The use of antibiotics at Buea Regional Hospital

Master thesis in Medicine
Frida Graumann

Supervisors:
Dr Gunnar Jacobsson
Dr Ndeso Atanga Sylvester

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Supervisors:

MD PhD Gunnar Jacobsson, Department of Infectious Diseases, KSS, Skövde, Sweden, Member of Swedish Strategic Programme for The Rational Use of Antimicrobial Agents and Surveillance of Resistance (STRAMA),

Dr. Ndeso Atanga Sylvester MPH, PhD, Director of Higher Institute of Applied Medical Sciences, Buea, Cameroon

UNIVERSITY OF GOTHENBURG.

Programme in Medicine

Gothenburg, Sweden 2014

Abstract

Master Thesis, Programme in Medicine. *The use of antibiotics at Buea Regional Hospital*, Frida Graumann, 2014, Institute of Biomedicine, Gothenburg, Sweden

Key words: Antibiotic resistance, antibiotic treatment, point prevalence survey, *E coli, K pneumoniae,* urine cultures, Cameroon

Background: Antibiotic resistance is a growing problem around the world. A rational use of antibiotics is one way to slow it down. Global action is needed.

Cameroon is a low-income country in the west central Africa. Here, there are no national guidelines for the use of antibiotics, and few studies have been made on the topic.

Aims: The main aim was to study the use of antibiotics at the Buea Regional Hospital. An additional aim was to investigate the prevalence of Gram-negative bacteria, mainly *Escherichia Coli* and *Klebsiella pneumoniae,* in urine among in-patients.

Methods: A modified point-prevalence survey (PPS) was conducted in three wards in the hospital during September-November 2014.

Urine cultures were performed. When Gram-negative bacteria were found, an Analytical Profile Index (API 20E, bioMérieux, Marcy l'Etoile, France) was used for species determination.

Results: 102 patients were included. Sixty-two of the patients (61 %) were on antibiotic treatment on the day of the study. Twenty-two urine samples were obtained, and 15 of these (68 %) showed bacterial growth. Seven were Gram-negative: 5 were *E Coli* and 2 were *K pneumoniae*.

Discussion: In Cameroon, the burden of infections is high, and the health care system is based on 'out-of-pocket' payments from the patients. This makes empirical antibiotic use common.

Conclusions: The proportion of patients on antibiotics was high, 61 %. More diagnostic methods, especially cultures, could be used prior to antibiotic prescription. More studies are needed on the use of antibiotics and antibiotic resistance in Cameroon.

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1. Introduction

1a. Antibiotic Resistance

Antimicrobial resistance is resistance of a microorganism to an antimicrobial medicine to which it was originally sensitive (as defined by the WHO). The antibiotics normally used will no longer have any effect, and the risk is greater that the infections will spread. [1] Microbes achieving resistance is a natural phenomenon. Antibiotic resistance can be obtained by the bacteria either through genetic mutations, or by transferring of genetic material, from another bacteria or via viruses. The antibiotic will kill or inhibit the sensitive bacteria while the resistant ones survive, creating a "selective pressure" which results in more of the resistant bacteria. [2] This means that when antimicrobial medicines are used, the process towards resistance speeds up.

Infections caused by resistant microorganisms have higher death rates, last longer, and are more expensive to treat because the first-line medicines do not suffice. Furthermore, efficient antimicrobials are important for prevention of infection when major surgery is conducted, and during cancer chemotherapy or other conditions when the immune defence is poor, e.g. HIV infection. [1]

The worst-case scenario for this increasing problem is a global post-antibiotic era, where antibiotics no longer have any effect on microorganisms. Common infections and minor injuries would be fatal. [3] According to the WHO, this is not something happening in a distant future, but could soon be our reality. [1]

Antimicrobial resistance and antibiotic resistance are sometimes used as synonyms, although the former is a wider concept. [1] Antibiotics are a subgroup to antimicrobials, which also includes antivirals, antifungals and anti-parasitic drugs. [4] In this study, only antibiotics were evaluated.

1b. *Escherichia coli* and *Klebsiella pneumoniae*

Escherichia coli (E coli) and *Klebsiella pneumoniae (K pneumoniae)* are two types of Gram-negative bacteria that are often part of the normal intestinal flora. However, they are both very common causes of urinary tract infections and blood stream infections, in hospitals and in the community. They both show an increasing resistance to antibiotics, worldwide. [3]

1c. Hospital-acquired infections

Many of the pathogens that have gained resistance to antibiotics, were first found in hospital milieu. [5] In hospitals, many patients with infections are gathered in the same place, and a lot of antibiotics are used, often broad-spectrum antibiotics. Health care staff and material can be carriers of pathogens. This all increases the risk for bacteria gaining resistance, and the spread of these same bacteria. Patients with a lowered immune defense are at risk, as well as patients who have undergone surgical procedures. [6], [7]

An infection occurring more than 48 hours after admission to a hospital is usually considered nosocomial or hospital-acquired. There exist different definitions of this type of infections [8], in this study the end limit was set as an infection occurring less than 30 days after discharge from a hospital. Infections that didn't classify as nosocomial were considered to be community acquired. [8]

The hospital-acquired infections have a much higher prevalence in low- and middle-income countries than in developed countries, according to some studies. [9] Some of the reasons for this can be poor hygiene and lack of equipment. [9] Not only do these infections contribute to an increased antimicrobial resistance, but they also create an economic burden for the society and for the patient. Additionally, they lead to longer hospital stays, and sometimes death. [10]

1d. Point prevalence surveys

A point prevalence survey (PPS) can be an efficient way to evaluate the use of antibiotics in a hospital [7] [11], and is a method that has been used for decades. [11] It is also a way to compare antibiotic use between hospitals and countries, when using a standardized model. [12] [13] A PPS is preferably conducted during one day [13], but sometimes a modified form of the PPS is used and one department can be investigated during several days. [13] [14]

In 2011-2012 ECDC[1] performed a large scale PPS in European hospitals [15], and in Sweden STRAMA[2] has conducted PPS's repeatedly 2003-2010. [16] In these studies, about 1/3 of the patients were on antibiotics on the day of investigation. [15] [16] In a nationwide PPS in the west-African country Benin, 64 % of the patients were on antibiotic drugs. [17]

1e. Urine cultures

Culturing is a common and relatively fast diagnostic method to find bacteria, and gives the possibility to perform antibiotic resistance testing. [18] This is a step towards getting a picture of the local resistance patterns, which can be helpful when prescribing antibiotics empirically. [19] Urine is a commonly used specimen for performing cultures. [20]

1f. Cameroon and Buea

Cameroon is a low-income country in the west central Africa. The population is about 22,8 million, in 2014. [21] The climate is tropical in the south and more desert-like in the north. [22] In 2000, the population below the poverty line was estimated to 48%. There are big income inequalities in the country [22] and connected to this, substantial differences in health outcomes. [23]

The country has one of the highest under-five child mortality rates in the world. The main reasons of this are malaria, pneumonia and diarrhoea. [23] The mortality rates in Cameroon

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[1] European Centre for Disease Prevention and Control

[2] Swedish Strategic Programme for The Rational Use of Antimicrobial Agents and Surveillance of Resistance

have improved very little over the past two decades, and life expectancy has declined. [23] Life expectancy in 2013 was 55 years. [22] The payment for health care is mainly "out-of-pocket", i. e. direct purchasing of health services when needed, paid for by the patient. Government spending on health care is low, and there are no good prepayment methods available. The government has launched a health insurance program, but only 1% of the population was covered in 2010. [23]

Buea is a city in the south west of Cameroon, on the slope of Mount Cameroon. In 2005 the population was about 90 000 inhabitants. It is a centre for administration and trade, and the capital of the South-west region of Cameroon. The climate here is humid. Buea has a university and a regional hospital. [24] [25]

1g. Study setting

Buea Regional Hospital is a government run regional hospital. It was initially a colonial military hospital. In 2003 it was rebuilt, and is since then a regional hospital, with 120 beds for inpatients, a pharmacy, a lab, and a TB lab. There are a number of different departments; among these are the surgical ward, medical wards and maternity ward. In addition the hospital has a HIV/AIDS unit and a dialysis centre. [26]

1h. Antibiotics in Cameroon

Although the major problem concerning health care in the country is probably the poor access to health care for the rural population and for the poor [23], the use of antibiotics and antibiotic resistance in Cameroon is also an important issue that needs to be studied more. On a national level, there are not enough statistics on health in general in Cameroon [23] and concerning the whole WHO African Region, which includes Cameroon, there is lack of accurate and reliable data on antimicrobial resistance. [27]

A systematic review performed in 2009, spanning from 1955 to 2008, showed that the antimicrobial resistance in the Central African region is increasing, as in the rest of the world.

[28] The WHO global report on antimicrobial resistance surveillance from 2014 indicates the same. [3]

In Cameroon, it is possible to buy antibiotics without prescription. This and the often-empirical antibiotic use in the hospitals [29] are problematic, and contribute to the evolution of antibiotic resistance here.

In a study on circulating currency from Buea, Cameroon performed in 2014, the majority of the bank notes were contaminated with microbes, and drug resistant pathogens were found among the isolates. [30] A study of antimicrobial susceptibility patterns in a hospital in Yaoundé, Cameroon, showed high drug resistance rates in most bacteria e.g. for the Gram-negative bacteria the overall susceptibility towards Amoxicillin was 13 %, towards Cefotaxime 67 % and towards Trimethoprim/sulfamethoxazole 27 %. [31] The isolates in this study were collected in 1995-1998, thus the resistance rate can be suspected to be higher today. These findings are of course alarming and make implementation of a rational antibiotic use even more important and urgent.

2. Aims

The main objective was to investigate the use of antibiotics at the Buea Regional Hospital. More specifically:

- Are guidelines for the use of antibiotics followed?

- If there are guidelines, are these local, national or WHO guidelines?

- Which are the indications for treatment with antibiotics?

- Are the antibiotics prescribed as therapeutic or prophylactic, and are the infections being treated community-acquired or nosocomial?

- What are the routes of administration for the antibiotics used?

- Which are the diagnostic methods for the use of antibiotics, especially cultures?

A second aim was to study the prevalence of *E coli* and *K pneumoniae* in urine from in-patients at the hospital, and to estimate the frequency of asymptomatic bacteriuria. The intention was to include at least 100 patients in the study.

3. Material and Methods

3a. Data collection

A modified point prevalence survey was conducted during 8 weeks, in Sep-Nov 2014. Initially the study was conducted in the surgical and medical wards, and later also the maternity ward was included.

