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Original Research Article

Epidemiological and bacteriological profile of neonatal bacterial infections seen in hospital pediatric in Antananarivo

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ABSTRACT

Background: Neonatal bacterial infection is one of the leading causes of new-born morbidity and mortality. Bacterial ecology is not known in our unit, no study has been devoted to this subject. This work aimed to determine the germs responsible for neonatal bacterial infections and their level of sensitivity to the usual antibiotics.
Methods: This is a retrospective descriptive study conducted in the Neonatology Department from January 1, 2018 to April 30, 2019 (16 months) including all newborns under 29 days hospitalized during the study period and possessing positive bacteriological results regardless of the site of collection (blood, urine, cerebrospinal fluid).
Results: The diagnosis of neonatal infection was confirmed in 47 cases, i.e. 26.1% of suspicions of neonatal bacterial infection hospitalized during the study period. The female predominance was found with a sex ratio of 0.81. The most frequently isolated germs are, in order of frequency, coagulase-negative *staphylococci* (10 cases), *Escherichia coli* (7 cases), *Enterobacter cloacae* (5 cases), *Klebsiella pneumoniae* (5 cases) and *Enterobacter aerogenes* (5 cases). Of the 47 cases studied, 16 cases were multidrug-resistant infections including 7 cases i.e. 14.9% of nosocomial infections. The majority of Enterobacteria are strains producing broad spectrum beta lactamases (12 cases to 22). The molecules that remained effective were mainly Imipenem and Amikacin.
Conclusions: Neonatal infection remains a real public health problem. The emergence of multi-resistant bacteria complicates the management. The knowledge of bacterial ecology on a wider population is an important asset in its prevention and management.

Keywords: Bacteriology, Multi-resistant bacterium, Neonatal infection, New-born

INTRODUCTION

Neonatal bacterial Infection (NNI) remains a major public health problem due to its high morbidity and mortality. Indeed, the World Health Organization (WHO) estimates the global occurrence of neonatal deaths at 2.8 million in 2015 and 47.6% are due to neonatal infection.[1] Neonatal mortality is falling too slowly, especially in Africa. These infections were the leading cause of hospitalization and the second leading cause of death for several African countries.[2] The main direct causes of neonatal mortality are prematurity (29%), serious infections (25%) and per natal asphyxia (23%) or their association.[2] Added to this is the emergence of multi-resistant bacteria during the last three decades which constitute a major problem by the cost, and the morbidity and mortality that they generate.[3] The epidemiology of primary and nosocomial bacterial infections varies over time and countries, which makes it impossible to extrapolate therapeutic proposals from one country to

another, both for the treatment of primary and secondary infections.[1,2] The bacterial ecology within hospital has not been studied to date. This led us to conduct this study to determine the epidemiological and bacteriological profile of neonatal bacterial infections in hospitalized newborns and their sensitivity to commonly prescribed antibiotics.

METHODS

The study was carried out at the Mother and Child Hospital Center at Tsaralalàna (CHUMET), in the Neonatology Department. This was a hospital seen at the downtown of Antananarivo, capital of Madagascar. This was a monocenter retrospective descriptive study from January 2018 to April 2019. The period of study was 16 months. All newborns under 29 days hospitalized during the study period and with positive bacteriological findings regardless of the site of collection (blood, urine, cerebrospinal fluid) were included in the study. Patients whose file was incomplete and/or microbiology was positive to *bacillus Koch* were excluded. The variables studied were the socio-demographic parameters of the patient (gestational age, age, gender, birth weight, neonatal resuscitation), the maternal pathologies during pregnancy, the modalities of delivery (vaginal or cesarean delivery), the adaptation to extrauterine life, the clinical and bacteriological parameters on admission, the sensitivity of the various germs to the usual antibiotics as well as the duration of hospitalization and the outcome of patients. All newborns included received one or more bacteriological examinations: either a blood culture, a cytobacteriological examination of the urine (ECBU) or a cytobacteriological examination of the Cerebrospinal Fluid (CSF).

