Democratic Republic of Congo
Ministry of Public Health

General Secretariat
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In Collaboration with the Kinshasa School of Public Health (KSPH)

Analysis of Bottlenecks Related to Demand, Supply, and Use of Antibiotics for the Treatment of Neonatal Sepsis in the DRC

In The Health Zones Of Bominenge (South Ubangui), Karawa (North Ubangui), And Kadutu And Bagira (South Kivu)

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(Translated from the French report) December 2015

With funding and technical support from Management Sciences for Health (MSH):
SIAPS Program and PROSANI Plus
and Save the Children (for the Global Technical Reference team of UNCoLSC for injectable antibiotics)

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CONTENTS

ABBREVIATIONS AND ACRONYMS

AFRINEST	African Neonatal Sepsis Trial
CDR	Central de Distribution Régionale des Médicaments (Regional Medicine Distribution Center)
CHW	community health worker
CHX	chlorhexidine digluconate 7.1%
C-IMCI	Community-based Integrated Management of Childhood Illness
COHZ	Central Office of Health Zone
DPM	Direction de la Pharmacie, du Médicament et des Plantes Médicinales (Directorate of Pharmacy, Medicines, and Medicinal Plants)
DPS	Division Provinciale de la Santé (Provincial Division of Health)
DRC	Democratic Republic of Congo
D10	Direction de la Santé de la Famille et de Groupes Spécifiques (Directorate of Family Health and Specific Groups)
ETAT	Emergency Triage Assessment and Treatment
FG	focus group
FEDECAME	Fédération des Centrales d'Achat et de Distribution des Médicaments (Federation of Central Purchasing and Distribution Services of Medicines)
GRH	General Referral Hospital
HC	Health Center
HZ	Health Zone
IM	intramuscular
IMCI	Integrated Management of Childhood Illness
IV	intravenous
KSPH	Kinshasa School of Public Health
LMIS	logistics management information system
MDG	Millennium Development Goals
MNCH	maternal, newborn, and child health
MPH	Ministry of Public Health
MSH	Management Sciences for Health
NEML	National Essential Medicines List
NPP	National Pharmaceutical Policy
PNAME	Programme National d'Approvisionnement en Médicaments Essentiels (National Procurement Program for Essential Medicines)
PNIRA	Programme National de lutte contre les Infections Respiratoires Aiguës (National Program for Acute Respiratory Infections)
PROSANI	Projet de Santé Intégré (Integrated Health Project)
PSBI	possible serious bacterial infection
SIAPS	Systems for Improved Access to Pharmaceuticals and Services
SNAME	Système National d'Approvisionnement en Médicaments Essentiels (National Essential Medicines Procurement System)
UNCoLSC	UN Commission on Life-Saving Commodities
WHO	World Health Organization

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SUMMARY

One of the principal causes of neonatal mortality remains neonatal sepsis, which causes nearly 500,000 deaths worldwide annually. In the Democratic Republic of Congo (DRC), the newborn mortality rate remains high at 28 per 1,000 live births. National policy recommends management of neonatal sepsis through hospitalization and a combination treatment of three injectable broad-spectrum antibiotics: an injectable β-lactam, such as ampicillin, benzylpenicillin, or procaine penicillin, associated with gentamicin and a third-generation cephalosporin. However, implementation of the recommended hospital treatment poses some operational issues.

To provide possible solutions to these issues, the African Neonatal Sepsis Trial (AFRINEST) was conducted jointly in the DRC, Nigeria, and Kenya. It demonstrated that, where referral to hospital was not possible, the treatment of sepsis cases in the newborn was possible with oral amoxicillin for seven days—instead of injectable penicillin—combined with gentamicin injections.

As a follow-up to AFRINEST, the current study focused on the identification and analysis of bottlenecks related to the demand, use, and supply of the injectable and oral antibiotics indicated for the treatment of neonatal sepsis with the goal of proposing possible solutions.

The study was conducted in four health zones (HZs) that were purposively selected: Bominenge (South Ubangi), Karawa (North Ubangi), and Kadutu and Bagira (South Kivu). Data were collected through individual and group interviews.

The following institutions were targeted for data collection: Ministry of Public Health (MPH) services involved in maternal, newborn, and child health (MNCH) and supply of antibiotics, such as the Direction de la Pharmacie, du Médicament et des Plantes Médicinales (DPM; Directorate of Pharmacy, Medicines, and Medicinal Plants) and the Programme National d'Approvisionnement en Médicaments Essentiels (PNAME; National Procurement Program for Essential Medicines); pharmaceutical depots and private pharmacies; Divisions Provinciales de la Santé (DPSs; Provincial Divisions of Health); Central Offices of the HZ (COHZs); health facilities (public and private) and community health workers (CHWS), as well as mothers with children under three months of age.

Like other investigations carried out in DRC, either about health in general or about medicines, this study confirmed that despite efforts to improve the coverage of essential medicines for child survival, the objectives are far from being achieved.

Bottlenecks identified through this study revolve mainly around the weakness of the essential medicines supply chain, which causes the unavailability of antibiotics for neonatal sepsis at health facilities; the inadequate training of health care providers on the application of standards and guidelines for management of neonatal sepsis and administration of injectable antibiotics; the high cost of antibiotics for neonatal sepsis; and the low awareness of targeted groups of the danger signs.

The following simple and feasible corrective measures were recommended:

- Updating and harmonization of standards and guidelines
- Training and support for health care providers in the application of the updated standards and guidelines as well as in the quantification of antibiotic requirements for neonatal sepsis
- Implementation and expansion of demonstration sites for the simplified regimen of newborn sepsis treatment to reduce barriers to the use of antibiotics in health facilities
- Strengthening of the essential medicines supply system, especially for pediatric forms of antibiotics and syringes
- Raising community awareness about the danger signs and the importance of taking the newborn to a health center as early as possible

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I. INTRODUCTION

1. Background

The health of the newborn, child, and mother is a major concern worldwide. There are approximately 5.9 million deaths of children under age five, of which nearly 2.7 million occur during the neonatal period (during the first 28 days) (UN Inter Agency Report, 2015).

Over the past three decades, the global mortality rate for children under five years of age declined by nearly 53%, while the mortality of newborns decreased by 47%. Neonatal deaths accounted for 46% of deaths in children under five (UN Inter Agency Report, 2015).

The DRC is among the 10 countries contributing to more than half (60%) the child mortality in the world and is among the six countries of the world, including three in Africa, contributing to 50% of the global burden of maternal mortality. The 2013–2014 Demographic and Health Survey found that child, infant, and newborn mortality rates are respectively 104, 58, and 28 per 1,000 live births. Furthermore, neonatal diseases, malaria, diarrhea, pneumonia, and malnutrition are responsible for over 80% of deaths of children under five in the DRC (UNICEF, 2011).

At the World Millennium Summit held in New York in September 2000, senior officials of UN member states pledged to achieve the eight Millennium Development Goals (MDGs). One of the MDGs aimed at reducing by two-thirds the under-five mortality rate in 2015, starting from the 1990 level. It is now established that the MDGs were not achieved in 2015. Other initiatives and approaches have been developed to intensify efforts to lead all nations toward achieving the MDG targets and the newly agreed Sustainable Development Goals.

Among such initiatives are (a) the UN Commission on Life-Saving Commodities (UNCoLSC), created to help countries with high rates of maternal, neonatal, infant, and child mortality eliminate bottlenecks related to universal access to 13 medicines that save the lives of mothers, children, and newborns; (b) the “Every Woman, Every Child” global movement that mobilizes and intensifies international and national action by governments, multilaterals, the private sector, and civil society to address the major health challenges facing women and children; and (c) “The Child Survival Call to Action: A Promise Renewed,”

In the DRC, the UNCoLSC contributes to ongoing efforts in the field of maternal, newborn, and child health and to strengthening the health system. The initiative on the 13 life-saving commodities provides the DRC a great opportunity to help bridge the remaining gap in MNCH. The joint efforts of the Congolese government and its partners, although important, cover less than half the HZs—and that not even completely. Most interventions target the public sector only; the private sector is barely supported.

The DRC is trying to accelerate the reduction of mortality of mothers and children through strategic, operational, and innovative responses to these challenges. The DRC Government and its partners, including the US Agency for International Development, the World Health Organization (WHO), the United Nations Children’s Fund, and the U.K. Department for International Development, support projects to improve the availability of essential products and to provide quality health services.

Moreover, the DRC as a stakeholder in the global strategy proposed by the UNCoLSC developed the first phase of its plan to eliminate bottlenecks. For this first phase, the DRC has proposed interventions aimed at eliminating bottlenecks related to the medicines, including weak governance; low product availability; poor monitoring, evaluation, and research; and low financial access—as well as specific bottlenecks for each of the 13 commodities.

2. The Situation of Neonatal Sepsis in the DRC

The recent Demographic and Health Survey reported a downward trend in neonatal mortality from 42 to 28 per 1,000 live births (MICS, 2010; DHS, 2013–2014). Despite this reduction, this mortality rate is considered high. One of the major causes of neonatal mortality in the world, and in the DRC in particular, remains neonatal sepsis, which causes nearly 500,000 neonatal deaths per year globally (Liu et al. 2015). With the assistance of its technical and financial partners, the DRC is working to accelerate the reduction of neonatal mortality.

As part of phase I of the national activities in the plan to eliminate bottlenecks to universal access to the 13 life-saving commodities for women and children, the MPH organized in August 2013, with technical and financial support from MSH, a sensitization workshop for policy makers and implementing partners on the introduction and use of chlorhexidine digluconate (CHX 7.1%) for umbilical cord care. The workshop resulted in the development of the strategic plan for the introduction and use of CHX 7.1% in umbilical cord care in DRC. The umbilical cord is one of the main entry points of sepsis in the newborn.

The management of newborn sepsis, as recommended by the WHO, is through hospitalization and treatment with injectable antibiotics: injectable β-lactams, such as ampicillin, benzylpenicillin, or procaine penicillin, associated with gentamicin. This recommendation poses some operational problems in DRC, primarily because most families in poor communities do not accept the referral to the hospital because of the distance to the hospital and the cost of this care, among other factors.

To provide alternative solutions to these issues, the AFRINEST trial study was conducted jointly in the DRC, Nigeria, and Kenya. It aimed to compare the efficacy of three simplified WHO-recommended antibiotic regimens for the treatment of neonatal sepsis in health centers (HCs) for infants ages 0–59 months with clinical signs of neonatal sepsis for whom referral to a hospital was not possible. The study demonstrated that the treatment of cases of newborn sepsis was possible with oral amoxicillin for seven days combined with gentamicin injection in an outpatient setting where referral is not possible (Tshefu et al., 2015). The study showed that two simplified regimens—oral amoxicillin and injectable gentamicin for seven days and oral amoxicillin for seven days with two days of injectable gentamicin—were equivalent to the standard injectable antibiotic regimen. For rapid breathing, which may represent 50% of the cases of possible serious bacterial infection (PSBI), oral amoxicillin for seven days were found to be equivalent to seven days of injectable penicillin and gentamicin.

