

Late Neonatal Bacterial Infection at the Brazzaville Teaching Hospital

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Abstract

Background: Late Neonatal Bacterial Infection (LNNBI) is a clinical and biological manifestations related to penetration and growth of specific causative bacteria in bloodstream occurring on the 4th-28th day of life. LNNBI still represents an important cause of mortality and morbidity among infants. **Objectives:** To determine the frequency of late bacterial infections in newborns, to describe the clinical and biological profiles and to identify the main responsible germs. **Methods:** Descriptive study data collection, conducted over a period of 10 months at the Brazzaville Teaching Hospital, of interest to newborns admitted from the 4th day of life for suspicion of neonatal infection, and those admitted for any other pathology and having presented an infection 48 hours after hospitalization, and in whom a bacterial culture and/or an inflammatory assessment confirmed or suspected infection. **Results:** During the study period, 1682 newborns were hospitalized, and 86 were hospitalized for a late neonatal bacterial infection, *i.e.* a frequency of 5.1%. There were 67 (77.9%) community infections and 19 (22.1%) nosocomial infections. The frequency of nosocomial infection was 1.1%. The main signs were fever in 65 cases (75.6%), and respiratory distress in 37 cases (43%). The most frequent localizations were bacteremia 32 (37.2%), pulmonary 21 (24.4%), digestive and meningeal in 11 cases (12.8%) each. The most common germ *Klebsiella* in 10 (50%) newborns was resistant to the usual antibiotics. The evolution was favorable in 71 cases (82.5%), and death occurred in 12 cases (14%). **Conclusion:** Late neonatal bacterial infection is common. The main responsible germs are gram-negative bacilli, in particular *Klebsiella* multi-resistant.

Keywords

Neonatal Infections, Germs, Antibiotic Resistance

1. Introduction

Neonatal bacterial infection is a clinical and biological manifestations related to penetration and growth of a specific causative bacteria in bloodstream within the first 28th days of life. It is said late when it occurs at 72 h after birth, a cut-off time point considered to adequately differentiate LNNBI from Early Neonatal bacterial infection (ENNBI) in terms of the spectrum of causative pathogens from the fourth day of life. [1] [2] The Global Burden of Disease (GBD) is estimated 1.3 million annual incident cases of neonatal infections and 203,000 infections-attributable neonatal deaths [3] [4] [5]; making it a public health problem [6] [7]. The incidence of late neonatal infection (LNNI) is inversely related to the degree of maturity and varies geographically from 0.61% to 14.2% among hospitalised newborns [8] [9]. Late neonatal bacterial infections (LNNBI) are subdivided into two nosological entities: community-acquired bacterial infections and nosocomial bacterial infections or healthcare-associated infections [10]. The bacterial ecology of LNNBI depends on the nosological variety of the infection, community or nosocomial and across the regions of the world. *Staphylococcus aureus* (*S. aureus*), *Escherichia coli* (*E. coli*) and *Klebsiella* are the most common germs in community infections; coagulase-negative staphylococci (CNS) represents the most frequent group of bacteria in nosocomial infections [1] [4] [11] [12] [13] [14]. In Africa and in particular in the Congo, few studies have been devoted to this subject.

This study carried out in the Neonatology Department at the Brazzaville Teaching Hospital aims to determine the frequency of LNNBI, specify its clinical and biological profile and determine the bacterial ecology.

2. Methods

This was a descriptive study with prospective data collection conducted from December 1, 2018 to September 31, 2019 (10 months). The study took place in the Departments of Neonatology and Bacteriology - Virology at the Brazzaville Teaching Hospital.

Our study population consisted of all newborns hospitalized in the neonatology department at the Brazzaville Teaching Hospital (B-TH) during the study period.

Newborns admitted to the neonatology department from the fourth day of life for suspected neonatal infection, those admitted for any other pathology and having presented an infection 48 hours after hospitalization for whom a bacterial culture and/or inflammatory workup confirmed or suspected infection were included.

The variables studied were collected from patients' files, hospital registers and parents's interview using a pre-established sheet.