The data was captured and analyzed on Epi-Info version 7 of the CDC/ WHO. Author used descriptive statistics to calculate frequencies and percentages. In some cases, author have also used PEARSON's Chi-square test to verify the binding force between the quantitative variables. The critical threshold of 0.05 was adopted to declare statistical significance.

The confidentiality of the information contained in the patient file has been respected.

RESULTS

Of the 180 hospitalized newborns suspected of having neonatal bacterial infection during the study period and who had undergone bacteriological examination, 56 cases (26.1%) met the inclusion criteria and 09 were excluded for incomplete records. A clear predominance of women was found with a sex ratio of 0.81. The average age was 6.07 +/- 2 days with extremes of 0 to 27 days. The vast majority were less than 7 days of life on admission (29 cases i.e. 61.7%). Nine newborns (19.1%) were born premature and 28 included, i.e. 46.8% had a birth weight of less than 2500 g. The most common infectious risk factors were prematurity (27 cases i.e. 57.4%), pathological leucorrhoea (23 cases i.e. 48.9%) and poor adaptation to extra uterine life (20 cases i.e. 42,6%) (Figure 1) Delivery mode was vaginal in 93.62% (44 cases) without the use of instrumental maneuvers and 10 were resuscitated at birth (Table 1).

Table 1: Socio-demographic parameters of the patient.

Paramètres		Frequency (n=47)	Percentage (%)
Gestational Age (WA)	< 34	4	8,51
	34 A 36	5	10,64
	≥ 37	38	80,85
Age (days)	<7	29	61,70
	≥ 7	18	38,30
Gender	Male	21	44,68
	Female	26	55,32
Birth weight (gram)	<1500	4	8,51
	1500 A 2500	18	38,30
	> 2500	25	53,19
Modalities of delivery	Vaginal delivery	44	93,62
	Caesarean delivery	3	6,38
Néonatal ressuscitation	Yes	10	21,28
	No	37	78,72

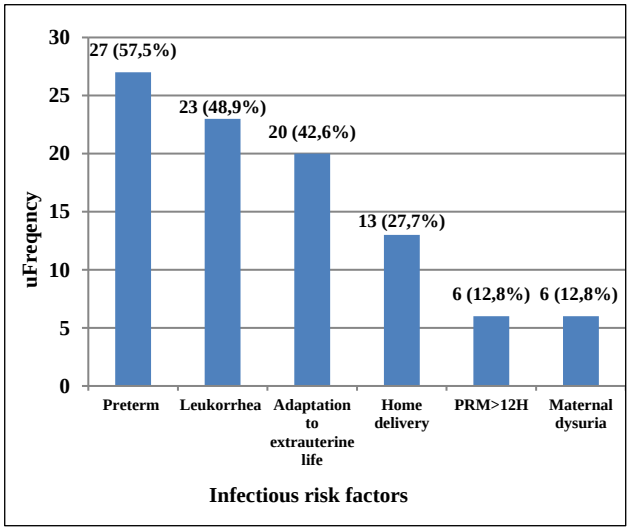

Figure 1: Infectious risk factors in new-borns included.

The most prominent clinical manifestations at the entrance were respiratory distress (21 cases or 44.7%), thermal dysregulation (21 cases or 44.7%) and neurological disorders (21 cases or 32.8%). Early neonatal bacterial infection was the most common in 61.7% (29 cases) of which in the very early neonatal period 48.98% (23 cases) was the first 72 hours of life in this study population. Outpatient diagnosis were sepsis

with no obvious call point (42 cases, 89.4%), neonatal meningitis (3 cases, 6.4%) and acute pyelonephritis (2 cases, 4.3%). Beta lactamases and aminoglycosides were the therapeutic classes prescribed in first-line treatment with a suspicion of neonatal bacterial infection at the beginning of hospitalization and were adapted according to the antibiogram.

The most common isolated were coagulase-negative *staphylococci* (10 cases), *Escherichia coli* (7 cases), *Enterobacter Cloacae* (5 cases), *Klebsiella pneumoniae* (5 cases) and *Enterobacter aerogenes* (5 cases) (Figure 2).