Because of this evidence, the WHO released new recommendations in September 2015: *Guideline: Managing Possible Serious Bacterial Infection in Young Infants When Referral Is Not Feasible*. These recommendations facilitate the administration of treatment for PSBI at the HC where referral is not possible. Table 1 shows the actual WHO recommendations taken from the guidelines.

Table 1: 2015 WHO Recommendations on Managing PSBI in Young Infants 0–59 Days Old When Families Do Not Accept or Cannot Access Referral Care

Number	Recommendation
1	**Community health workers and home visits for postnatal care** During home visits made as part of postnatal care, community health workers should counsel families on recognition of danger signs, assess young infants for danger signs of illness, and promote appropriate care seeking.
2	**Infants 0–6 days with fast breathing as the only sign of illness** Young infants 0–6 days old with fast breathing as the only sign of illness should be referred to hospital. If families do not accept or cannot access referral care, these infants should be treated with oral amoxicillin, 50 mg/kg per dose twice daily for seven days, by an appropriately trained health worker.
3	**Infants 7–59 days with fast breathing as the only sign of illness** Young infants 7–59 days old with fast breathing as the only sign of illness should be treated with oral amoxicillin, 50 mg/kg per dose twice daily for seven days, by an appropriately trained health worker. These infants do not need referral.
4	**Young infants 0–59 days old with clinical severe infection** Young infants 0–59 days old with clinical severe infection whose families do not accept or cannot access referral care should be managed in outpatient settings by an appropriately trained health worker with one of the following regimens: *Option 1:* Intramuscular gentamicin 5–7.5 mg/kg (for low-birth-weight infants, gentamicin 3–4 mg/kg) once daily for seven days and twice daily oral amoxicillin, 50 mg/kg per dose for seven days. Close follow-up is essential. *Option 2:* Intramuscular gentamicin 5–7.5 mg/kg (for low-birth-weight infants, gentamicin 3–4 mg/kg) once daily for two days and twice daily oral amoxicillin, 50 mg/kg per dose for seven days. Close follow-up is essential. A careful assessment on day 4 is mandatory.
5	**Young infants 0–59 days old with critical illness** Young infants 0–59 days old who have any sign of critical illness (at presentation or developed during treatment of clinical severe infection) should be hospitalized after pre-referral treatment.

The DRC has opted to set up demonstration sites for this new protocol, using option 2 (two days of gentamicin) before its scale-up.

II. OBJECTIVES

1. General Objective

The general objective of this study was to identify the bottlenecks related to demand, supply, and use of injectable and oral antibiotics such as amoxicillin, used for the treatment of newborn sepsis in the DRC.

2. Specific Objectives

Specifically, this study had the following objectives:

- Identify the law, policies, and regulations in effect as well as existing financing strategies in the field of neonatal sepsis in the DRC
- Review the procurement cycle and procedures and the quality assurance mechanisms for injectable and oral antibiotics available for the treatment of neonatal sepsis in the DRC
- Evaluate the availability, accessibility, use, and barriers to the use of injectable and oral antibiotics (ampicillin, procaine benzylpenicillin, gentamicin, and ceftriaxone or other third-generation cephalosporin) for the treatment of neonatal sepsis at all levels of care in the DRC
- Assess the knowledge, attitudes, and practices of mothers and health care providers (community volunteers and health professionals) related to the diagnosis and management of neonatal sepsis
- Propose strategies to put in place to increase the availability, accessibility, and proper use of injectable and oral antibiotics for the treatment of neonatal sepsis, especially in the implementation of demonstration sites and their eventual expansion

III. METHODOLOGY

1. Type of Study

This is a descriptive study using a mixed approach (quantitative and qualitative) for data collection.

2. Study Sites

The study was conducted in four health zones, which were purposively selected. These are the Bominenge HZ in the province of South Ubangi, the Karawa HZ in the province of North Ubangi, and Kadutu and Bagira HZs in South Kivu province.

The Bominenge and Karawa HZs had already been selected as a demonstration area for the management of neonatal sepsis in the context of the AFRINEST study. Consequently, they were of particular interest for this study.

Both South Kivu HZs were selected purposively because they are intervention zones supported by the PROSANI project with funding from the US Agency for International Development.

The provinces of North and South Ubangi only came into being after the recent administrative division in the DRC. They were both previously in the former province of Equateur.

3. Sampling

Information on laws, regulations, policies, standards, and guidelines for neonatal sepsis were collected at central level in Kinshasa from the following institutions: (a) D10; (b) the DPM, the Direction de Lutte contre la Maladie (Directorate of the Fight against Disease), and PNAME.

Information about the supply chain and quality assurance mechanisms for antibiotics to treat neonatal sepsis were obtained from the following institutions and key informants:

- *At the central level*: DPM, PNAME, the Fédération des Centrales d'Achat et de Distribution des Médicaments (FEDECAME; Federation of Central Purchasing and Distribution Services of Medicines), pharmaceutical stores, and private pharmacies

- *At the provincial level*: DPSs of Kinshasa, South Kivu, and South Ubangi (North Ubangi DPS is supplied by South Ubangi); the Centraux de Distribution Régionale des Médicaments (CDRs; Regional Medicine Distribution Centers) of Kinshasa (FEDECAME and CAMESKIN), South Kivu (DCMP/8th CPAC, BDOM, APAMESK), and South Ubangi (CAMENE); pharmaceutical stores and private pharmacies

- *At the peripheral level*: COHZs; the General Referral Hospitals (GRHs) and HCs (see table 1); private pharmacies

The availability, accessibility, use, and barriers to the use of injectable and oral antibiotics for neonatal sepsis were evaluated with the following institutions and key informants:

- *At the central level*: DPM, PNAME, FEDECAME, pharmaceutical depots, and private pharmacies

- *At the provincial level*: DPSs of Kinshasa, South Kivu, and South Ubangi (North Ubangi mainly supplied from South Ubangi); the CDRs of Kinshasa (CAMESKIN), South Kivu, and South Ubangi; pharmaceutical depots and private pharmacies

- *At the peripheral level*: COHZs; GRHs, and HCs (see table 2); private pharmacies; community volunteers and mothers of children under three months of age

The knowledge, attitudes, and practices of mothers and health care providers (community volunteers and health professionals) related to the diagnosis and management of neonatal sepsis were evaluated with four groups of mothers (six to eight participants per group); four groups of HC care providers; and four groups of CHWs from the selected HZs (one group per HZ).

Table 2: Type of health facility surveyed, by HZ and province

		Type of health facility				Total
DPS	**HZ**	GRH	HC	Referral HC	Health Post	
South Kivu	Bagira	1	8	0	0	9
	Kadutu	1	6	1	0	8
South Ubangui	Bominenge	1	7	0	1	9
North Ubangi	Karawa	1	6	0	0	7
Total		**4**	**27**	**1**	**1**	**33**

4. Operational Definitions

Clinical signs of neonatal sepsis: (from the national guidelines for essential and emergency care of the newborn, vol. 3, 2012)

Newborn with signs of danger of major infection such as weak or absent of sucking, lethargy or inactivity (little or no movement), fever (hot body) or hypothermia (cold body and extremities), constant crying, difficulty breathing, vomiting and abdominal distension, convulsions, red and swollen umbilicus, nauseous, severe jaundice; *with also history of* maternal fever, premature rupture of membranes more than 12 hours, unsanitary practices during childbirth, poor cord care, inhaled amniotic fluid, prolonged labor for more than 12 hours.

Knowledge of neonatal sepsis: a respondent mentions at least one danger sign suggesting a major infection, without prompting.

Management of neonatal sepsis: (from the national guidelines for essential and emergency care to the newborn, vol. 3, 2012):

- *At the HC or maternity unit level:* administer emergency care and refer to hospital. Emergency care includes:
    - Give the first dose of appropriate antibiotics: ampicillin 50–100 mg/kg + gentamicin 5 mg/kg intramuscular (IM) per dose

- *At the hospital level:* (a) proceed as at HC or maternity unit; (b) treat major infection according to the national Emergency, Triage, Assessment, and Treatment (ETAT) protocol below; (c) ensure counter-referral to the health center on baby's discharge.
    - Emergency, Triage, Assessment, and Treatment (ETAT) Protocol

The general protocol for curative treatment of all neonatal infections recommends a triple combination of broad-spectrum bactericidal antibiotics:

- β-lactam antibiotics: ampicillin 200 mg/kg/day in 4 intravenous (IV) doses
- Third-generation cephalosporins: cefotaxime 100 mg/kg in 3 IV doses
- Aminoglycosides: gentamicin: 3–5 mg/kg/day in 2 IM/IV doses
- In case of suspicion of anaerobes, metronidazole IV is indicated (8–10 mg/kg/day in 3 doses for 7 days).

The duration of treatment varies depending on the infection to be treated:

- Meningitis: 2–3 weeks
- Other infections: at least 10 days IV (2 weeks)

5. Data Collection Procedures

Survey organization

The study established a steering committee with members from the following institutions:

- The MPH's PNIRA
- MSH (SIAPS and PROSANI-Plus)
- Kinshasa School of Public Health

The role of this committee was (a) to read, enhance, and validate documents produced as part of this study (research protocol, including data collection tools, results, and preliminary report); (b) to participate in training supervisor teams; and (c) to monitor the progress of the study and the implementation of the recommendations.

Data collection

Data were collected by five teams of two supervisors with experience in conducting qualitative and quantitative surveys and previously trained in interviewing techniques with standardized questionnaires (quantitative approach) and interview guides (qualitative approach). The training of these teams was held in Kinshasa and lasted four days from October 13 to 16, 2015, including pretesting in health facilities to finalize the questionnaires.

One team collected the data in Kinshasa, the other four were divided among the four targeted HZs. Three teams also collected data at the provincial capitals of the three surveyed provinces (Kinshasa, Gemena, and Bukavu).

Data collection took place from October 19 to 30, 2015, in Kinshasa and from October 15 to 25, 2015, for the HZs of Bominenge (South Ubangi), Karawa (North Ubangi), and Kadutu and Bagira (South Kivu).

Interviews (individual and group) were conducted by teams of two supervisors. At the end of each working day, the team had to review the completeness and the correct filling in of questionnaires or the audio recording (for the qualitative component) to ensure the quality of the collected data.

