Scientific Research Publishing

Pharmacology & Pharmacy, 2026, 17(7), 215-228
https://www.scirp.org/journal/pp
ISSN Online: 2157-9431
ISSN Print: 2157-9423

Evaluation of Rational Antibiotic Use in Neonatology: The Angre University Hospital Experience

Leynouin Franck-Olivier Te Bonle[1,2*], Alain Aka Kacou[1,3], Melissa Cardenat[4], N'Guessan Aimé Brou[2], Aziz Flores Kamelan[1], Daniel Oula[1], Geneviève Irie-N'Guessan[2]

[1]Department of Pharmacy, Angré University Hospital, Abidjan, Côte d'Ivoire
[2]Pharmacology and Hospital Pharmacy Unit, Department of Pharmaceutical Sciences, UFR Pharmaceutical and Biological Sciences, Félix Houphouët-Boigny University, Abidjan, Côte d'Ivoire
[3]Medicinal Chemistry and Organic Chemistry Unit, Department of Pharmaceutical Sciences, UFR Pharmaceutical and Biological Sciences, Félix Houphouët-Boigny University, Abidjan, Côte d'Ivoire
[4]Department of Pediatrics and Specialties, Angré University Hospital, Abidjan, Côte d'Ivoire
Email: *tebonlefranck@gmail.com

How to cite this paper: Te Bonle, L.F.-O., Kacou, A.A., Cardenat, M., Brou, N.A., Kamelan, A.F., Oula, D. and Irie-N'Guessan, G. (2026) Evaluation of Rational Antibiotic Use in Neonatology: The Angre University Hospital Experience. *Pharmacology & Pharmacy*, **17**, 215-228.
https://doi.org/10.4236/pp.2026.177012

Received: July 1, 2026
Accepted: July 26, 2026
Published: July 29, 2026

Abstract

Introduction: Neonatal mortality is largely driven by preventable conditions, including maternal-fetal bacterial infections, which frequently require antibiotic therapy. Optimizing antibiotic use in neonatal care is therefore a major public health priority, particularly in low- and middle-income settings. This study aimed to describe antibiotic utilization patterns and assess prescribing practices in the neonatal unit of Angre University Hospital, Côte d'Ivoire. **Methods:** A prospective descriptive study was conducted among neonates admitted to the neonatal unit between November 1, 2022, and January 31, 2023. Data collected included demographic and clinical characteristics, indications for admission, and assessment of infectious risk. Antibiotic utilization pressure and compliance of prescribing practices with established clinical guidelines were evaluated. **Results:** The majority of neonates were admitted for suspected early-onset neonatal bacterial infection. A male predominance was observed, with more than half of the deliveries performed by cesarean section and a considerable proportion of neonates presenting with APGAR scores below 6. Antibiotics were the most frequently prescribed medications, with the cefotaxime-gentamicin combination being the most commonly used regimen. Overall, 34.2% of antibiotic prescriptions did not meet predefined relevance criteria, mainly because the treatment had not been reassessed or adjusted based on available blood culture results. Bacteremia was microbiologically confirmed in fewer than one-third of cases, and staphylococci were the pre-

dominant pathogens isolated. **Conclusion**: In neonatology, where patients are highly vulnerable to infections, rational and guideline-adherent antibiotic use is essential to ensure effective treatment while minimizing the risk of antimicrobial resistance.

Keywords

Neonatology, Drug Prescriptions, Anti-Bacterial Agents, Rational Use, Neonatal Nursing Care

1. Introduction

The discovery of antibiotics marked a major therapeutic revolution in the mid-twentieth century. However, their excessive and inappropriate use has led to the rapid emergence of resistance, making antimicrobial resistance (AMR) a major global health threat. According to a recent analysis published in The Lancet, infections caused by antibiotic-resistant bacteria were directly responsible for 1.27 million deaths worldwide in 2019, highlighting the magnitude of this phenomenon [1].

