# The use of antibiotics at two paediatric wards at Kilimanjaro Christian Medical Centre (KCMC) in Moshi, Tanzania


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**Master Thesis**
**Supervisors: Gunnar Jacobsson and Grace Kinabo**

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Master Thesis in Medicine

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# Abstract

## Background

Antibiotic resistance is an increasing problem worldwide. Multiple studies report of high resistance rates in Tanzania. There are several factors contributing to antibiotic resistance including overuse and lack of surveillance systems. There is a need to monitor the actual usage of antibiotics in the health care systems in order to improve this and to combat the antibiotic resistance.

## Objectives

The objective of this study was to describe the usage of antibiotics among hospitalized children and to which extent diagnostic measurements were used, such as cultures, and also to describe the most common isolates found from cultures and its susceptibility patterns.

## Methods

A cross-sectional study conducted during October-November 2013 at Kilimanjaro Christian Medical Centre (KCMC) in Moshi, Tanzania. All children admitted to the neonatal ward and the general paediatrics ward were enrolled. Information was collected from medical files using a standardized protocol

## Results

Among 201 patients admitted, 72 % were inserted on antibiotics on the day of admission. The most common antibiotics were Ampicillin and Gentamycin; these were used in 44 % and 42 % of all antibiotic therapies respectively. Specimens were taken for culture 29 times, 34 % of these yielded bacterial isolates. The most common isolate was *Coagulase negative Staphylococci* (n=3) followed by *S. aureus* (n=2). One isolate, *Pseudomonas*, was found resistant to Gentamycin. In 53 % of the cultures ordered no results were found. Among febrile patients, specimens were taken for culture in 37 % of cases.

## Conclusion

There is a high usage of antibiotics at the paediatric wards at KCMC but this is also a referral hospital with many ill patients. The choice of therapy for the most common indications; respiratory illness and septicaemia mostly follow the local guidelines. Cultures are often ordered, but in more than half of them results are missing. There is a need to go over the routines to find out the reason for this and to increase the rates of cultures, especially among febrile patients.

# Background

Antibiotic resistance is an increasing problem worldwide. With microorganisms becoming resistant to therapy follows prolonged illness and greater risk of death. Some infectious diseases might become impossible to treat, and when first-line therapy is not improving the patient´s condition more expensive therapies must be used(1). Globally 6.6 million children under 5 died in 2012. The fourth Millennium Development goal (MDG4) is to reduce the under 5 mortality globally by two thirds between 1990 and 2015(2). In Tanzania the under-5 mortality rate was 54 deaths/1000 live births in 2012, which means they have reached their target goal, 54 deaths/1000 live births. Still 98 000 children under 5 died during 2012 in Tanzania, whereby 40 % during the neonatal period(3). This can be compared to Sweden were the under-5-mortality the same year was 3 deaths/1000 live births(4). In 2010 the leading cause of death among children under 5 in Tanzania was pneumonia and prematurity, counting for 15 % each. The same year 7 % of children under 5 died due to neonatal sepsis(5). More than 25 % of deaths under 5 in Tanzania 2010 occurred due to infectious diseases where effective antibiotic is a life-saving treatment.

Bacteria become resistant either through genetic changes like point mutations and gene amplifications, or by acquiring resistance from other bacteria by transfer of genes. In the latter, also called horizontal gene transfer, resistance genes are transferred on plasmids and other vectors. These can be transferred within the same species or between different. The human body consists of more bacteria than human cells. Ideally, antibiotic treatment would kill only the pathogenic bacteria. In reality though, both the pathogenic bacteria and the protective bacteria from the normal flora susceptible to the antibiotics used will be killed. Resistant bacteria survive and are then allowed to proliferate in absence of the protective

normal flora, this is called selective pressure(6). This explains how antibiotic use can lead to emergence of a resistance bacterial population within a patient.

There are several factors contributing to antibiotic resistance including overuse and lack of surveillance systems. Overuse includes treatment with antibiotics when there is no indication, for example for viral causes, treating inappropriate time, inappropriate dosage and wrong choice of antibiotics(7). According to WHO more than 50 % of all medicines are prescribed, dispensed or sold inappropriately in the world(8). Among outpatients seeing the doctor for cough and cold (not having pneumonia) in Gambia, 55 % were prescribed antibiotics(9). In the same study 45 % of patients with simple diarrhoea without dehydration were prescribed antibiotics. These being conditions were antibiotics are not indicated(10). In the developing countries antibiotics are often sold over the counter without prescriptions, this is also contributing to the overuse of antibiotics. There are several studies exploring this, in Tanzania for example, only 1/3 of the customers buying medicines had seen a health worker before(11). In this study antibiotic was relevant in 50 % of the cases. In Europe, countries using a lot of antibiotics also have higher resistance rates, while countries in northern Europe with lower consumption report lower resistance rates (12). There are some studies discussing the link between consumption of antibiotics and resistance trends. During the 1990s in Finland, Erythromycin resistance among group A streptococci was increased and new national treatment guidelines were issued to lower the usage of Erythromycin. This resulted in a decrease of Erythromycin resistance from 16.5 % in 1992 to 8.6 % six years later(13).

In Tanzania multiple studies report increasing frequency of antibiotic resistance. Though, one must remember that, since resources are limited in developing countries, blood cultures are often done on the most ill patients, which might result in more resistant bacterial results.

Among children with invasive bacterial disease at a district hospital, only 47 % of the isolated bacteria were sensitive to the first recommended antibiotics(14). In this study, 2/3 of the children with severe pneumonia had bacterial isolates resistant to Benzyl penicillin, which is the first recommended treatment according to WHO guidelines. Many studies report of high resistance rates among gram-negative enteric bacteria to commonly used antibiotics. In a study including neonates with sepsis at Bugando Medical Centre in Tanzania, *Klebsiella* was the most common isolate in blood cultures, 49 % of these were Extended Spectrum Beta Lactamase (ESBL) producing. Among gram-negative bacteria, *Escherichia coli* was the second most common isolate found. About 68 % of these two bacteria were resistant to Gentamycin and 90 % resistant to Ampicillin, these being the first choice of antibiotics for neonatal sepsis at this hospital. In this study only 1/3 of the neonates with resistant isolates survived, compared to 74 % of neonates with susceptible isolates(15). In another study in Tanzania, also including children with septicaemia, 25 % of the *E. coli* and 17 % of the *Klebsiella* isolates were ESBL-producing. The fatality among patients with ESBL-producing isolates was significantly higher in this study, 71 % died compared to 39 % of patients with non-ESBL-isolates(16). At Muhimbili National Hospital in Dar-Es-Salaam 23.3 % of the *Staphylococcus aureus* found in blood cultures were Methicillin-resistant (MRSA). In the same hospital 10 years earlier only 0.4 % of the *S. aureus* were MRSA(17).

In 2011 WHO published "WHO Global Strategy for Containment of Antimicrobial Resistance" where they recommend interventions against resistance. These are directed both to health care systems, governments, prescribers, pharmaceutical industries and the general community. Among the recommendations for interventions in hospitals, one is to monitor the usage of antimicrobials(18). In Sweden for example, the Swedish Strategic Programme against Antibiotic Resistance (STRAMA) regularly do point-prevalence studies to monitor the

use of antibiotics in Swedish hospitals(19). Point-prevalence surveys on the antibiotic usage are a type of cross-sectional studies that have become a well-established method to study the usage of antibiotics in the health care all over the world. These are done by counting how many patients who are treated with antibiotics at a particular time in proportion to the other in-bed patients at that time. In Europe a point prevalence survey on the usage of antibiotics in 21 countries in paediatric departments was done in 2008(20). In this study 32 % of the children received antimicrobials on the day of the survey. A few point-prevalence surveys have been done in Africa, for example in Malawi, where 40 % of the children (1 month-18 years) and 39 % of the neonates received antibiotics on the day of survey(21).