Questionnaires and interview guide used

Several types of data collection tools were used for each of the target groups, among them the following:

- Module 1: Health care providers of public and private health facilities (HCs, Referral HCs, and hospitals)
- Module 2: The team from the COHZ
- Module 3: Members of the DPS
- Module 4: Members of the central level of the MPH, including those responsible for MNCH and the D10; the DPM; and PNAME
- Module 5: The in-charges of the centers for purchasing and distribution of medicines
- Module 6: Interview guides for the five target groups of the qualitative component (mothers, health care providers of health facilities, CHWs, managers of pharmaceutical depots, and managers of private pharmacies)

6. Study Pretest

During the training of the research supervisors in Kinshasa, which lasted four days, the penultimate day was used to pretest the methodology and data collection tools that were used in this study, to ensure their understandability and the feasibility of their administration within the set time.

This pretest was conducted in the urban-rural HZ of N'sele, a site not included in the study and located in the outskirts of Kinshasa.

Supervisors were put in a real situation with appropriate targets. For the qualitative part, they carried out two focus groups and two in-depth key informant interviews. In addition, they visited two health facilities (a health center and a hospital) to apply the questionnaire to health care providers.

The results of the pretest were discussed during the last day of training, and minor modifications were made to finalize the data collection tools.

7. Data Treatment and Analysis

The questionnaires were numbered. The answers to open questions were examined carefully to develop the coding guide. Once the questionnaires were coded, double entry of data was carried out using Epidata software to ensure the quality of the encoded data.
After entering all the questionnaires, raw frequency tables were produced, and the internal consistency of responses was checked and missing data were adjusted for.

Statistical analyses were performed using SPSS software version 21. The frequencies of all the variables were produced as absolute numbers and proportions. The proportions were used to describe category-specific variables such as the level of knowledge about neonatal sepsis.

In-depth interviews and focus groups were recorded on Dictaphone. After each workday, supervisor teams had a debriefing session that was also recorded. Then the recordings were transcribed and translated into French (if the interview or discussion was conducted in a local language) by the transcription team officials.

The transcripts were reviewed in detail by the two study investigators and by an expert in qualitative studies to highlight the codes; then they were reviewed by the research supervisors. After obtaining a consensus on coding, transcripts were coded using Atlas software. The responses were analyzed for emergent themes. The results were interpreted and reported in narrative form.

8. Ethical Considerations

The protocol was approved by the Ethics Committee of the KSPH before the start of the study.

Before any interview was conducted, written informed consent (with signature of respondent) was obtained from the study participants.

Consent was required for participants in the focus groups so the in-depth interviews and focus groups could be recorded. Confidentiality and anonymity of the participants were maintained at all times; during the focus groups, participants' names were taken only to facilitate the conversation. They are not included in the reports.

Transport costs were reimbursed to the participants from the focus groups; five dollars' equivalent in local currency for HC health care providers and one dollar (in local currency) for the others.

In the field, survey questionnaires and the Dictaphone-recorded discussions were stored in a safe place. Access to these documents was restricted to the research team.

IV. PRESENTATION OF THE RESULTS

1. Policies, Laws, and Guidelines Relating to Neonatal Sepsis

In 2003 within the MPH, the D10 was created according to the terms of the Ministerial Decree of Public Service No. CAB/FP/JMK/CP/044/2003 of March 28. Its mission is to promote health of family and specific groups through integrated high-impact interventions targeting central, provincial, and HZ levels.

This MPH directorate coordinates MNCH interventions through the PNIRA/clinical Integrated Management of Childhood Illness (IMCI) program, the National Program for Diarrheal Diseases (PNMLD/Community-IMCI), and National Program for Reproductive Health.

The guidelines specifically related to the management of serious infection in newborns, such as neonatal sepsis, are contained in volume 3, *Essential and emergency care of the newborn*. They are supplemented for case management at hospital level by the document "Emergency, Triage, Assessment, and Treatment (ETAT)," dated 2007 and adapted from the WHO document published in 2007. Technical sheets for health facilities also form an integral part of these guidelines: "Technical Specifications for Care Providers: Essential and emergency care of the newborn," published in 2013.

The results of this analysis show that several guidelines exist for the management of neonatal sepsis, including MNCH standards and clinical IMCI guidelines, according to the level of care (for health centers and hospitals). However, these guidelines differ somewhat with regard to the dosage recommended for the antibiotic treatment of neonatal sepsis. The MNCH standards and guidelines recommend the following treatment protocol: ampicillin injection 50–100 mg/kg and gentamicin 5 mg/kg; whereas the IMCI clinical guidelines recommend ampicillin injection 100 mg/kg divided in three daily doses and gentamicin 2.5 mg/kg twice a day; and the ETAT protocol recommends ampicillin 200 mg/kg and gentamycin 3–5 mg/kg twice a day. In addition, it is important to note that the DRC ETAT recommendation of triple therapy: β-lactam antibiotic/third-generation cephalosporin/gentamicin differs from the WHO recommendation of a combination of β-lactam antibiotic and gentamicin or a third-generation cephalosporin.

Furthermore, 76% of health facilities surveyed (n = 33) had neither guidelines nor technical sheets for the treatment of neonatal sepsis at the time of the survey. The same situation prevailed at the central offices of the four HZs visited. Only at the South Kivu DPS was a copy of the guidelines present.

It should also be noted that other policy documents exist in the country, including in particular the National Plan for the Elimination of Bottlenecks to Access to Life-Saving 13 Medicines for Women and Children; the 2012–2015 Strategic Plan for Provision of Essential Medicines for Child Survival; and the 2008–2012Strategic Plan for PNAME. Most of these policy documents have expired and require updating in light of developments in the health context and new evidence such as that contained in this report.

2. Supply Chain

The DRC's National Pharmaceutical Policy (NPP) was developed and adopted in 1997 and revised in 2005. Its overall objective is to ensure an adequate supply and rational use of good quality, safe, effective generic essential medicines that are affordable for the majority of the population. In addition to the NPP, two laws serve as a legal framework for drug regulation: Decree N^{o} 27 of March 15, 1933, on the exercise of pharmacy and the Royal Decree of March 15, 1955, on the art of healing in the DRC.

The DPM was created within the MPH by Presidential Ordinance 82-027 of March 19, 1982. This directorate is the medicine regulatory authority. It exercises all regulatory functions, including granting authorizations for opening and running a pharmacy, granting licenses for imports of medicines, registration of medicines, pharmaceutical inspection, and quality control of pharmaceuticals. It also publishes and periodically updates the National Essential Medicines List (NEML). This list includes the International Nonproprietary Name of the medicine, dosage, dosage form, and level of use. Antibiotics for the treatment of neonatal sepsis are included in the NEML. However, some pediatric presentations of relevant antibiotics, such as amoxicillin 125 mg dispersible tablets and gentamicin 20 mg/2 ml injection, are not included.

In 2002, the MPH created the Système National d'Approvisionnement en Médicaments Essentiels (SNAME; National Essential Medicines Procurement System), with the support of partners, to implement the strategies of the NPP. Key procurement strategies were to centralize purchasing through a nonprofit central procurement unit (FEDECAME) and to decentralize distribution of medicines through 20 autonomous subregional distribution centers (CDRs) with nonprofit status.

To coordinate, supervise, and evaluate the implementation of SNAME, the MPH has created the PNAME, mandated to develop and promote a supply system for essential medicines. The SNAME consists of FEDECAME, the CDRs, the COHZs, and health facilities. Besides the SNAME, a for-profit private sector consists of importers and wholesale distributors, manufacturers, and retailers.

In theory, the CDRs are supplied by FEDECAME, the COHZs and the hospitals are supplied directly from the CDRs, and health facilities from the COHZs.

Registration of medicines

The antibiotics recommended for the treatment of neonatal sepsis are included in the NEML and are registered. However, certain forms of pediatric antibiotics are not included: amoxicillin 125 mg dispersible tablets and injectable gentamicin 20 mg/2 ml. They are not registered in the country either.

However, the DPM confirmed that it is relatively easy to register a product formulation with a different dosage if the product is already registered. The efficiency of the dosage has to be shown, and the cost has to be affordable.

Procurement

FEDECAME buys mainly from international suppliers based on orders from the CDRs.

All the tracer medicines for neonatal sepsis are procured by FEDECAME and the CDRs. Injectable gentamicin 40 mg/2 ml and 80 mg/2 ml and ampicillin 500 mg and 1 g are purchased from European suppliers but are manufactured in India. Benzylpenicillin is purchased from European suppliers in presentations of 1.2 MU, 1 MU, and 5 MU. Because of its once-daily dosing, ceftriaxone is preferred by providers as a third-generation cephalosporin over cefotaxime, which requires administration two or three times a day. Ceftriaxone is purchased from European suppliers in presentations of 250 mg, 500 mg, and 1g. The complexity of administration of injectable antibiotics for providers could be explained by the lack of a standardized presentation for them, especially when pediatric presentations are not always available.

South Kivu has three CDRs: CDR-BDOM, DCMP/8th CPAC, and APAMESK. South Ubangi has only one, referred to as CAMENE. In Kinshasa, CAMESKIN was visited.

The CDRs are supplied either by FEDECAME or from other suppliers, mostly international. The CDR-BDOM in South Kivu and Kinshasa CDR-CAMESKIN reported they sometimes purchase from local suppliers. With the exception of CDR-BDOM, all other CDRs reported at least one stock-out of antibiotics at FEDECAME during the year, varying in duration from one to three months. This is also a reason why the CDRs sometimes purchase from other suppliers.

The CDRs order essential medicines quarterly, based on average monthly consumption. All the CDRs stated that antibiotic forecasts are based either on morbidity or on consumption, depending on the central units, which indicates lack of a standardized method. These forecasts are made by CDR staff who have received appropriate training. There is not a standard periodicity for orders of the CDRs because some are placed every six months and others every two years.

All the CDRs surveyed, except CDR-BDOM, include some pediatric injectable antibiotics on the NEML in the forecasting process.

Three of the four health zones visited are supplied through their respective CDRs, except for Karawa HZ, which does not have a CDR in the province and so purchases either from private distributors or from the CDR-CAMENE in South Ubangi.

The main source of supply for about half the health facilities is the COHZ. Some health facilities are supplied directly from CDRs (31%) and sometimes obtain supplies from pharmaceutical stores (38%) or from private pharmacies (4%). This shows the pharmaceutical distribution chain in the public sector is not completely respected.

CAMENE CDR Bwamanda (Sud Ubangui)

Distribution

Antibiotics for neonatal sepsis are distributed through the system in the same manner as all other essential medicines. It is also not standardized.

In South Kivu, the transport of medicines is provided by the COHZs and the hospitals themselves or the CDRs. This is also sometimes the case for the DCMP/8th CPAC. In the provinces of Kinshasa and South Ubangi, the COHZs and the health facilities go to collect their supplies themselves.

Funding

The sources of funding at all levels of the health system for the purchase of essential medicines, including antibiotics for neonatal sepsis, are the facility's own funds and partner support.