The surgical ward has 9 rooms, with 23 beds in total. The medical ward is divided into a female and a male department. The female ward has 5 rooms, with 22 beds in total. The male ward also has 5 rooms, with 19 beds in total. The maternity ward has 8 rooms with in total 22 beds. During the period of the study, all adult patients in a ward were included. One ward was investigated at a time. The patients were informed orally about the study and their anonymity. Information about the patients was collected from the patients and from patients' files, on manually completed forms, using a protocol that was made before starting the study. (See appendix I) The focus was on the treatment with antibiotics.

If the patients' English was too poor, a nurse or a relative of the patient was asked to interpret. If this was for some reason not possible, the patient was not included in the study.

There was no specific time span between conducted studies. During the period that a ward was studied, a room where all the patients had been changed could be included again. When a second investigation of a ward was performed, only rooms with exclusively new patients were included. I. e., rooms were set as the smallest units investigated. During the study, lists with the patients' names and code numbers were saved and compared with the patient lists at the wards,

to avoid including the same patient twice. The lists were destroyed when the study was finished.

The surgical ward was evaluated 5 times, between 30 Sep and 13 Nov. The medical wards were evaluated 4 times, between 8 Oct and 12 Nov. In the maternity ward the study was conducted twice, between 6 Nov and 17 Nov.

Questionnaire: The information collected about each patient comprised of the following:

- Admission date, age, sex, date of investigation,

- Socioeconomic background: living conditions, number of people in the household, occupation, number of children alive,

- Medical history: HIV/AIDS, drug allergies, other chronic disease/s, daily medicines,

- If the patient had antibiotics prior to admission, i.e. during the 2 weeks before admission; and if so, the type of antibiotic used, indication, date of insertion, and if the antibiotic was on prescription or not,

- Diagnostic methods used: if the patient had any diagnostics done during this hospital stay, more specifically: blood samples of any kind, cultures from blood, urine, feces, or nasopharynx, x-rays, or other diagnostic measurements, marked as 'other' and specified. It was also noted what type of diagnostic method had been used, e.g. the type of x-ray, and the results, if available.

- Risk factors for nosocomial infections: if the patient had any risk factors like central venous catheter, or 'other' risk factors, e.g. urinary catheter or if the patient had undergone a surgical procedure.

- Vital parameters: here was noted the patients' blood pressure, pulse, pulse oximetry, respiratory rate, and temperature, on the date of admission.

- Current treatment with antibiotics: This was the focus of the study. It was noted if the patient was currently on antibiotic treatment, if the patient had multiple antibiotics, date of insertion, the type of antibiotic/s used, dose, and route of administration. It was stated

if the patient was actually given the antibiotic prescribed, and if not, the reason for this, if available.

- The indication for treatment: if the antibiotic was prescribed as a therapeutic or prophylactic treatment, and in the case there was an infection, if this was community acquired or nosocomial, and the type of infection.

The patients were asked about their socioeconomic background, their medical history, and if they had taken any antibiotics prior to admission. The rest of the information was taken from the patients' file.

Missing data: In case information could not be found about socioeconomic background, vital parameters, or indication for treatment with antibiotics, the question was marked as unknown. If no information about medical history or diagnostic measurements could be found, the question was marked as no. If the patient stated they had been on antibiotics prior to admission but didn't know the name of the antibiotic, or information about this could not be found in the patients' file, the question was marked as 'maybe'. If a file was missing or there were any ambiguities about medicine names, a nurse or doctor was asked.

3b. Exclusion criteria

Children under 16 years old; patients who could not give their oral consent to participation, either because of communication difficulties or because of their present health status (e.g. stroke patients, patients with cerebral malaria); patients who did not wish to participate. When a ward had already been studied, new patients in a room with a patient previously included, were not included as long as the 'old' patient remained.

3c. Urine cultures

Patients included in the PPS part of the study were asked for a midstream morning urine sample. Any patient who had been included in that part of the study and was still in the hospital

could be asked for this, regardless of their diagnosis, ward, and if treated with antibiotics or not. By using patients from the PPS, a lot of background information was obtained about the patients providing the urine sample.

Urine samples were collected in sterile urine cups marked with the patients' code number, sex and age. The colour and aspect of the urine was noted (see lab protocol, appendix II). The urine was then cultured on cystine lactose electrolyte deficient (CLED) agar plates using sterile loops (5 or 10 μl), and incubated at 34-36°C overnight. The following day colonies were counted and the number documented. If several different colonies were found on one plate, subcultures were done on new CLED agar plates, and incubated overnight. Gram staining was performed when bacterial growth was found, and the bacteria found to be Gram-negative were further analyzed with Analytical Profile Index (API) 20E (bioMérieux, Marcy l'Etoile, France) for exact species determination, following the manufacturer's instructions. The Gram-negative isolates found were stored in deep agar tubes marked with the patient's code number, species and date, for future further analysis.

The author of this report conducted the sample collection and informed the patients about the purpose. Laboratory staff from the hospital performed the laboratory work, or guided the author in the laboratory.

Antibiotic resistance testing was not performed in this study.

3d. Ethics

Ethical clearance was obtained from the Regional Delegate of Public Health in the South West Region of Cameroon (see appendix III). All patients were informed about the study aim and asked for oral consent, before inclusion. The patients were informed that the study was anonymous. Those who were asked for a urine sample were informed about the purpose and that this was not a part of their treatment. Each patient was given a number, and the list with the names and the numbers was stored confidentially, and destroyed after the study was finished.

3e. Statistical methods

The data was analyzed using IBM SPSS Statistics version 22. A p-value of <0.05 was considered statistically significant. Chi-square was used for proportions.

4. Results

4a. Study population

In total, 102 patients were included in the study. Eight patients chose not to participate, 3 patients didn't speak English (with no translator available), 20 patients were considered too ill to give their informed consent, and 5 patients who were to be asked to participate, unfortunately passed away. Forty-seven patients were not included because they stayed in a room with a previously included patient, and 4 patients who were initially included, but stayed in a room with a previously included patient, were excluded.

Patients from three departments were included, the surgical, medical and maternity wards. Each ward was studied during 1-8 days, depending on the number of patients available in the ward at that time. Forty-three patients (42 % of total) were included from the surgical ward, 40 (39 %) from the medical wards, and 19 (19 %) from the maternity ward. Fifty-one of the patients (50 %) were men and women, respectively. The age span was 16 to 85 years with a mean age of 45 years and a median age of 40 years.

The length of the hospital stay at inclusion varied from 0 to 72 days, with a mean time of 6 days, and a median time of 4 days. The total length of the hospital stay was not noted in this study.

Sixty-two patients (61 %) stated they lived in a city while 40 (39 %) lived in the countryside. Thirty-two patients (31 %) were currently not working or retired, and 31 (30 %) had some type of office work, including teachers and businesspersons. Seventeen (17 %) were farmers or had a physical outdoor work.
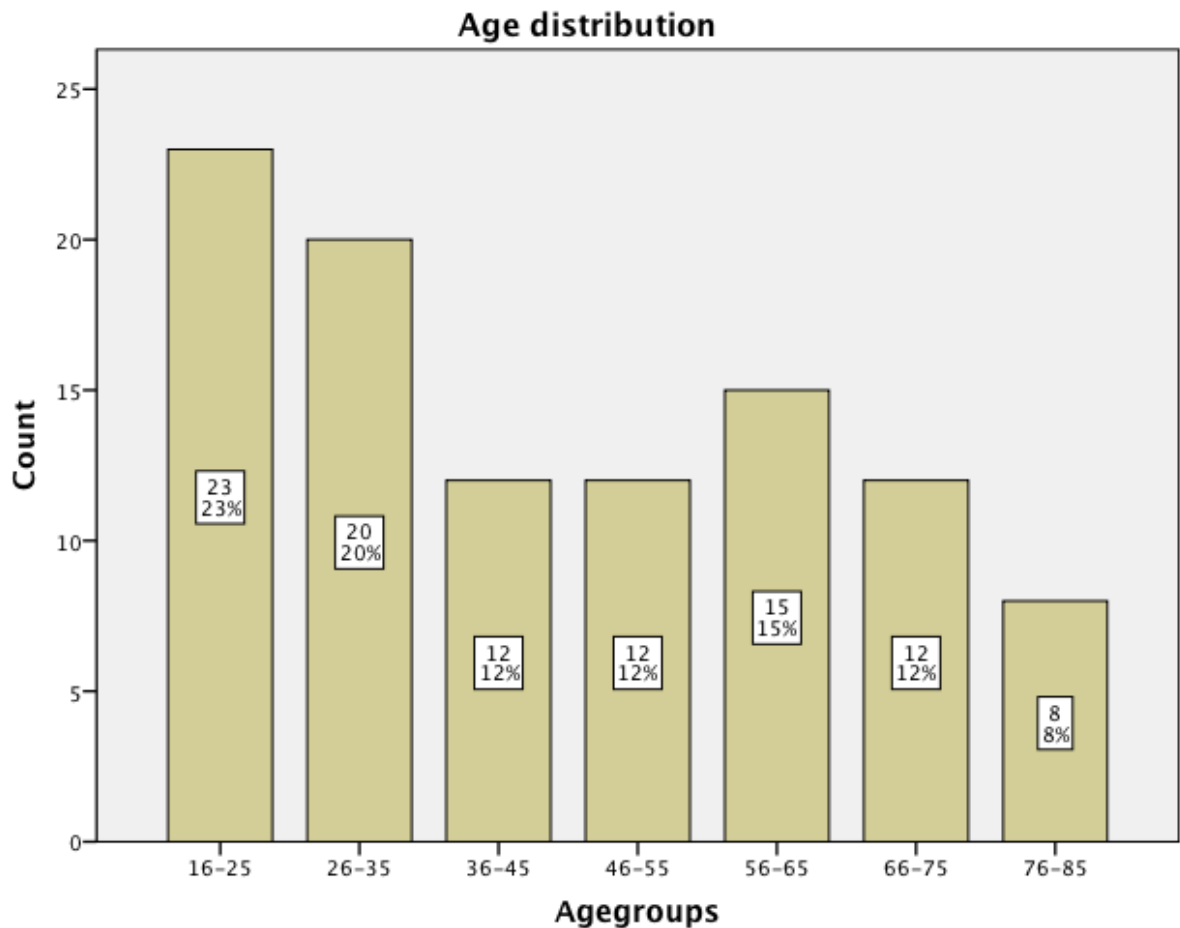
Figure 1. Age distribution according to age groups.

Table 1. Number of patients in different occupation groups.