At KCMC, management of the children is guided by "KCMC paediatric management schedules"(22), a book written by paediatricians at KCMC where they adapt the WHO guidelines for common illnesses with limited resources(10). Recommended treatment and choice of antibiotics is listed in this book. For example, Ampicillin and Gentamycin is recommended for severe pneumonia and septicaemia.

As described above, the antibiotic resistance is widespread in Tanzania; this in combination with high burden of infectious diseases is a scary reality. To be able to treat the patient appropriate it is crucial that hospitals use the available diagnostic tools when necessary. There is a need to monitor the actual usage of antibiotics in the health care systems in order to improve this to combat the antibiotic resistance. The broad objective of this study is to describe the use of antibiotics and to which extent diagnostic measures are used at a paediatric department in Tanzania, and also to describe the most common isolates found from cultures and its resistance patterns.

### Specific Aims

- How many of the in-bed patients at the paediatric ward are initiated on antibiotics on the day of admission?

- Which antibiotics are used?

- Which diagnoses are treated with antibiotics?

- How often are blood cultures, malaria slides or other diagnostic measurements ordered?

- Which are the most common pathogens found in blood cultures and other ordered cultures?

- What are the susceptibility patterns of the isolates found?

# Methods

## Setting

This study was conducted at the paediatric department at Kilimanjaro Christian Medical Centre (KCMC) in Moshi, Tanzania, during October to November 2013. KCMC is a referral hospital for over 11 million people in Northern Tanzania(23). The paediatric department consists of three wards, P1, P2 and P3. P3 is a neonatal ward with a capacity of about 50 neonates. They have a total of six rooms where the neonates are divided depending on cause of care, for example there is one room for preterm babies, one room for term babies and one room for infectious diseases. P1 is general paediatrics with 35 beds and P2 has some beds for general paediatrics but is mostly for surgical patients. Children up to the age of 13 years were admitted to P1 but during the study period one patient was 15 years.

The hospital has handwritten medical files in English. There is a bed sheet by each bed where the on-going medical treatment is listed. There is no intensive care unit (ICU) for children, but sometimes beds are borrowed on the ICU for adults. The hospital has no working CT-scan (since 2 years), but has normal x-ray and availability to do ultrasound and echocardiography.

## Study population

All the patients admitted to the neonatal ward (P3) and the general paediatrics ward (P1) from 9th October to 10th November 2013 were included in the study (n=217), no matter if they were being treated with antibiotics or not. Patients were excluded if the medical file was unavailable (n=16). To facilitate the data collection, the medical patients on P2 were not included in the study and since no arrangement had been done with the department for surgery, no surgical patients were included either. Some of the patients admitted to the neonatal ward came directly from the labour ward at KCMC, the rest of the patients were either referred from another hospital or came directly from home.

## Study design

This was a cross-sectional descriptive study. Information was collected from the medical files using a standardized protocol (*Appendix 1*). Information was only taken from the day of admission to the ward but cultures that were ordered at that time were followed up for the results. The results from cultures were gathered from the laboratory for cultures taken 9th October to 3rd of November. For patients admitted after this, unfortunately no results from cultures could be registered. It would have been too complicated to track the results of the other diagnostic workup ordered (see which ones below) so I chose to only focus on results from cultures. A pilot study was done during two days including 7 patients before starting the main data collection. A short summary of the protocol used (See *Appendix 2* for further definitions) follows.

## Study protocol

### *Basic data*

Background information about the patient; age, sex, weight, date of admission and if the patient was referred from another hospital. Birth order and information about if the parents are alive.

### *Medical history*

Information regarding HIV-status, heart diseases, respiratory diseases, renal impairment, liver diseases, Diabetes Mellitus and anaemia was noted. In general, a patient was classified to have for example a heart disease if this was written in the file. Information if the patient was being treated with immunosuppressive medicines or malaria treatment within 2 months prior to admission.

### *Urinary catheters or surgical procedure?*

Information regarding presence of urinary catheters and if any surgical procedure was performed during the day of admission. At KCMC they very seldom (never) use central venous catheters on children and they don´t have respirators on the paediatric wards, so these two alternatives were taken away from the protocol.

### *Antibiotics prior to admission*

Antibiotic treatment within two months prior to admission that was mentioned in the file from the day of admission. Also its indication, if known.

### *Diagnostic workup*

Cultures ordered on admission date; including blood cultures, urinary cultures, stools analysis and liquor from lumbar punctures. Information about if blood chemistry (full blood picture, including Hb and WBC) or x-ray were ordered and blood slides for malaria parasites.

### *Current antibiotic treatment*

Type of antibiotic used, its indication and administration.

### *Vital parameters*

Vital parameters from the day of admission, including systolic blood pressure, heart rate respiratory rate, saturation and temperature.

### Statistical methods

Descriptive statistics were calculated using SPSS Statistics version 21. Mean values, medians and percentages were calculated. Excel was used for creating charts and tables.

## Ethical considerations

The paediatric department and its head of department, Dr Grace Kinabo, ethically approved the study. All gathered information was handled confidentially; no individual patient can be identified from the collected data. Only the hospital registration numbers were used to collect the data, so all information gathered was anonymous.

# Results

## Basic data

A total of 217 patients were admitted to the neonatal ward (P3) and the general paediatrics ward (P1) during the study period, 9th October to 10th November 2013. Of these, 16 patients were excluded because the file was unavailable. Thus 201 patients were included in the study, 96 (48 %) from general paediatrics and 105 (52 %) from the neonatal ward. Of these, 93 (46 %) were girls and 99 (49 %) were boys, information about sex was missed to fill out for 9 patients (4 %) The median age was 1.5 years in the general paediatrics and 1 day in the neonatal ward. See table 1 and 2 below for further distribution according to age and sex in the two wards. Of the patients at P1, 20 (21 %) were older than six years, and among neonates, 83 (79 %) were only 1 day old. The results will not be divided into further age groups than neonates (<28 days) and general paediatrics (28 days-15 years), since they would have included too few patients then.

**Table 1 Patiens at the general paediatric ward: Distribution of age and sex**

| | ***General paediatrics (P1)*** | | |
|---|---|---|---|
| | *Nr of patients* | *Percentages* | *Median age (years)* |
| **Girl** | 45 | 47 % | 2.0 (range 5 months-14 years) |
| **Boy** | 48 | 48 % | 1.4 (range 1 month-15 years) |
| **Unknown sex**[a] | 3 | 3 % | 1.1 |
| **Total** | 96 | | **1.5 years** (range 1 month-15 years) |

[a]; *Not found in the file or missed to fill in information*

**Table 2 Patients at the neonatal ward: Distribution of age and sex**

| | ***Neonatal ward (P3)*** | | |
|---|---|---|---|
| | *Nr of patients* | *Percentages* | *Median age (days)* |
| **Girl** | 48 | 46 % | 1 (range 1-15) |
| **Boy** | 51 | 49 % | 1 (range 1-21) |
| **Unknown sex**[b] | 6 | 6 % | 1 |
| **Total** | 105 | | **1 day** (range 1-21) |

[b]; Not found in the file or missed to fill in information.

Among the newborn children (1 day old), 30 (36 %) had a low birthweight <2500 g, according to the WHO definition (24). Unfortunately no information about the gestational age was collected, so I cannot draw conclusions whether the low birth weight was due to preterm birth or to restricted foetal growth, or to a combination of these two. 50 patients (25 %) were referred from another hospital to KCMC. No information about the length of hospital stay from the referring hospital was found in the files.

## Medical history

A total of 24 patients (25 %) at the general paediatric ward (P1) had one of the listed diseases.