Only the CDR-DCMP/8th CEPAC felt these funds were sufficient for the purchase of the amount of injectable antibiotics needed. Alternatives to dealing with the insufficient funding mentioned by respondents included advocacy to the government and partners, prioritizing the purchase of highly consumed products, and splitting purchase quantities. Clearly, the last two options could affect the availability of antibiotics with low consumption, such as amoxicillin 125 mg dispersible tablets, although oral amoxicillin has proven effective in the treatment of neonatal sepsis in the AFRINEST study.

Of the health facilities surveyed (n = 33), 80% purchase antibiotics with their own funds, which are mostly generated from the sale of medicines to patients. The profit margin was estimated at 25–50% of the purchase price. It should be noted that the price of injectable antibiotics in the surveyed health facilities was standardized across only 30% of health facilities.

This dependence on attendance at the health facilities may explain the irregularity of orders, which are made monthly for some (66%), quarterly for others (16%), or when funds are available (18%). The orders are mostly reported to be based on average monthly consumption (88%).

Respondents from 60% of health facilities surveyed stated that there was a mutual insurance company for health in their community, and 73% covered care of the newborn. However, providers felt that despite the existence of these mutual funds, the population does not subscribe to them because of lack of information and financial means.

All these parameters accentuate the community's lack of financial accessibility to care.

Logistics Management Information System

The logistics management information system (LMIS) is not standardized. Data from the CDRs and FEDECAME are apparently not incorporated in the LMIS.

Three of four health zones, with the exception of the Bominenge HZ, reported having an LMIS that includes antibiotics for neonatal sepsis. However, considerable variability was observed in the type of information reported and the level of reporting and analysis of this information as reported by COHZ respondents.

3. Availability

The availability of antibiotics for the treatment of neonatal sepsis was assessed in the health facilities, the COHZ pharmacies, the Kinshasha DPS, the CDRs, and FEDECAME. In addition to a respondent reporting whether a product was available, the physical presence of cited products was inspected for confirmation. Ceftriaxone was studied rather than cefotaxime as the third-generation cephalosporin preferred by health workers. As previously mentioned, the usual presentation of gentamicin injection in the health system is 80 mg/2 ml.

All the surveyed antibiotics were available at FEDECAME except amoxicillin 250 mg dispersible tablets.

At all five CDRs visited, gentamicin 80 mg/2 ml, amoxicillin syrup, and injectable ceftriaxone were available. However, gentamicin 40 mg/ml was found in stock at the CDR-DCMP/8th CPAC (South Kivu). The amoxicillin 250 mg dispersible tablet was available at the CDR-APAMESK (South Kivu). Ampicillin and benzylpenicillin injections were not available in all the CDRs, as shown in table 3.

The negative impact of the unavailability at CDR level of antibiotics that are needed for the proper management of neonatal sepsis in the health facilities is easily understood. However, the presence of gentamicin 80 mg/2 ml injection and amoxicillin syrup in all the surveyed CDRs is encouraging, especially given the expected implementation of the new simplified regimen for the management of neonatal sepsis.

Table 3: Availability (%) of antibiotics for treatment of neonatal sepsis in CDRs (n = 5)

Antibiotics	Availability
1. Gentamicin 80 mg/2 ml amps	100%
2. Gentamicin 40 mg/2 ml amps	20%
3. Gentamicin 40 mg/1 ml amps	20%
4. Ampicillin 500 mg inj vial	60%
5. Benzylpenicillin inj vial	80%
6. Amoxicillin dispersible tablet 250 mg	20%
7. Amoxicillin syrup or suspension (250 mg/5 ml)	100%
8. Ceftriaxone inj vial (1 g/vial)	100%

Gentamicin injection 20 mg/ml and amoxicillin 125 mg dispersible tablets were not available at any CDRs because they are not included in the NEML and so are not used in health facilities. In all pharmacies of the four COHZs surveyed, injectable gentamicin 80 mg/2 ml and amoxicillin syrup were available. Ampicillin 500 mg injectable vials were available in only two COHZs while benzylpenicillin injection and amoxicillin syrup were available in only one COHZ.

The availability of medicines at the time of the surveyors' visit in health centers and hospitals is shown in figure 1.

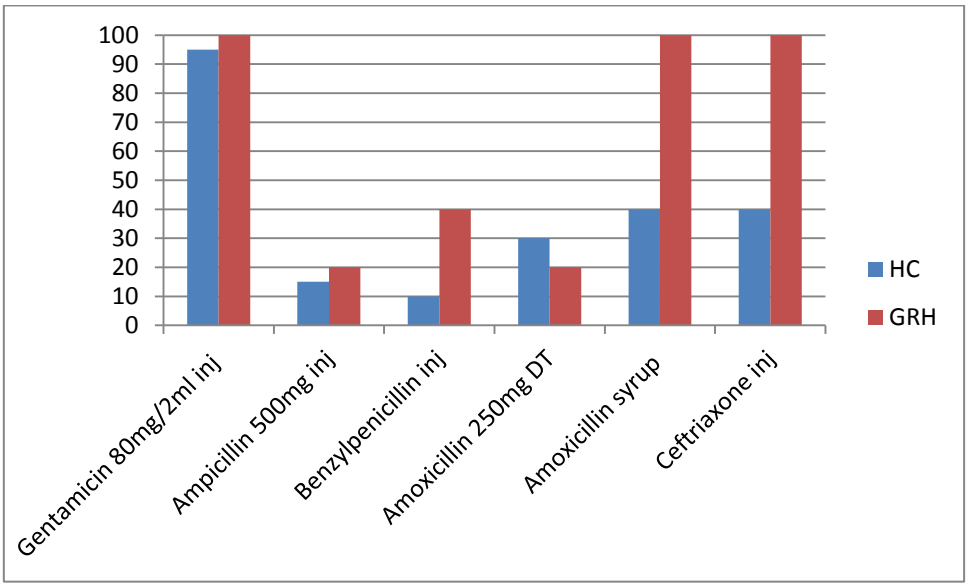

Figure 1: Availability (%) of tracer antibiotics by type of health facility, GRH (n = 5) and HC (n = 21)

As in the CDRs, the adult presentation is the most available in the health facilities.

At GRHs, gentamicin injection 80 mg/2 ml and ceftriaxone were available in all hospitals.

At health centers, antibiotics were not very available (injectable ampicillin, benzylpenicillin, and amoxicillin dispersible tablets); more than half the HCs were out of these antibiotics, except for gentamicin 80 mg/2 ml, which was available in 95% of the HCs.

One of the medicines recommended in treatment of sepsis—injectable ampicillin—is the least available in all health facilities (20% of GRHs and 15% of HCs). In addition, injectable ceftriaxone or other third-generation cephalosporin, which is supposed to be used exclusively at GRH level, was found in 40% of the health centers.

We also assessed availability of syringes, particularly pediatric syringes, because they are necessary for administration of pediatric doses of injectable antibiotics. Syringes of 1 ml were available in only Karawa COHZ of (North Ubangui) while in the three other COHZs only 5 ml syringes were in stock.

At the health facility level, 5 ml syringes were available in all health facilities while 1 ml and 2 ml syringes were available in only one HC in the HZ of Bagira.

4. Diagnosis and Treatment

Knowledge of the signs of neonatal sepsis

Health facility service providers

In all health facilities, respondents said they knew the signs of neonatal sepsis. However, only a small proportion (23%) cited lethargy or inactivity, which shows that in fact the level of awareness is still low.

Figure 2 shows the signs commonly cited by respondents in the surveyed health facilities.

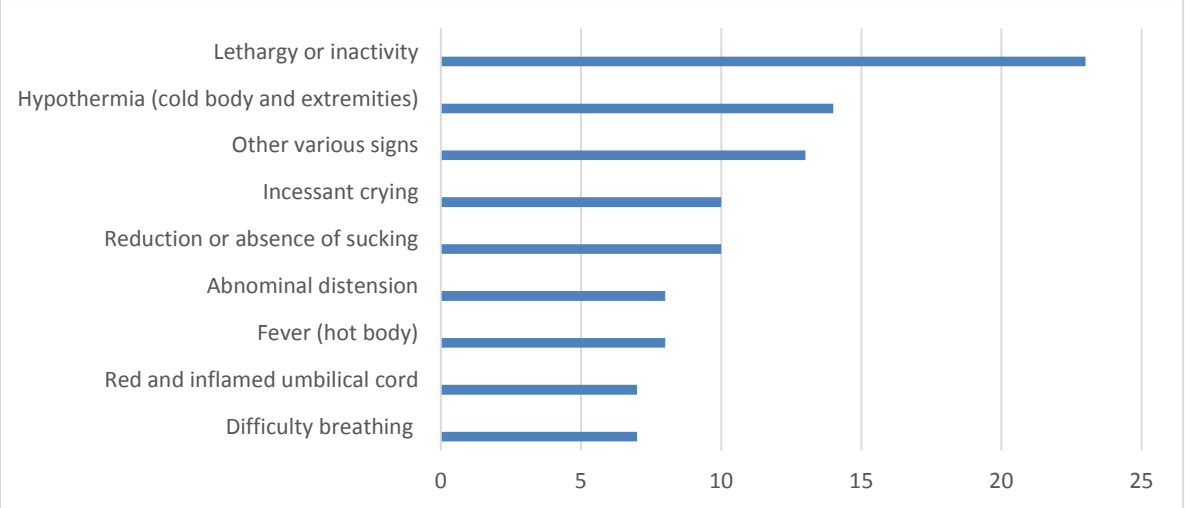

Figure 2: Signs of neonatal sepsis cited in health facilities (n = 26)

Community Health Workers (CHWs)

The results demonstrate that the CHWs also have a low knowledge level of danger signs/warning of major infection in the newborn. The most obvious signs were cited by very few: fever (7/30), refusal to suck (3/30), incessant crying (3/30), respiratory difficulties (3/30), severe jaundice (3/30), convulsion (2/30), and diarrhea (2/30).

> *"The child is not able to suck; if the mother wants to breastfeed the child, he refuses; either he has repeated fevers. We can say that the child is not in good hands."* **FG CHWs, Kadutu**

With respect to their role in diagnosis and/or management of neonatal sepsis, the majority of CHWs reported having home visits in their respective communities to carry out health education sessions (15/19) with the mothers of newborns.

> *"We also have the role to teach the population on the danger signs because not all households know these signs. For example, if a child is sick with a red and inflamed umbilical cord and his mom or a family member does not know the sign of the danger; they will not know to take the child quickly to a health center. Thanks to the CHWs, the mother may take the child to the health center earlier."* **FG CHWs, Kadutu**

A minority of those CHWs surveyed is responsible for follow-up of newborns to detect danger signs and to refer them to a health center in an emergency (2/19) or to recommend home treatment (2/19).

> *"During home visits or by invitation of the family, I can recommend to give something for fever, if the temperature is high, ORS if there is diarrhea, and encourage them to go to the health center."* **FG CHWS, Bagira**

> *"Our role is to monitor the newborn, to recognize danger signs, track the child's health status and send the mother to health center nurses."* **FG CHWS, Karawa**

The majority of CHWs (16/19) said they had been trained in the identification of danger signs in the newborn as part of the C-IMCI strategy. However, some new recruits (3/19) have not yet received training on neonatal sepsis.