	Frequency	Percent
Farmer/outdoor work	17	17
Not working/Retired	32	31
Office work	31	30
Driver	3	3
Student	13	13
Works in hospital	6	6
Total	102	100

Medical history

Sixty patients (59 %) were previously healthy. Forty-two patients (41 %) had one or more

chronic diseases. The most common disease was hypertension, occurring in 23 cases (23 %).

Six patients (6 %) had HIV/AIDS.

Risk factors for nosocomial infection

In total 38 patients (37 %) had some type of risk factor for nosocomial infection. The most common was a current surgical procedure, e.g. major surgery or pleural tap, present in 31 patients (30 %). In this group of patients, 14 (14 % of total) had also a urinary catheter and/or wound drain or suprapubic tap.

Five patients (5 %) had a urinary catheter. One patient (1 %) had a dialysis catheter. No patient had a central venous catheter. No statistically significant correlation was found between these risk factors and prevalence of nosocomial infection (p-value 0.31).

Vital parameters

For 77 patients (75 %) there were vital parameters from the day of admission in the file. The majority, 74 patients (73 %), had a blood pressure taken, and 69 (68 %) also their pulse. Fourteen patients (14 %) had a systolic blood pressure lower than 110 mmHg, and 28 patients (27 %) had a pulse higher than 100 bpm. Forty-one patients (40 %) had their temperature taken, and 6 of these (6 % of total) had a temperature of 38.5°C or higher. No patients had pulse oximetry done.

There was no statistically significant correlation between current antibiotic treatment and tachycardia, i. e. pulse 100 bpm or higher (p-value 0.42), or between current antibiotic treatment and systolic blood pressure under 110 mmHg (p-value 0.24), or temperature of 38.5°C or higher and current antibiotics (p-value 0.66).

4b. Use of antibiotics

On the date of the study, 62 patients (61 %) were on treatment with one or more antibiotic/s while 40 patients (39 %) were not on any antibiotics. Eighteen patients (18 %) were currently on two, and 7 patients (7 %) were on three or more antibiotics.
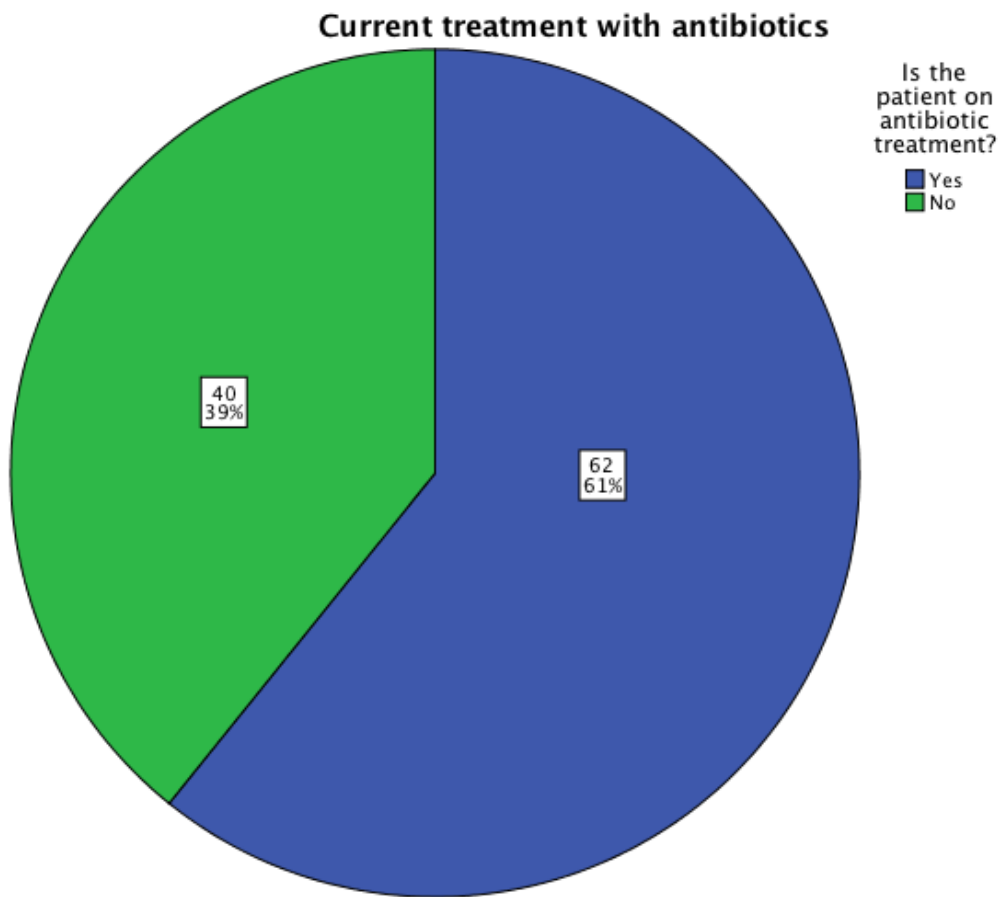
Current treatment with antibiotics

Is the patient on antibiotic treatment?
- Yes
- No

40
39%

62
61%

Figure 2. Number of patients currently on antibiotics.

Table 2. Frequency of multiple antibiotics

	Frequency	Percent
No antibiotics	40	39
One antibiotic	37	36
Two antibiotics	18	18
Three or more antibiotics	7	7
Total	102	100

In the surgical ward, 56 % of the cases were currently on antibiotics. In the medical wards (male and female) in total 55 % of the cases were on antibiotics. In the maternity ward, 84 % were on antibiotics. There was no statistically significant correlation between type of ward and antibiotic prescription (p-value 0.07).

Table 3. Patients currently on antibiotics (treatment and prophylaxis) in the different wards.

Ward	Patients	Patients on antibiotics	Percent
Surgical ward	43	24	56
Medical ward	40	22	55
Maternity ward	19	16	84
Total	102	62	61

Guidelines and local routines for antibiotic prescription

It was found that there are no Cameroonian guidelines for antibiotic prescription. However, in the maternity ward there are local routines for antibiotic use regarding deliveries, according to the nurse in charge. These routines are: After every vaginal delivery the woman is given Amoxicillin capsules, 500 mg 2x2 for 5 days. This is because of the non-sterile vaginal examinations. In case there was a ruptured membrane for more than 24 hours, the woman instead is given Rapiclav (Amoxicillin/Clavulanic acid) 1g x2 for 7 days. When there is a caesarian section, Ceftriaxone 2g is given during the surgery, and then 1g x2 for 2 days.

Antibiotics received by the patient

Of the patients treated with antibiotics during the present hospital stay (current or previous treatment), 39 (49 % of this group) had information that this was given in their files. For 24 patients (30 %) sometimes it was not written in the file if the patient had received the antibiotics, and in 14 cases (18 %) the nurses had not signed in the file that the antibiotic had been given. Two patients (3 %) who were prescribed antibiotics didn't buy them.

Earlier antibiotics and antibiotics prior to admission

Of all the patients included in the study, 50 (49 %) had had one or more antibiotic/s earlier during the present hospital stay. Twenty of the patients currently not on antibiotics (20 % of total) had earlier had antibiotics.

Fifteen patients (15 % of total) had been on antibiotics during the two weeks prior to the current hospital stay. In 23 cases (23 %) it was unknown if the patient had been on antibiotics or not, and the remaining 64 patients (63 %) had not been on antibiotics. Twenty-six patients (26 %) had got the medicine prescribed from a doctor, 1 (1 %) had got it without prescription and for 12 patients (12 %) it was unknown if on prescription or not.
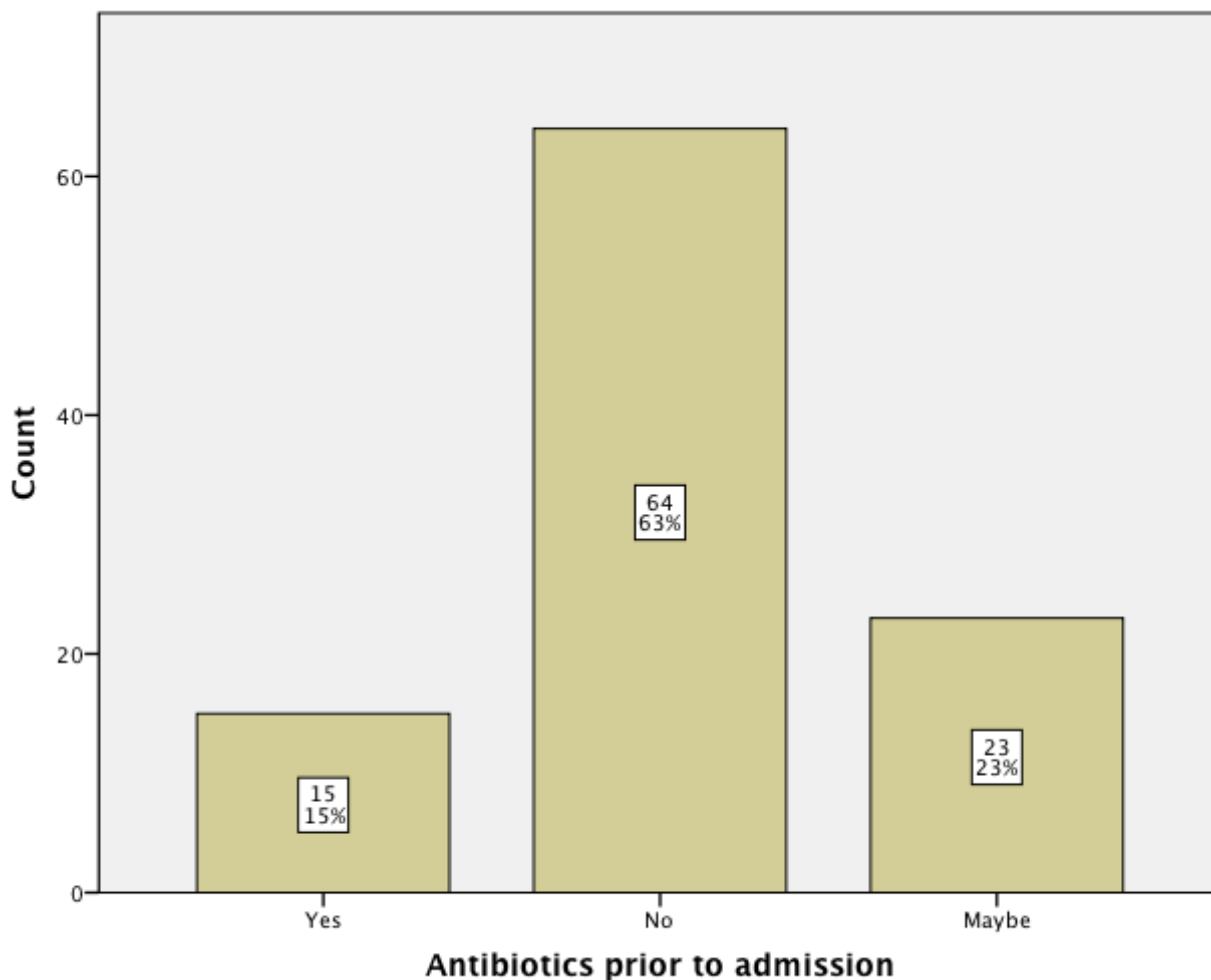

Figure 3. Number of patients using antibiotics during the 2 weeks prior to admission.