Table 2: Bacteriological parameters and patients' outcomes.

Bacteriological Parameters		Frequency (n=47)	(%)
Bacteriological examination	Blood	42	89,36
	Urine	2	4,26
	Cerebrospinal fluid	3	6,36
Type of infection	Community acquired infection	40	85,11
	Nosocomial infection	7	14,89
Bacteria found	Sensitive to usual antibiotics	34	73,34
	Multi-resistant bacteria	13	27,66
Length of stay (days)	< 5	6	12,76
	5A10	18	38,30
	> 10	23	48,94
Patient outcome	Recovered	36	76,60
	Deceased	11	23,40

Table 3: Resistance profile of the main germs encountered.

Isolated bacteria	Sensitive to usual antibiotic		Multi-resistant bacteria	
	Frequency (n=47)	(%)	Frequency (n=47)	(%)
Coagulase-negative staphylococcus	9	19.15	1	2.13
Escherichia coli	5	10.67	2	4.25
Enterobacter aerogenes	2	4.25	3	6.38
Enterobacter cloacae	0	0	5	10.67
Klebsiella pneumoniae	3	6.38	2	4.25

Of the 47 cases studied, 13 cases or 27.7% were Multi-resistant bacterial infections (Table 3) including 7 cases of nosocomial infections or 14.9%. The majority of Enterobacteria were strains producing Broad-Spectrum Beta Lactamases (ESBL). The resistance profile of the main bacteria to the different antibiotics is summarized in Table 4. The molecules that remained effective were mainly Imipenem and Amikacin. The duration of hospitalization was 11 +/- 4 days on average, with extremes of 1 to 99 days. Author deplored 11 cases of deaths (23.4%) among the cases retained in the study (Table 2).

Table 4: Pharmacological antibiotic sensitivity patterns.

Bacterial isolated	Antibiotic resistance
Coagulase-negative staphylococcus	Ampicillin, amoxicillin, amoxicillin-clavulanic acid, cefixime, gentamicin, chloramphenicol
Escherichia coli	Amoxicilline, amoxicillin-clavulanic acid, ceftriaxone, cefixime, gentamicine, ciprofloxacine, trimethoprim-sulfamethoxazole
Enterobacter aerogenes	Amoxicilline, amoxicillin-clavulanic acid, ceftriaxone, cefixime, gentamicine, ciprofloxacine, tobramycin, nitrofuran
Enterobacter cloacae	Amoxicillin, amoxicillin-clavulanic acid, ceftriaxone, quinolone
Klebsiella pneumoniae	Amoxicilline, amoxicillin-amoxicillin-clavulanic acid, ceftriaxone, cefixime, gentamicin, ciprofloxacin, nitrofuran

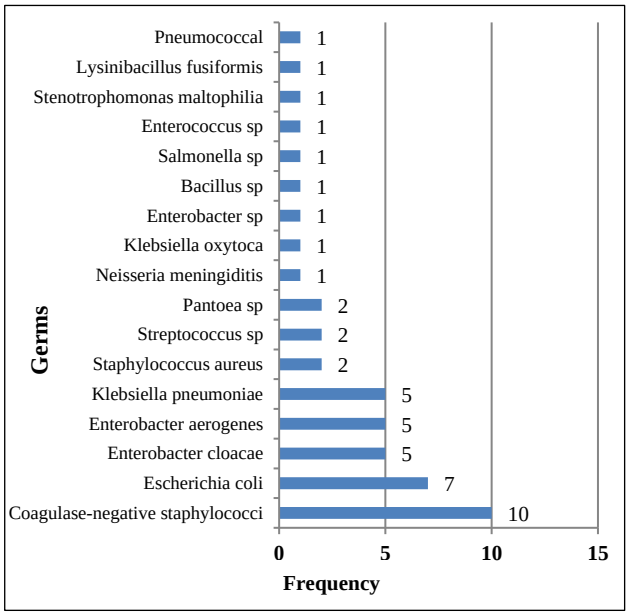

Figure 2: Germs responsible for neonatal infections.

In bivariate analysis, author did not identify any factors significantly related to neonatal morbidity and mortality.

