

Evaluation of Antibiotic Prescribing in the Pediatric Department of Gabriel Touré Teaching Hospital, Bamako, Mali

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Abstract

Objectives: The main objective was to evaluate antibiotic prescribing in the Department of Pediatrics at Gabriel Touré teaching hospital. **Methods:** This was a prospective descriptive study conducted from September 1 to November 31, 2018, in the Department of Pediatrics at Gabriel Touré teaching hospital. All children aged 0 to 15 years hospitalized for any pathology during the study period and having received at least one antibiotic had been included. **Results:** We collected 445 children's records out of 1032 admissions during the study period, representing a hospital frequency of 43.1%. The sex ratio was 1.3%. The 2 - 5 age group accounted for 48.1%. Fever was the reason for consultation in 45.6% of cases. Patients' general condition was altered in 60% of cases. The fathers were blue-collar workers in 65.4% and the mothers housewives in 85%, and had no education in 42.9% and 64.5% respectively. Hepatomegaly was present in 18.2%, splenomegaly in 9.6% and peripheral adenopathy in 3.1%. The site of infection was pulmonary in 37.6% and ENT in 9.2%. Bacterial infection was assumed on admission in 54% of cases, and meningitis in 57.7%. The discharge diagnosis was malaria in 54.6%, severe acute malnutrition in 18.6% and meningitis in 6.7%. The death rate was 3.8%. Neutrophilic leukocytosis was present in 47.3% of patients. CRP was positive in 85% of patients. Blood cultures taken in 27.6% of patients were positive in 5. CSF analysis in 30% of patients showed elevated leukocytes in 6.5%. No cultures were positive. Antibiotic prescription was justified by infectious hypotheses in

43.1% of patients. β -lactam antibiotics were prescribed in 98.6%. Antibiotic therapy was not adapted to national/international recommendations in 68.3% of cases, and was not justified in 16.3% of cases on D5 of hospitalization.

Conclusion: Antibiotic use was justified in more than half of patients, but remained inadequate in almost two-thirds of cases, in line with national and international recommendations.

Keywords

Antibiotic Prescription, Hospitalization, Child

1. Introduction

Antibiotics are substances of natural or semi-synthetic origin capable of inhibiting or destroying some microbial species [1]. The era of antibiotics began in earnest in 1941, following the industrial production of the penicillins discovered in 1929 by Flemming [2]. The discovery and development of antibiotics (ATBs) was a major scientific breakthrough in the 20th century, revolutionizing the history of medicine by making it possible to effectively treat numerous bacterial diseases which, until then, had generally been fatal. Indeed, until the last century, infectious diseases still accounted for a significant proportion of deaths, and the spread of antibiotics combined with the widespread use of vaccinations greatly curbed them [3] [4]. Since then, infectious pathology and antibiotic treatment have undergone rapid change, marked on the one hand by the emergence of new pathogens, and on the other by the development of antibiotic resistance, despite the introduction of new molecules [5]. Antibiotics account for a significant proportion of drug prescriptions: one in four prescriptions includes an antibiotic [6]. However, their use requires a great deal of rigor, as improper handling can increase their disadvantages, notably the occurrence of side effects, the risk of unnecessary expenditure and, above all, the spread of bacterial resistance [2] [6] [7] [8]. The health consequences and economic costs of antimicrobial resistance (AMR) are estimated at 10 million human deaths per year and a 2% to 3.5% drop in global gross domestic product (GDP), or USD 100,000 billion by 2050 [9]. One of the major causes of antibiotic resistance is the uncontrolled and inappropriate use of antibiotics [2] [8] [10]. One of the principles of controlling bacterial resistance is therefore to ensure the proper use of antibiotics, in order to avoid the emergence and spread of multi-resistant bacteria, and to reduce the cost of treatment and the length of hospital stays [11] [12]. Faced with the scale of the problem, the WHO, at its World Assembly held in May 2015, adopted a Global Action Plan (GAP) to combat antimicrobial resistance, which defines five objectives. Goal 4 of this plan is to Optimize the use of antimicrobial drugs in human and animal health [13]. Several studies carried out in Africa show a high rate of antibiotic prescribing in paediatric hospitals [14] [15] [16]. Our study contributes to the evaluation of antibiotic prescribing in our pediatric department,

with the following hypotheses:

- The rate of antibiotic prescribing remains high in paediatric hospitalization;
- Antibiotic prescribing complies with recommendations.