The African continent is disproportionately burdened by this threat. Data reveal an increasing prevalence of multidrug-resistant strains, notably methicillin-resistant *Staphylococcus aureus* (MRSA) and Gram-negative bacilli producing extended-spectrum beta-lactamases (ESBLs) and carbapenemases [2]. This alarming situation, where up to 80% of *Staphylococcus aureus* infections can be resistant, renders first-line antibiotics ineffective [3]. In Côte d'Ivoire, this trend is confirmed by studies showing extremely concerning resistance levels, reaching, for instance, over 90% for third-generation cephalosporins, which are nonetheless essential molecules [4].

Within this challenging epidemiological landscape, neonatal care settings are especially high-risk environments. Due to the immaturity of their immune system, newborns are particularly susceptible to severe nosocomial infections. In fact, bacterial infections are one of the leading causes of neonatal mortality, all of which are preventable through accessible and available quality healthcare, including access to effective antibiotics [5].

The inherent difficulty in confirming an infection diagnosis in newborns often leads to the inappropriate use of antimicrobials, thereby compromising the goal of rational use as a cornerstone of quality care. This practice fosters the emergence and spread of resistant strains, establishing multidrug-resistant bacteria as a critical public health issue in neonatal intensive care units [6].

As a national reference center, Angré University Hospital undertook an evaluation of antibiotic prescribing practices in its neonatology unit. Given the paucity of recent, context-specific data in this intensive care setting, a detailed assessment was deemed necessary. This study therefore aimed to evaluate prescription com-

pliance with predefined criteria derived from the local neonatal protocol and french neonatal guidelines, identify discrepancies and formulate evidence-based recommendations to optimize antibiotic therapy.

2. Materials and Methods

A prospective descriptive study was conducted in the neonatology and neonatal intensive care unit of Angré University Hospital from November 1, 2022, to January 31, 2023.

2.1. Study Population and Eligibility Criteria

All newborns admitted to the neonatal intensive care unit (NICU) during the study period were eligible. Newborns discharged against medical advice or transferred to another healthcare facility were excluded from the analysis, as were those with incomplete medical records.

The study database did not contain a separate list of eligible and excluded newborns. Therefore, exclusions could only be described based on the available analytical data. This point was taken into account when interpreting a possible selection bias.

2.2. Data Collection

Data were extracted from patients' medical records and treatment sheets, as well as from the medical biology department's database. Variables included sociodemographic profile, reasons for hospitalization, infectious risk, laboratory data, and blood culture results in newborns. Regarding prescribed antibiotics, in addition to consumption data, dosage, duration of treatment, and any changes or interruptions in treatment after obtaining microbiological results were recorded. Missing laboratory data were considered as such and were not imputed. For the quality assessment of prescriptions, the absence of blood cultures limited the analysis of therapeutic adjustments guided by microbiological results; these cases were interpreted separately from those for which a blood culture result was available but not used for therapeutic adjustment.

2.3. Definition of Early-Onset Neonatal Bacterial Infection and Infectious Risk Assessment

In this study, early neonatal bacterial infection was classified as probable or microbiologically confirmed and defined as occurring within the first 72 hours of life. A confirmed early neonatal bacterial infection was defined as a clinically consistent infection with a positive blood culture validated by the medical biology department. A probable early neonatal bacterial infection was defined by the presence of compatible maternal or perinatal risk factors and/or neonatal clinical signs, with or without elevated inflammatory biomarkers, in the absence of microbiological confirmation.

Two clinical risk assessment tools were used:

- The **Houenou score** [7] (Table 1), developed for screening suspected maternal-fetal infections, whereby neonates classified with moderate-to-high risk were deemed eligible for antibiotic therapy.
- The **RIB-MF score** [8] (Table 2), employed to inform the decision to initiate antimicrobial treatment.

Table 1. Houenou infectious score [7].

Score Criteria	Scoring	
	No	Yes
Maternal temperature > 38˚C	0	1
Premature rupture of membranes	0	1
Maternal evacuation	0	1
Prematurity or low birth weight without clear cause	0	2
APGAR* score ≤ 6	0	2
Meconium-stained or discolored amniotic fluid	0	2

Interpretation: 1 ≤ Score 1 ≤ 2: Low risk; 3 ≤ Score 2 ≤ 4: Moderate risk; Score 3 ≥ 5: High risk. *APGAR: Appearance, Pulse, Grimace, Activity, Respiration.

