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Research Article

An assessment of antimicrobial prescribing at a tertiary hospital in north-western Nigeria

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Background: Inappropriate antibiotic use is a public health problem worldwide. Misuse of these agents is one of the drivers of antimicrobial resistance (AMR), which is believed to be the next pandemic. Consequently, auditing antimicrobial prescription patterns can provide useful information on the scope and extent of this problem.

Objective: The aim of this study was to describe outpatient antimicrobial drug prescribing at the National Health Insurance Scheme (NHIS) unit of Ahmadu Bello University Teaching Hospital, Zaria, Nigeria.

Methodology: This was a descriptive drug utilization study carried out prospectively during a 2 week period in May 2015. Six objective World Health Organization (WHO) indicators were used to assess the rationality of antimicrobial prescribing at the site. Data collected on antimicrobials included type, route of administration, dose and dosing frequency as well as length of therapy. Average costs (both prescription and antibiotic) were obtained by dividing the total drug costs by the relevant number of drugs.

Results: A total of 167 prescriptions were analyzed. The average number of drugs per encounter in the facility was 3.7. Fifty seven percent of antimicrobials were prescribed using their generic names, while the average duration of treatment was 8.9 days. Thirty seven prescriptions (22%) contained more than one prescribed antimicrobial, out of which 7 were potentially pharmacologically antagonistic. Only 21% of the prescriptions had indications in line with the National Standard Treatment Guidelines (STG's). Average cost of prescribed antimicrobials was about NGN 2,238 (approximately US$11).

Conclusion: Several problems associated with rational antimicrobial prescribing were identified. There is a definite need for suitable interventions to help improve antimicrobial drug prescribing at the site.

Keywords: Anti-infective agents, Costs, Drug use review, National Health Insurance, Nigeria

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1. Introduction

Since their introduction into Medicine in the 1940s, antimicrobial or antibiotic agents have become some of the most widely used drugs in the world. The 2011 World Medicines Situation Report states that inappropriate antibiotic use, especially overuse and misuse is a serious global public health problem (Holloway and vanDijk, 2011). Inappropriate antimicrobial use is a major driver of antimicrobial resistance (AMR). AMR develops when a microorganism (bacteria, fungus, virus or parasite) is no longer responsive to a chemotherapeutic agent to which it was originally sensitive (WHO, 2014). Several organizations including the World Health Organization (WHO) and the World Economic Forum (WEF) recognize the danger posed by AMR and are currently working on measures to control it. While AMR is a global problem as earlier stated, it is of particular importance to the African continent. Africa has the largest infectious disease burden in the world, and infectious diseases continue to contribute to the bulk of illness related morbidity and mortality on the continent (WHO, 2003). Other harmful consequences of irrational antibiotic use include adverse drug events, wastage of scarce resources (especially in

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resource poor settings like sub-Saharan Africa) and even death.

Most effective interventions to ensure or influence rational antimicrobial use require good quality data on the scope or extent of the problem. Monitoring antimicrobial prescription and consumption behavior can provide valuable information needed to inform therapy decisions, assess public health consequences of antimicrobial abuse and evaluate the effect of resistance containment interventions (WHO, 2014). Surveillance of antimicrobial use in health facilities can be carried out by evaluating certain objective indicators as recommended by the WHO (MSH, 2012). These indicators can be used in most antimicrobial usage studies and provide a simple tool for quickly and reliably evaluating critical aspects of antimicrobial use in hospitals.

There is conflicting data on antimicrobial prescription patterns in Nigeria. The WHO estimates that about 60% of antimicrobial prescribing in the country is irrational (Tamuno and Fadare, 2012). Other hospital based estimates range from over 30% to as high as 80% (Chukwuani et al, 2002; Odusanya, 2005; Akande et al, 2009; Adebayo and Hussain, 2010). However all of these studies were carried out in other parts of the country except the north-west, which is where this work was carried out. This study set out to add to existing data on this topic, while gathering baseline information that could serve as a basis for designing appropriate interventions & policies to improve antimicrobial prescribing.

2. Methodology

2.1 Study Setting

This study was conducted at the National Health Insurance Scheme (NHIS) unit of the Ahmadu Bello University Teaching Hospital(ABUTH) Zaria, – a tertiary facility providing healthcare services to citizens of Kaduna and other states within the North-Western region of Nigeria. It provides both general outpatient and specialist medical care, while also serving as the Teaching Hospital for the Faculties of Medicine and Pharmacy of Ahmadu Bello University, Zaria.