2. Material and Methods

2.1. Study Setting

Our work was carried out in the general pediatric department of the Gabriel Touré teaching hospital in Bamako. In addition to general pediatric, neonatology and pediatric emergencies. The pediatric department includes:

- A pediatric oncology unit;
- A sickle-cell and haemophilia unit;
- A center of excellence for the care of HIV-infected children and follow-up of children born to HIV-positive mothers (PMTCT);
- A nutritional care unit (URENI);
- A mother-kangaroo care unit (MKC) for premature and low-birth-weight babies.

The Pediatric Department is the national benchmark for pediatric care, and a training center for health students and future pediatricians. With the exception of neonatology patients, all other patients from other units pass through the general paediatrics department before their definitive diagnosis or during ad hoc hospitalizations.

2.2. Type and Period of Study

This was a prospective descriptive study conducted from September 1 to November 31, 2018, in the Department of Pediatric at Gabriel Touré Teaching Hospital.

Inclusion criteria:

- To be aged between 0 and 15 years;
- To be hospitalized in pediatrics and to have received at least one antibiotic;
- Have a usable medical record.

Non-inclusion criteria:

All children who did not meet the inclusion criteria were excluded from our study.

2.3. Ethical Considerations

For this study, we obtained authorization from the administrative authorities of the Gabriel Touré teaching Hospital to use the records. The information gathered from the files remained confidential.

2.4. Operational Definition

- MAM: Acute malnutrition is moderate if the weight/height ratio is between -2 and -3 z-score.
- SAM: Acute malnutrition is severe if the weight/height ratio is less than -3 z-score.
- Hyperleukocytosis: If the white blood cell count exceeds $10,000/\text{mm}^3$.

- Thrombocytopenia: If circulating platelet count is below 150,000/mm³.
- C-Reactive Protein (CRP) positive: If greater than 6 mg/L.

2.5. Criteria for Judging Antibiotic Prescription

Judgment on the quality of antibiotic therapy was based on the recommendations for the management of infectious diseases in children available in 2018 [17] [18] [19].

- Antibiotic therapy was justified on admission if an infectious hypothesis was posed or systematically used in a malnourished.
- At Day 5 of hospitalization, it was only justified if the infection was confirmed by blood cultures or retained in the face of biological/radiological examination results in favor of an infection or systematically in a malnourished child.

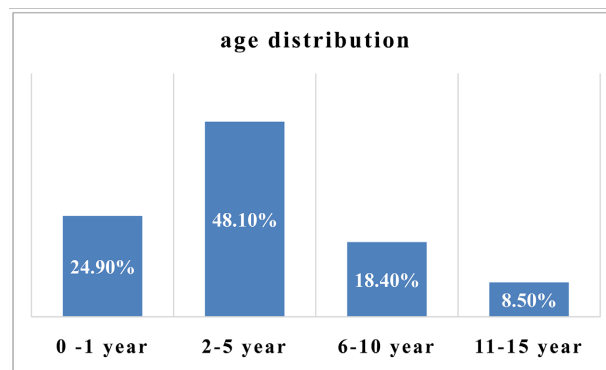
3. Results

3.1. Socio-Administrative Characteristics

We collected 445 children's files out of 1032 admissions during the study period, representing a hospital frequency of 43.1%. Males accounted for 57%, with a sex ratio of 1.3% (Figure 1). The 2 to 5 age group accounted for 48.1% (Figure 2). Fathers and mothers were respectively blue-collar workers (65.4%) or housewives (85%), and had no education in 42.9% and 64.5% of cases. Patients had been referred by a health facility in 71% of cases.