**Table 3 Medical history of patients at the general paediatric ward (P1)**

| General paediatrics | *Nr of patients* | *Percentages* |
|---|---|---|
| **Heart disease** | 11 | 12 % |
| **HIV** | 8[a] | 8 % |
| **Diabetes Mellitus** | 2 | 2 % |
| **Respiratory disease** | 1 | 1 % |
| **Renal impairment** | 1 | 1 % |
| **Anemia** | 1 | 1 % |

[a];whereby 5 patients had AIDS

Heart disease was the most common finding, 11 children (12 %) had heart related problems, followed by HIV which 8 children (8 %) had. None of the neonates had any of the listed diseases. Observe that it wasn´t noted if the child was HIV-exposed, meaning if the mother had HIV, so HIV-status among the neonates is unknown. This was due to the fact that this part of the medical file was understood first when the majority of data was already collected. Two of the children from the general paediatrics had been treated with antimalarial within two months prior to admission and no patient had any drug allergy.

## Catheter or surgical procedure?

Only one patient at the neonatal ward had a urinary catheter. No surgical procedure was ever performed during the first day of admission. Regarding the referred patients, no surgical procedure was ever performed at the referring hospital, according to the files.

## Current antibiotic treatment

A total of 144 patients (72 %) were inserted on antibiotics on the day of admission (At P1 68 patients (71 %), at P3 76 neonates (72 %)). Of these, 124 patients (86 %) received >1 antibiotic and 96 % of all treatments were given intravenously. Co-Trimoxazole was the only treatment given orally. Ampicillin and Gentamycin were the most common drugs, 85 % of the patients were inserted on Ampicillin and 79 % on Gentamycin (Fig 1). In figure 2, the proportions of antibiotics used are showed, Ceftriaxone being the third most used drug.

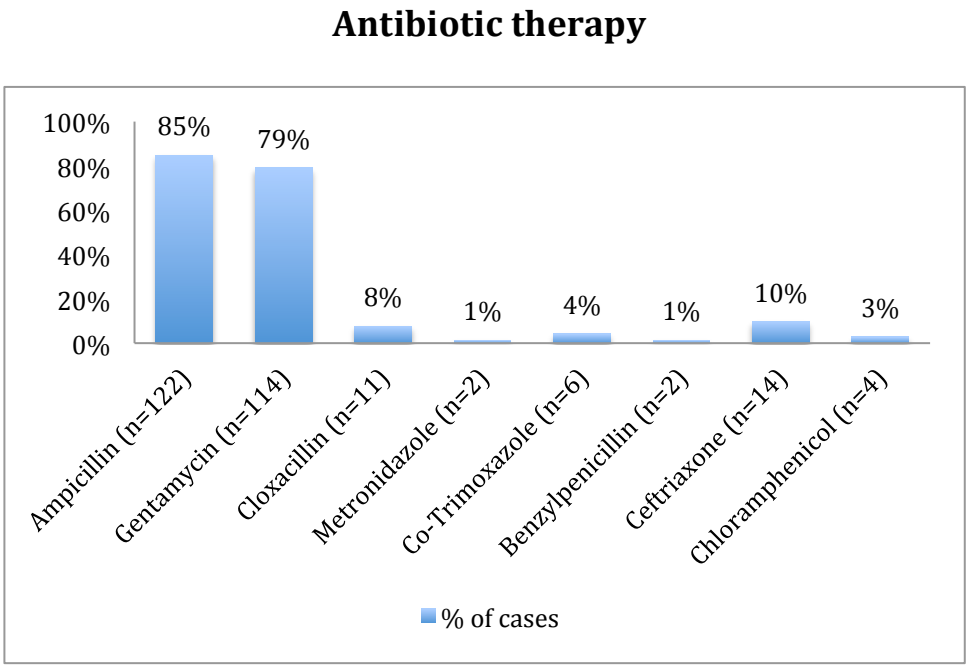


**Fig 1** *This chart shows the antibiotics used in both the neonatal ward and the general paediatrics ward. It shows percentage of patients who were inserted on a specific antibiotic..*

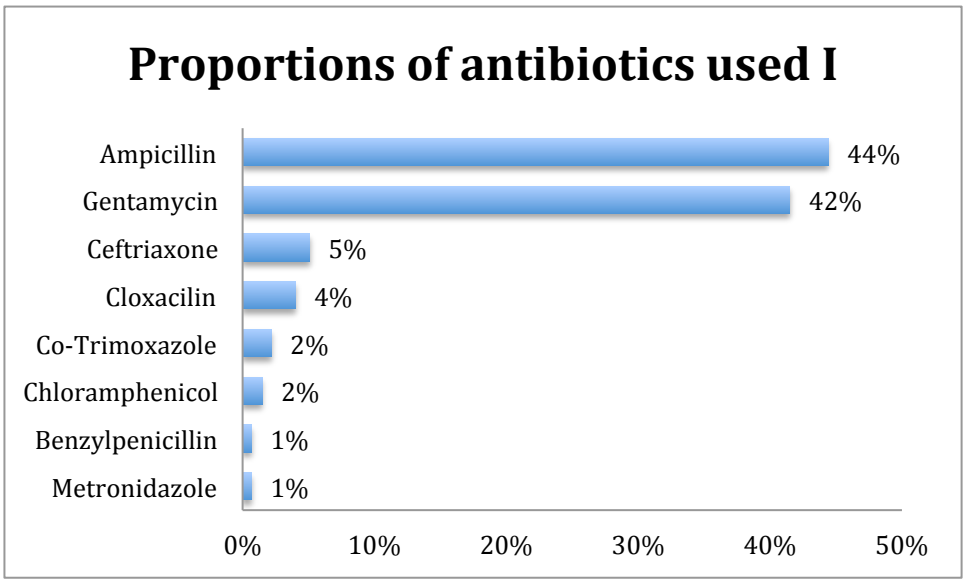


**Fig 2** *This chart shows the proportions of antibiotics used in both wards. It shows percentage of all antibiotics given that were of a certain type, for example 44 % of all antibiotic therapies given were Ampicillin.*

By looking at the antibiotic usage separately in the two wards, Ampicillin and Gentamycin were still the top used drugs (figure 3). In the neonatal ward this was followed by Cloxacillin which was used in 6 % of antibiotic therapies, and in the general paediatric ward, Ceftriaxone was the third most used drug, used in 12 % of antibiotic therapies. So only three different types of antibiotics were used in the neonatal ward.

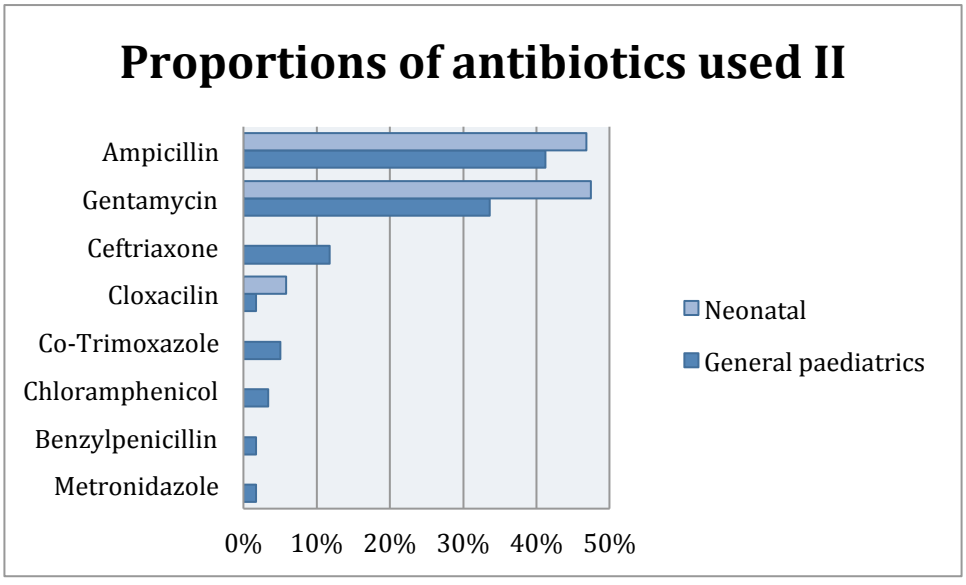


***Fig. 3*** *This shows the proportions of antibiotics used at the neonatal ward and general paediatric ward separately.*

