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Research Article

Analysis of Antibiotic Prescription at the Pr Bocar Sidy SALL University Hospital of Kati as a Prelude to the Development of a Therapeutic Formulary: Compliance with the AWaRe Classification of the World Health Organization

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Abstract

Introduction: Prescribing antibiotics has become one of the most critical actions in hospitals. This is linked to the risk of misuse of these drugs and its impact on bacterial resistance. Our objective through this study was to analyze the compliance of antibiotic prescriptions with the WHO AWaRe classification at the Pr BSS University Hospital of Kati before the development of the therapeutic form.

Materials and Methods: This is a descriptive cross-sectional study from January 1 to December 31, 2021. Patients in outpatient consultations with 650 prescriptions prescribed and hospitalized patients with 371 patient records in which there is an accessible and usable antimicrobial treatment were included.

Results: In this study, 48.29% were female and 51.71% were male. The majority of prescriptions were made by specialist doctors, i.e. 632 prescriptions. The majority of prescriptions were made by specialist doctors with 632 prescriptions. The number of antimicrobials received per patient varied from 1 to 4 while it was 0 to 5 for antibiotics. The molecule most prescribed in outpatient settings was amoxicillin + clavulanic acid with 144 prescriptions and that in hospitalization was metronidazole with 187 prescriptions. The antibiotics prescribed were respectively in the WHO "AWaRe" classes as follows: 54.46% for the "Access" class, 44.55% for the "Watch" class and 0.99% for the "Reserve" class. . These results are a little different from the WHO recommendation on this subject.

Conclusion: The non-compliance of the trend of antibiotic prescriptions with the WHO AWaRe classification would be due to the absence of validated standard protocols for antibiotic prophylaxis and antibiotic therapy in the structure.

Keywords: Prescription Analysis; Antibiotics; AWaRe Classification

Introduction

The terms «antimicrobials» or «antimicrobial agents» simply refer to all types of natural or synthetic medicines that may decrease the multiplication of microorganisms or destroy them [1]. Global action plans to address antimicrobial resistance recognize that AMR is a global public health threat [2]. It is clear that the effectiveness of antimicrobials is now threatened by the emergence of treatment-resistant pathogens around the world, which jeopardize the health of populations. There is therefore a risk of re-emergence of incurable infections, an increase in mortality and considerable additional costs. The use of antibiotics in the animal sector and the use of pesticides in the ecosystem are factors that

promote this emergence in both animals and humans [3,4]. In view of these phenomena, the World Health Organization (WHO) in 2017 developed a classification approach called «AWaRe». It is a strategy that divides the different antibiotics into three classes. These classes reflect the level of oversight and accessibility that the listed antibiotics should have. This categorization is based on international recommendations, the spectrum of molecules and their resistances. It aims to rationalize the use of antibiotics and to control bacterial resistance to antibiotics [4]. A study carried out in Bamako showed a high level of resistance of E. coli to beta-lactams with amoxicillin it was 84.97%, 84.56% to cefalotin, 84.37% to ticarcillin, 57.14% to cefotaxime, 52.63% to ceftazidime and 50% to amoxicillin-clavulanic acid [5].

Assessing antibiotic use patterns over time allows trends comparable to those of resistance patterns to be identified. Similarly, these data can inform decision-making on the implementation of strategies that will limit the development of resistance [6,7]. It is in this context that the Pr Bocar Sidy SALL University Hospital Center of Kati, in the phase of standardization of treatment protocols through the development of the therapeutic formulary, has been interested in the analysis of the compliance of antibiotic prescriptions with the AWaRe classification of the World Health Organization.

Materials and Methods

Study framework

The study took place at the Pr Bocar Sidy University Hospital in Kati (Mali). The patients recruited were all from the medical-clinical departments. The hospital has a capacity of 203 functional beds and has nine medical-clinical departments, three surgical departments, three paramedical units and three medico-technical services [8].

The WHO «AWaRe» classification has been used to rationalize the use of antibiotics by classifying them in: Access Group (for first/second line antibiotics), Attention Group (for antibiotics with high resistance selection power) and Reserve Group (for antibiotics of last resort) [7].

Type and period of study

This was a descriptive cross-sectional study on antibiotic prescribing from January 1 to December 31, 2021.

Study population

It is made up of patients admitted to the hospital either for an outpatient consultation or for hospitalization and who have benefited from a medical prescription.

