

**ANTIBIOTICS STEWARDSHIP IN DIARRHOEAL CASES
AMONG CHILDREN UNDER FIVE YEARS IN PRIMARY CARE
SETTINGS IN MASERU, LESOTHO**



Proposal for MPhil in Family Medicine

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Declaration

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1 Introduction

The global rise in antibiotic resistance has resulted in increasing difficulty in the treatment of infectious disease. A mere three decades after the discovery of antibiotics, resistance was first detected.¹ Penicillin resistance was detected in the early 1950s, but since then resistance to almost all known antibiotics has developed.¹ The projected global mortality rate as a result of this growing problem, is 10 million deaths per year by 2050.² Hence, from the late 1990s, the concept of antibiotics stewardship has been rapidly adopted worldwide in the struggle against antibiotics resistance in order to preserve the effectiveness of antibiotics.^{3,4,5,6}

Antibiotics stewardship programmes (ASP) are well organised programmes which aim to guide healthcare providers to adopt evidence-based patterns in prescribing antibiotics. The overall rationale is to reduce antibiotic over prescription which leads to resistance. Evidence shows that ASPs can effectively control over prescription of antibiotics, without influencing overall mortality.⁷ The principles of ASPs maybe used in different settings, ranging from fulfilling educational purposes to informing policymakers.⁷

Globally, ASPs are effective, and various strategies are continually used to improve the reliability of existing programmes.⁷ These strategies are categorised as either restrictive or enabling strategies. Examples of restrictive strategies include appointing designated antibiotic prescribers or reducing the variety of antibiotics available on ordering lists. Enabling strategies mainly improve knowledge about resistance, for example via educational and training programmes. It is important to empower all levels of people in the system, including healthcare providers, patients, and administrators.⁷

Despite the importance of ASPs, there is still a lack of awareness of the need to protect patients by reducing antibiotic resistance in the sub-Saharan region. Scant evidence exists of applications of ASPs and there is also little knowledge of the concept or its importance. Most of the research has been conducted in South Africa. A study in Cape Town demonstrated that when rolled out on a greater scale such a programme could deliver sustained reductions in antibiotic consumption, and achieve cost-savings within 4 years that could pay for the programme itself.⁸ Another local study demonstrated that health care providers are not following the guidelines for antibiotic use. For instance, patients with viral bronchitis were more likely to be prescribed an antibiotic than those with bacterial bronchitis.⁹ The need for raising awareness amongst health care providers has been recognized, even at undergraduate level. In South Africa, 92% of medical students feel that antibiotics are overused, and 87% agree that resistance is a significant problem. The majority (95%), report that they would appreciate more education on the appropriate use of antibiotics, and only 33% felt confident to prescribe antibiotics.¹⁰

Raising awareness at population level is also an important intervention. The common belief that antibiotics can cure everything is prevalent. In Nigeria, 54% of the population has some knowledge of antibiotics, 62% use antibiotics over the counter without prescription, and only 27% adhere to prescribed antibiotics. About 26% of patients use leftover antibiotics in case of fever, and only 9% feel that antibiotic misuse may affect the economic status of Nigeria. Twenty-seven percent of Nigerian doctors acknowledge that pharmaceutical companies affect their

prescription practice. While 57% of doctors prescribe according to their personal experience, 88% state that they use standard treatment guidelines in their hospitals. In contrast to public opinion, 95% of doctors think that antibiotic misuse affect the economic status of the country, and 96% suggest training of doctors and education of patients as a solution to antibiotic misuse.¹¹

In Lesotho, antibiotics are prescribed by both doctors and nurses mostly in the empiric treatment of infections. In the absence of comprehensive antibiotic prescribing guidelines, decisions to prescribe antibiotics are based solely on opinions of healthcare providers.¹² A survey in Lesotho in 2013 showed that only 17% of doctors and nurses routinely request microscopic identification prior to prescribing antibiotics, and only 32% routinely request a sample for culture sensitivity tests. The researchers' search of the literature revealed no records of studies investigating factors that affect decisions of healthcare providers to prescribe antibiotics in Lesotho. It is therefore relevant to conduct this study for purposes of providing baseline information in formulating policies on appropriate prescribing of antibiotics.

