MAKERERE UNIVERSITY

COLLEGE OF HEALTH SCIENCES

SCHOOL OF MEDICINE

CLINICAL EPIDEMIOLOGY UNIT

ANTIBIOTIC PRESCRIPTION PRACTICES AND ASSOCIATED FACTORS AMONG HEALTH WORKERS IN MANAGING PNEUMONIA AMONG CHILDREN (<5 YEARS) AT MENGO AND LUBAGA HOSPITALS

KAMOGA GONZAGA CENA (BPHS, MUST)

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SUPERVISORS

DR. MOSES OCAN PhD, Msc. Pharmacology, BSc (Biochemistry)

DR. FREDDY KITUTU PhD, Msc. Clin.Pharm, Msc. CEB, B.Pharm

A RESEARCH DISSERTATION SUBMITTED TO THE DIRECTORATE OF RESEARCH AND GRADUATE TRAINING IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE AWARD OF THE DEGREE OF MASTER OF SCIENCE IN CLINICAL EPIDEMIOLOGY AND BIOSTATISTICS OF MAKERERE UNIVERSITY

NOVEMBER 2024

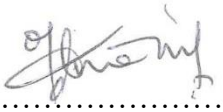
DECLARATION

I **Kamoga Gonzaga Cena** declare that this is my original work and has not been published before in any institution for academic purposes.

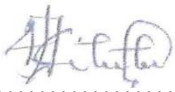
Signature  .....Date.....08 Nov 2024.....

This work was done under the supervision and approval of my supervisors:

Dr. Moses Ocan, PhD, Msc. Pharmacology, BSc (Biochemistry)

Signature  …….Date……01 Nov 2024…….

Dr. Freddy Kitutu, PhD, Msc. Clin.Pharm, Msc. CEB, B.Pharm

Signature  ……..Date……01 Nov 2024…….

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ABBREVIATIONS

ARTIs:	Acute Respiratory Tract infections
CAP:	Community Acquired Pneumonia
CDC:	Centers for Disease Control and Prevention
Hib:	Haemophilus influenzae type b
IV:	Intravenous
LMICs:	Low- and Middle-income countries
PCV:	Pneumococcal Conjugate Vaccine
SOMREC:	Makerere University School of Medicine Research and Ethics Committee
UCG:	Uganda Clinical Guidelines 2022
UNICEF:	United Nations International Children's Emergency Fund
WHO:	World Health Organization

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OPERATIONAL DEFINITIONS

Antibiotic prescription practices: These were classified as either appropriate or inappropriate prescription practices.

Inappropriate antibiotic prescription: Antibacterial drugs that were prescribed without adhering to the Uganda Clinical Guidelines (UCG) 2022's recommendations for treating pneumonia (Ministry of Health Uganda, 2022), and the pneumonia treatment protocols by Mengo and Lubaga hospitals i.e.

i. A child aged less than 5 years admitted with pneumonia who was not receiving IV antibiotic treatment in accordance with the UCG, Lubaga treatment protocol for pneumonia and Mengo treatment protocol for pneumonia.

i. A child aged less than 5 years who was receiving more or less than 50 mg/kg of ampicillin, more or less than 80mg/kg of ceftriaxone, more or less than 15mg/kg of Amikacin, and more or less than 7.5 mg/kg of gentamicin in one delivered dose.

ii. A child under the age of five who was receiving IV treatment of ampicillin plus gentamicin, ceftriaxone plus gentamicin and ceftriaxone plus amikacin for less than five days and more than 7 days without having had meningitis or septicemia as co morbidities, which required 10 and 21 days of treatment respectively

Pneumonia: Children that had at least two of the following signs were considered as having pneumonia (Bradley et al., 2011).

- Difficulty in breathing and respiratory distress.
- Cough
- Abnormal temperature $\geq 38^{o}C$
- Abnormal white blood cell count.
- Chest radiograph indicating pneumonia
- Health clinician diagnosis of pneumonia within the first 48 hours of hospitalization.

ABSTRACT

Introduction: Pneumonia is a major cause of morbidity and mortality in children under five years in low-and middle-income countries like Uganda. Inappropriate antibiotic prescription contributes to antimicrobial resistance and poor treatment outcomes.

Objectives: To evaluate the antibiotic prescription practices and associated factors among children under five years admitted with pneumonia in the pediatric wards of Mengo and Lubaga hospitals in Kampala, Uganda.