Inclusion criteria

The following were included in our study

- All patients seen in outpatient consultations with a prescription prescribed at the University Hospital Prof. BSS in Kati on which at least one antimicrobial exists;
- All hospitalized patients have an accessible and usable patient record on which antimicrobial treatment exists.

Non-inclusion criteria

The following were not included in our study:

Outpatients with a prescription prescribed outside the Pr BSS University Hospital in Kati and those not part of our study period.

Sampling

A simple random sample was carried out from outpatients either (n=650 prescriptions) and inpatients or (n=371 patient records). The minimum sample size was calculated by the SCHWARTZ formula

T= 72.03

To be exhaustive in the collection of data, we deliberately chose to take 100 samples per department because of 50 prescriptions and 50 patient records for the services that do the consultation and hospitalization and 100 prescriptions for the services that only do the consultation.

- t= 95% confidence level (typical value 1.96)
- m= margin of error at 5% (typical value 0.05)
- p= frequency of antibiotic prescription in hospital (assumed value 0.75)

The sample size could not be reached at the level of the intensive care unit because of the restrictive measures put in place in this department following the COVID19.

Data Collection Techniques and Tools

Data collection was carried out in two groups

1st group

We collected, through a questionnaire filled in by the interviewer, the study variables found on patients' prescriptions from outpatient consultations. At this stage, prescriptions from hospitalized patients were excluded;

2nd group

We collected, through a questionnaire completed by the investigator, the study variables found in the records of patients in hospital. At this stage, outpatient records were excluded.

Data analysis

The collected data, figures and tables were generated, compiled and analyzed using Microsoft Office Excel 2010 software. The socio-demographic variables were age and sex; therapeutic and clinical variables were prescribed antimicrobials and prescriber profile; quantitative variables were antimicrobial prescribing frequencies; qualitative variables were the percentages of antibiotics in the AWaRe classes, the number of antimicrobials and antibiotics prescribed per patient.

The compliance of the requirements was assessed on the basis of the WHO recommendations.

Possible administrative and ethical considerations

A collection authorization issued by the general manager of the hospital was acquired before the start of the collection. Each document (prescription and patient file) has been identified by a unique code, so anonymity has been preserved. Verbal informed consent from each patient included in the study was obtained. No name or specification that could identify the patient appeared in the document. The study took place in a context of routine practice and did not require any additional requirements on the patient resulting in an additional expense or burden.

Results

Socio-demographic data

In total, the prescriptions of 1021 patients were analyzed. The sample consisted of outpatients (n=650 prescriptions) and inpatients (n=371 patient records) with at least one antimicrobial in their treatments. The extreme ages of the patients were five months for the lower bound and 92 years for the upper bound. The curve peaked in the 25-35 age group with a total of 110 patients. The male sex represented 51.71% of the sample compared to 48.29% for the female sex.

Of the 650 prescriptions examined, 311 were made by medical specialists, 182 by medical assistants, 150 by general practitioners, six by interns and one by a midwife. As for the patient files, they were initiated only by specialist doctors in 321 cases and by general practitioners in 50 cases.

Prescribing data

Of all the cases studied

- From the analysis of the 650 prescriptions, antibiotics were prescribed 814 times, antiparasitics 163 times, 57 times for antifungals and 11 times for antivirals on prescriptions.
- As for the files of the 371 patients, there were 700 respectively for antibiotics; 53 for antiparasitics; 44 for antifungals and 1 time for antivirals.

Number of antimicrobials prescribed per patient

Our study found that the number of antimicrobials per prescription was:

- 1 for 541 prescriptions;
- 2 for 98 ordinances and;
- 3 for 11 prescriptions.

In addition, in the patient files, we found:

- 1 antimicrobial in 321 cases;
- 2 antimicrobials in 48 files,
- 3 antimicrobials in 1 folder and
- 4 antimicrobials in 1 folder.

Number of antibiotics prescribed per patient

As for the number of antibiotics received per patient, it was

- 0 for 67 prescriptions;
- 1 for 404 ordinances;
- 2 for 141 ordinances;
- 3 for 28 ordinances;
- 4 for 7 prescriptions and
- 5 for 3 prescriptions.

In addition, in the patient files, we found

- 0 antibiotics in 18 cases;
- 1 antibiotic in 131 cases;
- 2 antibiotics in 144 cases;
- 3 antibiotics in 47 cases;
- 4 antibiotics in 18 cases and
- 5 antibiotics in 13 cases.