The researcher considered identifying a disease that can be accurately diagnosed at primary care level, is prevalent in our setting, and is not primarily treated with antibiotics. Two groups of diseases meet these criteria, namely respiratory conditions and diarrhoeal disease. It was then decided to focus on diarrhoeal disease, considering the complexity of respiratory conditions. The choice of diarrhoeal disease as subject was then narrowed down to its incidence in children under five. The most common causes are viruses followed by food allergies; food poisoning; and previous antibiotic overuse.¹³

Mortality due to acute diarrhoea in < 5 year old patients in Lesotho was estimated at 10% in 2015.¹⁴ Acute diarrhoea is mainly caused by viral infections. The recommended guidelines on the correct prescription of antibiotics in children with diarrhoea is the South African guidelines, Integrated Management of Childhood Illnesses (IMCI).¹⁵ Lesotho does not have its own specific guidelines, and the use of the IMCI guidelines is recommended in Lesotho. Selection of the South African guidelines is based on the proximity of geographical setting and the possibility of similar resistance patterns.¹⁶

However, to our knowledge there is no current evidence of the degree of implementation of IMCI by primary care providers. How are the principles of antibiotics stewardship applied in the treatment of children under five years with diarrhoea in primary care settings in Maseru, Lesotho?

2 Aim and Objectives

2.1 Aim

The aim of this study is to describe the application of the principles of antibiotic stewardship in the treatment of children under five years with diarrhoea in primary care settings in Maseru, Lesotho.

2.2 Objectives

- To describe the application of the principles of the use of antibiotics in children under five years with diarrhoea
- To compare the antibiotic prescribing pattern for children under five years with diarrhoea between nurses and doctors

3 Methodology

3.1 Study design

The study design is a descriptive survey. Data was collected from patient's health booklets on the use and prescription pattern of antibiotics on cases of diarrheal diseases in under five children. The research design was used to evaluate or measure the results against the known standards described in the Integrated Management of Childhood (IMCI) Illnesses guidelines.

3.2 Setting

This study took place in Maseru, which is one of the 10 districts of Lesotho. The Maseru District, with its capital city Maseru, contains the largest urban area in the country. Maseru is located on Lesotho's western border adjoining the Free State province of South Africa, the frontier being marked by the Caledon River. Maseru borders on the Berea District in the north, the Thaba-Tseka District in the east, Mohole's Hoek District in the south, and the Mafeteng District in the southwest. The study took place in the rural part of the Maseru District. The district has three hospitals: one level-three referral hospital that is situated in the city centre, and two hospitals that provide primary care services in the rural area. In Lesotho, each patient has a health booklet that contains information on care received as an outpatient, as well as discharge summaries after hospitalisation. These booklets are used by all the primary healthcare providers, and the information was used in this study as health records.

3.3 Study population and sampling strategy

The researcher chose primary care settings because of the implementation of the relevant guidelines in these settings.

The researcher randomly selected the two rural hospitals to assess the prescription pattern among doctors considering that they are the only ones prescribing at hospital level and two health centres to assess nurses' prescription patterns at this level. The two hospitals are St Joseph Mission Hospital and Scott Mission Hospital. Saint Joseph is attached to the Lesotho National University, which has a school of nursing and covers about six health centres. It has 5 doctors and 75 nursing staff, and a bed capacity of 100. Scott Hospital has 6 doctors and 50 nursing staff with a catchment area of seven health centres and a bed capacity of 80. Both hospitals are running basic services such as an outpatient department, HIV corner, TB clinic, eye unit, mental health unit, and laboratory unit and inpatient facility. This study collected data from the outpatient clinic and the under-five clinic department run mainly by doctors. Most healthcare centres are run by four to five nurses, with one or two beds for observation and a delivery bed, with no laboratory services.

Data was collected from the booklets of 48 children who attended under-five clinics, 24 who attended hospitals and 24 who attended health centres. The patients' health booklets were screened for diarrhoeal cases. The researcher collected data from the patient's previous visits during the past two years as reflected in the health booklet. Data was recorded anonymously on a data capture sheet by the researcher. Coded data from each selected participant was then entered into an Excel spreadsheet. Diarrhoea was defined each time as loose stool, frequent stools, diarrhoea or watery stool, as recorded in the health booklets.

3.3.1 Selection criteria

Inclusion criteria:

- Children who were five years and younger at the time of the diagnosis.
- Records of diarrhoea available as defined above.

Exclusion criteria:

- History of hospitalisation during the episode.

3.3.2 Sample size

The researcher was assisted by the biostatistics unit of Stellenbosch University. A sample size of 23 per group (doctors and nurses) was needed to achieve 80% power to reject the null hypothesis of equal means. This allowed the researcher to have a general view of antibiotics use, and also to compare doctors' and nurses' prescribing patterns. Hence a total sample size of 46 diarrhoeal cases prescriptions for the two groups was needed.

