

# Profile of Newborns Hospitalized for Maternal Fetal Infection and Having a Positive CRP in the Pediatric Department of the Gabriel Touré CHU in Bamako, Mali

Oumar Coulibaly<sup>1\*</sup>, Hawa Gouro Diall<sup>1</sup>, Guédiouma Dembélé<sup>2</sup>, Mamary Coulibaly<sup>1</sup>, Fatoumata Léonie Françoise Diakité<sup>1</sup>, Lala Ndrayni Sidibé<sup>1</sup>, Leyla Maiga<sup>1</sup>, Ibrahima Ahamadou<sup>1</sup>, Abdoul Karim Doumbia<sup>1</sup>, Belco Maiga<sup>1</sup>, Adama Dembelé<sup>1</sup>, Pierre Togo<sup>1</sup>, Karamoko Sacko<sup>1</sup>, Mohamed Elmouloud Cissé<sup>1</sup>, Djeneba Konaté<sup>1</sup>, Fousseyni Traoré<sup>1</sup>, Aminata Doumbia<sup>1</sup>, Yacouba Aba Coulibaly<sup>1</sup>, Amadou Touré<sup>1</sup>, Bourama Kané<sup>2</sup>, Issa Amadou Touré<sup>3</sup>, Abdoul Aziz Diakité<sup>1</sup>, Traoré Fatoumata Dicko Traoré<sup>1</sup>, Mariam Sylla<sup>1</sup>, Boubacar Togo<sup>1</sup>

<sup>1</sup>Department of Pediatrics, CHU Gabriel Touré, Bamako, Mali

<sup>2</sup>Department of Pediatrics, Mali Hospital, Bamako, Mali

<sup>3</sup>Department of Pediatric Surgery, CHU Gabriel Touré, Bamako, Mali

Email: \*cheickcoull@live.fr

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## Abstract

**Objective:** Early bacterial neonatal infection (INBP) or maternofetal infection (early neonatal sepsis) remains a concern of the pediatrician due to diagnostic difficulties and its increased morbidity and mortality. No study has been done in Mali on the profile of newborns admitted for INBP with positive CRP, hence the initiation of this work with the aim of studying the epidemiological, biological and bacteriological profile of newborns with a bacterial maternal-fetal infection. **Method:** Longitudinal study descriptive (from 27 June to 3 September 2016) which concerned all newborns aged from 0 to 72 hours of life hospitalized for confirmed early bacterial neonatal infection with a positive C-reactive protein (CRP) in the neonatal department of the CHU Gabriel Touré. INBP was defined by the presence of maternal and neonatal infectious risk factors, positivity of CRP with a germ in the blood culture. **Results:** During the study period we included 244 newborns for probable maternofetal infection and who benefited from the CRP assay, 43 had a positive CRP, *i.e.* a frequency of 17.62%. The sex ratio was 2.30. The majority had a low birth weight (<2500 g) in 69.8% of cases. Mothers were aged 18 to 35 in 93%. The majority were out of school (43.8%) and housewives in 74.4%. The main reasons for consultations were prematurity and/or low birth weight, respiratory distress and neonatal distress, *i.e.* 46.5%, 25.6% and 11.6% respec-

tively. Among the 43 newborns with a positive CRP, the blood culture returned positive in 79.1% (n = 34). We deplore 2 deaths (4.7%). The main bacteria were gram-positive cocci (*Staphylococcus aureus* 53.01% and *Streptococcus agalactiae* 4.10%), gram-negative bacilli (GNB) type *Enterobacteriaceae* (*Klebsiella pneumoniae* 11.25% and *E. coli* at 5.70%) and non-fermentative GNBs (*Pseudomonas aeruginosa* 2.80% and *Acinetobacter baumannii* complex 2.24%). **Conclusion:** Maternal-fetal infection is a hospital pathology frequently encountered in the neonatal period. Its clinical presentation is dominated by respiratory distress, neurological disorders and low birth weight.