The most common indication for treatment was respiratory tract infections (n=45), followed by septicaemia (n=31) and prophylactic usage (n=20) (figure 4). By looking at the wards

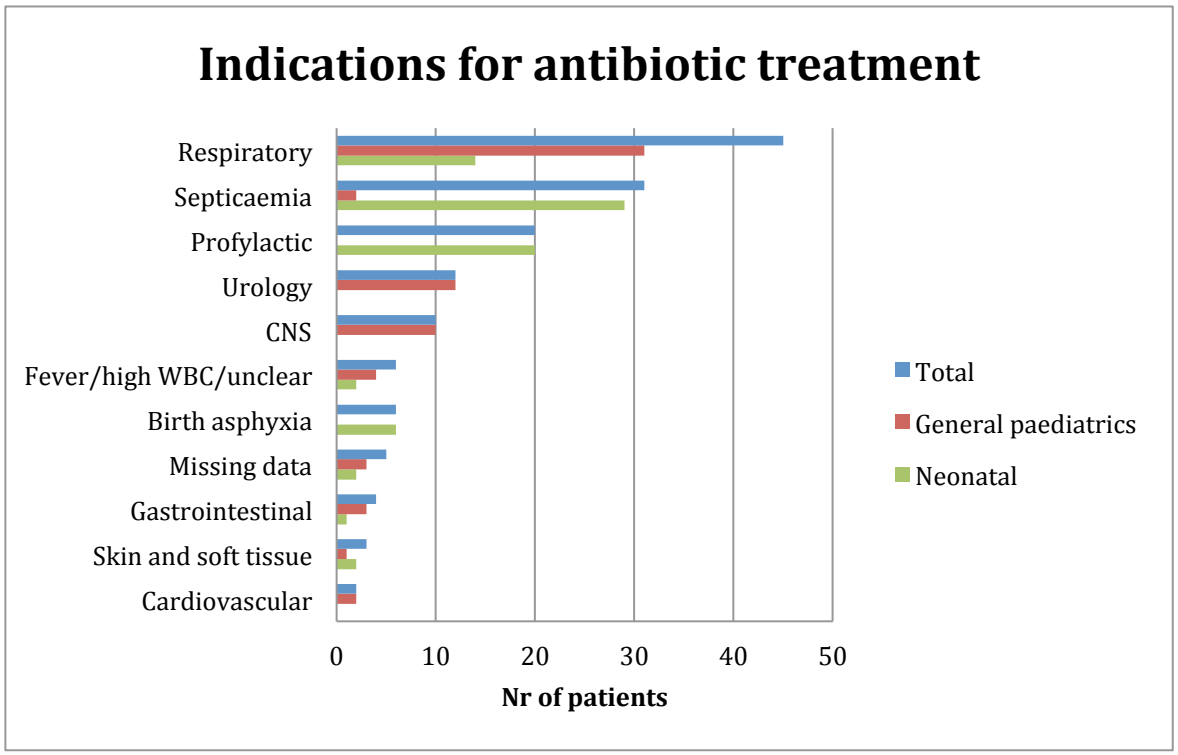


***Fig. 4*** *This chart shows the indication for antibiotic therapy both among all patients and by looking separately at the two wards. Observe that this is number of patients, not percentages.*

**Table 4 Top 3 indications for antibiotic therapy**

| General paediatrics | Neonatal |
|---|---|
| Respiratory (n=31) | Septicaemia (n=29) |
| Urology (n=12) | Profylactic (n=20) |
| CNS (n=10) | Respiratory (n=14) |

separately there were some differences between the most common indications. Among the neonates the top three indications were septicaemia, prophylactic use and respiratory (Table 4). Neonates who received treatment because of risk of infection were classified as prophylactic. Unfortunately no more specified information was collected regarding the prophylactic use, but no patient had surgical prophylaxis. Among the older children; respiratory, urology and CNS were the most common indications.

## Choice of treatment in certain conditions

Since Septicaemia and respiratory illness were the most common indications, I take a closer look on the choice of therapies for these.

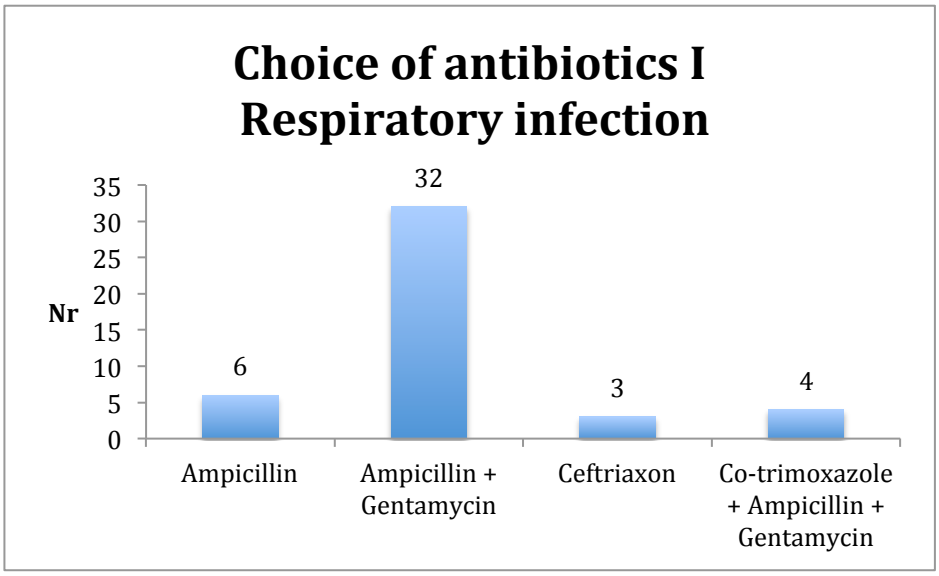


**Fig. 5** *Choice of antibiotics for children with respiratory infections (nr of patients).*

The most common treatment for respiratory infections was the combination of Ampicillin and Gentamycin, which 32 patients received (71 %) (Fig 5). Only 3 patients received Ceftriaxone.

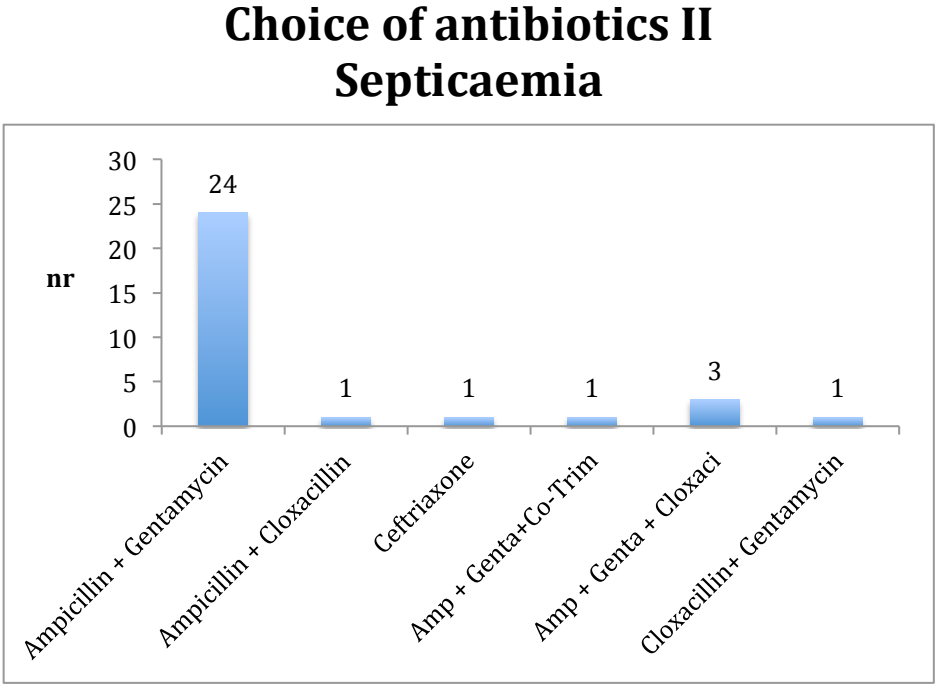


**Fig. 6** *Choice of antibiotics for children with septicaemia (nr of patients).*

The most common choice of antibiotics for septicaemia was also the combination of Ampicillin and Gentamycin in both wards, 24 patients (77 %) received this. (fig 6). Observe that the majority of patients with sepsis were neonates.