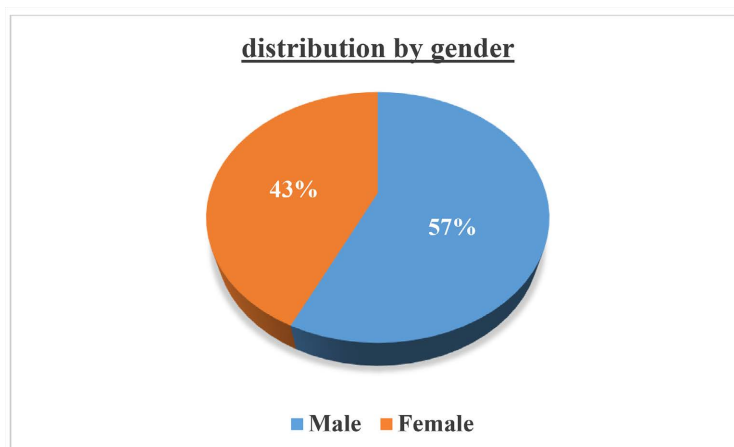
3.2. Clinical Features

Fever was the reason for consultation in 45.6% of cases, followed by headaches (10%). General condition was impaired in 60% of patients. On physical examination, hepatomegaly was present in 18.2%, splenomegaly in 9.6% and peripheral adenopathy in 3.1% (Figure 3). The site of infection was pulmonary in 37.6% and Otolaryngological in 9.2%. Bacterial infection was assumed on admission in 54% (Figure 4) of cases, and meningitis in 57.7% (Table 1). The discharge diagnosis was malaria in 54.6%, severe acute malnutrition in 18.6% and meningitis in 6.7%. The death rate was 3.8%.



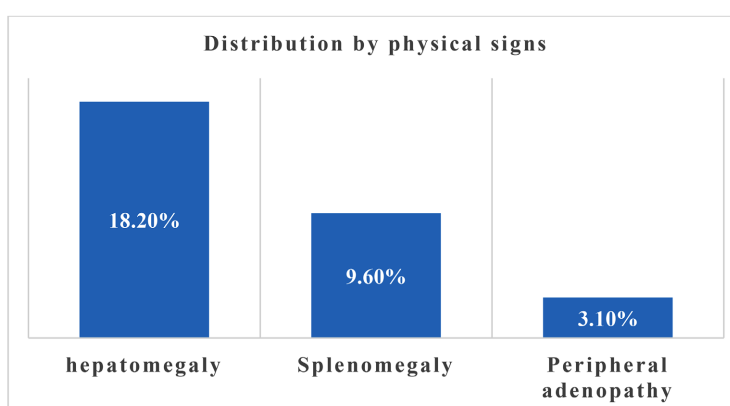
The 2 - 5 age group was the most represented, with a rate of 48.1%.

Figure 1. Age distribution of patients.



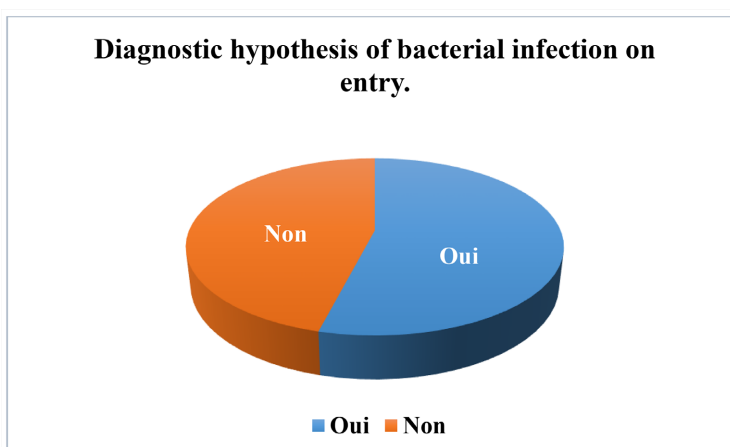
Males were the most represented, with a sex ratio (M/F) of 1.3.

Figure 2. Distribution of patients by gender.



Hepatomegaly was the physical sign most frequently found on palpation.