Methods: This was a cross-sectional study that collected data retrospectively from inpatient registers of children under five years with pneumonia admitted at Mengo and Lubaga hospitals. All in-patient records at the pediatric wards in the year 2022 that met the eligibility criteria were reviewed. Data was collected using a data abstraction tool. A data entry screen was developed in Epi-data using checks, data entered in duplicate. The data was then transferred to STATA version 14 and cleaned prior to the analysis. Data analysis involved univariate, bivariate, and multivariate analyses using modified Poisson regression methods at 95% confidence level.

Results: From the 678 files assessed for inappropriate antibiotic prescription, 375 (55.3%) were male, with a median age of 15 months and a median weight of 9.8 kg. Most files (99.7%) had a confirmed pneumonia diagnosis. The majority (82.0%) had two antibiotics prescribed, predominantly ceftriaxone and gentamicin (28.6%). Inappropriate antibiotic prescription prevalence was 39.7%, with 95.3% based on UCG, 48.7% on Lubaga's protocol, and 40.5% on Mengo's protocol. Bivariate analysis indicated age, weight, and hospital stay duration as significant factors. Multivariate analysis revealed that weight (aPR: 0.979, p=0.027) and hospital stay duration (aPR: 0.959, p=0.049) were significantly associated with inappropriate antibiotic prescriptions.

Conclusion: This study highlights a significant reliance on dual antibiotic therapy for children under five with pneumonia in Mengo and Lubaga hospitals, with ceftriaxone and gentamicin being the most prescribed combination. High inappropriate antibiotic prescription rates based on UCG

guidelines suggest deviations from recommended practices. Notably, child weight and hospital stay duration were linked to inappropriate prescription, emphasizing the need for enforcement of guideline adherence by health workers and continuous healthcare provider training to optimize antibiotic use and combat antimicrobial resistance.

CHAPTER ONE: INTRODUCTION

1.1 Introduction

Pneumonia is the leading cause of morbidity and mortality in children under five, with 1,400 cases per 100,000 children and 700,000 deaths annually (UNICEF, 2022). In East Africa, pneumonia was reported to have a prevalence of 34% (Beletew et al., 2020) and in Uganda, the pneumonia prevalence was reported to be 5.3%(Ministry of Health, Uganda)

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The Pneumonia-causing agents vary depending on the age, infection source and other child defects for example immunodeficiency (Wojsyk-Banaszak & Bręborowicz, 2013). Viruses are the most common cause of community-acquired pneumonia in children under five, which declines with age (Messinger et al., 2017). Children may also develop pneumonia when infected with bacteria including *Streptococcus pneumoniae*, *Haemophilus influenzae* type b (Hib), and *Staphylococcus aureus* (Das et al., 2016; Messinger et al., 2017). Identifying the cause of pneumonia can increase the likelihood of successful treatment (Grief & Loza, 2018).

The mainstay of treatment for pneumonia is antibiotics (World Health Organization, 2020), with over 80% of children with pneumonia receiving antibiotic prescriptions (Akkerman et al., 2008; Petersen &Hayward, 2007). Antibiotic misuse can have detrimental effects on both the general populace and specific patients. Overuse can lead to the emergence of resistant pathogens, while underusecan lead to treatment failure, illness escalation, and even death (CDC, 2024).

Antibiotic resistance is a global concern that can lead to serious illnesses (World Health Organization, 2020).. It can also lead to less-than-ideal treatment outcomes, longer hospital admissions, disease relapses,patient toxicity, greater treatment costs, and higher morbidity and death rates (Ayukekbong etal., 2017; Mashalla et al., 2017).

Countries have in turn adopted strategies to combat antibiotic resistance, such as Antibiotic Stewardship Programs, which aim to optimize the choice, dosage, and duration of antibiotic medication (Majumderet al., 2020). Countries can further use clinical recommendations and policies to harmonize treatment procedures and encourage appropriate antibiotic use, and implement strict antibiotic prescribing policies such as prior authorization requirements and restricted indications, to limit antibiotic usage to specific interventions (World Health Organization, 2012). Clinical symptoms are used to guide paediatric antibiotic therapy in sub-Saharan Africa due to a lack of microbiologic diagnostic facilities (Williams et al., 2018).

Research reports indicate frequent inappropriate antibiotic use, including polypharmacy, prescriptions for non-recommended illnesses, as well as prescriptions for unclear diagnoses, and incorrect durations (Atif et al., 2018; Bilal, Osman and Mulugeta, 2016; Machowska and Stålsby Lundborg, 2018; Mbonye et al., 2016).