## Diagnostic workup

During the whole study period, 76 cultures (including blood, urinary, stools and CSF) were ordered. For all the cultures ordered between 9th October to 3rd November, results were collected with assistance from the laboratory staff. During this period cultures were ordered 62 times, but there were only results in 29 of these cases (47 %). In figure 7 the distribution of

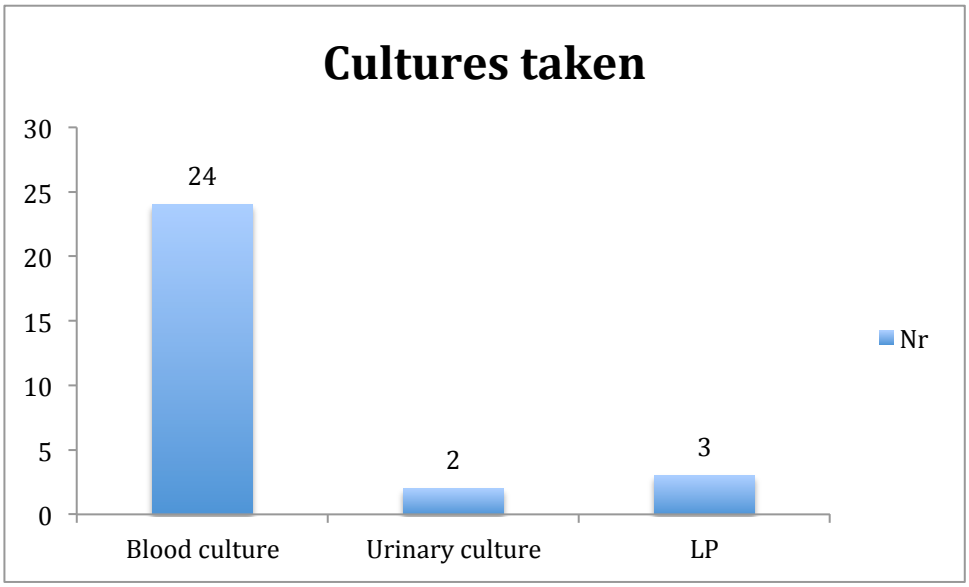


**Fig 7** *Number of cultures actually taken 9th October to 3rd November*

cultures *actually taken* during this period can be seen, the majority being blood cultures. During this time period, 159 patients were admitted, thus cultures were taken in 18 % (29/159) of these. Of the 159 patients admitted during this period, 114 were inserted on antibiotics, thus in 25 % (29/114) of patients on current antibiotic treatment a culture was taken. There were a total of 9 positive blood cultures, 5 from general paediatrics and 4 from the neonatal ward, and 1 positive result from a lumbar puncture (Table 5). The results from urinary cultures were both negative. Thus 34 % (10/29) of the cultures taken were positive.

**Table 5 Isolates from blood cultures and liquor**

| **Isolates from blood cultures** | n (%) |
|---|---|
| *Coagulase negative Staphylococci* | 3 (13) |
| *S. aureus* | 2 (8) |
| *Pseudomonas* | 1 (4) |
| *S.viridans* | 1 (4) |
| *Enterococcus* | 1 (4) |
| *Coliform** | 1 (4) |
| No bacterial growth | 13 (54) |
| Environmental contamination** | 2 (8) |
| Total | 24 |
| | |
| **Isolates from Liquor** | |
| Pseudomonas | 1 |
| No bacterial growth | 2 |

**Gram negative rods;**As it said on the labresults, don´t know what KCMC:s definition of this is.*

The most common bacteria isolated in blood cultures were *Coagulase negative Staphylococci* and *S. aureus*, which accounted for 3 (13 %) and 2 (8 %) of all the isolates from blood (Table 6). *CNS* could be skin contamination. In one lumbar puncture *Pseudomonas* was found. No resistant bacteria were found from the blood cultures, intermediate sensitivity was found for *S. aureus* and *S. viridans* for Ampicillin and Clindamycin respectively (Table 6). Pseudomonas isolate from liquor was resistant to Gentamycin. In Sweden, Pseudomonas is considered resistant to Ceftriaxone (25), but was found sensitive here. No assessment concerning the quality of the laboratory was available. *S. aureus* was never tested for Oxacillin, which is the first drug of choice for this bacteria, and Pseudomonas was tested for three antibiotics which it is intrinsic resistant against (Table 6).

**Table 6. Susceptibilty pattern for the 7 isolates found**

| **Bacteria** | Type of isolate | GEN | AMP | SXT | CRO | OXA | ERY | CLI | CTX | OXA | CIP |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ***S. aureus*** | blood | | S | S | | | | S | S | | |
| ***S. aureus*** | blood | S | I | | | | S | S | | | |
| ***Pseudomonas*** | blood | S | S | S | S | | | | | S | |
| ***S. viridans*** | blood | S | S | | | | S | I | | | |
| ***Enterococcus*** | blood | S | | S | S | | | S | | S | |
| **Coliform** | blood | S | | S | S | | | | | | |
| ***Pseudomonas*** | liquor | R | R[a] | R[b] | S | | | | | R[c] | S |

GEN; Gentamycin, AMP; Ampicillin, SXT; Co-Trimoxazole; CRO; Ceftriaxone, ERY; Erythromycin, CLI; Clindamycin, CTX; Cefotaxime, OXA; Oxacillin, CIP; Ciprofloxacin. R; resistant, S; sensitive, I; interminant

[abc] *Pseudomonas* is always resistant to these.

An overview of the diagnostic tools used among all patients can be seen in figure 7. In 37 % of cases full blood picture (FBP) was taken, this includes Hb and white blood count (WBC). The majority of the x-rays ordered were chest x-ray which was ordered 33 times.

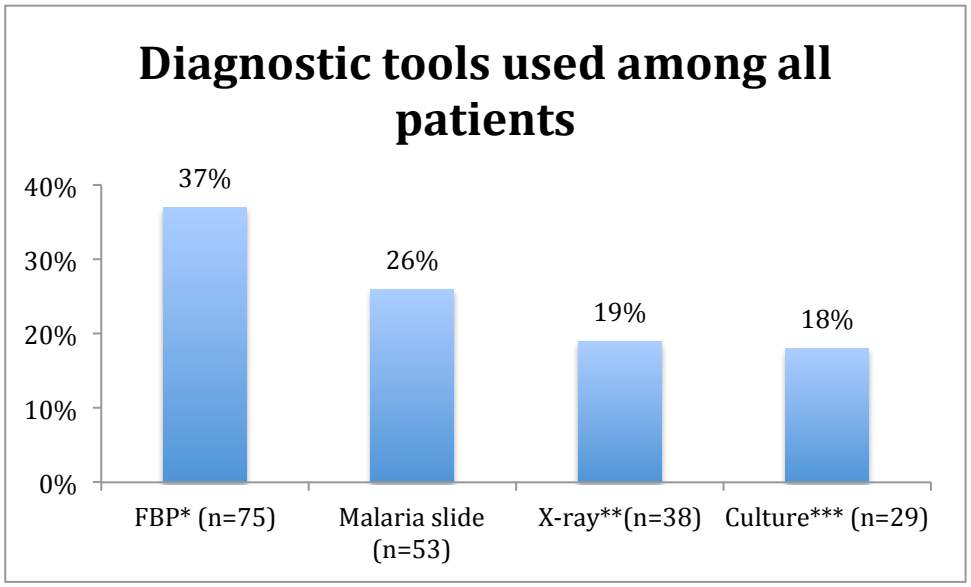


**Fig 7** *This chart shows the diagnostic tools used among all admitted patients.*
**FBP;full blood picture including Hb and WBC;**x-ray; including chest x-ray, abdominal ultrasound or extremities; ***culture;including blood-, urinary-culture or stools analysis. OBS this only include cultures* ***taken*** *during 9th Oct to 3rd Nov.*