The NHIS was introduced in 1999 by the Nigerian government, to facilitate fair financing of health care costs for citizens through pooling of financial resources and cost burden-sharing. ABUTH is a participating Health Care Provider (HCP) on the Scheme, and has over 15,000 enrollees. The unit provides both out and in-patient services and is one of the busiest in the hospital. The unit also keeps excellent records, which is why it was chosen for the study

2.2 Study Design

The study was a descriptive drug utilization study. Data was collected prospectively, in line with WHO guidelines on antimicrobial utilization studies in hospitals (MSH, 2012).

It was carried out over a 2-week period in May 2015, as a similar audit carried out by Ntšekhe et al (2012) in Botswana utilized a similar time span.

2.3 Data Collection

Any outpatient Prescription containing at least one antimicrobial, presented to the NHIS pharmacy unit during the study period was included in the study. Only patients who had been prescribed antimicrobials to treat Tuberculosis were excluded. Data was collected from patients' prescription sheets and records. A collection form was designed and used by the investigators to record basic demographic data and information on all prescribed drugs. Data collected on antimicrobials included type, route of administration, dose and dosing frequency, length of therapy and cost.

2.4 Data analysis

Several WHO indicators exist to describe antimicrobial usage in hospitals. The objective indicators used for this study, were specifically chosen because they would provide information on particular areas of interest to the investigators. The indicators used in this study included:

- Average number of medicines per encounter.
- Percentage of medicines prescribed by generic name.
- Average medicine cost spent on antibiotic per encounter.
- Percentage of prescriptions in accordance with treatment guidelines.
- Average duration of prescribed antimicrobial treatment.
- Percentage of medicines prescribed from the Essential Drugs List (EDL) or hospital formulary

Two of the indicators measured in this study assessed the degree of compliance with official prescribing guides/documents, namely the National Standard Treatment Guidelines (STGs) and Essential Drugs List (EDL). Thus, verbal enquiries directed at all prescribers within the unit (6 in total) were made to confirm their knowledge of the existence of these documents, to which all of the prescribers responded in the affirmative. Further analysis of the data was also carried out to characterize antimicrobial prescribing patterns for specific indications. Drug prices were copied from the prescription sheets after the pharmacists working at the unit had finished costing the prescriptions. Average costs (both prescription and antibiotic) were obtained by dividing the total drug costs by the relevant number of drugs. Exchange rate at the time of the study was $1= NGN 205. Data collected was coded and entered into an Excel 2013 spread sheet. The data was analysed using the Statistical Package for the Social Sciences (SPSS) software version 20. Descriptive statistics was used to report the data obtained, with percentages, mean and median used where appropriate.

2.5 Ethical Considerations

Ethical clearance was obtained from the Hospitals' ethics committee before the study began (Ethical approval number **ABUTH/HREC/TRG/36**). Patient names or any other identifying information were not recorded on the data collection sheets after their folders had been successfully identified. All the data collected was handled confidentially.

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3. Results

A total of one hundred and sixty seven (167) prescriptions were successfully analyzed. Around 51% of patients were male and majority were older than 18 (67.1%). All the encounters had at least one drug prescribed, with 55% (92 prescriptions) containing at least 4 drugs. The average number of antimicrobials per encounter was 1.22. Of the 207 antimicrobials prescribed, the beta-lactams were the most prescribed drug class (57%). The quinolones accounted for 17%, followed by the nitroimidazoles (13%). Conversely, the aminoglycosides, chloramphenicol and the lincosamides were rarely prescribed, accounting for only about 6% of the antimicrobials surveyed. The oral route was the most utilized (80%), with other routes (intra venous & topical) accounting for the rest. Analgesics including Paracetamol & Non-Steroidal Anti-inflammatory Drugs (NSAIDs) were the most frequently co-prescribed drugs (35%), anti-malarial agents (17%) and antihistamines (15%) were also frequently prescribed. **Table 1** shows the WHO indicators evaluated during the study.

Thirty seven prescriptions (22%) contained more than one prescribed antimicrobial. Frequently encountered antibiotics combinations were mostly beta-lactams with nitroimidazoles (usually Metronidazole) and quinolones with Metronidazole. However, some combinations were potentially problematic due to pharmacological antagonism between the two antibiotics and these can be seen below in **Table 2**.