Inappropriate antibiotic use was reported in Indonesia, Turkey and Mongolia between 28%-57% (Ceyhan et al., 2010; Dorj et al., 2013; Yusuf, Murni and Setyati, 2017). A Norwegian study found thatonly half of children receiving antibiotics for community acquired pneumonia, CAP, had a bacterial infection, suggesting that many cases of pneumonia are viral or caused by other non-bacterial factors (Selvåg and Christian Magnus Thaulow, 2021). It is therefore important to develop better diagnostic tools to accurately distinguish between bacterial and non-bacterial causes of pneumonia to avoid unnecessary antibiotic use. Causes of inappropriate antibiotic prescriptions were identified and categorized at individual, healthcare facility, and community levels (Desalegn, 2013; Shet, Sundaresan and Forsberg, 2015). These factors included; pressure from patients and caregivers, the number of patients at healthcare facilities, concerns connected to health professionals, prolonged medicine stockouts, and availability of guidelines and reference material (Adisa, Orherhe and Fakeye, 2018; Amaha, Berhe and Kaushik, 2018; Andrajati, Tilaqza and Supardi, 2017).

Inappropriate antibiotic prescription is a common issue in children and may be reflected in regionalpolicies. Research has focused on public hospitals, with limited information on private, not-for- profit hospitals in Uganda. This study aimed to assess the antibiotic prescription practices and associated factors among children under the age of five admitted to Lubaga and Mengo Hospitals with pneumonia in 2022.

1.2 Problem Statement

Despite established national guidelines for treating pneumonia in young children, non-adherence to these protocols remains a challenge in Uganda. Studies have repeatedly documented inappropriate antibiotic use across public healthcare facilities, indicating widespread deviation from recommended practices (Abeja et al., 2022; Kiguba, Karamagi, and Bird, 2017; Ocan et al., 2017). This issue is not limited to Uganda alone; a similar trend was reported in Tanzania, where 70.1% of cases deviated from treatment guidelines (Wiedenmayer et al., 2021).

Inconsistent adherence to guidelines can lead to inappropriate antibiotic use, which undermines effective pneumonia treatment and contributes to the growing problem of antibiotic resistance. However, current research on this issue has primarily focused on public hospitals, with limited insight into prescription practices within private, not-for-profit hospitals. As a result, little is known about how these facilities manage pneumonia treatment for children under five, despite the critical role they play in Uganda's healthcare system.

This study seeks to fill this knowledge gap by examining antibiotic prescription practices in private, not-for-profit hospitals treating pediatric pneumonia. By investigating adherence to national guidelines within this context, the study aims to identify trends and areas for improvement, contributing to more effective antibiotic stewardship and resistance prevention efforts.

1.3 Research Questions

1. What antibiotic agents are prescribed for treatment of pneumonia in children under five years in Mengo and Lubaga hospitals, Uganda?
2. What is the prevalence of inappropriate antibiotic prescription among children under five years with pneumonia at Mengo and Lubaga hospitals?
3. What factors are associated with inappropriate antibiotic prescription among children under five years with pneumonia at Mengo and Lubaga hospitals?

1.4 Study Objectives

1.4.0 General Objective

To assess patterns of antibiotic prescription, prevalence of inappropriate antibiotic use, and associated factors, in the treatment of children under five years admitted with pneumonia at Mengo and Lubaga Hospitals.

1.4.3 Specific Objectives

1. To determine the antibiotic agents prescribed for treatment of pneumonia in children under five years admitted in Mengo and Lubaga hospitals.
2. To determine the prevalence of inappropriate antibiotic prescription among children under 5 years admitted with pneumonia at Mengo and Lubaga hospitals.
3. To determine the factors associated with inappropriate antibiotic prescription among children under 5 years admitted with pneumonia at Mengo and Lubaga hospitals.