The variables studied were socio-demographic in relation to the newborn, including age at admission, sex and origin; those related to parents are age, level of education, occupation and socio-economic level. The variables related to preg-

nancy and childbirth are gestation, parity, prenatal visits, place and route of delivery, risk factors for neonatal infection. Clinical and paraclinical variables: presenting complaint; clinical signs on admission; anthropometric parameters; gestational age; complete blood count, C-reactive protein, cerebrospinal fluid analysis, and cultures.

Data entry and analysis were performed using Microsoft Excel 2013 and SPSS 20.0 software. The qualitative variables were expressed in frequency and percentages, the quantitative variables in mean and their standard deviations. The Student's T test, the corrected chi-square and the Odds ratio (OR) with a confidence interval of 95% were used for the univariate analysis in order to compare the means and the percentages. If there was a relationship, the significance level was 5%.

3. Results

Out of a total population of 1682 admitted during the study period, 86 were admitted for a late neonatal infection, *i.e.* a frequency of 5.1%, including 67 cases/86 (4%) for a community infection and 19 cases/86(1.1%) for a health acquired infection. The frequency of health acquired infection is 19 cases for 1682 admissions, *i.e.* 1.1%

We collected 51 newborn males (59.3%) and 35 females (40.7%) the sex ratio was 1.45

The newborns were full term in 58 cases (67.4%), had a normal birth weight in 51 cases, *i.e.* 59.3%. The average age at admission was 11.6 ± 7.9 days, extreme (4 - 27 days); there was a risk factor for late infection $n = 58$ cases (67.4). These were: previous antibiotic therapy $n = 21$ cases (36.2%); resuscitation care $n = 23$ cases (39.7%) and previous hospitalization $n = 14$ cases (24.1%).

Clinical signs found were fever in 65/86 (75.8%), respiratory distress in 37/86 (43%), in 18/86 (20.9%) each decreased tonus and primary reflex disorders as mentioned in **Table 1**.

Bacteremia was the most represented site with 32 cases (37.2%) followed respectively by pulmonary 21 cases (24.4%), digestive 11 cases (12.8%) and meningial 11 cases (12.8%).

The blood count performed in 84 newborns (97.7%) was abnormal in 60 cases (71.4%). These were: an abnormality of white blood cells $n = 24$ cases (40%) including leukopenia $n = 8$ cases (13.3%) and hyperleukocytosis in 16 cases, *i.e.* 26.7%; anemia in 50 cases (83.3%); and thrombocytopenia in 23 cases (38.3%). CRP: was obtained in 80 cases (92%), it was high in 59 cases (73.8%). Blood culture performed in 31 cases (36%), was positive in 14 cases (45.2%). Analysis of cerebrospinal fluid was obtained in 26 cases (30.2%), and a germ was isolated in 4 cases (15.4%). Stool culture was indicated in 3 cases (3.5%) and pyoculture in 2 cases, all positive (2.3%). Bacteria found were *Klebsiella* in 10/20 (25%), *Enterobacter* in 4/20 (20%), *E coli* and *Enterococcus* in 2/20 (10%) each see **Table 2**. According to the type of infection *Klebsiella* (45.4%), *Enterobacter* (27.3%), *E coli*

Table 1. Distribution of newborns hospitalized for LNNBI according to the clinical aspects.

Clinical aspects	n (effective)	%(percentage)
Fever	65	75.8
Respiratory distress	37	43
Decreased tonus	18	20.9
Primary reflex disorders	18	20.9
Cough	17	19.8
Seizures	12	14
Diarrhea	11	12.8
Jaundice	9	10.5
Altered consciousness	8	9.3
Behavior disorders	8	9.3
Vomiting	5	5.8

Fever (75.8%) and respiratory distress (43%) were the most predominant signs.

Table 2. Distribution of newborn hospitalized for LNNBI according to the type of bacteria.

Bacteria	n (effective)	% (percentage)
<i>Klebsiella</i>	10	25
<i>Enterobacter</i>	4	20
<i>Escherichia coli</i>	2	10
<i>Enterococcus</i>	2	10
<i>Pseudomonas</i>	1	5
<i>Citrobacter</i>	1	5
Total	20	100

Klebsiella (25%) and *Enterobacter* (20%) were the most found bacteria.