Table 2. Classification of patients according to the maternofetal bacterial infectious risk (RIB-MF) before paraclinical investigation [8].

RIB-MF	Medical History	Clinical Signs	Management
No risk	–	–	No antibiotics Monitoring
Low risk: Possible infection	+	–	No antibiotics, Paraclinical workup
	-	+	
High risk: Probable infection	+	+++	Paraclinical workup, Antibiotic therapy
	–	+++	
	+++	–	

2.4. Blood Culture Procedures

The investigators did not directly participate in blood sample collection, blood culture processing, or microbiological identification. In accordance with standard institutional practice, neonatal blood cultures are obtained by peripheral venipuncture or, when clinically indicated, by umbilical catheter after antisepsis. It is recommended to collect at least 1 mL of blood, and up to 2 mL when possible, particularly in newborns who have previously received antibiotics. Blood cultures are incubated for at least 5 days. Positive blood culture results and bacterial iden-

tification were validated by medical biologists according to standard laboratory procedures. However, detailed information on the actual blood volume collected, the number of blood culture bottles obtained per neonate, the antiseptic agent used, and adherence to recommended sampling procedures was not systematically available in the study database. The specific criteria used to distinguish contamination from true bloodstream infection, particularly for coagulase-negative staphylococci, were also unavailable and could not be independently reassessed by the investigators.

2.5. Measurement of Antibiotic Consumption

To assess antibiotic use pressure, we computed the penetration rate (number of antibiotic treatment days per 1000 days of hospitalization) [9], applying the following formula:

$$PI = \frac{Q}{P \times DDD} \times 1000$$

where: PI = Penetration index; Q = Quantity of antibiotic consumed (in grams); P = Number of patients-day in hospital; DDD = Defined Daily Dose.

2.6. Analysis of Antibiotic Use

The primary criterion was the proportion of antibiotic prescriptions deemed appropriate according to a composite quality criterion. This criterion was predefined according to the neonatology department's internal protocol, aligned, where applicable, with french neonatology guidelines. Five aspects were evaluated:

- the justification for the indication;
- the appropriate choice of antibiotic;
- the dosage within the recommended range (mg/kg/day);
- the appropriate duration of treatment;
- and reassessment or adjustment based on blood culture results and clinical progress.

Prescriptions were classified as appropriate when all five predefined criteria were met. Inappropriate prescriptions were further categorized as debatable or unacceptable. A prescription was considered debatable when the indication and antibiotic choice were appropriate but one or more deviations concerned dosage, treatment duration, or treatment reassessment based on microbiological findings. A prescription was considered unacceptable when the indication for antibiotic therapy was not justified, the antibiotic choice was inappropriate for the clinical condition, an unnecessary antibiotic combination was prescribed, or the treatment regimen posed a potential risk to patient safety.

2.7. Statistical Analysis

Data were analyzed descriptively. Qualitative variables were summarized as counts and percentages. For the main proportions relevant to the study objectives, 95% confidence intervals (95% CIs) were calculated using the Wilson score method.

Given the single-center design, limited sample size, and incompleteness of several laboratory variables, no multivariable analysis was performed.

2.8. Ethical Considerations

For the purposes of our study, an administrative procedure was followed to obtain approval from the Medical and Scientific Directorate of the Angré University Hospital Center for access to patient records. Data were collected confidentially and with patient anonymity maintained.

3. Results

3.1. Study Population

A total of 139 neonates were included in the study. The majority of patients (95%) were admitted to the neonatal unit within the first 24 hours of life. A male predominance was observed, with a sex ratio of 1.57. Nearly half of the neonates (49.6%) were born at term, and 52.5% were delivered by cesarean section. The main reasons for hospitalization were an APGAR score < 6 (54.7%), respiratory distress (46.8%), and prematurity (23.7%).