> *"Yes, we have received training to know when the child shows danger signs of the disease. The training was given in 2010 at the COHZ."* **FG CHWS, Bominenge**

However, the general impression is that they have not fully mastered these signs—hence, the need to strengthen their capacity through the organization of training courses or through supervision visits.

Mothers

The results of the group discussions with mothers on knowledge of danger signs of major infection in the newborn show that a small proportion of them seem to know these signs. The signs most mentioned were fever (5/23), refusal to suck (3/23), incessant crying (3/23), and vomiting (3/23). In addition, some other less obvious signs were mentioned by individuals:

for example, sunken or bulging fontanelle, convulsion, jaundice, inflamed and smelly umbilicus, and low birth weight.

> *"When the child is weak, it does not suck any more, and then I say this child really has a problem, particularly that it refuses to suck, that means he is sick."* **FG mothers, Kadutu**

> *"It may have something that extends out of the head but you don't know because he has a lot of hair, and it is in the hospital that they will tell you that he is sick."* **FG mothers, Bagira**

This low level of knowledge is exacerbated by the delay in seeking health care at a health facility. The mothers explain this delay in several ways, including the following:

The slight majority (9/17) mentioned that they have to wait for the decision of the head of the household, as the provider of funds necessary to take the baby to the hospital:

> *"I cannot go straight to the hospital because it is the father who must pay."* **FG mothers, Bagira**

Nevertheless, some (6/17) did not agree, mentioning the risk that the baby would run as a result of waiting for the father to return to the house and make a decision:

> *"I do not want to wait; otherwise the child will die in my arms. And if the child dies, they will ask what did the child die of? And you will say that you were waiting for your husband or your mother-in-law to take him to the hospital? Yet you could inform anyone, even a little girl of the neighborhood, leaving a message that you had gone to with the child to the hospital."* **FG mothers, Kadutu**

Self-medication is practiced at home before going to a health facility:

> *"If my child falls ill, I wait first and, then I give him paracetamol; he could get better, and other times you give the medicine but he continues to be sick so I take him to the hospital."* **FG mothers, Bagira**

The high cost of care in the health facility requires that a family first has to mobilize the necessary funds before taking the baby:

> *"If you do not have all the money, they will give the treatment the first day and will ask you to find the rest of the money to continue the treatment; if not, they stop treatment on the second day. You are obliged to return home with the child like that."* **FG mothers, Bominenge**

The majority of mothers surveyed (8/14) say they preferred injectable antibiotics although some of them recognized disadvantages associated with it:

> *"Injections are better because some children refuse to swallow tablets and sometimes they vomit."* **FG mothers, Bominenge**

"I don't like injections; they are painful, but for my baby, I prefer them because tablets are bad for babies." **FG, mothers, Bagira**

"Injections work quickly on the child." **FG, mothers, Bominenge**

Management of neonatal sepsis in health facilities

The median number of cases of neonatal sepsis seen in the health facilities surveyed in the last three months is five cases with an interquartile space of 11 cases. Figure 3 shows the number of health facilities that treat neonatal sepsis by type of structure:

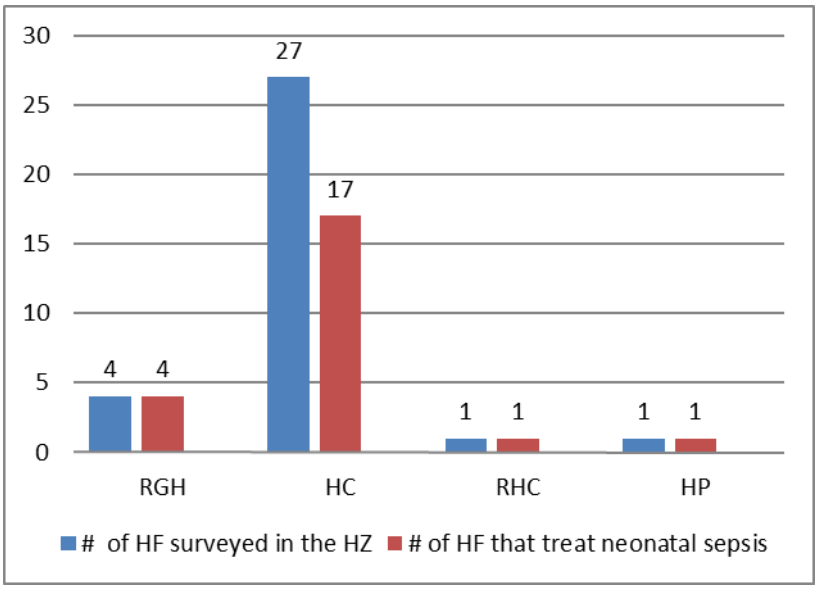

Figure 3: Number of health facilities that treat neonatal sepsis by type of facility

At the HCs, the MNCH guidelines recommend the administration of injectable ampicillin and gentamicin as a pre-referral treatment and then urgent referral to the hospital for complete treatment.

At the hospital level, the C-IMCI ETAT protocol is recommended.

Given the results, it appears these guidelines are not respected. Indeed, cases of neonatal sepsis are treated in health centers as well as hospitals. In addition, many different treatment regimens, ranging from a single antibiotic to the triple therapy, are used that are not in line with the standard protocol.

Thus, of the 17 HCs that say they treat cases of neonatal sepsis, only 12% cited the recommended combination of injectable ampicillin and gentamicin. The other combinations mentioned are not recommended in the national guidelines and are shown in figure 4.

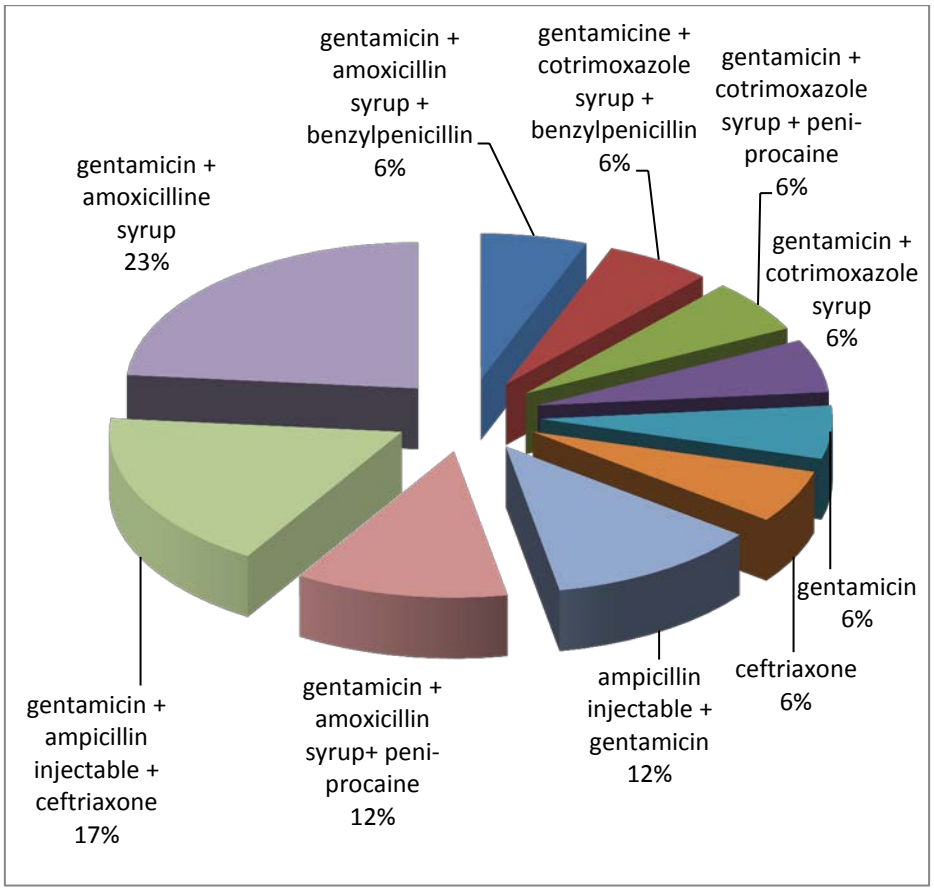

Figure 4: Therapeutic regimens for neonatal sepsis cited by HC service providers (n = 17)

This noncompliance with the norms was confirmed during the evaluation of the quality of care in the same health centers. Ten files of cases of neonatal sepsis during the last six months were randomly selected from among all the records available at each targeted health facility. If the required number of cases was not met, all eligible cases were analyzed.

Paradoxically, antibiotics that were cited by respondents as those recommended for treatment of newborn sepsis were not the same as those found in the analysis of the case records. So some discrepancy remains between what the respondents say is done and what is actually done. In total, 84 cases of newborn sepsis were able to be collected and analyzed.

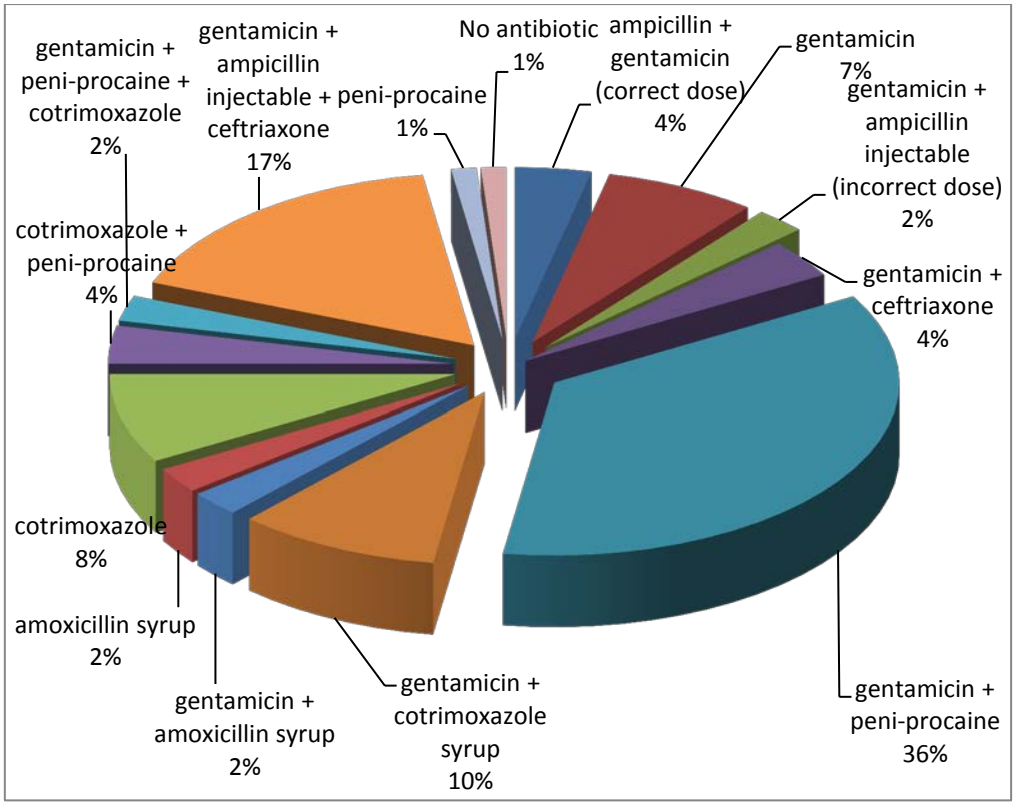

Figure 5: Treatment combinations for newborn sepsis from records in HCs (n = 84 records from 17 HCs)

Figure 5 shows more than 10 different combinations of antibiotics found in the treatment records of newborn sepsis studied in the health centers, but only 4% of the cases of sepsis studied were managed correctly.