DISCUSSION

The literature data on primitive or nosocomial neonatal bacterial infections are diverse and varied. Studies have already been carried out in some hospitals in Madagascar, but they are not many.[4-6] This study is the first in author's institution. Bacterial ecology in the neonatology department at CHUMET has not been studied before. Being monocentric and retrospective, it has some limitations. Sample size did not provide conclusive results for neonatal morbidity and mortality. Antibiotic intake by mother or newborn before hospitalization is unknown. Bacteriological examinations were very limited because of their high cost for most hospitalized patients and incomplete clinical data were classified as exclusion criteria. Only newborns with positive bacteriological findings were included in the study. This study will serve as a database for future research to improve the management of hospitalized neonates for primary or nosocomial bacterial infections. The importance of this study lies in the fact that it can highlight information necessary to make important decisions to permanently inflect the trend of neonatal mortality but equally the rate of Multi-resistant infection that is currently in full emergence.[2,3]

Maternal, neonatal and infant mortality remains the most important indicators of the state of any community health.[4] The high vulnerability of newborns was found in this study.[4-6] Author also confirm that this population alone accounts for a large part of the global morbidity and mortality rate.[5] The high proportion of neonatal bacterial infections found in this study is consistent with literature.[3-6] The risk attributed to the female gender was found with a sex ratio of 0.81, unlike in the literature where male predominance is reported by several authors.[7]

Early neonatal infection was the most common in 61.7% (29 cases), of which 23 cases in the first 72 hours of life most often reflecting vertical transmission from mother to child before or during delivery.[8] This trend of frequent early neonatal infection was lower compared to that found in Douala in 2015 by Kemeze (96.8%) but higher than that of Chiabi in Yaounde in 2011 (34.7%) and by Chemsi in Casablanca in 2015 (6.2%) where prevalence was significantly lower.[7-9] This can be explained by differences in the definition of early neonatal infection. Indeed, some authors consider the early neonatal period as that which goes from 0 to 3 days.[10] In this study, author used the definition of the National Agency for Health Accreditation and Assessment which considers the early neonatal period as 0-7 days. Premature and low birth weights accounted for a significant proportion of inclusions similarly to studies in Douala, Yaoundé and Fianarantsoa.[2,5,8] Infection was therefore frequent in premature infants and that joins the results of other African as well as European studies.[10,11] This observation could be explained by the fact that premature infants are weak because of their immaturity which exposes them more than others to infections. The most common infectious risk factors apart from prematurity were pathological leucorrhea (23 cases i.e. 48.9%) and poor adaptation to ectopic life (20 cases 42.5%). For Kemeze et al, neonatal resuscitation and Prolonged Membrane Rupture (PMR) were the most common associated factors.[7] In Cameroon, Chiabi et al, in 2011 found neonatal resuscitation, PMR and peripartum fever as the most frequent associated factors. Indeed, PMR, peripartum fever and unexplained prematurity are major criteria for NINT defined by ANAES.[8] Most infected neonates were of low birth weight (<2500 g). These results are similar to several African studies.[10] They are different from that of Chabni et al, in Algerian as they found a low representation of low birth weight in the infection.[11] This predominance of infection in low birth weight could be explained by the fact that this study population was dominated by low birth weights and premature infants, unlike that of Shah et al, where most of the newborns had a birth weight ≥2500 g. Thermal regulation disorders, neurological disorders and respiratory distress, which represent the clinical manifestations most frequently found in neonatal bacterial infection, were also found in this study, however, with a clear predominance of respiratory distress. Besides, thermal dysregulations have been dominated by hypothermia in author's series. Author had 47 positive bacterial cultures out of 180 made, an incidence of IBN positivity of 31% similar to those of Kemeze et al, and Chiabi et al.[7,8]