Therapeutic and prophylactic use of antibiotics

For the patients currently on antibiotics, the use was therapeutic in 34 cases (55 % of patients on antibiotics), prophylactic in 26 cases (42 %), and the indication was unknown in 1 case (2 %). In 1 case (2 %) the patient was on two antibiotics, one prescribed as therapeutic and one with unknown indication.
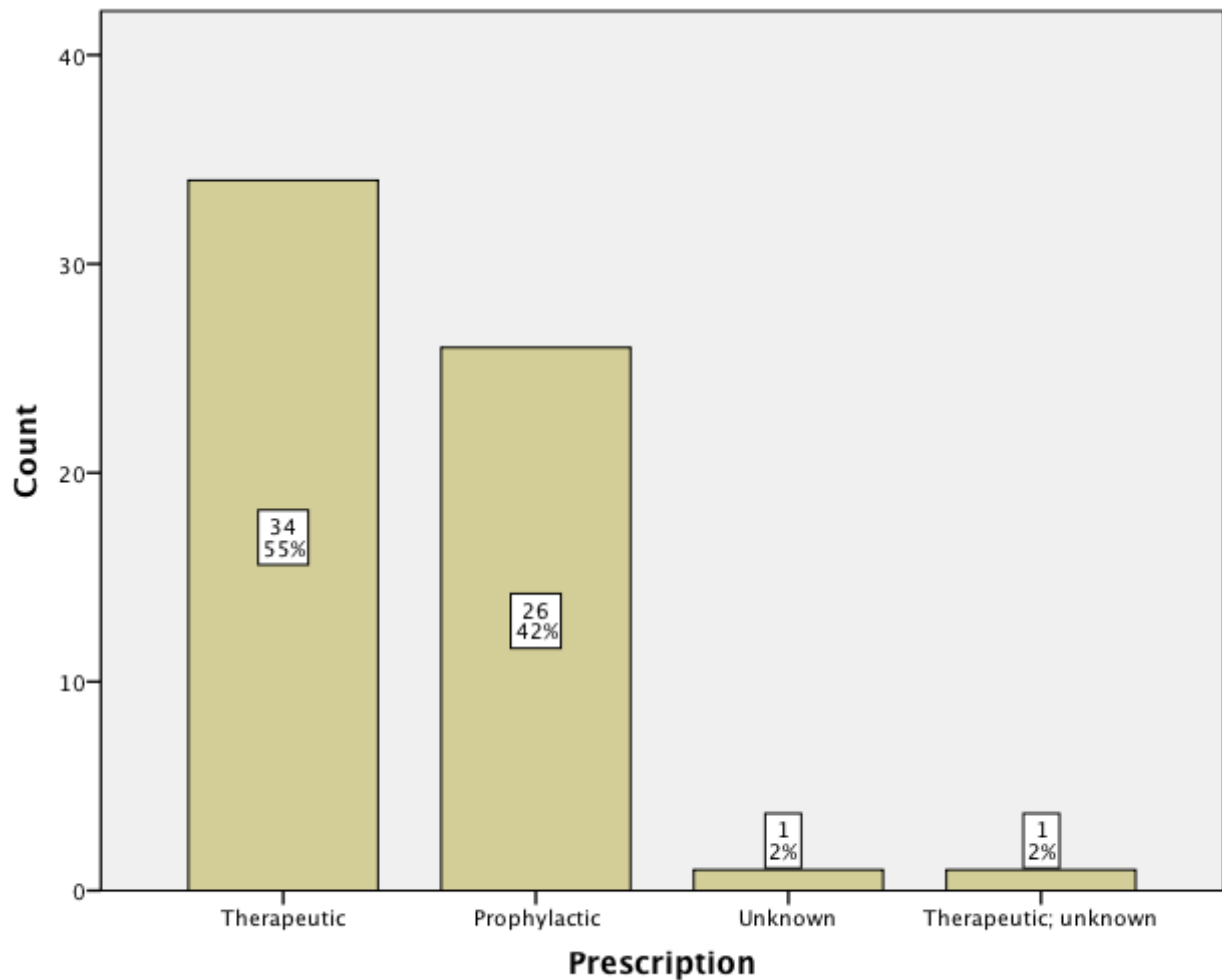
Figure 4. Therapeutic and prophylactic prescription of antibiotics. In one case, a patient on two antibiotics was prescribed one with therapeutic and one with unknown indication.

Reasons for admission

The patients were grouped according to their present health issue. The biggest group was infection/sepsis/fever with 31 patients (30 %), followed by patients who underwent surgery, with 19 patients (19 %), trauma with 14 cases (14 %), and giving birth (including caesarian sections), 13 patients (13 %).

Seven patients (7 %) were admitted for 'other' reasons, this includes readmission for control of earlier surgery (1 patient), collapse/fainting (2 patients), stomach pains (1 patient), and CNS lesion other than infection or stroke (3 patients).
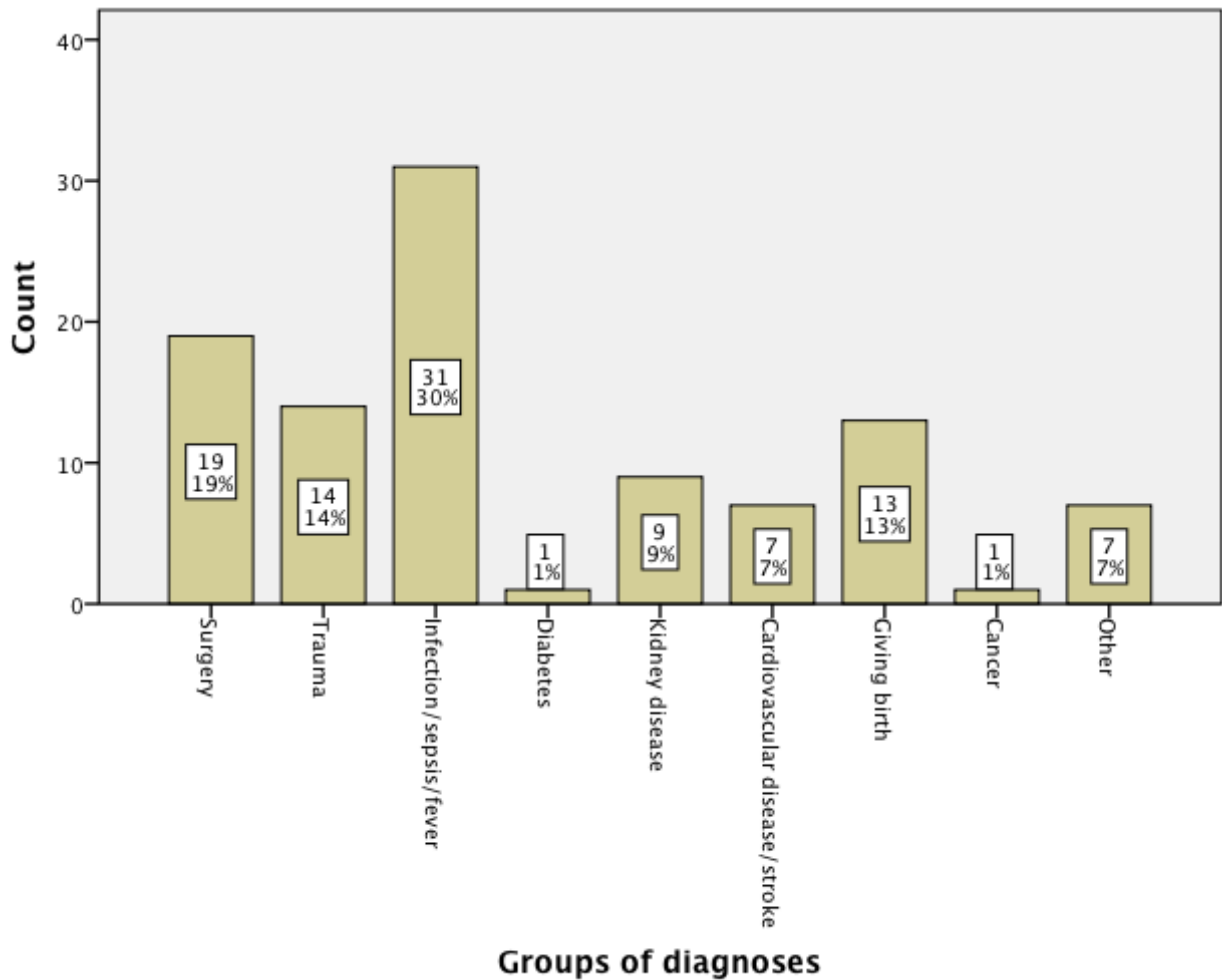
Figure 5. Reasons for admission. Patients grouped according to present health issue.

Twenty of the patients (20 %) had been admitted from another hospital or readmitted. For the remaining 82 patients (80 %) this was not the case, or there was no information about this.

Community acquired and nosocomial infections

Forty-three patients (42 % of total) were considered to have an infection, and in 21 of the cases (21 %) the infections were classified as community acquired, 8 cases (8 %) were considered to be nosocomial and in 14 cases (14 %) the infections were of unknown origin.

Indications for antibiotic prescription

Of the 62 patients who were prescribed antibiotics, the biggest group was the patients receiving antibiotics as prophylaxis, 26 patients (42 % of those receiving antibiotics). This includes patients who underwent surgery, patients who gave birth, and trauma patients. Therapeutic indications were: Six patients (10 %) had a wound infection, 6 patients (10 %) had a gastrointestinal infection and 5 (8 %) had a pulmonary infection. Four patients (6 %) had a urinary tract infection, 3 (5 %) had a pulmonary *and* a gastrointestinal infection and for 3 patients (5 %) the focus of infection was unknown.