(18.2%) were found in community acquired infections and in Health acquired infections: *Klebsiella* (55.6%), *Enterococcus* (22.2%), *Pseudomonas* and *Enterobacter* in 11.1% of cases each see **Table 3**. Resistance to antibiotic were found in 100% of cases for Ceftriaxone and Ceftazidim, thus for Imipenem and meropenem there was not antibiotic resistance see **Table 4**.

The hospitalization mean length was 10.9 ± 5.3 days (extremes: 2 and 27 days). A favorable outcome was seen in 71 cases (82.5%), complications were observed in 3 cases (3.5%) represented by hydrocephalus. Death occurred in 12 cases (14%).

4. Discussion

The hospital frequency of late neonatal bacterial infection is 5.1% at the B-TH.

Table 3. Distribution of bacteria according to the type of infection.

Bacteria	community-acquired infection		Health Acquired Infection	
	n (effective)	% (percentage)	n (effective)	% (percentage)
<i>Klebsiella</i>	5	45.4	5	55.6
<i>Enterobacter</i>	3	27.3	1	11.1
<i>Escherichia coli</i>	2	18.2	-	
<i>Enterococcus</i>	-	-	2	22.2
<i>Pseudomonas</i>	-	-	1	11.1
<i>Citrobacter</i>	1	9.1	-	
Total	11	100	9	100

klebsiella came first regardless of the type of infection followed by: -*Enterobacter* in community-acquired infection; -*Enterococcus* in Health Acquired Infection.

Table 4. Distribution of type of bacteria according of antibiotic resistance.

	<i>Klebsiella</i> n = 10	<i>Enterobacter</i> n = 4	<i>E. coli</i> n = 2	<i>Pseudomonas</i> n = 1	<i>Enterococcus</i> n = 2
<i>Amoxicillin</i>	100	NP	100	NP	NP
<i>Amox Ac clav</i>	NP	NP	100	NP	50
<i>Ceftazidim</i>	80	50	100	100	NP
<i>Cefotaxim</i>	NP	50	0	0	0
<i>Ceftriaxone</i>	100	100	100	100	100
<i>Imipenem</i>	0	0	0	0	0
<i>Méropenem</i>	0	0	0	0	0
<i>Gentamycin</i>	100	75	0	NP	NP
<i>Amikacin</i>	0	0	NP	NP	NP
<i>Ciprofloxacin</i>	50	75	NP	100	0
<i>Vancomycin</i>	10	0	0	NP	50

Acronym: NP = not specified; Amox Clav AC = amoxicillin Clavulanic acid; *E. coli* = *Escherichia coli*. Resistance to antibiotic were found for Ceftriaxone and Ceftazidim (100%) of cases, thus for Imipenem and meropenem there was not antibiotic resistance see.

This frequency is similar to that of Vergnano *et al.* in England (6.1%), Hammoud in Kuwait (7.3%) [15] [16]. Higher frequencies are observed by Tsai *et al.* in Taiwan (14.2%) and Van den Hoogen in the Netherlands (13.9%) [9] [17] [18]. The methodological differences, in relation to the age of recruitment, justify the discrepancies observed between the different studies.

In our study, health acquired infection represents 1.1% of the causes of hospitalization. The frequencies of health acquired infections vary between countries and between neonatal intensive care units in the same country. Nejari and

Maoulainine in Morocco have a respective frequency of health acquired infection of 2.03% and 13% [19] [20]. In France, it is 5.9% [21], in Turkey 6.4% and in China the frequency is 0.8% [22] [23]. The high frequencies in these different departments are mainly due to the more important practices than in our department of invasive procedures recognized as risk factors of health acquired infection [11] [24].

Classically, LNNI are acquired postnatally from the child's environment. Transmission is horizontal from the mother or made by caregivers when handling the child [18]. Other risk factors are prematurity, a history of prolonged hospitalization and broad-spectrum antibiotic therapy, prolonged parenteral nutrition and prolonged mechanics ventilation [18]. We reported risk factors in 67.4% of cases. These are: neonatal resuscitation (39.7%), previous hospitalization (36.2%) and previous antibiotic therapy (24.1%). These factors have been reported by various authors at varying frequencies [9] [12] [22].