3.4 Data collection

Data was collected retrospectively from patients' health booklets as they reported for under-five services at the clinics of both hospitals and health centres. Parents were informed about the study during the regular health education sessions held at the clinics, and were asked to give their consent for information to be collected from their children's health booklets. Routinely, nurses provide health education to all the mothers on a specific topic before starting other activities of the day. After the health education sessions, the researcher reviewed each health booklet for which consent has been obtained, and coded data from each selected participant was then entered into an Excel spreadsheet.

3.4.1 Data collection tool

Coded data from each selected participant was entered into an Excel spreadsheet, after which the data was checked and cleaned using the Excel filter tool.

3.5 Data analysis

The researcher conducted the descriptive analysis of the data with the help of the Biostatic Department of Stellenbosch University. The data was imported to the Statistical Package for Social Sciences (SPSS) version 23.0 for statistical analysis. Non parametric tests were used to compare median scores of providers and institutions. A p-value of 0.05 was regarded as significant.

4 Ethical considerations

Ethical clearance to conduct this study was obtained from the HREC of the Lesotho Ministry of Health, and Stellenbosch University.

5 Results

The records of prescriptions of 48 patients were included in the analysis. The prescriptions were for patients <five years old, with diarrhoea, written by either a nurse or a doctor from one of four institutions. Adherence to antibiotic prescription guidelines in primary health care settings in Maseru, Lesotho is low. Only 43.8 % of the prescriptions were adherent to the guideline recommendations. (Table 1)

Table 1: Antibiotics prescription according to Standard Treatment Guidelines and Essential Medicines List. (1=yes, 0=no)

| | | Frequency | Percent | Valid Percent | Cumulative Percent |
|-------|-------|-----------|---------|---------------|--------------------|
| Valid | 0 | 27 | 56.3 | 56.3 | 56.3 |
| | 1 | 21 | 43.8 | 43.8 | 100.0 |
| | Total | 48 | 100.0 | 100.0 | |

The main reasons for non-adherence were identified from the 56 % of incorrect prescriptions. In 87.5% of these prescriptions, antibiotics were prescribed inappropriately. The majority of these antibiotic prescriptions were inappropriate or unnecessary antibiotic prescriptions (92.6%), while in only 7.4 %of prescriptions, antibiotics were omitted when indicated. The most commonly incorrectly prescribed antibiotics were Cotrimoxazole, Metronidazole and Amoxicilline.

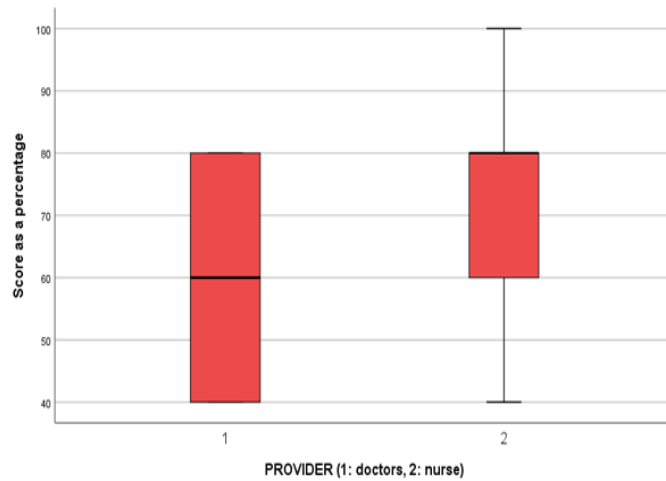
Comparison of the prescription patterns for nurses and doctors, show a not quite significant difference in median score in the antibiotic prescribing pattern between nurses and doctors ($p=0.069$). However, institutions one and two only had doctors and institutions three and four only had nurses, therefore provider was much linked to institution. (Table 2) Although there were no difference between provider prescriptions, there was a significant difference in median score between the four institutions ($p=0.009$). Pair wise comparisons showed that institutions one and three were different ($p=0.014$) as well as three and four ($p=0.035$). As a result we cannot say that institution three was better than one, since it was only nurses in institution three and only doctors in institution one. However, since institutions three and four were different, we can say that nurses in institution three scored better than those in institution four.