3.2. Biological Investigations

Laboratory tests were performed in 84.2% of newborns (117/139), including 21 C-reactive protein (CRP) measurements and 96 procalcitonin measurements. Elevated inflammatory markers were detected in 41% of newborns (48/117), with 8 positive CRP results and 40 elevated procalcitonin levels.

3.3. Infection Scores and Therapeutic Decision

The proportion of neonates classified as requiring antibiotic therapy differed markedly between the Houenou score and the RIB-MF classification (Table 3).

Early neonatal bacterial infection was ultimately the most frequent discharge diagnosis (114 cases).

Table 3. Distribution of neonates according to infection risk.

Score	n/N	% (95% CI)	Therapeutic Decision
Houenou Score			
1 (Low risk)	85	61.2 (52.9 - 68.9)	No antibiotics
2 (Moderate risk)	42	30.2 (23.2 - 38.3)	Antibiotics
3 (High risk)	12	8.6 (5.0 - 14.5)	
RIB-MF Score			
Low (Possible MFI)	25	18 (12.5 - 25.2)	No antibiotics
High (Probable MFI)	114	82 (74.8 - 87.5)	Antibiotics

3.4. Bacteriological Analysis

Among 114 newborns for whom blood cultures were requested, results were available for 63 (55.3%; 95% CI: 46.1 - 64.1). The reasons why blood cultures were not performed or completed in the remaining cases were not systematically recorded in the study database. Of the 63 newborns for whom blood culture results were available, 34 had positive cultures (54.0%; 95% CI: 41.8 - 65.7). Microbiological confirmation was obtained in 34 of the 114 newborns treated for early neonatal bacterial infection (29.8%; 95% CI: 22.2 - 38.8). Positive blood culture results and bacterial identification were validated by medical biologists according to routine laboratory procedures. Gram-positive cocci, mainly staphylococci, were the most frequently identified microorganisms (Table 4).

Table 4. Distribution of identified microorganisms.

Microorganisms	Number	Percentage
Gram-positive cocci	**19**	**55.9**
Coagulase-negative *Staphylococcus*	14	41.2
Staphylococcus aureus	3	8.8
Staphylococcus epidermidis	2	5.9
Gram-negative bacilli	**6**	**17.6**
Klebsiella pneumoniae	3	8.8
Escherichia coli	3	8.8
Other bacteria	**9**	**26.5**

3.5. Antibiotic Consumption Evaluation

Antibiotics comprised 53.4% of the medications utilized in neonatal therapy. The general profile of drug consumption is presented in Figure 1. Three principal antibiotic classes constituted the majority of prescriptions, as summarized in Table 5.

Table 5. Antibiotic consumption by family and molecule.

Antibiotics	Penetration Index**
J01D (other β-lactams): Cefotaxim	**47.21**
J01M (quinolones): Ofloxacin	**8.02**
J01G (aminoglycosides)	**16.83**
• Amikacin	1.54
• Gentamicin	15.29