A total of 45 patients had fever (35 patients during 9th Oct-3 Nov), defined as a temperature ≥

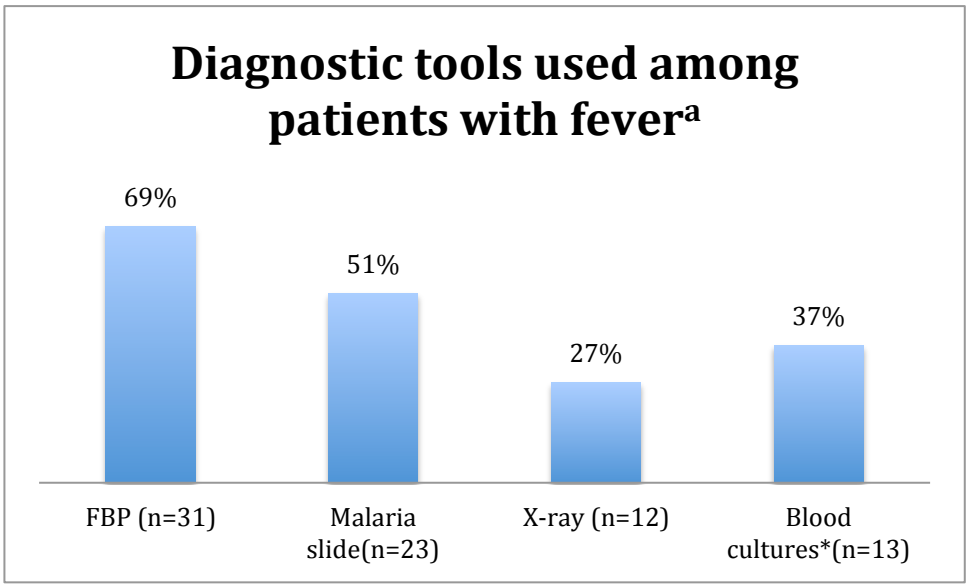


**Fig. 8** *Diagnostic tools used among patients with fever*
*[a];Fever defined as temperature ≥ 38 C, *Blood cultures; OBS this only include blood cultures taken during 9th Oct to 3rd Nov among patients with fever during this period (35 cases).*

38 degrees. Among patients inserted on antibiotics the mean temperature was 38.0 C on the general paediatric ward and 37.0 C among the neonates. Among patients with fever at the general paediatric ward, malaria slides were taken in 22 patients (71 %), and among neonates, in 1 patient (7.1 %). In figure 8 is an overview over diagnostic tools used in the both wards among children with a temperature ≥ 38 degrees. Among these, blood cultures were taken in 37 % of cases and full blood picture in 69 % of cases (fig 8).

## Antibiotics prior to admission

A total of 31 patients (15 %) had been treated with antibiotics within two months prior to admission. Of these, 20 (65 %) had received the antibiotics at the hospital before being referred to KCMC (Table 7). Observe that regarding patients who were not referred, no information was collected about if the treatment was with/or without prescription or given on a hospital. By looking only at the general paediatric ward, 26 patients (27 % of P1) were treated with antibiotics prior, and 5 patients (5 % of P3) at the neonatal ward. Of all the

**Table 7 Characteristics of patients treated with antibiotics prior to admission**

| | ***Nr of patients*** | ***Percent*** |
|---|---|---|
| **Referred** | 20 | 65 % |
| **Combination of >1 antibiotic** | 17 | 55 % |
| | | |
| *Choice of antibiotic* | ***Nr*** | ***Percentage of cases*** |
| **Ampicillin** | 17 | 55 % |
| **Gentamycin** | 15 | 48 % |
| **Cloxacillin** | 6 | 19 % |
| **Ceftriaxone** | 6 | 19 % |
| **Erythromycin** | 4 | 13 % |
| **Unspecified** | 2 | 7 % |
| **Ciprofloxacin** | 1 | 3 % |
| **Cefixime** | 1 | 3 % |
| **Chloramphenicol** | 1 | 3 % |
| **Co-Trimoxazole** | 1 | 3 % |

patients receiving antibiotic prior to admission, 55 % received Ampicillin and 48 % received Gentamycin (Observe that the total percentages are >100 % since many patients received more then one antibiotic) (Table 7).

The most common antibiotic used was Ampicillin and Gentamycin, both among referred and non-referred patients. From the diagram (fig 9) one understands that some of the patients who weren´t referred also received their treatment either as in-bed patients or in outpatient clinics (since for example Gentamycin is an intravenous drug). The most common indication was respiratory tract infections (26 %) followed by gastrointestinal illness (16 %) and urology and fever (13 % each) (Table 8).

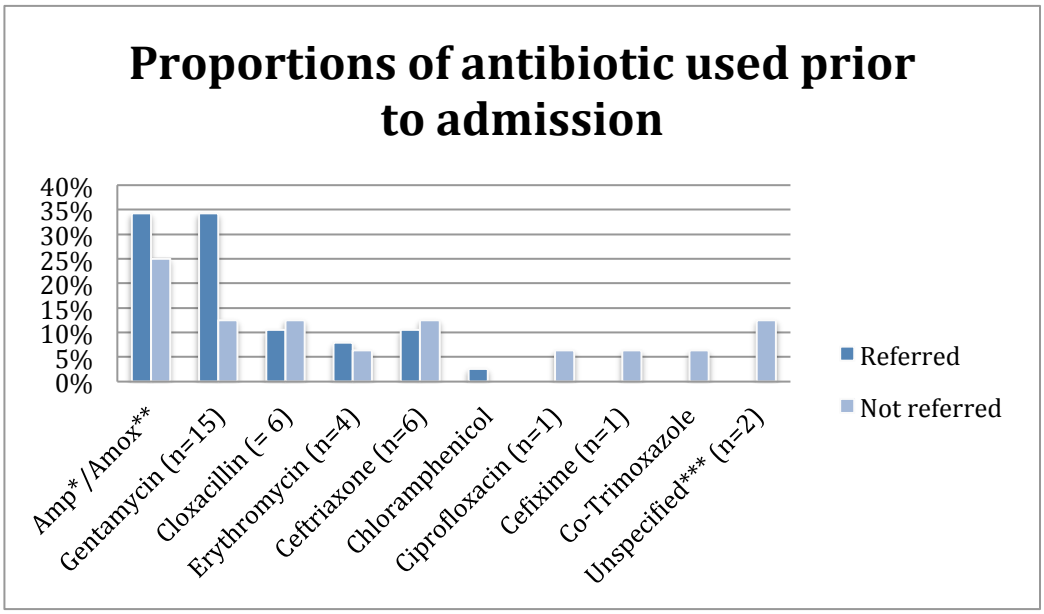


***Fig. 9*** *Proportions of antibiotics used prior to admission among referred and non-referred patients. Observe that this is percentage of all antibiotic therapies, for example 34 % of all antibiotic therapies among referred patients were Ampicillin.*
**Amp; Ampicillin. **Amox;Amoxicillin ***Unspecified meaning that the patient had been treated with antibiotics prior, but no information regarding which type of antibiotic*

**Table 8** Indications for antibiotic therapy prior to admission

| | *Nr of patients* | *Percentages* |
|---|---|---|
| **Respiratory** | 8 | 26 % |
| **Gastrointestinal** | 5 | 16 % |
| **Urology** | 4 | 13 % |
| **Fever** | 4 | 13 % |
| **Other**[a] | 3 | 10 % |
| **Septicaemia** | 3 | 10 % |
| **Unclear**[b] | 3 | 10 % |
| **CNS** | 1 | 3 % |

[a]bee bite, jaundice and birth asphyxia
[b]No information could be found regarding indication.