## Keywords

Early Bacterial Neonatal Infection, Clinical Profile, Neonatal Mortality

## 1. Introduction

Neonatal mortality remains a major public health challenge in the world with 2.7 million annual deaths, eighty percent of these deaths occur in the developing world in particular sub-Saharan Africa and South and South Asia [1] [2]. Currently, neonatal bacterial infections are the third leading cause of newborn death worldwide, behind prematurity and childbirth-related mortality, and account for 10% of deaths before the age of 5. The mortality gap between high- and low/middle-income countries may be explained by inadequate monitoring of some pregnancies, the lack of systematic screening for pre- and per-partum risk factors of INBP, and immediate postnatal surveillances of the newborn in poorly done maternity hospitals are factors that increase the morbidity and mortality of INBP in developing countries [3]. The etiology of early bacterial neonatal infections (INBP) also differs depending on the level of development. In industrialized countries, group B streptococcus (GBS) remains the predominant germ [4], despite systematic screening between the 34<sup>th</sup>-35<sup>th</sup> week of pregnancy and intrapartum antibiotic therapy in the event of colonization [5]. In developing countries, early neonatal bacterial infections (INBP) are mainly caused by multi-drug-resistant gram-negative bacilli with increased neonatal mortality rate, particularly *Escherichia coli* and *Klebsiella* spp. [3] [6] [7] [8]. This is due to the lack of financial means for access to the best-indicated antibiotics in these developing countries [9]. Specific and sensitive early markers, with a high negative predictive value, would therefore be particularly appreciated in neonatal medicine. The neonatologist will mainly use the complete blood count, C-reactive protein (CRP) by repeating the assays and sometimes the blood culture. In the neonatal department of the Pediatrics Department of the CHU Gabriel Touré, neonatal infection is the third leading cause of hospitalization and death after prematurity and perinatal asphyxia [10]. In the African context, knowledge of an epidemiological and clinical profile of confirmed neonatal bacterial infection is necessary to ensure rapid treatment, especially in regions where the performance of con-

firmatory diagnostic examinations is not possible. where the initiation of this study on the epidemiological and clinical profile of newborns admitted for maternofetal infection with a positive CRP in order to improve our practice.

## 2. Material and Methods

The study took place in the neonatology service of the pediatrics department of the CHU Gabriel Touré in Bamako. It is the only national reference service for the care of newborns in Mali. We carried out a prospective cross-sectional study that focused on the clinical and biological characteristics of hospitalized newborns from June 27 to September 3, 2016 ((2 months and 8 days)). Newborns less than or equal to 72 hours hospitalized for suspected early neonatal sepsis (maternal and neonatal infectious risk factors and/or clinical signs) in the neonatal service of the pediatric department of the CHU Gabriel Touré in Mali have been included in this study. The suspicion of INBP was based on the presence of maternal and neonatal infectious risk factors and/or clinical signs. The following immediate pre, per and postpartum infectious risk factors were retained: rupture of membranes greater than or equal to 18 hours, rupture of the water bag before 37 weeks, maternal fever greater than 38°C in 48 hours before or after childbirth, maternal genital and/or urinary tract infection in the last month of pregnancy, tinted or meconium amniotic fluid, unexplained fetal distress or prematurity, twin with confirmed BNI, respiratory problems and/or unexplained neonatal heart disease. When at least one of these factors was present, a blood culture was performed on admission, as well as the C-Reactive Protein (CRP) at the 12 hours of life and the complete blood count (CBC) at the 24<sup>th</sup> hour of life. The blood sample for blood culture was inoculated on fresh sheep blood agar (5%) and on cooked blood agar supplemented with Polyvitex. The incubation was done for 24 to 48 hours under 5% CO<sub>2</sub>. An antibiogram by diffusion in agar medium was carried out on all the isolated strains. Partial results of the fresh state (presence or absence of leukocytes and bacteria) were communicated to the clinicians after 24 to 48 hours to allow them to orient their therapeutic approach. Thus, the following operational definitions have been adopted:

- A confirmed case of INBP: any newborn baby at most three days old presenting one or more clinical and/or biological signs with positive blood culture.
- A suspected case of INBP: any newborn with at least one infectious criterion in the history associated with one or more clinical and/or biological signs with negative blood culture.

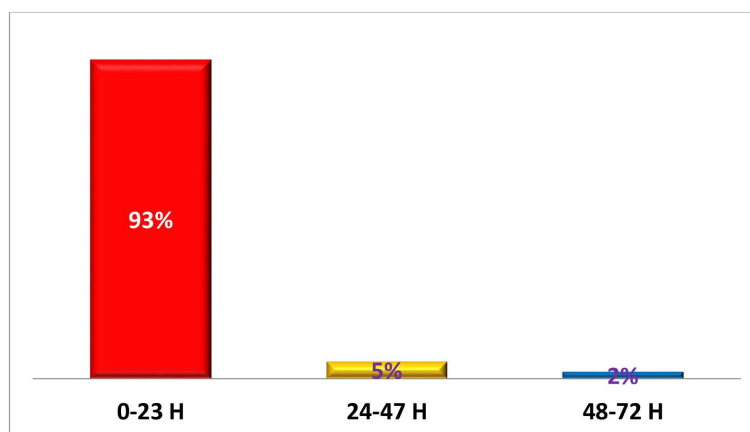
### Data processing

Data were entered and analyzed on SPSS software.