1.5 Justification

Pneumonia remains a significant health threat for children under five in Uganda, ranking as the second leading cause of death in this age group (Ministry of Health Uganda, 2015). This infection is caused by various microorganisms, with *Haemophilus influenzae* and *Streptococcus pneumoniae* being the most common bacterial culprits in Uganda (Nantanda et al., 2008). Studies have shown high prevalence rates of pneumonia among children in Ugandan hospitals, including viral and bacterial pneumonia (Nantanda et al., 2013; Kiconco et al., 2021) Accurate and judicious use of antibiotics is critical in treating pneumonia to prevent the rise of antibiotic resistance (Yantzi, van de Walle, and Lin, 2018). However, limited diagnostic capabilities often result in unnecessary antibiotic prescriptions, which can exacerbate resistance issues and limit effective treatment options (Ciccone et al., 2022). Prescription practices are influenced by various factors, including drug availability, cost, and the socio-economic background of patients, which may compromise the appropriateness of these

prescriptions (Erah, Olumide, and Okhamafe, 2003). Furthermore, a lack of stringent regulatory oversight has led to inconsistent adherence to treatment protocols, with some prescribers opting for more expensive antibiotics even when they are not needed (Godman et al., 2017; WHO, 2018).

Although inappropriate antibiotic use has been reported in public hospitals in Uganda (Kibuule, Kagoya, and Godman, 2016; Nantongo et al., 2022; Obakiro et al., 2021), little research has focused on private, not-for-profit hospitals. This study therefore provides valuable insights into antibiotic prescribing patterns within this healthcare setting, focusing on children under five with pneumonia, to highlight areas where improvements can enhance patient outcomes and combat antimicrobial resistance.