Treatment of neonatal sepsis in the four hospitals surveyed was found to be better than at the HCs, but the proportion of cases managed properly in accordance with ETAT protocol is still low. Among 30 treatment records analyzed, only 40% of cases were given the correct treatment combination correctly as per ETAT protocol with the three following antibiotics: gentamicin + injectable ampicillin + ceftriaxone (or other third-generation cephalosporin) in the correct dosage. An additional 27% of cases were given the correct medicines but not in the correct dose, as shown in figure 6.

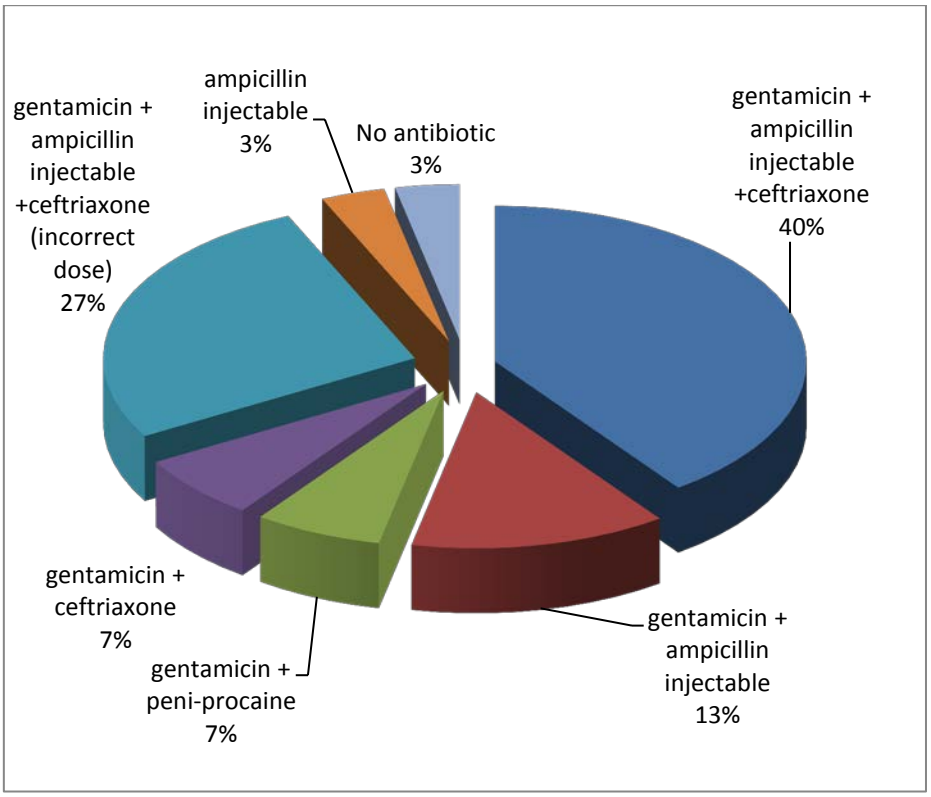

Figure 6: Therapeutic treatment combinations for newborn sepsis found in GRH records (n = 30 treatment records from 4 hospitals)

This situation is quite worrying, especially because different regimens for treatment of neonatal sepsis were cited by hospital health care providers. Regimens cited included the following:

- The combination of injectable ampicillin and gentamicin
- The combination of gentamicin and amoxicillin syrup
- The combination of gentamicin, injectable ampicillin, ceftriaxone, and injectable amoxicillin
- The combination of gentamicin, injectable ampicillin, ceftriaxon, augmentin syrup, and metronidazole

The low level of knowledge of signs and of correct management of neonatal sepsis by HC and GRH health care providers could be owing to the lack of specific training on neonatal sepsis treatment. The standards recommend that HC and hospital health care providers need to be regularly trained/refreshed in management of emergency care and treatment of the newborn.

In fact, 66% of service providers in the 17 health centers and all those surveyed in hospitals (n = 4) stating that they manage cases of newborn sepsis have not yet received training in this area. Even those who reported having been trained in newborn sepsis received training more than two years ago.

It could also be explained by the lack of knowledge of standards and guidelines, which have not been adequately disseminated. Only 24% of health facilities had a copy of the technical sheets or guidelines for treatment of newborn sepsis at the time of the survey.

Respondents from three COHZs said they sometimes assessed the level of knowledge of health care providers on the standards and guidelines. The Bominenge COHZ acknowledged that they are not, because the newborn sepsis management protocol from the School of Public Health for the AFRINEST Project is not consistent with the national guidelines. The demonstration HZ sites applied the simplified regimen.

Administration of injectable antibiotics

The incorrect preparation and administration of injectable antibiotics might also hamper the proper management of neonatal sepsis by health care providers. There are no standard operating procedures for the preparation of injectable antibiotics, and no health care providers who were interviewed reported reading the instructions for use when preparing the injection. Each injectable antibiotic has a different approach for its preparation.

Storage

Most surveyed health care providers (73%; n = 33) admitted they stored preparation for reuse of the antibiotic another time. For example, with respect to the ampoule of injectable gentamicin, the ampoule opening is closed with a piece of tape after the first use and stored at room temperature until it is needed again.

Most respondents (79%) say they reuse the injectable antibiotic only during a maximum of 24 hours, according to the guidelines, while others reuse it during a period ranging from two days to a week. In 73% of cases, the antibiotic is stored at room temperature, which is acceptable if it is not a reconstituted injection, but if it is a reconstituted antibiotic, it is not an acceptable practice because it allows the medicines to deteriorate, which could be dangerous for the baby.

Storage of medicines in the Bogbaguma HC, Bominenge Health Zone

Administration

Less than half (36%) of surveyed health care providers (n = 33) believe that the administration of injectable antibiotics is not easy. Most (70%) surveyed health care providers (n = 33) believe the use of oral amoxicillin would be a good alternative.

Regarding the barriers identified by providers when using injectable antibiotics in newborns, especially in case of major infection such as sepsis neonatal, they are as follows:

- The difficulty of finding the vein and/or location of injection (42%)
- The lack of materials, equipment, or supplies to administer the injection (35%)
- The lack of cooperation of the newborn and/or caregiver (23%)
- Fear of post-injection complications (23%)
- The high cost of treatment (13%)
- The difficulty of calculating the correct dose (7%)
- Other various reasons (7%)

It is worth noting that the vast majority of these barriers could easily be addressed by capacity-building sessions and supervision visits by the health zone and/or provincial staff.

All four COHZ respondents and three provincial-level respondents said the prescription of antibiotics was also among the items to be supervised.

In this regard, all three DPSs encounter irrational use of injectable antibiotics during their supervisory visits, where health care providers prescribe antibiotics with no real indication and prescribe too many antibiotics.

Other findings are health care providers' difficulty in calculating the correct dosage of antibiotic to administer (as reported by the South Kivu and South Ubangi DPSs) and frequent stock-outs (South Kivu DPS). These stock-outs could also be caused by irrational use of injectable antibiotics, which points to a need to organize trainings on management of neonatal sepsis to improve the quality of the treatment and to improve the management of stock of injectable antibiotics.

Referral of cases

At the health center level, the standards recommend that in case of major infection, the health care provider give the first dose of treatment and then refer urgently to the hospital. This rule is not respected, because in all the health facilities surveyed, cases have been treated as evidenced by the 84 treatment records analyzed in this study.

The signs for which the health center should refer the case, according to the health center respondents are shown in figure 7.

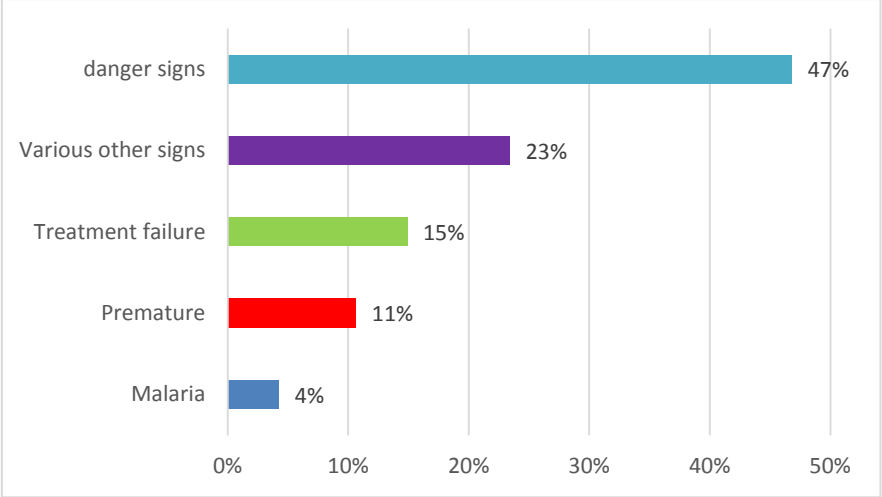

Figure 7: Reasons for referral of newborns

The majority of respondents (97%) stated that they refer cases of newborn sepsis to the hospital, after administering first doses of treatment, which consists of various antibiotics (58%), antipyretics (23%), and other adjunctive therapies (14%).

Regarding the monitoring of the outcome of the newborn after the referral, the majority of health center respondents (91%) said they do follow-up, but this is only done systematically by 39% of respondents. Reasons that the health care providers gave for not following up systematically are the following: they received feedback from the hospital (33%); lack of transportation for monitoring the referred cases (33%) while others did not provide sound reasons (34%).

Only 30% of health care providers believe the mothers would follow the advice to go to hospital, 61% felt that the mothers would maybe follow the referral advice, and 9% say they would not do it.