# Discussion

In this study 72 % (n=144) of the patients admitted to the general paediatrics and neonatal ward during the study period were inserted on antibiotics on the day of admission. The most common antibiotic therapies were Ampicillin and Gentamycin. Specimens were taken for culture 29 times, 34 % of these yielded bacterial isolates and the remaining were negative.

From the beginning this was supposed to be a point prevalence study examining the use of antibiotics since this is a well-established method and there are lots of studies to compare the results with. Though after having been in the local setting, the study design changed due to difficulties in performing an adequate point prevalence study. This makes it more difficult to compare the results to other studies; no other study has been done with the same design, only looking at how many of the patients that are inserted on antibiotics during the first day of admission. To clarify, both this study and the point prevalence studies (done in several countries) are cross-sectional studies, the differences being the inclusion criteria, point prevalence studies include *all* in-bed patients during *one* day. This study include the newly admitted patients consecutively.

Many point-prevalence surveys (PPS) on paediatrics have been done around the world; for example, in 21 countries in Europe, 32 % were treated with antibiotics on the day of the survey(20)(Swedish PPS 2010 31 % of children(19)), and in Malawi 41 % of children (1 month-18 years) and 39 % of the neonates were on antibiotics(21), in Turkey, 55 % of the children had on-going antibiotic treatment during the day of survey(26). Thus there is a big variation in different settings. The point-prevalence studies also include patients with nosocomial infections. At a first glimpse one might say that no patients had infections with a nosocomial onset in this study (defined as initiation of antibiotic therapy 48 h after admission), but since 25 % of the patients were referred from another hospital this is not

known for them. Since I cannot really compare with point prevalence studies, I can´t make a conclusion saying it is much that 72 % of the admissions were inserted on antibiotics. In this setting where infectious diseases are common; at a referral hospital where the most ill children are referred, where they don´t have an ICU or respirator, and many new-borns have a low birth weight, one might expect a high rate of antibiotics. In the end, what is interesting is if the treatment given is appropriate or not.

The most common antibiotics used were Ampicillin and Gentamycin in both wards; these were used in 44 % and 42 % of all antibiotic therapies respectively. The most common indications were sepsis among the neonates, and respiratory illness among the older children. Among patients with respiratory illness, 71 % received a combination of Gentamycin and Ampicillin, the recommended treatment for very severe pneumonia according to the local guidelines(22). Among patients with sepsis, 77 % received Ampicillin and Gentamycin, this is also one of the recommended treatments according to the local guidelines(22). Thus the choices of antibiotics for these conditions were adequate, as long as the diagnose was valid. This is of course a limitation of the study, a patient was categorized to having for example pneumonia if it said so in the file, no matter how the diagnose was set. Even though the treatment did follow local guidelines, resistance exist to both Ampicillin and Gentamycin, for example, of E-coli isolated from blood among febrile children in Tanzania, only 10 % and 45 % were sensitive to Ampicillin and Gentamycin respectively(14). Cultures are important to choose the appropriate treatment.

For patients admitted 9$^{th}$ October to 3$^{rd}$ November, cultures; including blood, urinary or CSF, were ordered 62 times but there were only results in 47 % of cases. So in the end, cultures were taken only 29 times, this being 25 % of patients inserted on antibiotics. So in more than

half of the cases either the culture wasn´t taken, it was lost on its way to the laboratory, or somehow lost on the laboratory. At KCMC the routine is that blood cultures should be taken on all patients with fever (according to the head of department), but this was only done in 37 % of febrile patients (>38 degrees). When being at KCMC and talking to the doctors, interns and medical students it often seemed to be a problem that test results were lost or that the laboratory couldn´t analyse a certain test some days. For example, specimens from lumbar punctures couldn´t always be analysed. Lack of resources to handle so many cultures might also be an explanation or that the parents of the children couldn´t afford these tests.
Blood slides for malaria parasites were ordered in 71 % of all patients with fever at the general paediatrics ward and full blood picture including Hb and WBC was ordered in 69 % of patients with fever at both wards. Both of these tests being an important part of the investigation in febrile patients.

Among the 29 cultures taken, 34 % (n=10) yielded growth, with *CNS (n=3)* being the most common isolate followed by *S. aureus (n=2)*. *CNS* could be a skin contamination. From the data collected it is not known if the cultures were taken before the antibiotics was given. A high percentage of positive isolates was found in this study. This can have many explanations, one of them being that the cultures that were actually taken might have been done on the most ill patients. For example, in another study from Tanzania, among children under five with fever, 6.6 % had bacteria in blood. In that study they took specimens for culture in each patient who had a temperature >37.5 degrees(27). Among children admitted to hospital for febrile illness in Mwanza, 9.4 % had bacteria in blood(14). Since so few cultures were taken in total in this study at KCMC it makes it difficult to make any conclusions. One of the isolates, *Pseudomonas*, was found resistant to Gentamycin, this resistance is of growing concern in many countries. Of *Pseudomonas* isolated at Bugando Medical centre in Tanzania

during 1998-99, 4 % were resistant to Gentamycin(28), and of Pseudomonas isolated from urine and wounds in Nigeria 1999-2001, 34 % and 26 % were resistant to Gentamycin respectively(29).

In Sweden the Swedish reference group for antibiotics (SRGA) publish information about which antibiotics that should be included when doing susceptibility testing of a certain bacteria. For example, *S. aureus* should be tested for Oxacillin, Aminoglycosides, Quinolones, Vancomycin, Clindamycin, Rifampicin and Linezolid(30). This may of course vary between different countries and in developing countries the availability of laboratory material may be limited. In this study, *S. aureus* was never even tested for Oxacillin, which is the first drug of choice for this bacteria, and Pseudomonas was tested for three antibiotics which it is intrinsic resistant against (Table 6). Unfortunately no assessment of the laboratory was available. By knowing more about the laboratory this could help to explain the routines regarding their susceptibility testing.

An important question is of course if the physician in charge actually did pay attention to culture results or results from blood chemistry. During the first two weeks when attending the ward rounds I did get the impression that they do. Two times I observed when they actually did change therapy after results from cultures.

In order to really study how appropriate the usage of antibiotics is it is probably easier to focus on separate diseases, only looking on pneumonia for example. Obviously empiric treatment is common in this setting. It would be interesting to know more about the local bacterial flora, which bacteria are the most common in blood or urine at *this* hospital among the children? Depending on the results, the empiric therapy could be more adapted to the local setting.

## Strengths and weaknesses

As mentioned earlier, a limitation of this study is that it is based on medical files. Especially when it comes to diagnostic measurements used and indications for treatments. Regarding the diagnostic tools used, the question is how much of the ordered investigations that were actually carried out. The cultures ordered were followed up for the results and this did indeed show that more than half of the results were missing. So one might expect that not all the other diagnostics ordered were actually done. Regarding the indications for treatment, the question is if the patients really did fulfil the criteria for the diagnose that he/she was said to have in the file. It would have been interesting to follow the patients and to see what the discharging diagnose was, did it change? For example, one patient initially treated for meningitis was discharged three days later with the diagnose "vaso-vagal collapse".

Not knowing the routines or the local setting is also a limitation even though I did spend almost two weeks just trying to learn about the system at the wards. Since this is a setting with limited resources, I don´t know how many of the decisions that were done because of economic constraints. Maybe the cost of taking more cultures leads to less available medications (because it´s to expensive). As mentioned earlier, it would have been interesting to know more about the routines at the laboratory. I do think it would have been easier to focus either on the neonatal ward only or to the general paediatrics ward only. That way the study protocol could have been more directed for example to the neonates and it would have been easier to just focus on one ward. On the other hand the strength of the study is that 201 patients were included and that wouldn´t have been possible only including one ward.

