacteria/tested bacteria (% susceptible). Antibiotic acronyms according to WHONET: PEN: penicillin; AMP: ampicillin; OXA: oxacillin; SAM: ampicillin-sulbactam; TZP: piperacillin-tazobactam; FOX: cefoxitin; CTX: cefotaxime; CAZ: ceftazidime; CRO: ceftriaxone; FEP: cefepime; ATM: aztreonam; IPM: imipenem; MEM: meropenem; ETP: ertapenem; AMK: amikacin; GEN: gentamicin; CIP: ciprofloxacin; LVX: levofloxacin; LZD: linezolid; VAN: vancomycin; SXT: trimethoprim-sulfamethoxazole. Fi: frequency. Intermediate sensitivity: *E. coli,* 7 SAM and 1 GEN; *S. fluorescens* 1 MEM.

The antibiotics shown for each microorganism are those suggested by CLSI M100-ED30, approved for clinical use by the FDA. Source: clsi.org free resources

Empirical Antibiotic Therapy

The combination of ampicillin and an aminoglycoside was used in 64.1% of the patients (25/39) (amikacin in 20 of 25 and gentamicin in 5 of 25), ampicillin plus a cephalosporin in 17.9% (cefotaxime 5 of 39; cefepime 2 of 39), and cefepime plus vancomycin or meropenem in 17.9%.

DISCUSSION

This research describes the clinical, microbiological, and epidemiological characteristics of neonatal meningitis in three reference institutions in the city of Medellín. Local data are limited, and this knowledge is required for the correct and timely approach to empirical treatment.

This study identified *Streptococcus agalactiae* and *Escherichia coli* as the predominant agents, revealing an etiological similarity with high-income countries and a difference concerning studies carried out in South America. In Peru, Guillen et al. (22) describe *Escherichia coli* and *Listeria monocytogenes* as the most prevalent (17% and 13% respectively), while *Streptococcus agalactiae* was less common (3%). On the other hand, in Brazil (23), a wide variety of enterobacteria is reported with a significant presence of *Staphylococcus aureus* (11.7%) and *Neisseria meningitidis* (8.8%). These differences reaffirm the need to study the local etiological profile and the inconvenience of

defining empirical therapy by extrapolating data from other countries, even if they may be similar socioeconomically.

Based on the onset of clinical manifestations, neonatal bacterial meningitis (NBM) is classified into early meningitis (which occurs in the first 72 hours of life) and late meningitis (which occurs after the first three days of life). In the early form, the most common agents are those that colonize the maternal genital tract, GBS and *Escherichia coli,* primarily (8). GBS has been described in 35% of screening cultures in asymptomatic pregnant women (24). In contrast, *Staphylococcus aureus,* coagulase-negative staphylococci (CoNS), *Pseudomonas aeruginosa,* and other Gram-negative bacilli found in the hospital environment cause late meningitis (4).

Our data shows that 3 of 17 meningitis cases due to *Escherichia coli* and 8 of 7 due to GBS started before 72 hours of life. Together, they constitute 91.7% of the total cases of early-onset infection. It is also observed that there are almost three times more cases where the infection had a late onset compared to those with an early onset. The importance of these microorganisms in late sepsis is highlighted, where intrapartum antibiotic prophylaxis has no impact. Even if mothers have a negative culture in prenatal screening, the literature reports late meningitis by GBS transmitted by breast milk or cross-contamination. It also warns that not all meningitis cases due to *Escherichia coli* are exclusively of vertical transmission, as this bacterium is highly frequent in neonatal infections associated with health care (25-28).

CNS are more frequently isolated in late neonatal infections acquired in the hospital, mainly bacteremia associated with the use of invasive devices (29-30). Although they are not usually found in neuroinfection, up to 12% of neonatal meningitis cases can be due to CNS (30). In this study, three (7.1%) were identified with clinical correlation in CSF cytochemistry. All patients were premature, with a birth weight less than 1500 g and a late onset of the disease. In addition, they had an epicutaneous central catheter, and 2 of 3 of the neonates underwent umbilical catheterization. Despite their low frequency (but great importance) in patients with prolonged hospital stays, each case should be carefully evaluated not to underestimate these bacteria as causal agents of meningitis in the neonatal stage (31).

This research identified three infections by *Pseudomonas* spp., a frequent opportunistic bacterium in hospital-acquired infections (29). However, cases of meningitis have been described by vertical transmission of this bacterium when mothers are vaginal carriers (32). One of the newborns infected with *Pseudomonas aeruginosa* was not associated with a hospital stay, as it had an early presentation of the disease, and this microorganism is unusual at this stage. Although no microbiological information was available from the mother, given the characteristics of this case, it is feasible to think that it could have been an infection due to vertical transmission.

Meningitis in the neonatal period presents with an insidious clinic and is usually secondary to bacteremia with clinical manifestations of late sepsis (33). The most common clinical manifestations are fevers, irritability, and respiratory problems, while the least common are seizures and a bulging fontanel (22).

The findings in this study correlate with what is mentioned in the medical literature regarding irritability and fevers as the main symptoms in NBM. It is highlighted that in 17% of the patients no symptoms were evidenced, and a similar behavior has been found in other studies (34-35). The absence of symptoms reaffirms the importance of the patient's comprehensive evaluation through the analysis of the hemoleukogram, vital signs, maternal screening, membrane rupture time, and other risk factors suggestive of systemic infection that justify the lumbar puncture and CSF analysis.