The group 'other' includes 1 patient with acute pelvic inflammatory disease, 1 patient with suspected pulmonary *and* urinary tract infection, 3 patients with kidney disease, 2 patients with malaria, 1 patient with chronic otitis media, and 1 patient with an abscess.

Table 4. Indications for antibiotic prescription. The diagnoses are suspected or confirmed. GI= Gastrointestinal infection.

Indications for antibiotic prescription

	Frequency	Percent
Pulmonary infection	5	8
Urinary tract infection	4	6
Wound infection	6	10
Gastrointestinal infection	6	10
Other	9	15
Prophylaxis	26	42
Pulmonary + GI	3	5
Unknown focus	3	5
Total	62	100

Types of antibiotics used

The most commonly used group of antibiotics was Cephalosporins, prescribed to 29 patients (47 % of those on antibiotics); to 12 patients (19 %) as monotherapy, and in combinations with other antibiotic/s to 17 patients (27 %).

The second most common group was Metronidazole, prescribed to 19 patients (30 %), as monotherapy to 3 patients (5 %) and combined with another antibiotic to 16 patients (26 %). Thirteen patients (21 %) were prescribed a Quinolone/fluoroquinolone antibiotic, six patients (10 %) as monotherapy. Thirteen patients (21 %) were prescribed a Penicillin antibiotic, 6 patients (10 %) as monotherapy. Penicillin combinations (different brand names of Amoxicillin+clavulanic acid), was prescribed to 9 patients (15 %), of which 8 patients (13 %) as monotherapy.
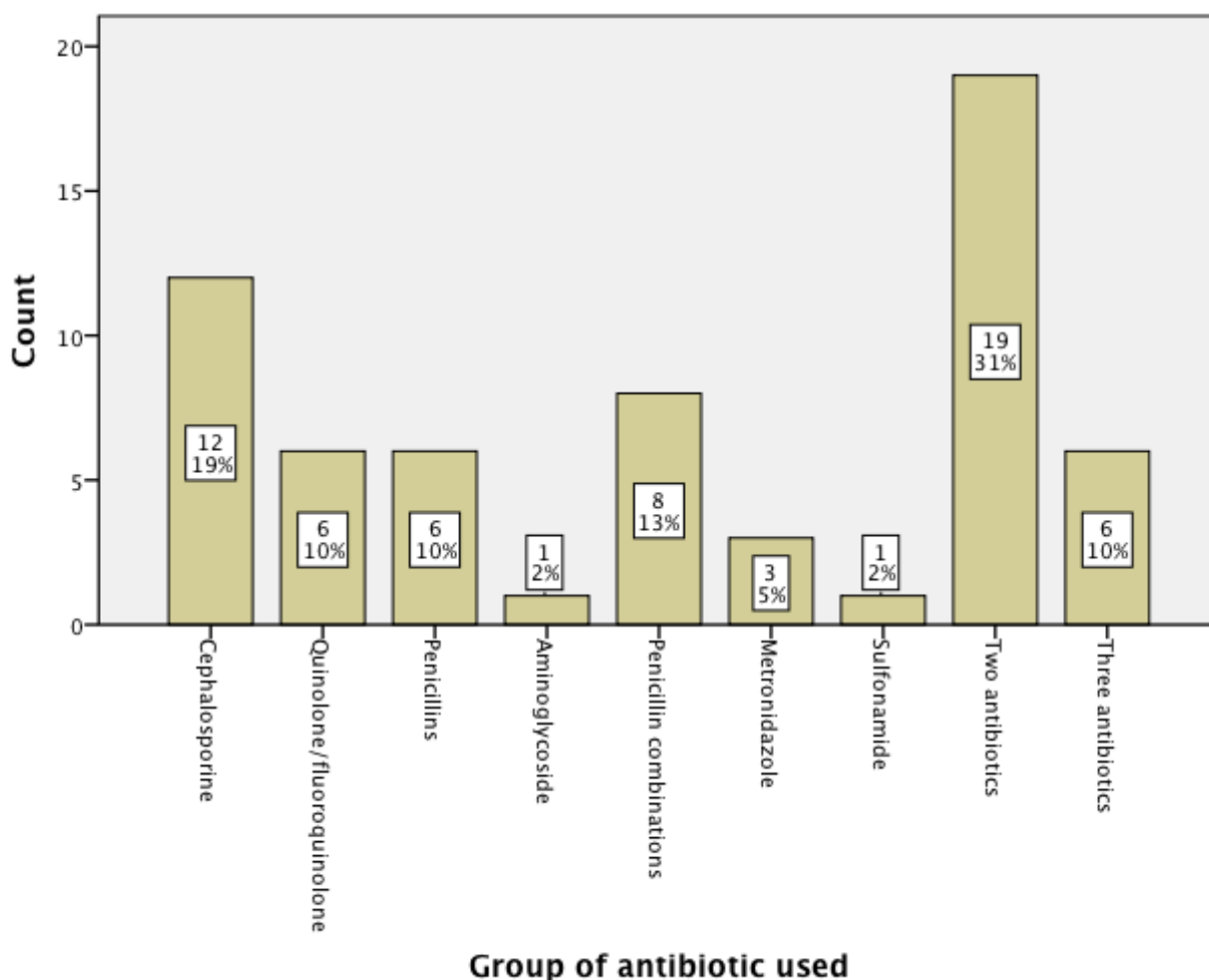

Figure 6. Antibiotic groups. Number of patients who were prescribed an antibiotic group, as monotherapy, or prescribed multiple antibiotics (two or three). The percentage is of patients with antibiotic prescription.
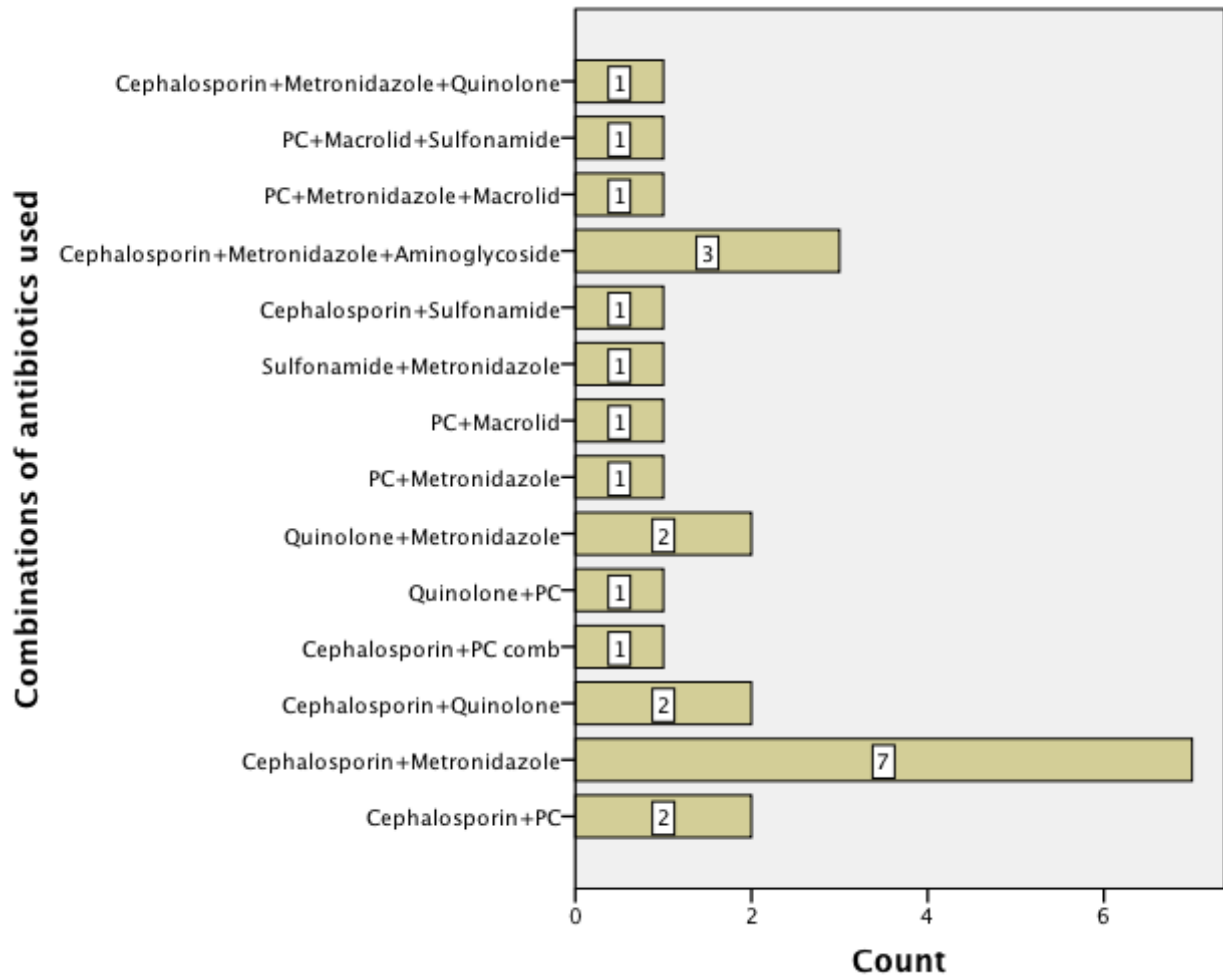
Figure 7. Multiple antibiotics. Number of patients who were prescribed different combinations of antibiotics, when two or more were combined. PC = penicillin. PC comb = penicillin combinations.

The most commonly used antibiotic was the Cephalosporin Ceftriaxone, which was prescribed to 26 patients (42 % of patients on antibiotics), as monotherapy or in combination with another antibiotic.