The clinical signs of neonatal bacterial infection, whether early or late, are not very specific, hence the variability of clinical signs. Fever (75.6%), respiratory distress (43%), hypotonia and primary reflex disorders (20.9% of each) were the most frequent signs in Brazzaville. Zhinling in China reports fever (53.06%), jaundice (30.6%) and weak response to stimuli (34.69%) [25]. Mishra *et al.* in Nepal reported feeding difficulties, thermal disturbances, incessant crying, irritability and lethargy [26].

The most frequent infectious sites during our study are bacteremia (37.2%) and pneumopathy (24.4%) overall and according to nosological entities. Our results are similar to those reported by Jaballah in Tunisia, and Chemsî and Abba *et al.* in Morocco [11] [12] [27] on a population of children hospitalized for a health acquired infection. For Abba, bacteremia and pneumopathy are associated respectively with the umbilical venous catheter and mechanical ventilation. In our practice, these localizations can be associated with peripheral venous infusion, oxygen support with nasal tube and manipulations of the entourage. The meningeal location, 12.8% in our study, is reported by Abba in 3.3% of cases in his population. The absence of urinary tract infections is attributable to the non-practice of urine culture in the department.

In our study, gram-negative bacilli were responsible for 90% of cases of neonatal bacterial infections. According to the nosological entities, gram-negative bacilli are involved in 100% of community-acquired infections and 77.8% of health acquired infections. *Klebsiella* represent 50% of germs. This was also observed in others countries and clinics in which Gram-negative bacilli including *E. coli*, *Klebsiella*, and *pseudomonas* species are in the forefront [8].

Seboui *et al.* in Tunisia [28] observe that gram-negative bacilli are responsible for 89.7% of community infections, the germs being *E. coli* and *Enterobacter sp.* These same authors also report a majority of health acquired infection in Gram-negative bacilli (95.45%), *Klebsiella* (45.45%) is the most frequent germ [28]. Pathak in India [29] has a predominance of *Staphylococcus aureus* followed by *Klebsiella* and *E. coli* in community-acquired infections, and *Klebsiella*

in health acquired infections. In the United States [30] and others developed countries [1] coagulase-negative *Staphylococci* and *E. coli* are the main etiologies of late neonatal infections according to a review from 1928 to 2003. We are witnessing a transition in bacterial ecology, *Klebsiella* and other *Enterobacteriaceae*, once known to be responsible for health acquired infections, are today also responsible for community infections as observed in our study and in those carried out by other authors [16] [31] [32].

The germs involved in late neonatal bacterial infection at the B-TH are multi-resistant to common antibiotics, in particular *Klebsiella*, the most common germ is resistant to amoxicillin and ampicillin (100%), ceftazidime (80%), ceftriaxone (100%) and gentamicin (100%). Antibiotics remaining active on germs in our practice are Imipenem, Meropenem, Ciprofloxacin and Vancomycin. Resistances of varying degrees have been reported by Shehab El-Din, Tallur, and Mohsen [31] [33] [34]. Antibiotic resistance in bacteria is now a public health problem according to the WHO [35]. Inappropriate prescriptions of antibiotics, their use in self-medication and in animal husbandry are the main causes of the emergence of resistance [35].

This study has enabled us to achieve our objectives nevertheless as all research work there are some limitations. Firstly, link to the methods of the study, it was a monocentric, hospital-based study so results found can't be generalized to the entire population. Secondly financial constraint, this study is carried out in a developing country where there is no social security in the health care system, thus all care is charge to parents who had low-income resource in 76% of cases.

5. Conclusion

Late neonatal bacterial infection is common. Clinical symptoms and localizations are usual. The main responsible germs are gram-negative bacilli, in particular *Klebsiella*. These multi-resistant germs lead us to recommend as therapeutic measures the strengthening of asepsis measures and the limitation of the prescription of antibiotics.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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