The most prescribed antimicrobials

Antibiotics (see Table I)

The five most prescribed antibiotics (prescriptions + patient records) are:

- Metronidazole 279 prescriptions;
- Ceftriaxone 276 prescriptions ;
- Amoxicillin + clavulanic acid 263 prescriptions;
- Ciprofloxacin 146 prescriptions and
- Amoxicilline 117 prescriptions.

Antibacterial	Prescription Frequency	Frequency on patient record	Cumulative frequency
Fusidic acid	2	0	2
Amikacine	0	3	3
Amoxicilline	90	27	117
Amoxicillin + clavulanic acid	144	119	263
Azithromycin	30	5	35
Benzathine benzylpenicilline	1	0	1
Bispirazole	1	0	1
Cefadroxil	1	2	3
Cefixime	19	24	43
Cefixime + clavulanic acid	2	1	3
Cefotaxime	30	12	42
Cefpodoxime proxetil	3	0	3
Ceftazidime	0	3	3
Ceftriaxone	119	157	276
Ceftriaxone + sulbactam	3	1	4
Cefuroxime	1	1	2
Ciprofloxacin	91	55	146
Ciprofloxacin + tinidazole	5	5	10
Clarithromycin	3	1	4
Clindamycine	4	1	5
Cloxacilline	1	0	1
Cotrimoxazole	4	11	15
Doxycycline	7	3	10
Erythromycin	1	0	1
Flucloxacillin	4	0	4
Fosfomycine	2	0	2

Framycetine	14	0	14
Gentamicin	38	57	95
Josamycine	1	0	1
Levofloxacine	4	1	5
Lincomycine	2	0	2
Meropenem	3	0	3
Metronidazole	92	187	279
Nitrofurantoin	2	1	3
Norfloxacine	34	0	34
Ofloxacine	12	1	13
Oxytetracycline	4	0	4
Phenoxymethylpenicilline	2	0	2
Neomycin+ metronidazole	11	7	18
Neomycin + polymycin b	11	4	15
Rifamycine	0	5	5
Roxithromycin	0	1	1
Spectinomycin	2	0	2
Spiramycine	0	2	2
Tetracycline	0	1	1
Thiamphenicol	3	0	3
Tinidazole	2	1	3
Tobramycine	9	0	9
Vancomycine	0	1	1

Table 1: Frequency of antibacterial prescribing.

Pest control (see Table II)

The four most prescribed antiparasitic drugs (prescriptions + patient records) are:

- Artesunate 62 prescriptions ;
- Albendazole 55 prescriptions ;
- Artemether + lumefantrine 39 prescriptions and
- Quinine 22 prescriptions.

Antifungals (see Table IV)

The three most prescribed antifungals (prescriptions + patient records) are:

- Fluconazole 33 prescriptions;
- Nystatin 28 prescriptions and
- Clotrimazole 15 prescriptions.

Antivirals (see Table II)

The most prescribed antiviral (prescriptions + patient records) was Aciclovir 10 prescriptions.

«AWaRe» classes of antibiotics prescribed on prescriptions and in patient records

Antibiotics listed on the prescriptions were respectively in 50.86% of cases in the «Access» class, 47.78% of cases in the «Watch» class and 1.35% of cases in the «Reserve» class.

In patient records, the «Access» class accounted for 58.63%, the «Watch» class was 40.80%, and 0.57% of cases were in the «Reserve» class.

Antiviral	Prescription Frequency	Frequency on patient record	Cumulative frequency
Acyclovir	9	1	10
Lamivudine	1	0	1
Tenofovir	1	0	1

Table 2: Frequency of Antiviral Prescribing.

Pest Control	Prescription Frequency	Frequency on patient record	Cumulative frequency
Albendazole	49	6	55
Artemether	8	2	10
Artemether + luméfantrine	29	10	39
Arterolane + piperaquine	3	0	3
Artésunate	28	34	62
Ivermectine	1	0	1
Mebendazole	1	0	1
Niclosamide	1	0	1
Praziquantel	4	1	5
Quinine	22	0	22
Secnidazole	2	0	2
Sulfadoxine + pyrimethamine	15	0	15

Table 3: Frequency of Prescribing of Antiparasitic Drugs.

Antifungal	Prescription Frequency	Frequency on patient record	Cumulative frequency
Amphotericin B	2	0	2
Cyclopyroxolamines	2	0	2
Clotrimazole	6	9	15
Econazole	6	7	13
Fluconazole	16	17	33
Griseofulvine	2	0	2
Ketoconazole	1	0	1
Miconazole	4	0	4
Nystatine	17	11	28
Terbinafine	1	0	1

Table 4: Frequency of Prescribing of Antifungals.