1.6 CONCEPTUAL FRAMEWORK

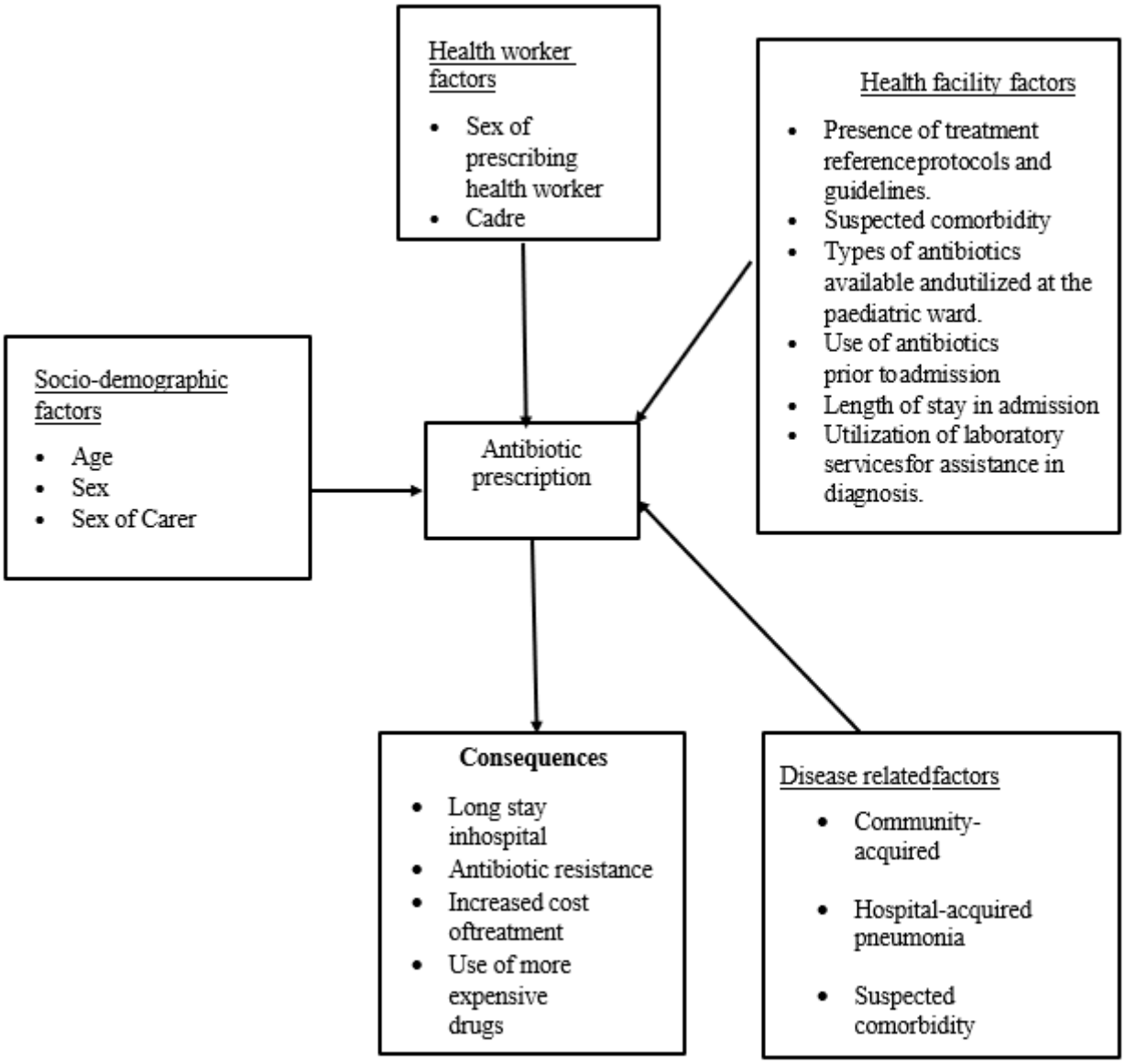

Figure 1: Conceptual Framework showing the factors associated with antibiotic prescription

Narrative of the conceptual framework

Socio-demographic factors, disease-related factors, health worker-related factors, and health facility-related factors were considered to have an impact on the practices of prescribing antibiotics.

Age, gender, and sex of the patient's caregiver were among the socio-demographic factors considered for each patient.

The factors related to the health facility included: The availability of treatment reference protocols and guidelines, the kinds of antibiotics available and used in the pediatric ward, the length of stay during admission, the use of laboratory services for assistance in diagnosis, and the use of antibiotics by the patient prior to admission.

The factors that pertained to health workers included the cadre and sex of the prescribing health worker. The disease-related factors included suspected comorbidity, nature of pneumonia, that is whether it was obtained in a hospital or in the community.

The conceptual framework highlighted the consequences of inappropriately prescribing antibiotics to children under the age of five, including extended hospital stays, higher treatment expenses, the usage of more expensive medications, and the emergence of antibiotic resistance.

1.7 Scope of the study

The study collected data in antibacterial agents prescribed for the management of pneumonia at Mengo and Lubaga hospitals between January and December 2022. This was done between August and September 2023. Additionally, it shed a light on the sociodemographic factors, health worker related factors and health facility related factors influencing how antibiotics were prescribed for children under five who were admittedto Mengo and Lubaga hospitals with pneumonia.

CHAPTER TWO: LITERATURE REVIEW

2.1 Burden of Pneumonia in children under five years

According to the World Health Organization, pneumonia is a major cause of morbidity and mortality in children under five years old, accounting for almost 16% of all fatalities in this age group with Low- and middle-income nations most affected (World Health Organization, 2021). In Uganda, the prevalence of pneumonia among children lies between 15.6% and 25.6% (Kiconco et al., 2021; Nantanda et al., 2021).

2.2 Etiology of Pneumonia in Children

Children under the age of five are susceptible to the frequent and possibly fatal pneumonia. It results from a lung tissue infection. The symptoms of pneumonia, which can range in severity from moderate to severe, include coughing, fever, breathing difficulties, and chest pain. Children who have underlying medical disorders like HIV/AIDS or asthma are more likely to acquire pneumonia (World Health Organization, 2021).

Inflammation and fluid build-up in the lungs are its hallmark symptoms, and it is brought on by a variety of pathogens, including bacteria, viruses, fungi, and parasites. Chest pain, fever, difficulty breathing, and coughing are just a few of the symptoms that children with pneumonia may face. Pneumonia can range in severity from mild to severe, and consequences like respiratory failure, infection, and death can result from it (American Lung Association, 2022).

2.3 Management and Treatment of Pneumonia in children under five years

The diagnosis and therapy of pneumonia depend greatly on hospital management. In this population, treating pneumonia requires a combination of tactics, including the use of suitable diagnostic techniques, antibiotic therapy, and supportive care (World Health Organization, 2014). The quick identification and diagnosis of the disease is one of the most important aspects of hospital management for paediatric pneumonia. A comprehensive clinical examination is partof this, and diagnostic tools like a chest x-ray and pulse oximetry are used to solidify the

diagnosis. Appropriate antibiotic therapy should be started as soon as feasible after a pneumonia diagnosis has been made (Atkinson et al., 2007). When treating bacterial pneumonia, antibiotics are frequently employed, but antiviral drugs might be used to treat viral pneumonia. If the child is having serious breathing problems, oxygen therapy may additionally be required (American Lung Association, 2020).