One hundred and twenty one (72%) of prescriptions analyzed had a written indication within the patients' folder for antimicrobial use. These indications covered a wide range of infectious diagnoses affecting various body systems including respiratory, skin and soft tissue, genito-urinary and gastrointestinal (mostly typhoid fever). Out of these, only 35 (21%) were in line with the national standard treatment guidelines, 10 prescriptions (6%) had disease conditions not covered in the STG's. A popular indication for antimicrobial use in the unit was for Upper Respiratory Tract Infections (URTI's), 14% of prescribed antimicrobials (28 drugs) were prescribed for this purpose. **Table 3** shows the specific antimicrobial agents prescribed for this purpose

The average cost of a prescribed antimicrobial was 2,238 NGN (≈11 US$), while the average total prescription cost during the study period was 3,641 NGN (≈18 US$). Thus, antimicrobials accounted for around 62% of the total prescription costs. All the antimicrobials prescribed during the study period contributed 373, 816 NGN (≈1877 US$) to the total prescription costs of 608,173 NGN (≈3053 US$).

Table 1: WHO Prescribing indicators at the study site

Prescribing Indicator	Value
Average number of medicines per encounter	3.8 ± 0.11
Percentage of medicines prescribed by generic name.	57.0%
Average duration of prescribed antimicrobial treatment (days).	8.9 ± 0.67
Percentage of medicines prescribed from the Essential Drugs List (EDL)	91.0%
Percentage of prescription in accordance with treatment guidelines	21.0%
Average medicine cost spent on antibiotic per encounter	NGN 2,238(≈USD 11)

Table 2: Pharmacologically antagonistic antimicrobial combinations prescribed during the study period

Antimicrobial Drug Combinations	n
Cefixime + Doxycycline	1
Ciprofloxacin + Neomycin	1
Clindamycin + Ciprofloxacin	2
Amoxicillin + Clarithromycin	1
Ofloxacin + Doxycycline	1
Cefuroxime + Clindamycin	1

Table 3: Types of antimicrobials prescribed for URTI's during the study period

Antimicrobial name	N	%
Cefuroxime	13	46.3
Amoxicillin	6	21.4
Cefixime	3	10.7
Erythromycin	2	7.2
Ciprofloxacin	2	7.2
Others (Cotrimoxazole & Doxycycline)	2	7.2

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4. Discussion

Hazards associated with irrational use of antimicrobial agents cannot be over emphasized. Abuse and misuse of antimicrobials can lead to several consequences in terms of cost, drug interactions, prolonged hospital stays and development of resistance by pathogens. Auditing antimicrobial prescribing patterns can help provide valuable information that can be ultimately used to improve patient outcomes.

More than half of the prescriptions surveyed during this study contained at least 4 drugs, even though the average number of drugs per encounter was 3.7. Similar studies carried out in south east and south west Nigeria have reported values ranging between 1.53- 7.9 (Chukwuani et al, 2002; Mgbahurike et al, 2010; Anyanwu and Arigbe-Osula, 2012). Polypharmacy while often appropriate for some pathological conditions, can equally be problematic in others. It is becoming increasingly common, with a large Scottish study confirming a trend over time of increasing total numbers of drugs prescribed (Duerden et al, 2013). Polypharmacy can increase the risk of drug interactions and adverse drug reactions, while worsening medication compliance and quality of life of some patients (Duerden et al, 2013).

Analgesics especially NSAIDs were the most frequently co-prescribed drugs in this study. Analgesics are commonly used as adjunctive treatments in the management of infections, both for pain relief and to reduce fever. However, NSAIDs, while a very useful drug class, have recently been implicated as a cause of heart attacks and strokes (FDA, 2015). This is of particular importance, in the Nigerian context where an increasing number of middle aged adults have at least one cardio-vascular disease risk factor (Maiyaki and Garbati, 2014). It may be worthwhile for a future study to concentrate on the rationality or lack thereof of NSAID usage within the unit.

The duration of treatment with antimicrobials is important because under treatment or unduly long exposure to antimicrobials can contribute to the development of resistance (NPS, 2013). The average duration of antimicrobial usage in this work was 8.9 days, generally suggestive of appropriate prescribing. However, optimal duration of treatment with antimicrobials needs to be sufficiently long enough to control the infection, but short enough to encourage adherence to prescribed treatment. A study by Fernandes and colleagues (2013) showed a relationship between non-adherence to antibiotic therapy and treatment duration. The WHO currently estimates that patient adherence to prescribed treatment regimens (for any condition) is only about 50% (Holloway and vanDijk, 2011). This has led to a consensus in some quarters that poor adherence is presently a global public health problem. In light of this, prescribers need to find and strike a suitable balance when trying to decide on the optimal duration of treatment.