Low birth weight (LBW) and premature birth are described as risk factors for the development and fatal outcome of NBM (36,37). We found that 50% of the children were preterm babies, and

some NBM studies report prematurity in the order of 39% (21). The average gestational age in the four patients who died was 33 weeks, and the birth weight was 2214 g.

CSF analysis is one of the most critical tools in the early diagnosis of meningeal infection. However, it should not be the only decision-making criterion regarding the type of intervention provided to the newborn.

The negative predictive value of pleocytosis is not 100%. In this regard, Garges et al. (38) describe that up to 5% of neonates with meningitis can have a white blood cell count (WBC) in CSF between 0 and 1 WBCs/mm^3; and in 10%, it is ≤3, a finding consistent with what was found in this research, where there were cases without pleocytosis in CSF. A study that included 9,111 newborns reported that the use of 20 WBCs/mm^3 as a cut-off point in CSF caused a false diagnosis in 13% of neonates with confirmed meningitis (38). Something similar happens with CSF glucose and protein values that overlap in some cases between patients with and without NBM (39-40).

In this research, 14.3% of the children did not have alterations in proteins, and 40.5% did not have alterations in glucose; fatal cases showed an average glucose of 21.2 mg/dL and proteins of 749.1 mg/dL, which correlates with what is described regarding patients with very high protein values and hypoglycorrhachia having a higher risk of mortality or sequelae (40-42).

The cellular parameters of the hemogram are not very useful for the diagnosis of meningitis (38), but they can be predictors of a poor prognosis. Klinger et al. (43) mention that thrombocytopenia in patients with neonatal meningitis is an essential predictor of complications. Since in some cases it was explicitly expressed in the patient's clinical history that a traumatic lumbar puncture had occurred and the protein and cellular quantification in CSF showed abnormally elevated data, we decided to apply the correction based on the correlation of these analytes in CSF with their values in the blood. This study found thrombocytopenia in 39% of cases. Additionally, 26% of the children had leukopenia (<5x10^3 WBCs/µL in blood), a finding referred to by Garges et al. (38) as a predictor of poor prognosis in meningitis.

According to what was observed in this research, the results of the CRP (C-reactive protein) had great variation (Table 2), and we believe that the wide dispersion of the values is due to it being measured at different times for each case and that it is an acute phase reactant. Its increase will be proportional to the patient's condition. It has been reported that the utility of CRP in NBM is reduced (44). Some authors mention that peripheral blood laboratory parameters help distinguish whether an isolate is due to contamination, especially in CNS cases, an aspect that was taken into account in this research to determine if it was indeed an infection (30).

The maternal information that could be collected was very limited. The low socioeconomic stratum was predominant, which is expected given the type of population served in the hospitals included in the study. Regarding prenatal controls, 4 of 26 mothers attended less than four times, a fact that is a risk factor for neonatal sepsis and NBM (45), and that could be a reflection of the untimely nature of the Colombian health system in providing complete assistance and prenatal follow-up to pregnant women in vulnerable conditions (46). It is proposed for future research to compare the findings of this study with results in non-vulnerable populations treated in other medical centers.

There are very few NBM studies that include the antibiotic susceptibility of the isolated microorganisms. Some strains of *Escherichia coli* showed resistance to third-generation cephalosporins, such as ceftazidime in 2 of 7 isolates. This finding in such a small group of isolates is a limitation, but it is worrisome because cephalosporins are part of empirical treatment. Other authors declare the increase in resistance to these antimicrobials and the expansion of ESBL as a growing problem in the pediatric population (47-48). Even more important was the finding of two strains resistant to cefepime, the most commonly used empirical antibiotic in late neonatal sepsis for coverage of central nervous system infections.

The data obtained on empirical antibiotic therapy show that in clinical practice there is adherence to the protocols and recommendations established by clinical management guidelines for neonatal sepsis in Colombia since the suggested combination of ampicillin-aminoglycoside/cephalosporin was used in 82% of the cases; the other antibiotic regimens used, according to the literature, are also used in NBM under medical criteria (49-50).

It is advisable to periodically review antibiotic susceptibility, as resistance to third-generation cephalosporins may compromise the effectiveness of empirical therapy.

CONCLUSIONS

The causative agents of NBM were *Streptococcus agalactiae* and *Escherichia coli*, both in early and late-onset sepsis. Although the most common symptoms are irritability and fevers, a significant number of patients do not show clinical infectious manifestations and are only diagnosed as part of the comprehensive approach to late neonatal sepsis.

The most frequent alterations in cerebrospinal fluid were hyperproteinorrachia and pleocytosis; however, the absence of these does not rule out an infection in the central nervous system. This highlights the role of microbiological, molecular, and serological studies for diagnosis. The antibiotic regimen of empirical therapy is in line with Colombian and international clinical guidelines. Constant surveillance of local etiology is recommended independently for the neonatal stage.

LIMITATIONS

Given that only cases with positive isolation in just three hospitals were included, this work might not account for the actual etiological prevalence of NBM in Medellín. However, these institutions were strategically chosen as reference centers in the city, and the information presented is a first approach to the local situation of neonatal bacterial meningitis.

The fact that electronic medical records are relatively new in Colombia limited the time span that the study could cover. Information was not found on maternal conditions during pregnancy, duration of membrane rupture, prophylaxis, and screening for *Streptococcus agalactiae*. It was not feasible to follow up on the patient's medical history to capture information on sequelae. Additionally, no further verification of the finding of ESBL-producing organisms was carried out because susceptibility results for some antibiotics were not available. By establishing such rigorous inclusion criteria, there might be a selection bias and valuable data for the characterization of NBM could be overlooked.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest related to this publication.

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