«AWaRe» classes of antibiotics prescribed according to the qualification of prescribers

In terms of prescriptions, antibiotics prescribed by medical specialists were respectively 58.09%; 44.85% and 2.06% of the «Access» class; «Watch» and «Reserve».

For general practitioners, 48.12% of the antibiotics prescribed were in the «Access» class and 51.88% of cases were in the «Watch» class.

The interns prescribed antibiotics from the «Access» class 60% and 40% from the «Watch» class.

As for medical assistants, 52, 31% of the antibiotics prescribed were in the «Access» class, 46.76% were in the «Watch» class, and the «Reserve» class accounted for 0.93% of cases. The antibiotic prescribed by the midwife was of the «Access» class.

In terms of patient records, the antibiotics listed were prescribed by medical specialists respectively 57.05%, 42.31% and 0.63% of the «Access», «Watch» and «Reserve» classes.

For general practitioners, 72.86% of the antibiotics prescribed were in the «Access» class and 27.14% of cases were in the «Watch» class.

Discussion

In our study, the most represented age groups were [20-25] years and [25-30] years with respectively 95 and 110 people in the workforce, i.e. 20.07% of the sample. This result is similar to that of Mariko, who in her study found that the age group of [20-30] was in the majority with 21.4% of her sample [11]. Compared to the result obtained by Dembélé, with the majority age group [20-39] years old, i.e. 43.33%, the age group [20-40] years old in our study was also in the majority with 35.45% [12]. Also the age range of [25-45] years in our study accounted for 31.83%, a result similar to that Mbia in his study found the age group of 26 to 45 years in the majority with a percentage of 33.8% [13]. More than half of our sample, 51.71%, were male, which is a similar result to those of the authors cited above.

The majority of prescriptions (prescriptions and patient records) were made by specialist doctors (632 prescriptions) followed by general practitioners with 200 prescriptions. However, it was noted that some prescriptions were made by medical assistants (health technicians and senior health technicians) with 182 prescriptions, then by interns six prescriptions and midwives with one prescription. What should be said here is that the drafting of a prescription is the responsibility of doctors and certain health professionals, within the limits necessary for their professional practice (dental surgeons, midwives, physiotherapists, chiropodists, nurses). Doctors have a broad right to prescribe. However, their ability to prescribe may be limited for certain drugs that are prescribed only by certain specialists or hospital practitioners [14].

In terms of the number of antimicrobials per patient, it should be noted that most prescriptions (862) were limited to one. But exceptionally in one case, four antimicrobials were listed for the management of the same patient.

Patients who received a single antibiotic were the majority in the sample with 535 cases or 52.39%. But it is clear that some patients in their treatment have received up to five antibiotics, including 13 cases in patient files and three cases on prescriptions. A few similar cases have been reported in other studies, Dega found in his study that the number of antibiotic molecules prescribed as probabilistic treatment was 27.2% for mono-antibiotic therapy, 42.4% for dual-antibiotic therapy, 20.8% for tri-antibiotic therapy, 7.2% for quadri-antibiotic therapy and 2.4% for quintu-antibiotic therapy [15]. In his research, Ly found a percentage of 15.92% for mono-antibiotic therapy, 56.72% for dual-antibiotic therapy and 27.86% for tri-antibiotic therapy [16]. The interpretation resulting from these results could be due to the increasing increase in antibiotic resistance and the tendency of prescribers to combine antibiotics to obtain a synergy of action in the absence of the result of any antibiotic susceptibility test [17].

In our study, Metronidazole was the most prescribed antibacterial with a cumulative number of 279 or 18.42%, followed by Ceftriaxone with 18.22% and Amoxicillin + Clavulanic Acid with

17.37%. Our results are similar to that of Mariko who, in her study, found that the combination of Cefotaxime + Metronidazole followed by Ceftriaxone + Metronidazole were the most frequently prescribed, i.e. a percentage of 19% and 18.30% respectively [18]. According to Yalcouye, in his study, Amoxicillin + Clavulanic Acid was the most prescribed with 33.9% as monotherapy and the combination of Amoxicillin + Clavulanic Acid and Metronidazole was administered in 30.6% of cases [19]. Relatively, the frequent use of Metronidazole would certainly be justified by the fact that it is both an antibiotic and an antiparasitic. It inhibits nucleic acid synthesis and is used for the treatment of infections related to anaerobic bacteria as well as protozoa [20]. These results could be explained by the fact that they are among the antibiotics most commonly known to prescribers and are often used as prophylaxis in most surgical procedures.