# Conclusions

There is a high usage of antibiotics at the paediatric wards at KCMC but this is also a referral hospital with many ill patients in a setting with a high burden of infectious diseases. The choice of therapy for the most common indications; respiratory illness and septicaemia mostly follow the local guidelines. Cultures are often ordered, but in more than half of them results are missing. There is a need to go over the routines to find out the reason for this and to increase the rates of cultures, especially among febrile patients. This in order to guide the further management of patients and, when possible, change to more narrow-spectrum antibiotics.

# Populärvetenskaplig sammanfattning

Antibiotikaresistens är ett växande problem globalt. Antibiotika är en grupp vanliga läkemedel som används vid bakteriella infektioner. Det finns flera olika typer av antibiotika som har effekt på olika bakterier, man brukar tala om ett läkemedels antibakteriella spektrum. Om bakterien erhåller egenskaper som gör att den förlorar sin känslighet utvecklas antibiotikaresistens. Flera faktorer bidrar till detta, däribland felaktig användning av antibiotika när indikation saknas; till exempel vid infektioner orsakade av virus, felaktigt val av antibiotika och fel behandlingstid(7). Därför är det viktigt att antibiotikaanvändningen inom sjukvården övervakas, detta görs regelbundet i Sverige(19) och i vissa andra länder, men är mindre förekommande i utvecklingsländer såsom delar av Afrika. I Tanzania är det många som köper antibiotika utan recept och det bidrar än mer till felanvändning.

I denna studie, utförd på ett sjukhus i norra Tanzania, har antibiotikaanvändningen samt diagnostiken bland barn studerats. Hos patienter med tecken på infektion, såsom feber, är det viktigt med diagnostik för att ta reda på om det rör sig om en bakteriell infektion och i så fall vilken bakterie som orsakar sjukdomen. Detta för att kunna välja antibiotika med rätt antibakteriella spektrum och öka chanserna för ett snabbt tillfrisknande. I denna studie blev majoriteten av barnen som inlades insatta på antibiotika på inskrivningsdagen. De vanligaste sjukdomarna som behandlades med antibiotika var infektioner i luftvägarna och blodförgiftning, och vid båda dessa tillstånd gavs mestadels adekvat antibiotika enligt lokala riktlinjer. Diagnostik såsom bakterieodlingar ordinerades ofta, men i mer än hälften av fallen fanns inget resultat. Om detta berodde på att provet faktiskt inte togs eller på annat sätt försvann på laboratoriet är okänt. I en stor andel av de tagna proverna hittades bakterier och viss resistens påträffades också.

Denna studie genomfördes i Moshi på sjukhuset ”Kilimanjaro Christian Medical Centre”. Journaler från inskrivningsdagen utgjorde grund för datainsamlingen. Alla patienter som lades in på två av barnavdelningarna under oktober-november 2013 togs med i studien.

Sammanfattningsvis var valen av antibiotika adekvata vid de vanligaste infektionssjukdomarna men det finns ett avsevärt behov av att förbättra diagnostiken på sjukhuset. Särskilt att se över rutinen vad gäller ordinerade prover, men också utföra mer provtagning, särskilt bland patienter som uppvisar allvarliga tecken på infektion såsom hög feber.

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# Appendix 1 – Study Protocol

Patient nr: Ward: Date:

***Basic data (1)***

Age _____
Sex Female _____ Male _____
Date of admission _____
Weight _____
Referred _____
Birth order _____ Unk ___
Is the mother alive No ___ Yes ___ Unk ___
Is the father alive No ___ Yes ___ Unk ___

***Medical History (2)***

Previously healthy No ___ Yes ___
HIV-positive No ___ Yes ___ Unk ___
Treatment for HIV No ___ Yes ___ Unk ___
AIDS No ___ Yes ___ Unk ___
Immunosuppresive treatment No ___ Yes ___ Unk ___
Heart disease No ___ Yes ___ Unk ___
Respiratory disease No ___ Yes ___ Unk ___
Liver disease No ___ Yes ___ Unk ___
Diabetes Mellitus No ___ Yes ___ Unk ___
Malaria treatment No ___ Yes ___ Unk ___
Anemia No ___ Yes ___ Unk ___
Renal impairment No ___ Yes ___ Unk ___
Drug allergies No ___ Yes ___, to _____
Unk ___

***Catheter or surgical procedure?*** *(3)*

Surgical procedure No ___ Yes ___ Unk ___
Urinary catheters No ___ Yes ___ Unk ___

***Antibiotics prior to admission (4)***

Antibiotic prior to admission No ___ Yes ___ Unk ___
Type _____ Unk ___
Indication _____ Unk ___

***Diagnostic workup (5)***

Blood cultures No ___ Yes ___ Unk ___

Results _____ Unk ___
Resistance patterns
_____ Unk ___

Other cultures Urinary ___ Wound ___ Sputum___ Drainage ___ Throat ___ Nasopharynx ___
No ___ Unk ___
Results _____ Unk ___
Resistance patterns

_____ Unk ____
Blood chemistry _____ Unk ____
Malaria workup No ____ Yes ____ Unk ____
X-ray No ____ Yes ____

***Current antibiotic treatment (6)***
Current antibiotics No ____ Yes ____ Unk ____
Date of insertion _____ Unk ____
Indication _____ Unk ____
Type prescribed
_____ Unk ____

Dose _____

Administration _____ Unk ____
Nosocomial onset _____ Unk ____

***Vital parameters (7)***
Blood pressure _____ Unk ____
Respiratory rate _____ Unk ____
Saturation 02 _____ Unk __
Temperature _____
Heart rate _____

# Appendix II - Explanation of study protocol

All the patients at the ward will be registrated in the study, no matter if they are being treated with antibiotics or not. The following information will be collected from the patient files.

**Basic data (1)**
**- Patient number:** The hospital registration number
**- Age**
**- Sex**
**- Date of admission**
- **Weight**
**- Birth order:** Number 1 being the oldest
**- Is the mother of the patient alive?**
**- Is the father of the patient alive?**

**Medical history (2)**
In general a patient was classified as having any of the following certain disease/treatment/condition if it said so in the file.
**- Previously healthy**
**- HIV-positive**: See below for information if the patient has treatment or not.
**- Treatment for HIV**
**- AIDS**
- **Immunosuppresive treatment:** Defined as Cortison or other apparent immunosuppressive treatment for cancer.
- **Heart disease**
**- Respiratory disease**
**- Liver disease**
**- Diabetes Mellitus**
- **Malaria treatment:** Within 2 months prior to admission
**- Anemia**
**- Renal impairment**
**- Drug allergies:** Regarding antibiotics.

**Catheter or surgical procedure? (3)**
- **Current surgical procedure**: Requiring incision, conducted during the first day of admission.
- **Urinary catheters**: All types, including urethral catheters, suprapubic catheters, nefro pyelostomy etc.

**Antibiotic treatment prior to hospital admission (4)** Within 2 months prior to admission.
**- Yes/No**
**- Type**
**- Indication**

**Diagnostic workup (5)**
**- Blood cultures**
**- Results:** positive/negative and eventual type of bacteria, see below.
- **Resistance patterns**
**- Other cultures:** Urinary, sputum, wound, drainage, throat, nasopharynx,
- **Results:**
**- Resistance patterns**
**- Blood chemistry:** Full blood picture which includes white blood cell count (WBC) and Hemoglobine (Hb). HIV-test.
**- Malaria workup**
**- x-ray**

**Current antibiotic treatment (6)**
**- Yes/no**
**- Date of insertion**
**- Indication:**
**- Type prescribed**
**- Administration:** Intravenous or oral administration
**Vital parameters (7)**
**Blood pressure**
**Respiratory rate**
**Saturation O2**
**Temperature**
**Heart rate**