Isolated organisms and their antibiotic resistance profile allowed us to classify infections as primary or nosocomial neonatal bacterial infection, but also as neonatal bacterial infection with susceptible or Multi-resistant organisms. The overall bacterial profile in series, revealed a predominance of Cocci Gram positive with *coagulase-negative staphylococcus* in the first position and Bacteria Gram Negative (BGN) with *Escherichia Coli* in the lead. Next are *Enterobacter Cloacae* (5 cases), *Klebsiella Pneumoniae* (5 cases) and *Enterobacter Aerogenes* (5 cases). This finding is similar to that of Kemeze et al, who found 44% of CGP and joining the studies made by Andrianarivelo et al, at Befelatanana with 41.08% *coagulase-negative staphylococci*.[4,7] It was also the most common germ in India in a study conducted by WHO in 2015 in six developing countries.[10] Concerning BGN, the results are similar to those of Chiabi et al, at Bertoua in Cameroon.[12] It has also been found in other countries such as Morocco in 2015, Tunisia in 2013 and India in 2015.[6,9,13] These results explain the first-line prescription of betalactamines associated with aminoglycosides in this study, with a suspicion of neonatal bacterial infection at the beginning of hospitalization. The most common clinical form was sepsis (89.4%). This result corroborates that found by Chiabi et al, in 2011.[5] Author found in author's series 03 confirmed cases of neonatal meningitis and 02 cases of

acute pyelonephritis which is much lower than those of Chiabi et al, and Kemeze et al.[7,8]

With respect to antibiotic susceptibility, infections with *Coagulase-negative staphylococci* (9 out of 10 cases) and *Escherischia coli* (5 out of 7 cases) had good sensitivity to betalactamine. The majority of Enterobacteriaceae were strains producing broad-spectrum beta lactamases (ESBL). The bacteriological profile of nosocomial infections dominated by BGN in this study was comparable to that reported in studies conducted in Casablanca, Cameroon and other developing countries.[8-10] This bacteriological profile was dominated by PGCs in developed countries.[10,14-16] The two *Escherichia coli* infections with ESBL-producing strains were community-acquired infections suggesting vertical maternal-fetal transmission resistant to most antibiotics tested but with good sensitivity of Imipenem and Amikacin. The 05 cases of Multi-resistant enterobacterial infections, all nosocomial, were Multi-resistant to Amoxicillin, Amoxicillin-Clavulanic Acid, Ceftriaxone, Cefixime, Gentamycin and Ciprofloxacin. *Klebsiella pneumoniae*, on the other hand, was sensitive to ciprofloxacin, which left us a cheaper alternative when the patient was unable to obtain Imipenem because of the high cost of this antibiotic. The resistance pattern of isolated organisms in this study is consistent with most African studies. In Morocco, negative grams were sensitive to third generation cephalosporins C3G (100%) and Ampicillin (48%) while in India they had better sensitivity to imipenem (92.8%), Amikacin (77.2%), Cefotaxime (66.7%) and Ampicillin (66.7%).[3,17] In Morocco, ampicillin had a better sensitivity on positive grams.[3] In India, PGC susceptibility was found to Vancomycin (100%), Cefotaxime (100%), Gentamycin (86%) and Ciprofloxacin (66.7%).[3]

Of the 47 newborns included in this study, author deplored 11 deaths, a rate of 23.40% which is lower compared to those found in Togo (33%), lower than the results of Cameroon (46.7%), Abidjan (26.7%) but much higher than those of Chiabi in Bertoua (5.2%).[2,7,8,10] Death rate can be explained by the reference delay since hospital does not have maternity, the unsuitable conditions of transport of newborns, the large proportion of premature newborns and low birth weights and poor compliance with laboratory examination and treatment due to lack of financial means.

CONCLUSION

At the end of this study, neonatal bacterial infections remain a real global public health problem. CGP and BGN are the bacteria most found in ecology with a very variable antibiotic resistance profile but confirming the emergence of Multi-resistant bacteria either in primary or nosocomial infections. They strongly suggest the need to improve prevention and control measures for mainly nosocomial bacterial neonatal infections, with emphasis on simple and important measures such as hand hygiene in hospitals or limited and rational use of antibiotics. Particular attention to compliance with antibiotic use rules and the need to establish epidemiological surveillance of nosocomial infections in hospitals in Madagascar is essential.

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