During focus group discussion, however, the majority of mothers (13/17) said that if the nurse advised them to take the child to hospital for better care, they would do so immediately:

> *"If the nurse refers me I will go immediately to the hospital and not to prayer groups. I respect the opinion of the nurse. I can tell you that when I fell pregnant I went to a clinic to give birth there and hoped to go back home thereafter, but I met nurses who after checking me, referred me to Ciriri hospital and I went directly."* **FG mothers, Kadutu**

A minority (2/17), however, said they would follow the referral advice, but after going first to their pastor to receive his blessing:

> *"If I was transferred to another hospital, I would go but after letting my Pastor know that so he could pray for me and his prayers can help me; for prayer to have an impact it is necessary that you have faith, that is why we say that where you are is where God is."* **FG mothers, Kadutu**

For some others (2/17), although they follow this recommendation, they believe that the referral would be recognition of failure to provide adequate treatment at the health center:

> *"Yes, I'll accept because it is the nurse himself who requested, and he did so because he failed and that's the reason for his request because he knows that all his superiors are at the hospital."* **FG mothers, Kadutu**

For those who would not follow the referral advice, the main reasons were long waiting time to receive care in hospital and high cost of treatment, especially treatment by means of injection.

> *"If you do not have enough money, your child will be given the treatment the first day and they will ask you to find the rest of the money so the treatment can be continued; if not, the second day they stop treatment. You are forced to go back home with the child without improvement.»* **FG mothers, Bominenge**

Focus group of mothers in the Bominenge HZ

Furthermore, opinions of CHWs are fairly divergent regarding the adherence of parents of newborns to referral. Some have claimed that parents have somewhat changed their behavior and readily agree to take the newborn to the hospital when they are given advice:

> *"To this day, people begin to hear our advice because it was in my community that a family often refused the vaccine; these days, I returned to the same family, they accepted me well and welcomed me and they begin to understand."* **FG CHWs, Kadutu**

Others said that parents hardly follow the referral advice and the CHWs need to insist and make several follow-up visits before recalcitrant parents agree to take their newborn with danger signs to the health center or hospital.

> *"There are those who accept and the others who refuse. Those who refuse for the first time and the second time, we appeal to the nurse in charge from the health center who also comes to talk to them, and they end up accepting after insistence."* **FG CHWs, Kadutu**

Some have admitted that parents would not follow the counseling or referral advice at all.

> *"No, some do not follow it; sometimes they hide the real reason for ignoring advice. Some hide under the pretext that they do not have money to go to the health center; yet, we sometimes offer ourselves as guarantor for the payment so that once the family finds money, they can pay."* **FG CHWs, BGA.**

Barriers to adherence such as noted by the CHWs are diverse: the habits and backward customs that would encourage parents to turn to traditional treatments; negative influences of other family members; and those related to religious beliefs (Kimbanguism, Jehovah's Witnesses), and especially the high cost of hospital care.

> *"Some families accept but tell you they do not have money; or ask if you can intercede for them with the health center. We often agree to plead for them at the health center and so the child is treated on credit in the health center."* **FG CHWs, Kadutu**

> *"Failure of the proper health-care seeking by some patients or the family, who start with self-medication, traditional healers, prayer rooms or go to private pharmacies before going to the health center. This causes late care seeking at the appropriate providers and can cause significant consequences."* **FG CHWs, Bagira**

Other barriers were related to poor quality of care in health facilities following the use of antibiotics of unknown quality or lack of a diagnostic laboratory, as illustrated in the following statement:

> *"The non-use of lab services in some health facilities does not reassure some patients about the diagnosis; the wrong choice of antibiotics by health care workers; the nonadherence to the prescription by parents; some ineffective medicines from several manufacturers that do not inspire confidence, some medicines do not treat the disease effectively."* **FG CHWs, Bagira**

A CHW noted a rather trivial fact that is more important than it seems, especially because it illustrates the importance of having appropriate clothing to go to a health institution:

> *"It's money problem and a problem of clothing: that is, at the health center you have to be well dressed. Mothers prefer to dress in wax prints, and when you do not have one you are ashamed go."* **FG CHWs, Karawa**

Two others noted the influence of the relationship existing between them and the community, explaining that sometimes the behavior of the CHW could negatively influence the attitude of the parents after the referral advice.

> *"... The obstacle is frequently at the CHW level: maybe you are not courteous and you do not know to talk with the entity to which you belong. Maybe you're the CHW and you've courted a daughter of this family where you have to go,. There it will be hard to sensitize in that family or you have an indignant behavior and it will be difficult ... "* **FG CHWs, Kadutu**

5. Private Sector

As in the public sector, it emerged from in-depth interviews conducted with the respondents in private pharmacies and medicine stores that the availability of antibiotics for neonatal sepsis is quite good for products such as gentamicin 80 mg/2 ml, injectable ampicillin, amoxicillin syrup, cephalosporin, and quinolones, whereas it is quite low for pediatric presentations in general, such as gentamicin 40 mg/1 ml. Amoxicillin 125 mg dispersible tablets are not available, and amoxicillin 250 mg dispersible tablets are quite rare.

According to the pharmaceutical sector survey report done in 2007, the private sector alone covers about 65% of the market. Understandably, the scarcity of a product in the private sector negatively affects availability in health facilities and consequently the quality of case management.

From the interviews, it appears that multiple supply chains exist for procurement, most of which are uncontrolled by the public authority, with obvious implications for the quality of the products in the Congolese market. It is therefore important to strengthen quality assurance mechanisms for essential medicines in general and particularly for injectable antibiotics, which are known to increase the risk of developing resistance if they are misused or of poor quality. Better quality assurance could be achieved in particular by strengthening the pharmacovigilance system.

Private pharmacies sometimes purchase injectable antibiotics from local medicine stores, sometimes from suppliers whose products come from abroad (Europe, China, and India) and sometimes from the wholesalers located in Kinshasa (Zenupha, Shalina, Moon Pharma, etc.). The medicine stores usually obtain medicines from local distributors located mainly in Kinshasa and also sometimes from the CDRs.

Both private pharmacies and pharmaceutical warehouses surveyed mentioned the lack of transport (especially by air) to transport medicines from Kinshasa to the provinces as one of the principal bottlenecks that hinders availability of essential medicines in general and especially injectable antibiotics. Very few airline companies regularly serve all parts of the country. According to owners, the lack of transport affects the prices of antibiotics, rendering them financially inaccessible for the majority of the population.

Medicine prices in the private sector are controlled by the Ministry of Economy, which fixes the profit margin (theoretically at 20% for wholesalers and 33% for pharmacies), whereas in the public sector, the prices are controlled by the MPH, which also grants approvals for opening private pharmaceutical establishments.

It would be important to promote local production of essential medicines to reduce taxes on imported products and therefore improve financial accessibility for essential medicines, including antibiotics for neonatal sepsis.

Similar to the public sector, there are no standard procedures to place an order in the private sector. Some are based on consumption, and others depend more on the availability of financial resources. Private pharmacies and pharmaceutical warehouses admitted they sometimes experienced stock-outs of injectable antibiotics. Private pharmacies have stated that there is a strong demand for injectable antibiotics, whereas most medicine stores have said the demand is quite low given the cost of these products. They also noted that it is

difficult to sell because of competition from the public sector, which is better established in the market.

Stock-outs of antibiotics are frequent and last on average nearly a week. If pharmacies order according to available funds, they cannot obtain the quantity they actually need. Moreover, as noted above, this practice may prejudice ordering of pediatric antibiotic presentations for neonatal sepsis. In addition, the receipt of the order is highly dependent on the availability of air-freight carriers, as explained above.

As for distribution, the respondents from private pharmacies identified health facilities and community members as their main customers. Sometimes sick clients also seek advice or prescription of a treatment; this is important to consider because in most cases, the attendants in pharmacies are not educated in the medical or pharmaceutical fields: they are mere sales persons. It might perhaps be worth training them in C-IMCI, as is done in some other African countries.

Respondents in medicine warehouses, in addition to pharmacies, also cited health facilities as their customers.

V. DISCUSSION

In the area of MNCH, in general, and specifically regarding treatment of the newborn emergencies, such as cases of neonatal sepsis, the DRC has implemented a series of policies and procedures to strengthen the quality of interventions and contribute to the reduction of neonatal mortality.

Among them, we can mention the creation in 2003 of the D10 within the MPH, whose mission is to promote family health and health of specific groups through integrated high-impact interventions targeting central, provincial, and HZ levels. In 2010, it updated the standard guidelines for health interventions in MNCH in collaboration with all partners operating in MNCH. This eight-volume document is entitled “Standards for health zones related to integrated interventions for maternal, newborn, and child health in the DRC." These different standards were used for implementing service and equipment levels in health facilities, while providing benchmarks for evaluation of implemented programs.

In addition, several other policies, standards, and guidelines exist in the field of MNCH in the DRC, but it must be emphasized, from the results of this analysis, we can see they are all insufficiently disseminated and applied at all levels of the health system. Moreover, it was noted that some discrepancies exist between them, especially in terms of dosage of antibiotics for neonatal sepsis, as was the case of the IMCI guidelines and those of MNCH for emergency care to the newborn. There were also differences between the ETAT protocol and the current WHO recommendations. The harmonization and updating of these guidelines is urgently needed, especially given current evidence that cases of neonatal sepsis can be effectively managed with a simplified regimen such as demonstrated in the AFRINEST study.

This finding is corroborated by the results of the health sector diagnosis conducted during the development of the Plan National de Développement Sanitaire (National Health Development Plan) 2011–2015.

Concerning regulations, standards, and guidelines for the pharmaceutical sector, this study showed that several laws exist, including those relating to the registration and authorization of marketing of pharmaceutical products and on the creation of the licensing commission of pharmaceuticals and other health products.

There is also a national system for supply, SNAME, consisting of centralized procurements through FEDECAME and decentralization of distribution through the CDRs, which are nonprofit organizations with management autonomy, operating nationwide.

Nevertheless, it should be noted that despite the establishment of this system, many problems still exist in the supply of antibiotics for neonatal sepsis, which this study has highlighted:

- Persistence of several parallel systems with multiple sources of supply and often uncontrolled diverse distribution channels that can enable the circulation of poor quality antibiotics
- Inadequate funding from the government for SNAME with respect to the supply of essential medicines in general as well as antibiotics for neonatal sepsis
- Nonstandardization of quantification methods from one CDR to another and in the whole health care system

- The high cost of essential medicines and especially injectable antibiotics, including those for the treatment of neonatal sepsis
- Lack of a policy to promote local production of antibiotics for neonatal sepsis
- Irrational use of antibiotics for neonatal sepsis
- Unavailability of pediatric forms of some antibiotics for neonatal sepsis, such as gentamicin 20 mg/ml and 40 mg/ml, amoxicillin 125 mg dispersible tablets, and 1 ml and 2 ml syringes
- Frequent stock-outs of antibiotics and supplies for neonatal sepsis
- Weak information system related to medicines and lack of data management tools for medicines including the LMIS

Regarding the availability and use of antibiotics for neonatal sepsis by health providers, the recommended combination is gentamicin and injectable ampicillin, but the study revealed that in health centers (n = 17) whereas gentamicin 80 mg/2 ml was available in 95% of those surveyed, injectable ampicillin was available in only 15% of them, making administration of the first pre-referral dose or the full treatment difficult and possibly explaining the noncompliance of providers and the irrational use of antibiotics by them. Indeed, only 4% of newborn sepsis treatment records (n = 84) showed correct case management.