Figure 3. Distribution of patients according to physical signs.



More than half of patients were discharged with a diagnostic hypothesis of bacterial infection.

Figure 4. Distribution of patients by diagnostic hypothesis of bacterial infection on admission.

Table 1. Distribution of patients according to bacterial infection hypothesis.

Infectious hypothesis	Number N = 239	percentage
Meningitis	138	57.7
Pneumonia	66	27.6
Sepsis	16	6.7
Meningoencephalitis	7	3
Urinary tract infection	4	1.7
Purulent otitis	2	0.8
Liver abscess	1	0.4
Tonsillitis	1	0.4
Endocarditis	1	0.4
Cellulitis	1	0.4
Ethmoiditis	1	0.4
Gastroenteritis	1	0.4
Total	239	100

Meningitis was the most common infectious diagnostic hypothesis.

3.3. Paraclinical Characteristics

CBC in 317/445 patients showed neutrophil hyperleukocytosis in 47.3%. CRP was positive in 85% of 225/445 patients. Blood cultures in 27.6% of patients were positive in 5. CSF analysis was carried out in 30% of patients, and showed elevated leukocytes in 6.5%. No cultures were positive. X-rays were performed in 3% of patients, but pathological in only 2%. The malaria RDT or thick drop was positive in 58%.

3.4. Prescription Analysis

Antibiotic prescriptions were justified by infectious hypotheses in 43.1% of patients. β -lactams were prescribed in 98.6% of cases, followed by aminoglycosides (23.6%). Prescription was monotherapeutic in 69%, bitherapeutic in 30% and tritherapeutic in 1%. Ceftriaxone accounted for 53.9% of monotherapy, and the ceftriaxone-gentamycin combination 61.2% of dual therapy. The parenteral route was used in 93% of patients. Antibiotic therapy was not adapted to national/international recommendations in 68.3% of cases. On day 5 of hospitalization, 67.6% of patients were on antibiotics. Antibiotic therapy was justified by a confirmed infection or retained on the basis of biology and/or radiology in 49.8%, systematic in malnourished patients in 21.9% and not justified in 16.3% of cases (**Table 2**). Duration of antibiotic therapy was 0-5 days in 42% of cases. The average duration was 7.30 days, with extremes of 1 and 25 days.

Table 2. Distribution of patients according to justification for antibiotic therapy on day 5 of hospitalization.

Justification for prescription on day 5 of hospitalization	Number	N = 301	Percentage
Infection confirmed or retained on the basis of biology and/or radiology	150		49.8
Systematic in malnourished patients	66		21.9
Clinical presumption of infection	27		9
Failure to rule out an infectious hypothesis at the outset	9		3
Unjustified prescription	49		16.3
Total	301		100

At day 5 of hospitalization, 67.6% of patients were on antibiotics, and infection was confirmed or retained on the basis of biology and/or radiology in almost half.

4. Discussion

4.1. Study Limitations

- **Keeping medical records:** we found that many records were incompletely filled in, thus reducing the size of our sample and the quality of the information collected.
- **Problem of confirming bacterial infection:** proving bacterial infection is always difficult in our department: blood cultures are only taken as part of a research protocol for children with invasive infections (meningitis, pneumonia, etc.). The hospital laboratory did not perform blood cultures or CSF cultures. The meagre means of most parents made it impossible to carry out basic check-ups.

4.2. Frequency

During the period of our study, 1,032 children had been admitted to the department and 445 had received at least one antibiotic, giving a hospital frequency of 43.1%. This result is higher than those of Senga P *et al.* in 1989 in Brazzaville, Congo [14] and Nadji A in Kuwait [20], with frequencies of 37.3% and 19% respectively. We note a clear reduction in the prescription rate in our department, compared with Kanta S [16] who found a frequency of 78.7% in the same department in 2007. This improvement is undoubtedly due to the many actions taken by the health department in the fight against antimicrobial resistance.