The World Health Organization (WHO) advises using oral amoxicillin as the first-line treatment for children with pneumonia when it comes to antibiotics. Antibiotics administered intravenously may be utilized when oral treatment is not an option(World Health Organization, 2014). The first-line antibiotic regimen for treating children under five admitted with pneumonia as recommended by the Uganda clinical guidelines is ampicillin 50 mg/kg body weight 6-hourly intravenous (IV) or 50,000 IU/kg of benzyl penicillin plus Gentamicin 7.5 mg/kg body weight administered once daily intravenously (IV)or intramuscularly (IM). This treatment is administered for five to ten days. Ceftriaxone 80 mg/kg IM or IV once daily for 5-10 days is also recommended as second line treatment, followed by oral Amoxicillin 40 mg/kg body weight 12 hours each day for 5 days once the condition improves (Ministry of Health Uganda, 2022). At Mengo hospital, the treatment protocol for pneumonia recommends ceftriaxone 80mg/kg plus gentamicin 7.5mg/kg as treatment for pneumonia. In Lubaga, the recommended regimen consists of ceftriaxone 80mg/kg plus amikacin 15mg/kg as treatment for pneumonia. These regimens are recommended for a period of between 5-7 days.

Supportive care is a crucial component of hospital management for paediatric pneumonia in addition to antibiotic therapy. For children who have hypoxemia, this entails giving them oxygen therapy, keeping them hydrated, and giving them nutritious food. Mechanical ventilation may be required in severe cases (Mantero et al., 2017).

2.4 Challenges in management of Pneumonia

There are numerous challenges in treating pneumonia. These challenges include those with

diagnosis, a lack of access to proper treatment and care, and a lack of funding in low- and middle-income nations (Graham, 2008).

The difficulty in getting an accurate diagnosis is one of the major issues with treating pneumonia in children (Chang et al., 2013; Nantanda et al., 2013). Pneumonia can present with a wide range of symptoms that might be vague and overlap with those of other respiratory disorders, making it challenging to differentiate between it and other illnesses (Nantanda et al., 2013). Also, in environments with low resources, it may be difficult to get diagnostic equipment like pulse oximetry and chest x-rays, which complicates the diagnosis even more (Kazi et al., 2022).

Lack of access to proper therapy and care is another problem in the treatment of paediatric pneumonia (Marangu and Zar, 2021). Antibiotics and other necessary medications may not always be available in settings with limited resources, and there may not always be competent healthcare professionals available to provide them (Kazi et al., 2022).

In low- and middle-income countries, a lack of resources makes it difficult to treat paediatric pneumonia. These nations frequently struggle to properly prevent and treat pneumonia because to a lack of healthcare staff, poor infrastructure, and restricted access to crucial diagnostic equipment and medications (Rahman et al., 2020; Yip and Hafez, 2015).

2.5 Rational medicine use in low- and middle-income countries

Rational medicine use, also known as appropriate or responsible medicine use, refers to the use of medications in a manner that maximizes the benefits and minimizes the risks for the individual patient (World Health Organization, 2002).

Studies have shown that inappropriate medicine use is a common problem in LMICs. One review of studies from LMICs found that over 50% of medications were prescribed, dispensed, or soldinappropriately (Mboya, Sanga and Ngocho, 2018; Nantongo et al., 2022; Ocan et al., 2017). This can include prescribing medications for conditions for which they are not indicated,

prescribing medications at incorrect doses or for too long a duration, and not providing appropriate information to patients about how to take the medication.

Inappropriate medicine use can have serious consequences for patients in LMICs, including increased risk of adverse reactions, treatment failure, and antibiotic resistance. It can also lead to financial burden for patients and their families, and can contribute to the overall burden of disease in the community (Melku, Wubetu and Dessie, 2021).

There are a number of strategies that have been proposed to improve rational medicine use in LMICs. One key strategy is to improve the education and training of healthcare providers in appropriate prescribing practices. This can include providing training on the appropriate use of specific medications, as well as training on how to conduct a thorough patient assessment and how to communicate effectively with patients (Asia, 2006).

Another strategy is to improve the availability of accurate and up-to-date information on medications. This can include providing healthcare providers with access to essential medicines lists and guidelines, as well as providing patients with information on how to correctly use their medications (Perumal-Pillay and Suleman, 2017).

2.6 Indicators of Inappropriate medicine use

Inappropriate medicine use can occur at various stages of the medication use process, including prescribing, dispensing, and consumption.