Correlation antibiotic prescription and socioeconomic data

There was no statistically significant correlation between present treatment with antibiotics and age group, sex, living conditions (urban/rural), occupation, number of people in household, or number of children alive.
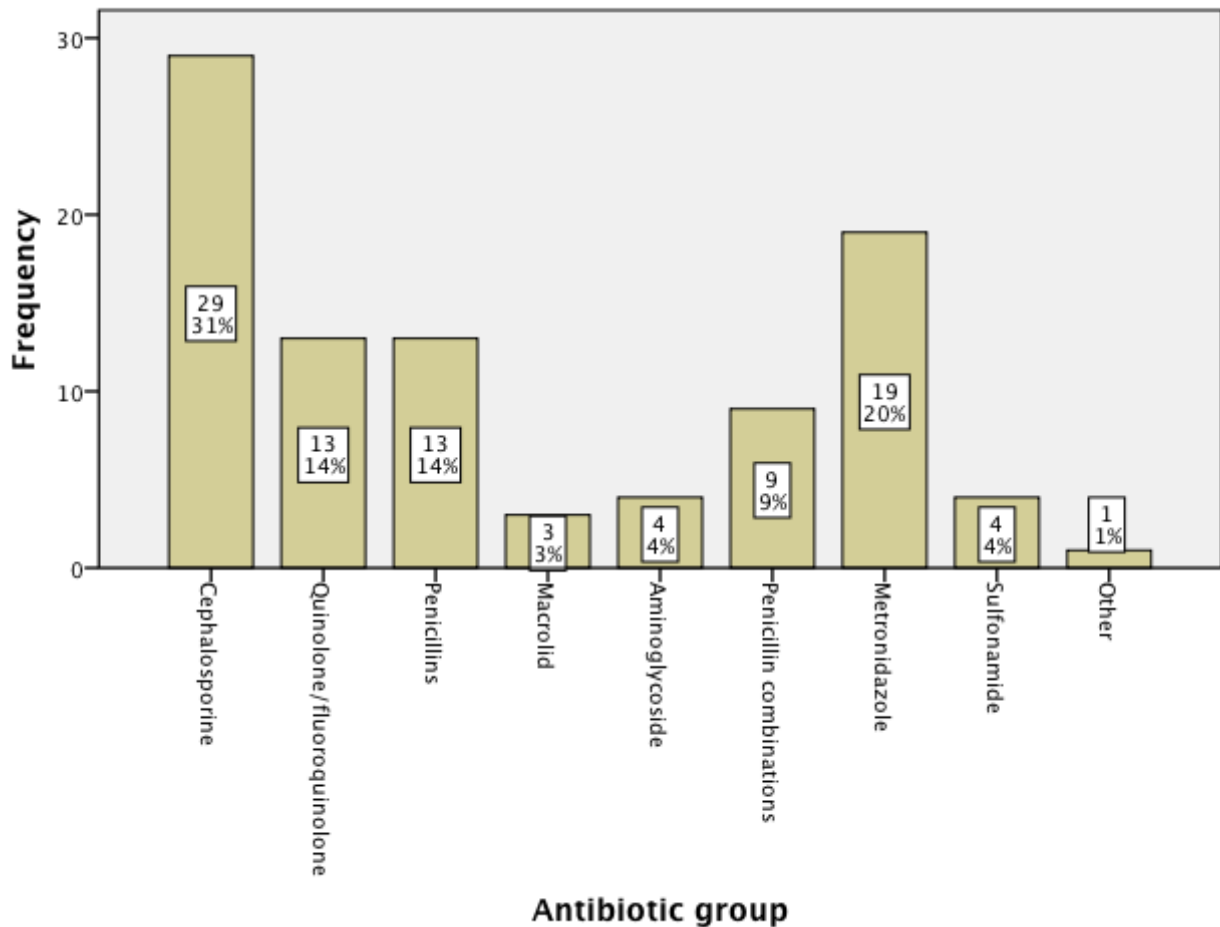
Figure 8. Total antibiotic prescription. Number of prescriptions of each antibiotic group. The percentage is of total antibiotic prescription. NB some patients had more than one antibiotic – the number of antibiotics prescribed is higher than the amount of patients on antibiotics.

Routes of administration

Of the patients currently on antibiotics, 18 (30 % of those on antibiotics) had intravenous (iv) treatment, and 29 (48 %) had per oral (po). Ten (17 %) had both iv and po administration, 1 (2 %) had both iv and po plus a third 'other' route of administration (i.e. intramuscular or subcutaneous) and 2 patients (3 %) had po and 'other' route of administration.
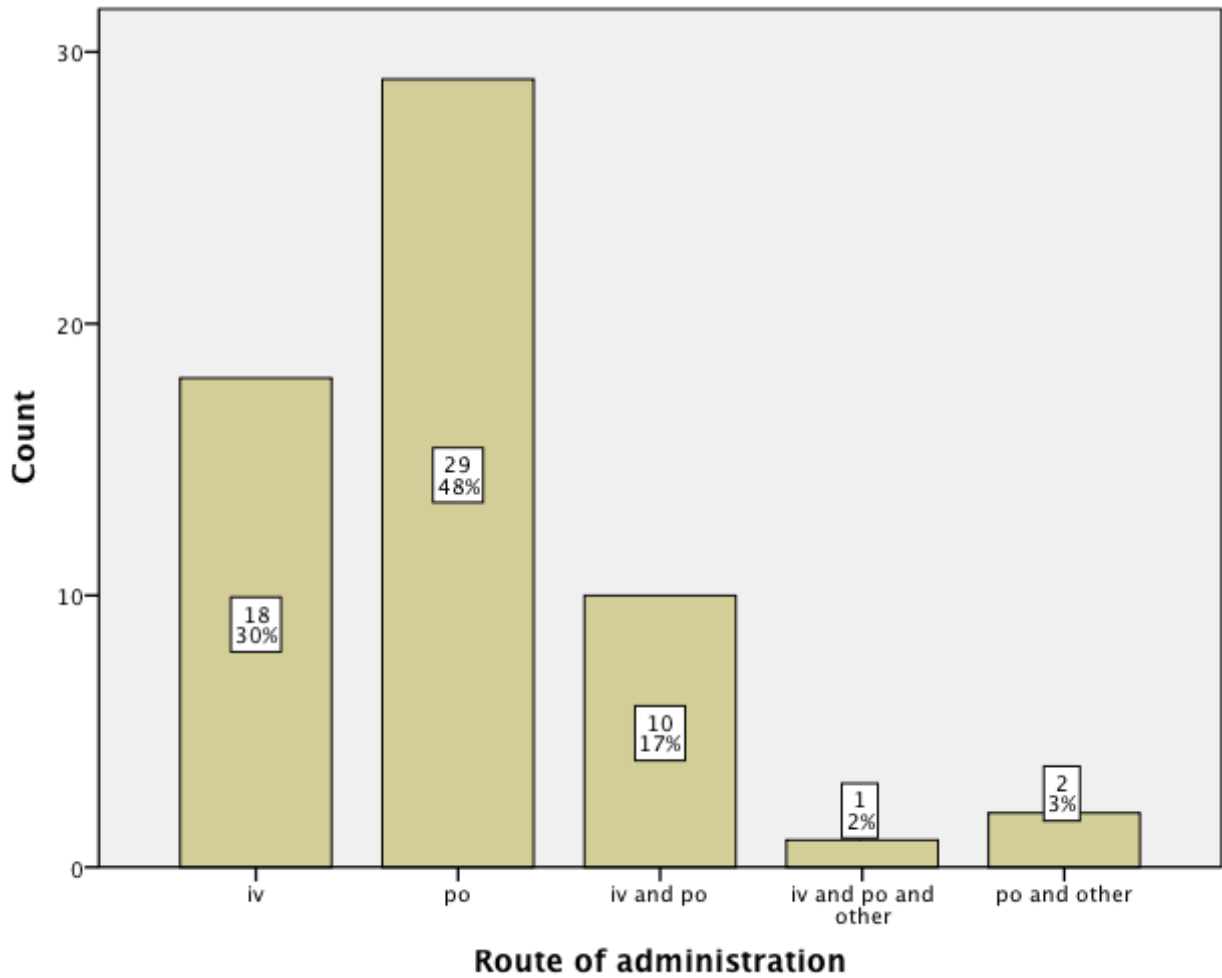
Figure 7. Routes of administration for the antibiotics used. IV= intravenous, PO = per oral. Other = subcutaneous or intramuscular administration. The percentage is of patients on antibiotics.

4c. Diagnostic measurements

Blood samples

The most common diagnostic measurement for patients currently on antibiotics was some kind of blood sample, 35 patients (56 %) had this done and it had been requested for another 6 patients (10 %). Two patients (3 %) had blood samples taken prior to admission.

Of the blood samples, FBC (full blood count) was the most common, taken in 25 cases (40 % of patients currently on antibiotics). For an additional 5 patients (8 %) it had been ordered but not yet done, and 4 patients (6 %) had FBC taken prior to admission. FBC includes Hb, leukocytes (with sub classes e.g. neutrophils), RBC, MCV,MCH, MCHC, and platelets. Serum electrolytes were taken for 11 patients (18 %), as a package or single electrolytes (e.g. potassium). Full blood sugar was taken for 9 patients (15 %). ESR (Erythrocyte sedimentation rate) was taken for 1 patient currently on antibiotics (2 %), and CRP was taken for 2 of these patients (3 %). Each of the two latter had also been ordered for 1 patient (2 %), respectively.

Cultures

No patients had cultures done from blood, urine or feces, or from the nasopharynx. In one case, a culture was done from knee aspiration fluid, with growth of *S Aureus*. Antimicrobial sensitivity testing of this isolate had been done, showing resistance to Amoxicillin, Erytromycin, Oxacillin, Cefazolin and Amoxicillin/Clavulanic acid, while sensitivity was found towards Tobramycin and Clindamycin.

Malaria testing

Malaria testing was done for 12 patients (19 % of patients currently on antibiotics) and had been requested, but not yet done, for an additional 7 patients (11 %).

X-ray

Of the patients currently on antibiotics, 9 (15 %) had some type of x-ray done, and for an additional 12 patients (19 %), x-ray had been requested, but not been done yet.
The most common types of x-ray for this group of patients were chest x-ray and CT brain, done for 4 patients (6 % of patients on antibiotics) respectively. One patient (2 %) had 'other' x-ray done, which in this case was x-ray of the skull.

Other diagnostic methods

34 of the patients currently on antibiotics (55 %) had some other types of diagnostic measurements done. Two patients (3 %) had stool analysis done, 5 (8 %) urine analysis, 7 patients ultrasound (11 %), 1 patient (2 %) wound swab, and 2 (3 %) a sputum test. Eleven patients (18 %) had more than one of these done or ordered.

Six of these patients (10 %) were grouped with 'other' diagnostics done, including patients who had diagnostics ordered but not yet done. Of this group 1 patient had skull x-ray done, 1 patient had a body fluid analysis done from a knee aspiration (the patient who also had a culture done, from the same fluid), 1 patient had a prostate biopsy taken, 1 had ECG ordered but not yet done, 1 had stool analysis ordered, and 1 had a body fluid analysis done from pleural aspiration.