4.3. General Patient Profile

Fathers and mothers were predominantly blue-collar workers (34.6%) and housewives (85%); they had no education in 42.9% and 64.5% of cases respectively. These results are in line with national surveys which found that 66% of women aged 15 - 49 had no education at all, compared with 53% of men in the same age group, the majority of whom were employed in agriculture (42% and 52% respectively) [21]. However, the purchasing power of parents has a positive impact on the care of sick children, which could partly explain the low rate of

complementary examinations in our study. Children aged 0 to 5 years were the most represented, with 73%. In Mali, children under 5 have a relatively high demographic weight. It is estimated at almost one person in five (18.1%), with variations between urban (15.3%) and rural (18.9%) areas. The numerical importance of this group reveals the extent of children's health needs, specifically in the field of vaccination [22]. Children are naturally sensitive and vulnerable to infections. Males predominate, with a sex ratio of 1.3. The same observation was made by Kanta S [16] and Konaté ND [23]. We have no precise explanation for this finding.

4.4. Clinical Features

▪ Vaccination status

The majority of patients (80%) were correctly vaccinated according to the EPI. This result is much higher than that of the national survey, which found that 45% of children had received all basic vaccinations [21].

▪ Mode of admission

The majority of patients (71%) had been referred by a health facility. This could be explained by the proximity and easy access of these structures, but also respect for Mali's health pyramid. All national hospitals and referral health centers refer to the pediatric department of the Gabriel Touré teaching hospital, which today constitutes a first reference structure in Mali for the care of children.

▪ Nutritional status

Patients aged 0 - 5 years presented malnutrition in 40%, 27% of which was severe, and those aged 6 - 15 years were thin in 20%. Our results are superior to those of the last national survey in which 27% of children had the chronic form, 9% the acute form and 19% were underweight [21]. This difference could be explained by the fact that our study subjects were already ill.

▪ Physical signs on entry and diagnosis on discharge

Fever (61%), altered general condition (60%) and hepatomegaly (18.2%) were the main physical signs on entry. Fever and hepatomegaly are infectious signs frequently encountered in both bacterial and parasitic infections. Assessment of general condition is subjective, which may explain the high number of patients whose general condition was judged to be impaired. Malaria was the most frequent discharge diagnosis, accounting for almost 55% of cases. Mali, like most countries in sub-Saharan Africa, records malaria as the leading cause of mortality and morbidity. In 2018, according to the health information system, 2,614,104 cases of confirmed malaria and 1,001 deaths were recorded. Malaria was the leading reason for consultation (39%) [21].

▪ Bacterial infectious diagnostic hypotheses

The majority of our patients entered with a bacterial infectious diagnostic hypothesis, *i.e.* 54% of cases. Meningitis was the first hypothesis (57.7%) followed by pneumonia (27.6%). This may be explained by the high proportion of infants in our sample with signs of meningitis and severe neurological malaria, malaria being the most frequent diagnosis. The same finding was made by Kanta S in

2007 in the same department, with 24.3% meningitis and 18.4% bronchopneumonia [16]; the remaining diagnoses were mainly malaria and dehydration. In contrast, Senga P *et al.* found in Congo that the main indication for antibiotics was pulmonary infections, accounting for 41% of cases [14].

▪ **Become**

At the end of our study, 82.7% of our patients were cured, 5.4% had neurological sequelae and 3.8% died. The high cure rate could be explained by the fact that malaria was the main discharge diagnosis. Malaria has a good prognosis if diagnosed early.

4.5. Paraclinical Characteristics

▪ **CBC/CRP**

The three quarters of patients had performed a blood cell count and 47.3% of cases had neutrophilic polynuclear hyperleukocytosis. CRP tests were carried out in more than half of patients (225), with the majority being positive (85%). The rate at which these tests are carried out is still low. They are routinely performed in cases of suspected bacterial infection, but feasibility is a problem due to the availability and purchasing power of parents.