Artesunate was the majority of the most prescribed antiparasitic with 62 prescriptions or 28.70%, followed by Albendazole with 55 prescriptions or 25.46% and Artemether + Lumefantrine with 39 or 18.05%. This result is a little different from that of Traoré in his study who found that Artemether + Lumefantrine was the most prescribed with 50.25% of prescriptions [21]. These high rates of antimalarials corroborate the endemic nature of malaria in our country. Faced with the observation of the failure of food and environmental hygiene as well as the extent of sanitation problems in schools which leaves something to be desired, the high frequency of Albendazole in our study would be justified.

The results of our study show that, among the antifungals listed, Fluconazole predominated with 33 prescriptions or 32.67%. In 2018, Dembélé in his study found that Fluconazole was the most consumed molecule with 17.66% [22].

Aciclovir was the most observed antiviral with a cumulative frequency equal to 10, i.e. 83.33% of prescriptions. This result is explained by the fact that prescriptions from antiretroviral patients were not included in the study.

The prescriptions made at the University Hospital Prof. BSS in Kati were analyzed according to the WHO's «AWaRe» classification, respectively 54.46% for the «Access» class, 44.55% for the «Watch» class and 0.99% for the «Reserve» class. This result is different from the «Access» class antibiotics (75%) listed in the national list of essential medicines [23] and that of the WHO recommendation (at least 60%) [24,25]. Also different from those of Zhussupova., *et al*. [26] in Kazakhstan and Xu [27] in western China. These studies found respectively that the consumption of medicines in the «Access» group was 39% in 2017 and 30% in 2019, and that those in the «Watch» group were 61% in 2017 and 68% in 2019. For the «Reserve» group, they were 0.03% in 2017 and 2.11% in 2019 [26]. On the other hand, antibiotics from the «Watch» group were the most consumed with 42.28%, followed by the «Access» group with 40.31% and finally the «Reserve» group with 0.11% [27]. From 2015 to 2018, the consumption of the «Access» group increased from 43.76% to 40.31%, for the «Watch» and «Reserve» group increased from 36.72% to 42.28% and from 0.11% to 0.06% [27]. Between January 2015 and December 2018, a study on *«Hospital Models of Antibiotic Prescribing in Adult Patients in 664 Hospitals in 69 Countries»,* the highest percentages of the «Access» class at the country level were observed in sub-Saharan countries such as Guinea Conakry 66.7%, South Africa 61.9% and Togo 59.8%. The «Access» requirement was lowest in Armenia 12.1%, Jordan 12.2% and China 15.1%. The percentage of Watch prescriptions was high in Armenia 87.9% and Jordan 84.4%, while Guinea Conakry 32.1%, South Africa 37.7% and the United Kingdom 39.5% recorded the lowest percentages of Watch prescriptions. The requirement of «reserve» was highest in Argentina 12.6%, India 7.8% and Brazil 7.1%. For a number of participating countries, such as Nigeria, Guinea Conakry, Togo, Laos, Kosovo, Kyrgyzstan and Armenia, did not report any «Reserve» group prescriptions [28].

In our study, the so-called «AWaRe» classification of prescribed antibiotics differs according to the qualification of the prescriber. As a result, it should be noted that only antibiotics prescribed on prescriptions by interns and in patient records by general practitioners complied with WHO recommendations with 60% and 72.86% of prescriptions respectively in the «Access» class. It was also observed that the prescription of antibiotics in the «Reserve» class was made by medical specialists (2.06% of prescriptions and 0.63% in patient files) but also a few cases were observed with medical assistants, i.e. 0.93% of prescriptions. This result could be explained

by the fact that at the time of our data collection, a standard antibiotic therapy protocol was not available at the Pr BSS University Hospital in Kati. However, it should be noted that the prescription is a medical act carried out by authorized professionals. Derogations may be made to the ability to prescribe in connection with the skills acquired [29].

Conclusion

At the end of the work, it can be seen that the prescription in general has not always complied with the WHO's «AWaRe» classification. It is due to the absence of the standard validated protocols of antibiotic prophylaxis and antibiotic therapy in the structure. The development and implementation of antibiotic prophylaxis and antibiotic therapy protocols, carried out in consultation with clinicians; microbiologists and pharmacists, through the therapeutic committee, should make it possible to improve practices and better control the spread of multi-resistant microorganisms. These must not inexorably involve a study of bacterial ecology and a definition of drugs that fall into the different «AWaRe» classes of the University Hospital Prof. BSS in Kati.

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