Antimicrobial combinations are often necessary in the treatment of some infections. Good combinations can be additive or potentiative, greatly increasing pathogen kill rates. However, when agents with antagonistic mechanisms of action are combined, increased toxicity and potential treatment failure may occur. Majority of surveyed prescriptions containing antimicrobial combinations were suitable, with the exception of 7 prescriptions that contained the above listed drug combinations. A 2004 Ethiopian study had previously reported results containing similar problematic combinations (Abula and Kedir, 2004). The combinations contain bactericidal agents in combination with bacteriostatic ones, causing pharmacological antagonism and increasing the risk of developing resistant strains. It should however be noted that amoxicillin in combination with clarithromycin is one of the currently approved antimicrobial combinations for the eradication of *H. pylori*. But with the prevalence of clarithromycin resistance in the population reaching levels of over 15% in several parts of the world, eradication rates of clarithromycin-containing triple therapy are decreasing clinically (Sanchez-Delgado et al, 2012).

The percentage of antibiotics prescribed from the Essential Drugs List (EDL) in this study was 91%. Similarly high rates (over 90%) have been obtained from other studies carried out within the Nigerian setting (Babalola et al, 2011; Tamuno and Fadare, 2012). The EDL is a list of drugs that are chosen based on the health care needs of majority of the population. The drugs on the list are widely available as generics and are generally affordable. It can therefore be assumed that the higher the compliance with this list, the more rational the drug prescription pattern. However in an interesting twist, the percentage of antibiotics prescribed using generic names was only 57%. This result would seem to suggest that the prescribers were still prescribing branded forms of the drugs on the EDL, thereby defeating the whole purpose. Generics are usually less expensive than their branded counterparts, reducing the financial burden on the patients. Generic prescribing also has the added benefit of reducing dispensing errors due to misidentification of the prescribed drug.

Only 121 prescriptions (72.5%) had a clearly documented indication for antimicrobial use, out of which 35 prescriptions (21%) had indications in line with the national standard treatment guidelines (STG) (FMOH Nigeria, 2008). Bad documentation and poor compliance with treatment guidelines are common problems encountered in antimicrobial prescribing. An NHS audit found suitable documentation of antimicrobial prescribing in only 75% of prescriptions in Scottish hospitals, though compliance with treatment guidelines was high at 81% (Malcolm et al, 2013). Other studies on antimicrobial prescribing have highlighted additional issues contributing to irrational antimicrobial prescribing in the Nigerian setting. These include poor usage of diagnostic testing and getting information on antimicrobials from unsuitable sources (Chukwuani et al, 2002; Adebayo and Hussain, 2010; Mgbahurike et al, 2010). Put together, all these factors paint an unpleasant picture of antimicrobial prescribing in the country, and highlight an urgent need for targeted interventions to improve rational prescribing.

Upper respiratory tract infections (URTI's) were a frequent indication for antimicrobial prescribing in this study accounting for 14% of all antimicrobials prescribed. Upper respiratory tract infections are frequently caused by viruses and generally should not require antibiotic therapy. Using antimicrobials for

URTI's is a general problem worldwide; with an outpatient study of more than 52,000 cases of URTI showing antimicrobial prescribing rates of 65% (Gill et al, 2006). Especially worrying in this case are the types of antimicrobial agents prescribed. Prescriptions during the study included second & third generation cephalosporins as well as ciprofloxacin and doxycycline. This would seem to suggest very serious misuse of these broad spectrum agents.

Globally antimicrobials account for a large chunk of drug expenditure (MSH, 2012), and the findings of this study corroborate that fact. Antimicrobials in this case accounted for around 62% of the cost of each prescription. Antimicrobial prescribing in other studies both within and outside the country have accounted for even higher values (Akande et al, 2009; Williams et al, 2011). Even though the patients in this case only pay a certain percentage of these costs, if the NHIS is to ensure universal health coverage for all citizens, drug therapies must be as cost effective as possible.

5. Conclusion

Several findings from the study highlighted problems with rational antimicrobial use at the unit. These problems include poor compliance with treatment guidelines, inappropriate use of antimicrobials for URTI's and relatively low generic prescribing. There is a need for suitable interventions (both educational and otherwise) to improve antimicrobial prescribing at the site, and pharmacists can put their expertise in drugs to good use here.

Conflict of Interest

The authors declare no conflict of interest.

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