Diagnostic results prior to antibiotic insertion

For the patients currently on antibiotics, in 21 cases (34 % of patients on antibiotics) there were some kind of diagnostic results available before antibiotics were prescribed. In 21 cases (34 %) antibiotics were prescribed before any diagnostics were requested, and for 13 patients (21 %) a diagnostic measurement was ordered, but no results were yet available when antibiotics were prescribed. In 7 cases (11 %) it was uncertain if there were diagnostic results prior to antibiotic insertion.

4d. Urine cultures

Only 22 urine samples were obtained, because the start of this part of the study was delayed. Of the 22 urine cultures conducted, 15 cultures (68 %) showed bacterial growth. Seven (32 %) were found to be Gram-negative and of these, API 20E tests showed that 5 (23 %) were *E Coli* and 2 (9 %) were *K pneumoniae*. Six (27 %) were Gram-positive. Two (9 %) were hard to determine if Gram-positive or –negative, hence subcultured and then repeatedly Gram stained,

with the result that both were Gram-positive. In 7 cases (32 %) there was no bacterial growth and no further analysis was done.
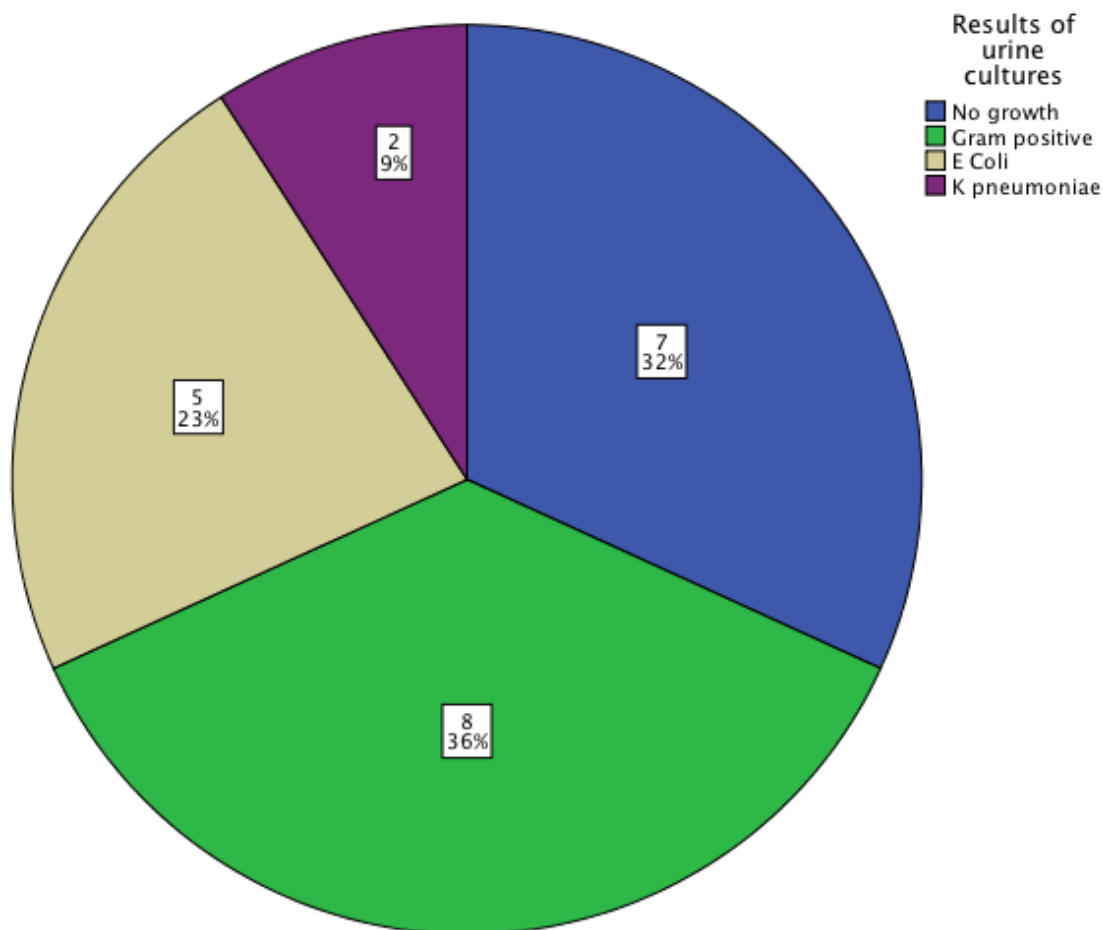
Figure 10. Bacterial growth in urine cultures performed.

For 87 % of the cultures with bacterial growth (13 of 15 cases) the patient had no symptoms from the urinary tract, or this was unknown, i.e. these could all be cases of asymptomatic bacteriuria.

Ten samples (45 %) were obtained from patients in the surgical ward, 3 (14 %) from the medical ward, and 9 (41 %) from the maternity ward. There was no statistically significant correlation between type of ward and bacterial growth (p-value 0.52).

Three of the patients (14 %) had a urinary catheter. All of these samples had bacterial growth (1 was *E coli*, 1 was *K pneumoniae* and 1 was Gram-positive).

Fifteen of the patients providing a urine sample (68 %) were currently on antibiotics. Six of these (40 %) had no bacterial growth in their sample, 4 (27 %) had Gram-positive bacterial growth, 4 (27 %) had growth of *E coli*, and 1 (7 %) had growth of *K pneumoniae*. There was no statistically significant correlation between antibiotic use and bacterial growth (p-value 0.23).

5. Discussion

5a. Antibiotics in Cameroon

In this study, 61 % of the patients were on antibiotics. This can be compared to other studies: As mentioned in the introduction, in the 2011-2012 ECDC[3] PPS in European hospitals, 32.7 % of the patients were prescribed antimicrobials [15], and in the Swedish STRAMA[4] PPS 2003-2010, about one third of the inpatients were on antibiotics on the day of the survey. [16] In a nationwide PPS in the west-African country Benin, 64 % of the patients were on antibiotic drugs. [17] Another study, a 1-day prevalence survey from Ghana in 1997, describes an antibiotic prescription to 57.8 % of the in-patients, with the highest prescription rate at the maternity ward, with 85.7 % of patients on antibiotics. [32]

Of course, one cannot directly compare a developing country like Cameroon, with developed countries in Europe. In Cameroon, the burden of infections is higher while health care resources are scarce, and poverty is widespread. The study methods also differ, as this study was a modified form of the PPS.

The percentage of patients on antibiotic treatment in this study correlates more with the Benin PPS, which seems likely, although one can be concerned about the high numbers. The proportions from the Ghanaian study are also similar to the findings here, however that study is

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[3] European Centre for Disease Prevention and Control
[4] Swedish Strategic Programme for The Rational Use of Antimicrobial Agents and Surveillance of Resistance

rather small, making it hard to draw any conclusions.

In Cameroon, antibiotics are mostly prescribed empirically. One reason for this is that the patients have to pay for everything themselves, from lab tests and the gloves that the nurses use, to surgeries performed. To give some examples, the blood sample Full blood count costs 4500 CFA, and one ampulla of Ceftriaxone (1g) costs 800-1000 CFA. A normal delivery costs 6000 CFA and a caesarian section 40 000 CFA. 500 CFA equals 1 dollar (in 2014). As stated in the introduction, the population below the poverty line was 48 % in 2000. Sometimes the doctors seem to prefer prescribing only an antibiotic, rather than making the patient pay also for lab tests.

There is a health care insurance launched by the government, but only about 1% of the population has got it. [23] There are also health care insurances offered by churches, but not everyone can afford it. Since the patient has to pay for all the healthcare, perhaps this keeps people from going to the hospital unless they really have to – in some cases the patients are very sick when admitted, which could contribute to a more generous antibiotic use.

Antibiotics can be bought without prescription, "in the street". [29] Only one patient stated they had bought antibiotics without prescription, when asked. It can be suspected that more patients had tried self-medication before coming to the hospital.

There are no Cameroonian guidelines for antibiotic treatments. One of the doctors in the surgical ward explained that in this hospital, the doctors look at European and American guidelines and modify them. This lack of local guidelines could affect the amount of antibiotics prescribed.

There was a difference between the wards in the proportion of patients on antibiotics, 56 % in the surgical and 55 % in the medical wards, while 84 % were on antibiotics in the maternity ward. Reasons for the higher percentage in the maternity ward can be that few patients were included from this ward (19 % of all patients studied) and that antibiotics were used on routine basis after every delivery. Most of the patients included from the maternity ward were women who had given birth, 68 % (13 of 19 patients), and hence stood on antibiotics. In addition, 2

patients (11 % of patients from this ward) had undergone surgery and had antibiotic prophylaxis, and 2 of the patients in the ward (11 %) had an infection and stood on antibiotics because of this.

The WHO recommends antibiotics in some cases after deliveries, but states that antibiotics cannot be recommended as a routine after every vaginal delivery, with the evidence available today. [33]

Field notes

Poor hygiene standards were observed in the area, which favors bacterial growth. In the hospital, each patient has to bring a relative or friend to take care of them and they themselves must bring bed linen, clothes and food. The toilets and washrooms are few and shared by many patients and their family members.

The nurses must buy their own hand sanitizer, this is not provided by the hospital, resulting in that it is rarely used. Gloves are used, but scarcely.

These factors of course affect the degree of sanitation in the hospital. The knowledge of the importance of good hygiene could also be improved in the society.

Community acquired and nosocomial infections

Eight patients (8 %) were considered to have a nosocomial infection, and 14 patients (14 %) had an infection of unknown origin. This can be compared to a European study where 6 % had a hospital-acquired infection. The same study states that these infections often are underestimated [15], which could also be the case here.

Of course, in this study these patient groups are very small, making it hard to draw any conclusions.

5b. Method

Oral consent was used instead of written, as one of the nurses explained that oral consent is more applicable in this context. Reading abilities may be poor – literacy was estimated to 71.3 % of the population, in 2010 [22] – and it may seem too formal with a letter to sign.

Initially the plan was to conduct the study in the surgical and medical wards, but the patient turnover wasn't very high here. To get a sufficient material, during the last weeks the study was also conducted in the maternity ward, and the intended number of patients was obtained.

When planning the study, the intention was to investigate if the use of antibiotics in the hospital was according to any guidelines, and if so, if these were local guidelines, or WHO guidelines for antibiotic treatment. Since there are no Cameroonian guidelines and there were few patients in each diagnosis group, this was not done.

5c. Diagnostics

Sometimes diagnostic measurements were requested by the doctor but not done. This could have different reasons. Some things had to be planned, for example the CT scans were done in another city. Sometimes the patient couldn't afford the diagnostics, with the result that they weren't done or delayed. Sometimes there were results but they hadn't been written in the file yet.