▪ **Blood cultures/CSF**

Blood cultures had been taken in 29.2% of patients and were positive in only 5, including two (2) cases of staining. Antibiograms were performed in 3 patients, and the germs found were *Streptococcus aureus* and *Salmonella* group D. As the hospital laboratory does not take blood cultures, they were only taken from patients included in the research protocol of the Center for Vaccine Development (CVD), which also analyzes CSF and pus free of charge. CSF analysis was carried out in 30% of patients, and showed elevated leukocytes in only 6.5%. Systematic CSF culture was negative in all patients. This CSF negativity could be explained by the almost constant prescription of antibiotics in the periphery prior to admission, thus decapitating the infection.

4.6. Thick Drop/Rapid Diagnostic Test for Malaria

RDT or thick drop was positive in 58% of cases. This result is consistent with the high number of malaria cases in our series.

4.7. Analysis of Antibiotic Prescribing

▪ **Justification for antibiotic therapy on admission**

Antibiotic prescription was justified by infectious hypotheses in most of our patients (43.2%). One of the fundamental points on which antibiotic prescription is generally based is a cluster of clinical arguments (an infectious focus on pulmonary or ENT examination, a cutaneous entry point...) or documented by a complementary examination. At the time of admission, most often at the time of on-call, the technical facilities and financial means of the parents/carers are not conducive to the performance of biological tests to rule out a diagnostic hypothesis,

leading to the frequent use of antibiotics. As severe acute malnutrition is a debilitating condition, antibiotic therapy was systematically used in its management, in line with the national protocol, in 16.6% of cases.

▪ **Antibiotic classes prescribed**

β -lactams were the most prescribed antibiotic family (98.6%) followed by aminoglycosides (23.6%). Our results are similar to those of Kanta S [16] in the same department, Senga P *et al.* [14] in Brazzaville, Congo, and Sanou I [15] in Ouagadougou, Burkina Faso, who found 98.6%, 89.5% and 62.6% respectively of β -lactam prescriptions. This could be explained by the fact that β -lactams have a broad spectrum of action and good tolerance in children, but are also better known by prescribers and more accessible to parents.

▪ **The number and combinations of antibiotics prescribed**

Most of our patients had received monotherapy (69%), and ceftriaxone was the most prescribed antibiotic (53.9%). In 2007, in the same department, Kanta S [16] found that the rate of bi-antibiotic therapy predominated, with 68% of cases, and that in mono-antibiotic therapy (32%), ceftriaxone was the most widely used (66.6% of cases). The most frequently used antibiotic combination (31%) was ceftriaxone + gentamicin, with 61.2% of cases. This combination was most frequently used in the series by Kanta S [16] and Koné MS [24].

▪ **Justification for antibiotherapy on day 5 of hospitalization**

At five days of hospitalization, 67.6% of patients were still on antibiotics, and infection was accepted on the basis of the CBC showing neutrophil hyperleukocytosis or elevated CSF leukocytes in almost half (49.8%). Routine prescription in malnourished patients accounted for 21.9% of cases. Proof of bacterial infection could only be obtained by blood cultures in 5 patients (1.1%), again within the framework of a research protocol. This could be explained by the difficulties encountered by the Gabriel Touré teaching hospital laboratory in carrying out basic bacteriological tests.

▪ **The quality of antibiotic prescribing**

As the pediatric department at Gabriel Touré teaching hospital does not have an antibiotic prescribing guide for prescribers, we used the recommendations for the management of pediatric infectious pathologies available in 2018. In 68.3% of cases, antibiotic therapy was not adapted to national and/or international recommendations. Koné DL [25], in his study of antibiotic use in pediatric bacterial infections in Koutiala, found incorrect prescription in 34% of cases. In Brazzaville, Congo, Senga P *et al.* found that in 18.2% of cases, antibiotic therapy had been abused [14].

5. Conclusion

Despite methodological limitations, this study has shown that the rate of antibiotic prescribing remains high; antibiotic use was justified in over half of patients, but remains inadequate in relation to national and international recommendations in almost two-thirds (2/3). More sustained action is needed on the part of health authorities to ensure the rational use of antibiotics, a key factor in the fight

against bacterial resistance to antibiotics.

Conflicts of Interest

The authors declare that they have no conflict of interest in relation to this publication.

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