There are a number of indicators that have been identified as markers of irrational medicine use. These include: high rates of prescribing antibiotics for viral infections: Antibiotics are only effective againstbacterial infections and not viral infections, prescribing antibiotics for viral infections is considered an indicator of irrational medicine use (World Health Organization, 2002). High rates of prescribing contraindicated medications: This refers to prescribing medications that are not recommended or not safe for a specific patient due to their medical history or otherfactors. High rates of prescribing medication at incorrect doses or for too long

a duration. High rates of prescribing, dispensing, or consuming medication that is not listed in the essentialmedicines list: This can lead to unnecessary use of medication and increased healthcare costs (World Health Organization, 2002).

2.7 Prevalence of Inappropriate antibiotic prescription practices

Exposure of disease-causing microorganisms to sub-therapeutic concentrations of anti-infective agents such as antibiotics leads to the emergence and spread of antimicrobial resistance (Sasi et al., 2020). This usually follows inappropriate use of antimicrobials. Antibiotic resistance is a major global health challenge that is fueled, in part, by the inappropriate or irrational use of antibiotics. Inappropriate prescription practices refer to the use of antibiotics when they are not indicated, the use of inappropriate doses or duration of treatment, and the use of suboptimal or outdated regimens (World Health Organization, 2002).

There are several studies that have been conducted to assess the prevalence of inappropriate prescription practices of antibiotics (Dache, Dona and Ejeso, 2021; EmyInumaru et al., 2019; Selvåg and Thaulow, 2021; Yusuf, Murni and Setyati, 2017). In Tanzania , study reported a 76.3% irrational antibiotics use (Mboya, Sanga and Ngocho, 2018). Another study in Iran reported a 69.8% prevalence of irrational prescription (Hashemi, Nasrollah and Rajabi, 2013). Furthermore, studies in Brazil, Norway and Indonesia reported prevalence of irrational prescription at 24.4%, 50% and 28.3% respectively (EmyInumaru et al., 2019; Selvåg & Thaulow, 2021; Yusuf, Murni and Setyati, 2017).

In Uganda there have been several studies on the prevalence of inappropriate antibiotic use (Abejaet al., 2022; Kibuule, Kagoya and Godman, 2016; Kiguba, Karamagi and Bird, 2016; Nantongo et al., 2022; Obakiro et al., 2022; Ocan et al., 2017; Okello et al., 2020). These studies have reported prevalence of inappropriate and inappropriate use of antibiotics within the range of 40% -83% .

Several factors have been identified as contributing to the high prevalence of inappropriate

antibiotic prescribing and these include : lack of knowledge and understanding among health care providers about appropriate antibiotics use : inadequate training in antimicrobial stewardship and the influence of pharmaceutical marketing and sales strategies (Machowska and Stålsby Lundborg, 2018). Patients also play a role in the inappropriate use of antibiotics as they may demand antibiotics from their healthcare providers or self -medicate with leftovers or expired antibiotics (Dache, Dona and Ejeso, 2021).

2.8 Factors associated with inappropriate antibiotic use

2.8.1 Socio-Demographic factors

Literature suggests that certain demographic factors, such as age, gender, and parental education, may be associated with inappropriate antibiotic prescription practices in children under five years of age. One study illustrated that there is a significant difference in proportions of inappropriate drug use when prescribing for children below 1 year compared to thoseat least 1 year old (Beletew et al., 2020). Further research is needed to fully understand these relationships and to identify potential interventions to address inappropriate prescribing practices in this vulnerable population.

Another study reported that prescribers were less likely to adhere to treatment guidelines when prescribing for males than when prescribing for female patients (Obakiro et al., 2022). A study in Bwizibwera also reported a 77.31% and 72.73% inappropriate prescription among females and males respectively. It further reported prevalence of 18%, 25.6%, 27.3% and 29.1% of inappropriate prescription among children aged 2-5months, 6-11months, 12-23months, and 24-59 months respectively (Abeja et al., 2022).

Another study in Indonesia reported inappropriate prescription among children of less than 1 yearof age (Yusuf, Murni and Setyati, 2017). Another study further reported that medicines obtained from a drug shop and are kept at home were 45% and 80% respectively, more likely to be used without a prescription for managing illnesses in children (Ocan et al., 2017).

2.8.2 Clinical factors

Several studies have investigated the clinical factors associated with irrational antibiotic prescribing practices among children under five years of age. One study conducted in primary care health facilities found that the lack of diagnostic testing was a common factor contributing to irrational antibiotic prescribing (Nantongo et al., 2022).