Sometimes there were diagnostic results available before an antibiotic was prescribed, but there might not be a correlation between the diagnostic measurement performed and the prescription of the antibiotic.

5d. Urine samples

The urine samples obtained were obviously too few to draw any conclusions from. Unfortunately the start of this part of the study was delayed which made the sample size smaller than intended.

The proportion of cultures with bacterial growth was high. The patients were informed how to collect the midstream morning urine, but perhaps this was not correctly done, which could lead to contamination of the samples. The laboratory work was conducted with help from experienced staff; hence the risk for methodological errors was low. A high proportion of the cultures with bacterial growth, 87 %, could be cases of asymptomatic bacteriuria as there was no information about urinary tract symptoms in the files for these patients.

5e. Limitations of the study

The author's knowledge about the culture can be a limitation, as well as language difficulties. Although English is the official language in this part of Cameroon, other languages are spoken, and the Pidgin English is commonly used, especially among the older population. Sometimes interpretation by relatives was used, which can be a source of misunderstanding.

The patients' files are written by hand, and are sometimes difficult to read. Some doctors were French-speaking, and would write in French. In that case, a nurse was asked to translate.

The medicine names in Cameroon are different from the Swedish. When in doubt if a certain medicine was an antibiotic, a nurse or doctor was asked, and if needed medicines were searched for on the Internet.

Sometimes not all the information about the patient's treatment could be found in the patient's file, each patient also has their own treatment book, and there is a report book in the nurses' station where notes are taken as well. Especially in the maternity ward the patients' files could lack information, instead most of the information was to be found in the report book in this ward.

When the patients were admitted via the Emergency ward, sometimes not all the information from the emergency file was transferred to the file in the ward. If the information in the patients' file was scarce, it was searched for in the patients' book or in the report book, if possible.

The nurses were supposed to sign the medicine list in the patients' file when a medicine was administered, but this was not always done.

Also the author's lack of experience of performing this type of study could be a limitation.

6. Conclusions and Implications

The prescription of antibiotics at the Buea Regional Hospital is mostly empirical and the amount of patients on antibiotic treatment is high.

More diagnostic methods, especially cultures, could be used prior to antibiotic prescription in the hospital, but the main problem here is poverty and the lack of a health care insurance system. Local guidelines for antibiotic prescription, like those in the maternity ward, could be useful.

Almost no cultures were performed during the study period. If more cultures were done, that would give a picture of the local resistance patterns, which would be useful for the empirical prescription of antibiotics.

The hygiene standards in the hospital could be improved.

More studies are needed on the use of antibiotics and the antibiotic resistance patterns in Cameroon.

7. Populärvetenskaplig sammanfattning på svenska*

Antibiotikaresistens är ett växande problem globalt. Att bakterier blir resistenta mot antibiotika är något som sker naturligt hela tiden, men detta påskyndas då antibiotika används, framförallt om mycket antibiotika används och när det används på fel sätt. Resistensen innebär att infektioner kan bli mer långvariga och svårare eller omöjliga att behandla, vilket medför mer lidande för den drabbade, och större kostnader för samhället.

Kamerun är ett låginkomstland i västra Centralafrika där sjukvårdens resurser är knappa, samtidigt som infektionssjukdomar är vanliga. Patienten måste själv betala för all vård, inklusive labprover. Kamerun har inga nationella riktlinjer för antibiotikaförskrivning.

Det har publicerats få studier om hur antibiotika används i Kamerun. De som finns visar på en ökande antibiotikaresistens.

I den här studien undersöktes antibiotikaanvändningen på Buea Regional Hospital, ett sjukhus i södra Kamerun. 102 vuxna patienter deltog i studien som genomfördes med korta intervjuer och informationssökning i patientjournaler. Det visade sig att 61 % av patienterna i studien fick antibiotika, på dagen de undersöktes. Liknande studier i Europa har visat på en antibiotika-användning på ca 33 %. Antibiotikan förskrevs dessutom i princip alltid empiriskt, d v s utan att resultat från bakterieodlingar var tillgängliga, vilket gör det osäkert om rätt typ av antibiotika används eller om antibiotika behövs alls.

Som ett tillägg till studien gjordes odlingar på urin från patienter på sjukhuset, för att leta efter Gram-negativa bakterier. Gram-negativa bakterier är bakterier med en viss typ av cellvägg, som kan orsaka infektioner, bland annat i urinvägarna. Det förekommer en ökande antibiotikaresistens hos Gram-negativa bakterier. Det gjordes totalt 22 urinodlingar, och i 15 av dessa (68 %) växte bakterier. I 7 odlingar påvisades Gram-negativa bakterier.

Det observerades att den hygieniska standarden på sjukhuset kan förbättras avsevärt. Bristfällig hygien bidrar till att bakterier sprids. I kombination med hög förskrivning av antibiotika finns en risk för att bakterierna som sprids också är resistenta mot flera antibiotika.

Mer provtagning och fler bakterieodlingar innan antibiotikaförskrivning på sjukhuset kunde vara önskvärt, men framförallt är problemen här brist på resurser, fattigdom och avsaknad av ett fungerande försäkringssystem för hälso- och sjukvård. Om patienten inte själv behövde betala för provtagning och annan diagnostik skulle detta sannolikt göras oftare, vilket skulle kunna minska antibiotikaanvändningen.

En studie av antibiotikaanvändningen uppmärksammar att detta är en viktig fråga och kan i sig påverka förskrivningen av antibiotika, där studien utförts. Bakterieodlingar kan ge en bild av vilka bakterier som är vanliga i ett sjukhus upptagningsområde, vilket sedan kan följjas upp med testning av antibiotikaresistens för dessa bakterier. När man vet detta är det större chans att antibiotikan som används verkligen fungerar.

I den här studien undersöktes bara ett sjukhus, och under en relativt kort period. För att få en bättre uppfattning om hur antibiotika används i Kamerun, behöver fler och större studier göras.

8. Acknowledgements

First I want to thank all the patients who participated in the study, and their relatives and friends who helped with translation and communication whenever needed. I'm very grateful. I want to thank my supervisors Dr Gunnar Jacobsson and Dr Ndeso Atanga for support and advice, as well as Dr Susann Skovbjerg for input and advice concerning the laboratory part. I want to thank Mrs Rebecca Moki and Mr Henry Dilonga for their help and guidance with the laboratory work.

I also want to thank all the staff and the students at the Buea Regional Hospital, especially the nurses at the surgical and medical wards, for being so welcoming and helpful. Thank you!

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10. Appendices

Appendix I. Questionnaire

Questionnaire
Hospital:
Ward:
Room:
Date:

Patient data
Patient nr:
Admission date:
Age:
Sex: M / F

Socioeconomic background
Living conditions: urban area/rural area
Number of people in household:
Occupation:

Number of children alive:

Medical history
HIV/AIDS: Yes/No
Treatment for HIV/aids   Yes/No
Drug allergies: Yes/No
    If Yes, specify:

Other disease/s: Yes/No
    If Yes, specify:

Other treatment/s: Yes/No
    If Yes, specify:

Antibiotics prior to admission   Yes/No
Type:

Indication:

Date of insertion:
With presciption   Yes/No

Diagnostic methods
Blood culture   Yes/No
Blood sample   Yes/No
Urine culture   Yes/No
Feces culture   Yes/No
Nasopharynx culture   Yes/No
X-ray   Yes/No
Other, specify:

Risk factors for nosocomial infection
Central venous catheter: Yes/No
Other, specify:

Vital parameters on date of admission
Blood pressure:
Pox:
Respiratory rate:
Temperature:

Current treatment with antibiotics Yes/No
Date of insertion:
Type of antibiotic/s:

Dose:

Route of administration: p o / i v
More than one antibiotic used: Yes/No
Is the antibiotic prescribed given to the
    patient: Yes/No

    If no, specify why:
Other antibiotic given   Yes/No
No antibiotic given   Yes/No
    If no antibiotic given, specify why:

Indication for treatment with antibiotics
Therapeutic: Yes/No
Prophylactic: Yes/No
Community acquired infection:
                            Yes/No/Unknown
Nosocomial infection:
        Yes/No/Unknown

Type of infection
Pulmonary infection   Yes/No
Urinary tract infection   Yes/No
Wound infection   Yes/No
Gastrointestinal infection   Yes/No
Other, specify

Appendix II. Lab protocol

Study of E. coli and K. pneumoniae in urine cultures

Sample ID	Sampling date	Number of colonies	cfu/mL	Species by API 20E	Stored in deep agar tube

Appendix III. Ethical permission

REPUBLIQUE DU CAMEROUN
Paix – Travail – Patrie

MINISTERE DE LA SANTE PUBLIQUE

DELEGATION REGIONALE
DU SUD OUEST

Tel: 33 32 22 10   General office
      33 32 22 62   Regional Delegate
      33 32 29 43   Drug Programme
pdph_sw@yahoo.com

REPUBLIC OF CAMEROON
Peace – Work – Fatherland

MINISTRY OF PUBLIC HEALTH

REGIONAL DELEGATION
FOR THE SOUTH WEST

BUEA the, 7th August 2014

THE REGIONAL DELEGATE

Ref: ___R11___/MINSANTE/SWR/RDPH/PS/ 229/78   TO:

Miss Frida Graumann
Medical Student
University of Gothenburg, Sweden

Subject: An Administrative Authorization to carry out a study on
"The Use of Antibiotics at the Regional Hospital Buea"

Your Application dated 1st August 2014 to carry out a study on *"The use of Antibiotics at the Regional Hospital Buea"* to fulfil the requirements for a Doctor of Medicine Degree was received and examined at the Regional Delegation of Public Health for the South West on Friday 5th August.

The results of your study may be a beginning of an early solution to nosocomial infections in our health facilities.

With the hope that information obtained from patients will be kept highly confidential and anonymous, I wish to inform you that an *Administrative Authorisation has been granted to carry out your study in the Regional Hospital Buea.*

I wish to hereby call on the Administration of the Regional Hospital to give you their greatest collaboration.

My best Regards

The Regional Delegate of Public Health
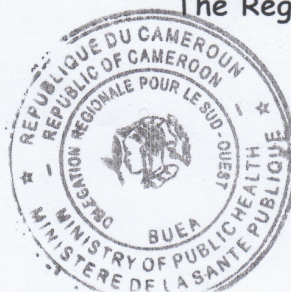
Dr. Abome Njile Victor
S.W Regional Delegate of Health