Table 2: Institutional Score as a percentage

| Institution(1, to 4) | | | | Score as a percentage | | | |
|----------------------|---|--|---|-----------------------|--------|------------------|------------------|
| | | | | Valid N | Median | Percentile 25 | Percentile 75 |
| Institution(1, to 4) | 1 | Provider's prescription (1: doctors, 2: nurse) | 1 | 12 | 60 | 40 | 60 |
| | 2 | Provider's prescription (1: doctors, 2: nurse) | 1 | 12 | 60 | 40 | 80 |
| | 3 | Provider's prescription (1: doctors, 2: nurse) | 2 | 12 | 80 | 70 | 90 |
| | 4 | Provider's prescription(1: doctors, 2: nurse) | 2 | 12 | 60 | 40 | 80 |

However, for the sample as a whole, nurses tended to score better than doctors

Figure 1



6 Discussion

The study findings confirm the global need to address antibiotic prescribing principles practice in primary care. Eighty percent of antibiotics prescribed for human use are in primary care.¹⁷ Adherence to antibiotic prescription guidelines in primary health care settings in Maseru, Lesotho is low. Only 43.8% of prescriptions for children (< 5 years) with diarrhoea in four primary care settings were aligned to the principles of antibiotic stewardship. Nurses' adherence to guidelines of antibiotic prescribing pattern was slightly better than doctors. There was a difference in the institutional' performances.

There has been limited published research and evaluation of antibiotic prescribing in primary care in Lesotho. Our finding of a low adherence rate (43.8%) is similar to another study done in Cape Town Metro, South Africa where the adherence rate was found to be 45.1%.¹⁷ Although these rates seems low, another study from Botswana showed inappropriate prescription rates of 74% of all cases; including cases with acute respiratory infection and cases with diarrhoea. Interestingly this study included mainly nurses (97%). It is important to be aware that adherence to guidelines in primary care has been shown to vary significantly depending on the condition being treated.¹⁹ Studies have shown poor guideline adherence for respiratory problems, urinary tract infections, tonsillitis and acute diarrhoea.^{18,19}

The antibiotics that were commonly misused (Cotrimoxazole and Metronidazole) in our study is also reportedly misused in other studies in developing countries such as South Africa and India.¹⁹ One of the reasons for this could be the fact that these drugs are relatively cheap and available in the public sector. There is also a misconception amongst the public about the value of the healing properties of antibiotics.

There was a difference in the performance between institutions, which was also reported in a similar study in Cape Town.¹⁷ Some studies have shown a difference because of socio economic circumstances.^{17,19} Some of the reasons could be that institutions are situated in different socio-economic areas, and managed by different . Adherence can also be influenced by the type of health care provider and their years of experience. As any human decision, it can be influenced by individual attitudes and perceptions.

This study found that nurses' adherence to guidelines was slightly better than doctors, which aligns with other studies where performance in both groups were mostly the same.¹⁸ However some evidence show that nurses appear to consider adherence to guidelines as a symbol of professionalism, whilst doctors' prescriptions tended to follow unwritten rules.^{20,21} Evidence from another study show that 3% of doctors in Lesotho prescribed antibiotics to satisfy patients' requests or expectations, but 33 – 42% of nurses reported that they were influenced by patients' requests and expectations.¹² Patient demand has a strong influence on providers prescribing decisions. However, some of the other studies were not based on antibiotic stewardship but on a qualitative perception or other aspects of adherence to guidelines.

Limitations

Considering the paucity of available data, this study only analysed data on generic medication and not details of dosages used. Another limitation is that Lesotho does not have its own guidelines and the IMCI that they are using does not recommend specific antibiotics but when indicated, it refers to local sensitivity and resistance pattern. Hence, we used the South African guidelines to assess this adherence.

We did not measure and analyse the clinical experience and judgements of individual health care providers. This could have informed us more about the demographic differences between nurses and doctors, although we did include two facilities for each group of health care provider.

Recommendations

The study findings confirm the global need to address antibiotic prescribing principles in primary care. The need for targeted interventional education of nurses and doctors is essential. Antibiotic stewardship principles training should be prioritized in undergraduate and postgraduate training programmes. Training should also be offered as continuing professional development or in service training to those health care providers already qualified or in practice.

Further studies should include qualitative assessments of healthcare workers' knowledge, attitudes and skills in antibiotic prescribing practices. This information could be used to inform the design of tailor made interventions suited to specific provider needs.

Another option will be to explore the possibility of appointing designated antibiotic prescribers at facilities. Reducing the variety of antibiotic options available for prescription could also be a

Institutions performing poorly should be targeted for interventions first. Barriers to adherence should be identified for specific institutions that are not performing well. These interventions could not only be educational interventions but also system level interventions.

To enable a more complete picture about antimicrobial resistance patterns and trends, surveillance systems should be set up. Standardizing data capturing of antibiotic prescription principles in all primary care clinics can help to inform future interventions.

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