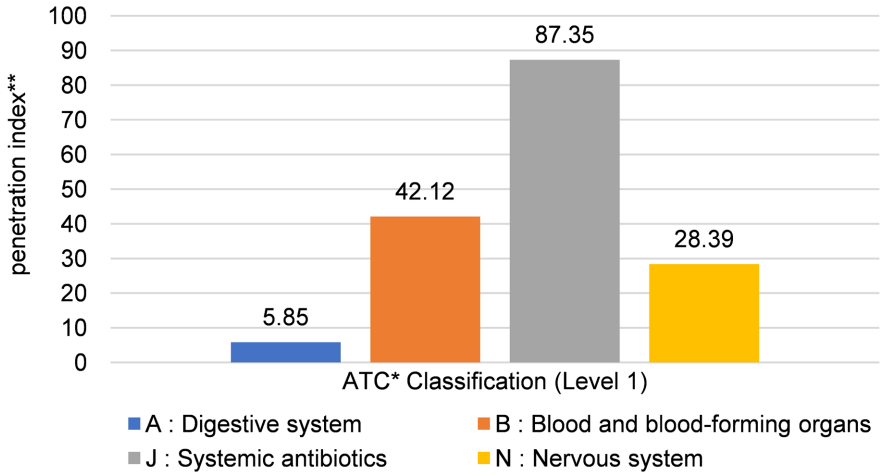
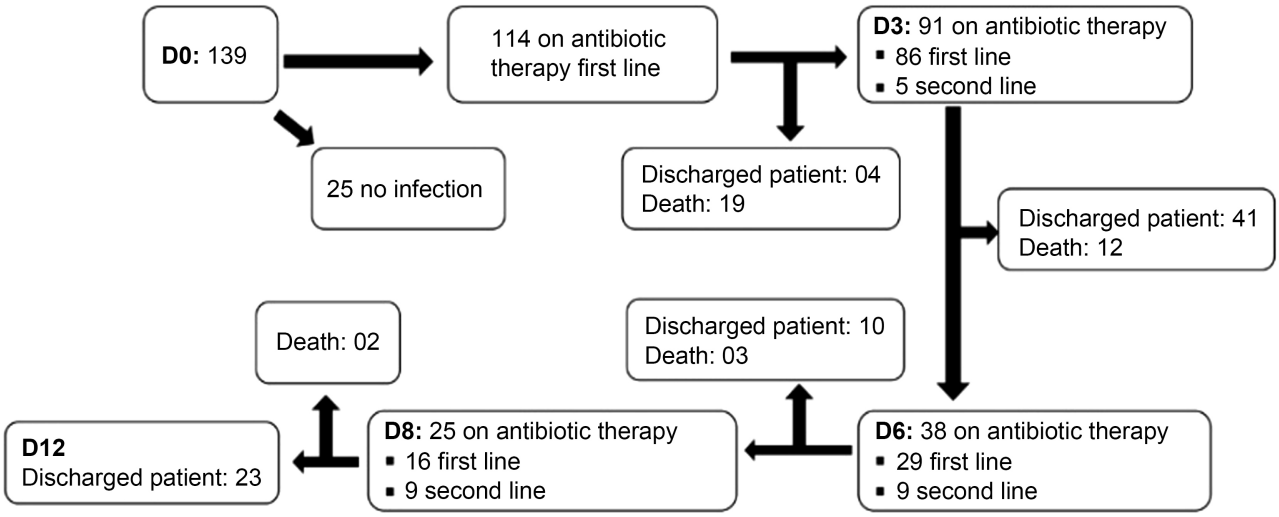


Figure 1. Drug consumption profile. *Anatomical Therapeutic Chemical; **Number of defined daily doses per 1000 hospital days.

3.6. Analysis of Antibiotic Prescribing

Figure 2 outlines the antibiotic prescribing strategy, which included a systematic re-evaluation of the treatment after 72 hours.

Deviations from guidelines were identified, primarily related to treatment adjustment according to blood culture results, dosage and treatment duration (**Table 6**). In total, 34.2% of all prescriptions were classified as inappropriate.



D: Day.

Figure 2. Antibiotic prescribing strategy.

Overall, 75 of 114 antibiotic prescriptions were classified as appropriate, whereas 39 prescriptions were classified as inappropriate (34.2%; 95% CI: 26.1 - 43.3). The main deviations from the predefined appropriateness criteria were unjustified continuation of antibiotic therapy after blood culture results became available, non-compliant dosage, and non-compliant treatment duration (**Table 6**)

Table 6. Pharmaceutical assessment of antibiotic prescriptions.

Compliance with antibiotic prescriptions				
Prescription Quality			Number (N = 114)	% (95% CI)
Appropriate prescription			75	65.8 (56.7 - 73.9)
Inappropriate prescription	Debatable	Non-compliant dosage	8	7.0 (3.6 - 13.2)
		Non-compliant treatment duration	2	1.8 (0.5 - 6.2)
		Unjustified continuation after blood culture	29	25.4 (18.3 - 34.1)
	Unacceptable		0	0
Identified Prescription Issues				
Administered doses				
Antibiotics	Reference Doses (mg/kg/day)	Prescription Quality		
		Appropriate	Debatable	
Cefotaxime + Gentamicin	100 - 200 + 3 - 5	109 (95.6%)	5 (4.4%)	
Ofloxacin + Amikacin	12 + 15	22 (88%)	3 (12%)	
Treatment Duration				
Antibiotics	Maximum Recommended Duration (days)			
Cefotaxime + Gentamicin	7 + 3	112 (98.2%)	2 (1.8%)	
Ofloxacin + Amikacin	7 + 3	25 (100%)	0	