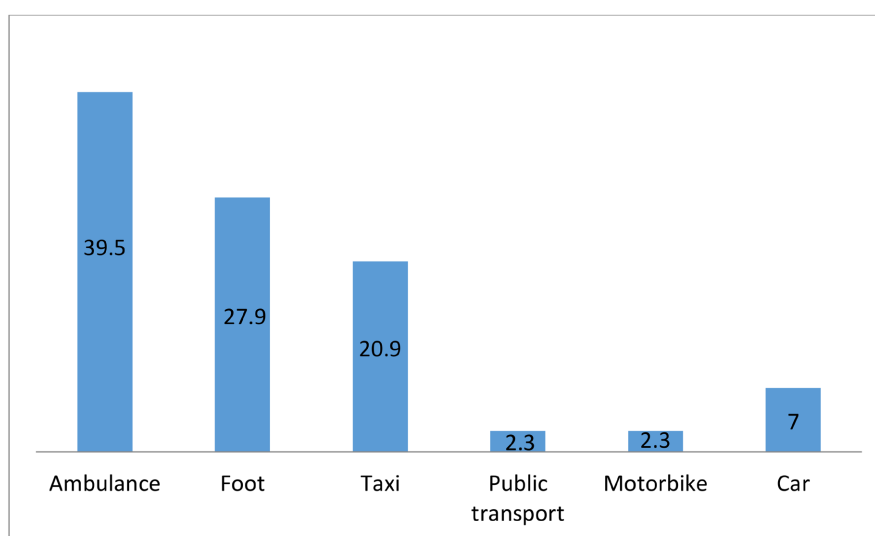
## 3. Results

During the study period, we included 244 newborns for probable maternofetal infection and who benefited from the CRP assay, 43 had a positive CRP, *i.e.* a frequency of 17.62%. There were 30 male (57.7%) and 13 female (42.3%) new-

borns, for a sex ratio of 2.30. The majority of newborns ( $n = 68$  [93%]) were admitted within the first 24 hours of life (**Figure 1**), the majority had a low birth weight ( $<2500$  g) in 69.8% of cases. In 39.5% of cases the newborns were referred to the ambulance. Mothers were aged 18 to 35 in 93%. They were mostly out of school (43.8%), primary level (27.2%), secondary (17.6%) and housewives in 74.4%. The majority of mothers had less than 4 ANC (67.4%) and 32.6% had 4 or more ANC. Vaginal delivery was the most frequent (81.4%), the Apgar score at the first minute was  $>7$  in 27.8% of cases and unspecified (62.8%), at the fifth minute it was  $>7$  in 39.5% of cases and not specified (60.5%). The vast majority of newborns made the consultation within the first 24 hours of life (86%). The ambulance was used as a means of transport in only 39.5% of cases (**Figure 2**). The main reasons for consultations were prematurity and/or low birth weight, respiratory distress and neonatal distress, *i.e.* 46.5%, 25.6% and 11.6% respectively (**Figure 3**). Anamnestic risk factors for infection were dominated by prematurity  $< 35$  weeks, maternal fever  $\geq 38^{\circ}\text{C}$ , unexplained fetal distress, opening