Availability at the HGR level was marked by the presence of gentamicin 80 mg/2 ml, amoxicillin syrup, and ceftriaxone, which were found in stock in all HGR pharmacies surveyed, but injectable ampicillin was available in only 20% of the hospitals surveyed. Only 40% of the case records of newborn sepsis (n = 30) analyzed showed correct case management. This is another example of an irrational use of antibiotics on the part of prescribers, probably linked to stock-outs of antibiotics, and raises questions about the quality of the management of neonatal sepsis at hospital level, which is supposed to be the reference structure with more qualified staff as compared to HCs.

This situation could be explained in part by the inadequate dissemination of the standards, as noted earlier. More than three health institutions in four (76%) did not have guidelines and job aids or flow charts on the management of neonatal sepsis.

Poor case management could also be caused by lack of reinforcement of in-service capabilities by on-the-job training. In fact, nearly 66% of health care providers in the HCs surveyed had not received training on the management of neonatal sepsis. Moreover, the lack of supportive supervision from the next higher level also affects this treatment.

Prescribing and dispensing without clearly set standards contribute to increasing irrational use of medicines. This situation was also seen in the Report of the Review of the Directorate of Pharmacy (DPM).

The study also identified barriers to the use of injectable antibiotics for neonatal sepsis for health facility providers. It emerged that the greatest barrier proved to be the difficulty in finding the vein or IM injection location (42%), followed by the lack of antibiotics and/or supplies (syringes, gloves, cotton wool) to administer the product (35%); fear of post-injection complications (23%); and the lack of cooperation of the newborn or mother (23%). Other barriers are the high cost of care (13%) and the difficulty of calculating the correct dose (10%).

It appears that the greatest barriers can easily be overcome by training sessions on the administration of injectable antibiotics (preparation of the solution, accurately calculating the

dose based on weight, and correct administration of the product), provision of job aids, and a regular supply of appropriate antibiotics for the treatment of neonatal sepsis in health facilities.

It is really necessary to disseminate the revised guidelines for the management of cases of major infection in newborns because the study found that more than half the HCs (53%) did not refer in the presence of a danger sign. Now it is clear that these are newborn emergencies that can be adequately cared for only in a hospital that has a qualified technical platform.

Moreover, even though some cases are referred in case of danger signs, families do not always follow the provider's recommendation. According to the providers interviewed, less than one case in three (30%) of those referred follows the recommendation every time and goes to the hospital for better care. The remainder follow the recommendation late or not at all (60%).

The reasons given by providers and mothers are the high cost of care and the great distance to travel to reach the hospital, especially since there is usually no means of transport in rural areas.

This situation is exacerbated by the fact that, as declared by the majority of interviewed mothers, the decision on health-care seeking is made by the household head who must provide the funds to take the baby to a health facility. Some mothers, however, make the decision themselves without waiting for the head of household; others also turn to the mother-in-law.

Moreover, following the erroneous ideas that disease always has a supernatural cause, many mothers increase the delay in using health facilities by going to the pastor to seek a spiritual response to the child's disease. Even in following the referral advice, some admitted that it was necessary—if not mandatory—first to make contact with the pastor before taking the child to the hospital.

Along the same lines, an assessment of barriers to access to treatment of neonatal sepsis was performed in the community (mothers with a baby under three months of age and CHWs), who identified the following barriers:

- Inadequate perception of the severity of signs in the newborn
- Late care seeking in a health institution following the practice of self-medication at home, recourse to pastors and/or traditional practitioners because of the belief in supernatural causes of disease
- Perceived poor quality of care after waiting for a long time when the case is referred, being given ineffective antibiotics, and lack of medical examinations in certain HCs that can support the diagnosis
- The high cost of care
- Lack of transportation

Most of these barriers have already been identified in previous analyses, including the national plan for the elimination of bottlenecks for access to 13 medicines that save the lives of women and children; the Strategic Plan for Coverage of Essential Medicines for Child Survival; the DRC pharmaceutical profile; and the PNAME strategic plan.

In addition, the same analysis was carried out in Nigeria, and most of the findings are consistent.

VI. STRATEGIES AND CONCLUSION

Table 4: Summary of Identified Bottlenecks and Recommendations

Activity	Bottlenecks	Recommendations
I. Antibiotic Procurement	Low funding for essential medicines, including antibiotics for neonatal sepsis	Advocacy with political authorities and technical and financial partners to strengthen SNAME to improve the availability of essential medicines, including antibiotics for neonatal sepsis Advocacy with political authorities for the adoption and implementation of a national pricing policy for essential medicines, including antibiotics for neonatal sepsis, *and* a policy of promoting local production of antibiotics for neonatal sepsis Strengthen the capacity of agents at FEDECAME, CDRs, and health facility staff in the management of essential medicines, including antibiotics for neonatal sepsis including in quantification Dissemination of National Pharmaceutical Policy, regulations, and standards, particularly with respect to SNAME and the NEML to leaders of MPH institutions at central, provincial, and peripheral levels; among health care providers; and to implementing partners Implementation and use at all levels of care standardized procedures and tools for management of essential medicines, including antibiotics for neonatal sepsis Implement a pharmacovigilance system Strengthen the national health information system's medicine component (SNIS-MED) Seize the opportunity offered by the efficiency of the simplified regimen for the treatment of neonatal sepsis to strengthen the implementation of demonstration sites and possibly scale up in other provinces In collaboration with the PNIRA and MSH, under PROSANI plus, develop an action plan for the implementation of these recommendations Within the framework of interventions PROSANI plus, support monitoring activities by the PNIRA of implementation of these recommendations
	Weak capacity of personnel to quantify needs for antibiotics for treatment of neonatal sepsis at all levels	
	Poorly functioning SNAME	
	Nonapplication of standards and regulatory texts in the field of procurement of essential medicines in the public sector, which recommend centralized purchasing for economies of scale and decentralized distribution	
	Several parallel systems with multiple sources of supply and diverse distribution channels	
	High cost of essential medicines, including injectable antibiotics for the treatment of neonatal sepsis	
	Lack of a policy promoting local production of antibiotics for neonatal sepsis, which can reduce the price of antibiotics both in the public and private sectors	
	Circulation of poor-quality antibiotics from multiple uncontrolled sources and a poorly functioning quality assurance system	
	Unavailability of pediatric forms of some antibiotics for neonatal sepsis, such as gentamicin 20 mg/ml, 40 mg/ml, amoxicillin 125 mg dispersible tablets, and 1 ml and 2 ml syringes	
	Frequent stock-outs of antibiotics and supplies for neonatal sepsis management	
	Poorly functioning information system related to medicines and lack of data management tools for medicines, including the Logistics Management Information System (LMIS)	

Activity	Bottlenecks	Recommendations
II. Use of Antibiotics for Neonatal Sepsis	Existence of several standards and guidelines for management of neonatal sepsis with discrepancies in dosage and differences from current WHO recommendations	Update standards and guidelines taking into account WHO recommendations, the results of this analysis, and the effectiveness of the simplified regime from the AFRINEST Study Development of standard operating procedures and job aids for the preparation and administration of injectable antibiotics Dissemination of updated guidelines and standards incorporating the simplified regime for the management of neonatal sepsis at all levels of the health system Establishment of an ongoing on-the-job training plan for health system staff on the updated guidelines and standards of newborn health in general and on the management of neonatal sepsis Reproduction and distribution of guidelines, standards, technical sheets, job aids for the treatment of neonatal sepsis at all levels of the health system Advocacy for the establishment and extension of a *mutuelle* health insurance system to ensure financial accessibility to quality health care as recommended in the national health policy Increase the number of CHWs trained in C-IMCI and implement an incentive policy for the CHWs Sensitize the community on danger signs in the newborn and the importance of going straight to a health facility as well as on the efficacy of the simplified regime of gentamicin in combination with oral amoxicillin for treatment of newborn sepsis, as shown in the AFRINEST study
	Unavailability of guidelines, standards, technical sheets on the management of neonatal sepsis in health system facilities at all levels	
	Irrational use of antibiotics for neonatal sepsis in most health facilities and lack of supporting material, such as job aids, bulletins, etc. on case management and treatment administration	
	Insufficient on-the-job training in the field of newborn health and the management of neonatal sepsis for the health system personnel at all levels	
	Insufficient financing system for health care services such as “mutuelles” that can contribute to improving financial access to quality care	
	Low coverage of the country with community care sites	
	Erroneous perception that injectable antibiotics are more effective than oral antibiotics	
	Limited knowledge by the community of danger signs in newborns and the importance of going immediately to a health facility	
	Inappropriate health-care-seeking behavior in health facilities	

VII. CONCLUSION

This study aimed at analyzing the bottlenecks associated with procurement and use of antibiotics for the treatment of neonatal sepsis in order to propose strategies that will contribute to the reduction of infant mortality in general and neonatal mortality in particular.

Like other investigations carried out in the field of health in general or in the field of medicines, this study confirmed that despite the efforts to improve the coverage of essential medicines in child survival, the objectives are far from being achieved.

Bottlenecks identified through this research revolve mainly around the low functionality of the essential medicines supply chain, which results in the unavailability of antibiotics for neonatal sepsis at health facilities.

Moreover, inadequate training of health care providers on the guidelines for management of neonatal sepsis and administration of injectable antibiotics, the high cost of antibiotics for neonatal sepsis, and low community awareness of the danger signs are the main bottlenecks associated with the use of antibiotics by these target groups.

The DRC has endorsed several international initiatives aimed at reducing maternal and infant mortality and has several plans, including one aimed at eliminating bottlenecks associated with provision of 13 life-saving medicines for women and children and the strategic plan for coverage of essential medicines for child survival.

This report will contribute to that effort by showing much still remains to be done to eliminate barriers to procurement and use of antibiotics for neonatal sepsis in the DRC. The proposed solutions are based on evidence from the study, and the report also serves as an advocacy tool for technical and financial partners working in the field of MNCH to continue supporting development of targeted interventions to improve the health of the newborn in the DRC.

Simple and feasible corrective measures were recommended, such as updating and harmonization of standards and guidelines; training and support to the health care providers in the application of updated standards and guidelines as well as in the quantification of antibiotics requirements for neonatal sepsis; implementation and expansion of demonstration sites to reduce barriers to the use of antibiotics in health facilities; and strengthening of the procurement system for essential medicines, especially regarding pediatric forms of antibiotics and syringes for neonatal sepsis. The PROSANI-Plus project should take advantage of the opportunity to offer technical assistance to PNIRA in the follow-up and monitoring of the implementation of these recommendations.

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