4. Discussion

4.1. Demographic and Clinical Characteristics of Neonates

A male predominance was observed in our study, consistent with existing epidemiological data from African settings. This finding is consistent with the documented increased susceptibility of male neonates to NBI in settings such as Bamako (57%) and Yaoundé (63%) [10] [11], although geographical variations exist, as evidenced by the sex ratio of 0.8 observed in Maradi [12].

The early admission of hospitalized newborns corroborates the early onset of NBI in our cohort, with most admissions occurring within the first 24 hours of life. This profile aligns with recent Malian observations [13] and fits within current definitions of early-onset neonatal infections [14].

Analysis of perinatal factors revealed a balanced distribution between cesarean sections and vaginal deliveries, reflecting variability in obstetric practices. Disparities exist in the literature: Kamaye [15] reported 61.5% cesarean sections, while Coulibaly *et al.* [13] in Bamako observed a predominance of vaginal de-

liveries (84.6%).

The finding that prematurity was not a major risk determinant in our cohort, in contrast to reports by Djidi [10] and Cohen *et al.* [14], underscores the heterogeneity of risk profiles across different settings.

4.2. Diagnostic Evaluation and Therapeutic Strategies

The observed discrepancy between the Houenou and RIB-MF scores in assessing the risk of neonatal infection significantly impacted antibiotic prescribing. This discrepancy raises important questions regarding the standardization of risk assessment tools in African settings, where most studies rely on conventional maternal and neonatal clinical risk factors and medical history [15] [16]. In our study, the RIB-MF score identified all newborns who were ultimately treated for probable early neonatal infection, while the Houenou score classified a smaller subgroup as being at moderate or high risk. This discrepancy suggests that the RIB-MF score may be more sensitive in identifying at-risk newborns and thus reducing the likelihood of undertreatment; however, its use could also increase antibiotic exposure in settings where microbiological confirmation is limited. The validity, sensitivity, and specificity of these two tools have not been fully established outside the contexts in which they were initially developed; therefore, their results should be interpreted as clinical decision-support tools rather than definitive diagnostic tests. These results underscore the need for locally conducted validation studies comparing the performance of clinical risk scores to standardized microbiological and clinical reference criteria. However, because the RIB-MF classification contributed to the initial therapeutic decision, the concordance between this score and the final diagnosis of probable infection should not be interpreted as independent evidence of diagnostic accuracy.

Our diagnostic approach systematically combined blood cultures with inflammatory biomarkers. Although the diagnostic performance of C-reactive protein (CRP) and procalcitonin (PCT) in the early stages of infection remains limited, serial measurement of these biomarkers is a well-established strategy to support decisions regarding the early discontinuation of antibiotic therapy [14]. The microbiological profile observed in our study, characterized by a predominance of Gram-positive cocci, particularly staphylococci, is consistent with data reported in West Africa [13] [15]. Although positive blood culture results have been validated as microbiologically significant by medical biologists in routine laboratory practice, the predominance of coagulase-negative staphylococci warrants cautious interpretation, as the specific criteria used to distinguish contamination from true infection were not available for independent reassessment. By contrast, our results differ from those reported in the European context, particularly in France. European data indicate that maternal-fetal infections are predominantly caused by Group B Streptococcus and *Escherichia coli* [14]. These differences may be attributed to variations in local epidemiology, screening practices, and socioeconomic factors. Additional comparative and multicenter studies are warranted to

better understand the underlying factors responsible for these regional differences and to optimize prevention strategies accordingly.

4.3. Antibiotic Practices and Resistance Challenges

The restriction to four main pharmacological classes reflects the persistent difficulties encountered in neonatal pharmacology in Africa, where marketing authorization for pediatric drugs remains limited. The predominance of antimicrobial use reflects the high prevalence of infections in our setting.