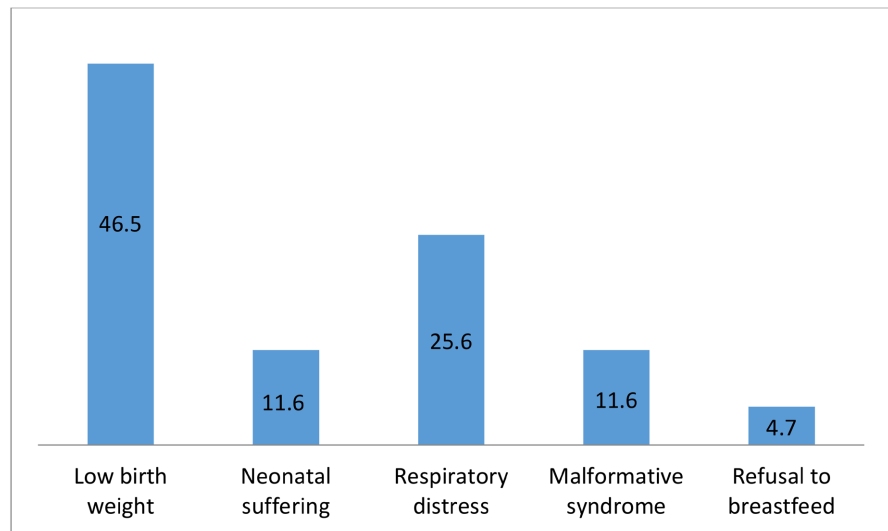


**Figure 1.** Age at admission.



**Figure 2.** Means of transport.

of the water bag > 18 hours, and fetid or meconium amniotic fluid, respectively 32.6%, 20.9%, 20.9%, 11.6%, 11.6% (**Table 1**). Among the 43 newborns with a positive CRP, the blood culture returned positive in 79.1% (n = 34). We deplore



**Figure 3.** The main reasons for consultation.

**Table 1.** Anamnestic risk factors for maternal-fetal infection.

Criteria	Frequency (n=43)	Percentage (%)
<b>Major anamnestic criteria for infection</b>		
Prematurity <35 SA	14	32.6
Maternal temperature $\geq 38^{\circ}$	9	20.9
Rupture of the water pocket before 37 SA	3	7
Opening of the water bag $\geq 18$ h	5	11.6
Twin diagnosed with maternal fetal infection	0	0
Clinical picture of chorioamnionitis	1	2.3
<b>Minor anamnestic criteria for infection</b>		
Unexplained fetal distress	9	20.9
Tinted or meconial amniotic fluid	5	11.6
Opening of the water bag $\geq 12$ h	0	0
Premature 35 weeks	2	4.7
<b>Other criteria</b>		
Fetid leucorrhoea	16	37.2
Dysuria	6	14
Urination burns in the last trimester	10	23.3
Maternal genitourinary infection	2	4.7
Home birth	0	0

2 deaths (4.7%). The main bacteria were gram-positive cocci (*Staphylococcus aureus* 53.01% and *Streptococcus agalactiae* 4.10%), gram-negative bacilli (GNB) type *Enterobacteriaceae* (*Klebsiella pneumoniae* 11.25% and *E. coli* at 5.70%) and non-fermentative GNBs (*Pseudomonas aeruginosa* 2.80% and *Acinetobacter baumannii* complex 2.24%).

#### 4. Discussion

Bacterial neonatal infection is the third cause of hospitalization at CHU Gabriel Touré with a frequency varying from 16.2% to 22.5% during the 2008-2012 five-year term [10]. The 2016 study carried out on confirmed BNIs revealed a frequency of 11.04%. Prior to 2008, the true frequency of INBP could not be appreciated. According to international literature, INBP is a common cause of hospitalization and is responsible for one-third of perinatal mortality [11]. In the present study, the overwhelming majority (93%) of hospitalized newborns were less than 24 hours old and 72.9% of outborn transfers were medicalized in only 39.5%. We know that improving the referral system for newborns leads to a reduction in neonatal morbidity and mortality [12]. In our study, seven out of ten newborns were premature and/or hypotrophic (69.8%). The frequency of premature babies was higher than that generally found in the literature, between 6 and 51.4% [13] [14]. This high rate of prematurity could be linked to illiteracy (63.5%), insufficient antenatal consultations and poor qualities, the existence of major maternal infectious risk factors. However, according to Vial-Courmont *et al.*, prematurity increases the risk of infection and when neonatal infection occurs, it is severe from the outset and may be responsible for heavy mortality and significant neurological sequelae. The same authors noted that infection is six times more frequent in feverish childbirth [15]. In the current study, one in five mothers (20.9%) was feverish during childbirth. In our series, other anamnestic criteria were used; fetid leucorrhoea (37.2%), prematurity < 35 weeks (32.6%), urination burns during the last trimester (23.3%), unexplained fetal distress (20.9%), of the water bag  $\geq$  18 h and the tinted or meconium amniotic fluid (11.6% each) (Table 1). NF Coly and Col in Dakar had retained a predominance of the concept of tinted amniotic fluid, *i.e.* 30%, followed by prematurity 18% and premature rupture of membranes 12% [16]. In Togo, the study by Balaka [17] found as anamnestic criteria, meconium amniotic fluid (24%), rupture of membranes for more than 12 hours (21%) and unexplained prematurity (19%). On the other hand, the signs in front of the clinical picture are respiratory and neurological distress of 40% and 48% respectively. For Nouaïli, [18] respiratory disorders predominated in 36.1% of cases, followed by neurological disorders (13.2%). A newborn baby presented with oral thrush on admission. In our work, respiratory distress represented 25.6%. Studies [19] [20] have shown that CRP is a key tool in the management of newborns suspected of MFI, with a sensitivity of 80% to 90%. The role of CRP in the duration of antibiotic treatment has also been studied. Serial CRP measurements may be useful in monitoring response to