Therapeutic protocols aligned with practices in other Ivorian university hospitals [16] but differed from West African regimens favoring ceftriaxone [13] [15] First-line treatment was based on the combination of cefotaxime and gentamicin, while the combination of ofloxacin and amikacin was used as second-line therapy.

The progressive phasing out of ceftriaxone in Côte d'Ivoire was driven by safety imperatives (calcium precipitation and risk of fetal erythroblastosis), illustrating how practices evolve based on pharmacological data [17]. In contrast, the divergence from French guidelines, which recommend amoxicillin-gentamicin combination [18], might be explained by local epidemiological specificities.

The high consumption of third-generation cephalosporins raises legitimate concerns about the emergence of bacterial resistance. This study argues for the implementation of antimicrobial resistance surveillance programs, the adaptation of therapeutic protocols to local epidemiology, the strengthening of diagnostic capacities and the continuing education of healthcare personnel.

4.4. Prescription Quality

Approximately one-third of antibiotic prescriptions did not meet the predefined appropriateness criteria. This finding is broadly consistent with the observations reported by Goulet *et al.* [19], while also reflecting context-specific prescribing challenges. The main deviations concerned treatment adjustment in response to blood culture findings, dosage issues, and treatment duration.

According to Maury *et al.*, optimal antibiotic prescribing requires the simultaneous application of a justified indication, an appropriate drug, an adequate dosage, and adjustment based on microbiological results [20]. However, non-compliance should not be interpreted solely as individual prescriber behavior. Several systemic constraints can explain the observed discrepancies: delayed blood culture results, insufficient laboratory capacity, difficulty in obtaining neonatal blood samples, socioeconomic barriers limiting access to diagnostic tests, clinical instability of newborns, and fear of undertreatment in cases of potentially severe sepsis. These constraints may incentivize clinicians to continue antibiotic therapy even when available microbiological data do not fully justify continued treatment. Therefore, an effective antimicrobial stewardship intervention in this context should combine prescriber training with diagnostic management, improved turnaround time for laboratory tests, a standardized 48- to 72-hour review, pharmacy-supported auditing and feedback, and local resistance monitoring.

4.5. Strengths and Limitations

This study has several strengths, including its prospective design, its focus on a neonatal unit in a resource-constrained setting, and its combined assessment of infection risk, antibiotic consumption, and prescription quality. However, several limitations should be acknowledged. The study was conducted at a single center over a short three-month period, limiting the generalizability of the findings and precluding the assessment of seasonal variations. Blood culture results were unavailable for a substantial proportion of neonates for whom they had been requested, and the reasons for these missing results were not systematically recorded. Consequently, the impact of missing microbiological data on treatment reassessment and prescription appropriateness could not be formally quantified. In addition, because the specific criteria used to distinguish contamination from true bloodstream infection were unavailable for independent reassessment, microbiological findings, particularly those involving coagulase-negative staphylococci, should be interpreted with caution. Finally, the use of DDD-based indicators is limited in neonates because DDDs are based on adult dosing assumptions and do not reflect weight-based neonatal exposure. The DDD approach was retained as an aggregate measure of antibiotic consumption rather than as an indicator of individual neonatal exposure. Days of therapy would provide a more appropriate complementary indicator in future studies.

5. Conclusion

This study highlights the complex challenges of neonatal care in sub-Saharan Africa, where a high prevalence of suspected bacterial infections coexists with significant diagnostic and therapeutic constraints. The predominance of staphylococci, whose interpretation must be cautious due to the risk of contamination by coagulase-negative staphylococci, underscores the importance of strengthening microbiological procedures and local surveillance of antimicrobial resistance. The high rate of non-compliant prescriptions, primarily due to insufficient adjustment of treatment following blood culture results, highlights the need to strengthen diagnostic management and implement structured programs for the appropriate use of antibiotics in neonatal units. Preserving the effectiveness of antibiotics remains essential to reducing neonatal morbidity and mortality in resource-limited settings.

Conflicts of Interest

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

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