treatment of infected newborns, determining the duration of antibiotic therapy and to recognize possible complications [21] [22]. In a cohort of 60 newborns with precocious sepsis, Ehl *et al.* [23] demonstrated that, after initiation of antibiotic treatment, CRP increased further, peaking and then subsequently decreased after 16 hours, with a CRP value returning to normal again, which may indicate that the duration of the antibiotic treatment has been sufficient to allow the antibiotics to be stopped, provided the clinical condition of the child and the results of the tests bacteriological came back negative. Thus, CRP has been proposed as a key parameter in the decision to guide the duration of antibiotic therapy [24]. However, CRP was not the only endpoint evaluated in these studies. In fact, other criteria are included in the decision of whether to stop antibiotics or not, namely, the clinical condition and the results of blood cultures. The contribution of bacteriology to deciding on the duration of antibiotic therapy is limited by the low rate of positive blood cultures, which varies in the literature from 2% to 10.2% [25] [26]. In our study, bacteriology was positive in 79.10% of hospitalized newborns. In the study by Franz *et al.* [22] concerning nosocomial bacterial infections, antibiotic therapy has only been started in symptomatic newborns with an elevated CRP, allowing treatment to be reduced to 71% of symptomatic newborns; the positive blood culture rate was 10%. In the prospective study by the same author, published in 2004 [26], only 13 newborns suspected of bacterial infection among 1291 had a positive blood culture. Variations in frequency could be explained by the different methodologies used. In our study, the bacterial ecology found during these INBP by transmission of maternal origin in utero or during childbirth is similar to that usually mentioned in another study of the West African sub-region with predominance of *Staphylococcus aureus* [27]. This predominance of *Staphylococcus aureus* during INBP could be due to the infection or colonization of many pregnant women by this bacterium which is mostly found during pregnancy according to Balaka *et al.* and not necessarily in connection with the conditions of precarious asepsis in neonatal units in Africa south of the Sahara [27]. *Staphylococci* and *enterobacteria* isolated in samples from pathological pregnancies are responsible for manifestations such as chorioamnionitis, prematurity with severe neonatal infections [15]. This can be illustrated by this work on bacterial genital carriage in the last trimester of pregnancy, which induced lesions such as endocervicitis (25%) and vaginosis (19.7%) and be the cause of the INBP [28]. In Morocco [29], it is above all certain Gram-negative bacilli that are isolated during MFI. They are *E. coli*, *Klebsiella pneumoniae* and *Enterobacter*. In some western countries, we note the emergence of GNBs which represented 78% of the germs isolated (*Klebsiella Pneumoniae*: 36% and *Escherichia coli*: 11% versus Group B *Streptococcus*: 4.5%) [29]. In the present study, we note the absence of *Listeria monocytogenes*. This could be explained by the lack of testing for bacteria in the cerebrospinal fluid in this work. In Mali, between 2003 (nosocomial and community germs) and 2016 (community germs), there was the emergence of new



strains such as *Streptococcus agalactiae*, *Escherichia coli*, *Acinetobacter baumannii* complex, and *Klebsiella pneumoniae* [29] [30].

## 5. Conclusion

At the end of our study, it emerges that maternofetal infection is a hospital pathology frequently encountered in the neonatal period. Its clinical presentation is dominated by respiratory distress, neurological disorders and low birth weight. The bacterial ecology is dominated by *Staphylococci* and *Enterobacteriaceae* (*K. pneumoniae* and *E. coli*). The evolution is favorable in 95.3% of cases and the rate of neonatal death due to IMF is 4.7%.

## Conflicts of Interest

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

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