A study done in Uganda reported that 77.1% of the prescribers had experience of 5 years and more in childcare. It further went ahead to report that 97.1% of the health facilities whose files were reviewed had a treatment reference tool i.e., the UCG and 62.9% had a Manual for Integrated Management of Neonatal and Childhood Illnesses (IMNCI 2012). However, the presence of treatment reference tools did not deter health workers from prescribing irrationally as 68.4% of the prescribed antibiotics were irrational (Okello et al., 2020). This study further reported that male health workers were more likely to prescribe irrationally. Another study found that a lack of knowledge and training on appropriate antibiotic use was a common factor contributing to irrational prescribing (Nkinda et al., 2022). Another study in India reported an oversupply of drugs and influence from medical representatives as some of the factors that influence irrational antibiotic prescriptions (Kotwani et al., 2010). Another study reported that irrational prescription was higher among health professionals that are not authorized to make these prescriptions (Nantongo et al., 2022).

Studies have also shown that the availability of medicines in private health facilities is generally higher compared to public health facilities, particularly in low- and middle-income countries (Ongarora et al., 2019). Additionally, studies have shown that the cost of medicines in private health facilities is often higher than in public health facilities, especially in low- and middle-income countries (Bizimana, Kayumba and Heide, 2020). This is due to a variety of factors, including the lack of price regulation, higher overhead costs, and the profit motive of private health facilities (Basu et al., 2012).

CHAPTER THREE: METHODS

3.1 Study design

The study employed a cross sectional study design and utilized retrospective data from patient files in the inpatient departments of Mengo and Lubaga hospital paediatric wards.

3.2 Study setting

The study was conducted at Mengo and Lubaga hospital paediatric wards between August and September 2023. Mengo and Lubaga Hospitals are private not for profit missionary hospitals in Uganda. The patients treated in these hospitals pay for their health care costs when they visit the hospital premises requiring, healthcare services. The two hospitals are among the oldest hospitals in Uganda and serve as referral centers for the surrounding areas located in Lubaga division and areas beyond. Mengo hospital is located on Namirembe Hill in Lubaga Division in northwestern Kampala, approximately five kilometers,by road, southwest of the Mulago National Referral Hospital. Lubaga hospital is located on Lubaga hill in Lubaga division in northwestern Kampala and about 6.5 kilometers by road south west of the Mulago national referral hospital.

The paediatric ward at Mengo hospital has about 30 beds and receives at least 5 children with severe pneumonia daily. In Lubaga hospital, the paediatric ward has a bed capacity of about 32 beds which admits at least 7 children with pneumonia daily.

3.3 Populations

3.3.1 Target population

Files of children under 5 years admitted with pneumonia at the paediatric wards in urban private not-for-profit hospitals.

3.3.2 Accessible population

Files of children under 5 years admitted with pneumonia at the paediatric wards in Mengo and Lubaga hospitals during the year 2022.

3.3.3 Study population

Files from the paediatric in-patient treatment registry of children aged under 5 years with pneumonia who were admitted during the year 2022 and met the eligibility criteria.

3.4 Eligibility Criteria

3.4.1 Inclusion Criteria

- The study included files of children aged between 1 day and 59 months admitted with pneumonia at Mengo and Lubaga Hospital paediatric wards during the year 2022 and had a prescription and diagnosis recorded even when the outcome of their treatment was death.

3.4.2 Exclusion Criteria

- Files where a diagnosis of pneumonia and Septicemia or meningitis as co morbidities were indicated.

3.5 Sample size determination

Objective 1:

For this objective, the Kish Leslie's formula was used.

$$N = \frac{Z^2_{\alpha/2} p(1-p)}{d^2}$$

N – was the number of participants that were included in the study for this objective, Z = the level of confidence at 95% i.e., 1.96, d was the precision level at 5%, p – estimated proportion of the inappropriate antibiotic prescription in Mengo and Lubaga hospitals.

A 77.86% prevalence of ceftriaxone prescription from a study among 131 children was assumed (Ali, Ahmed and Lohana, 2013). A sample size of 265 was calculated. Twenty percent missing data was anticipated in the calculation of the sample size. Hence, the final sample size was 316. But due to clustering at the health facility level, the sample size was adjusted using a design effect of two hence the estimated sample size was 316*2 which gave a sample size of 632 participants.

Objective 2:

For this objective, the Kish Leslie's formula was used.

$$N = \frac{Z^2_{\alpha/2} p(1-p)}{d^2}$$

N – was the number of participants that were included in the study for this objective, Z = the level ofconfidence at 95% i.e., 1.96, d was the precision level at 5%, p – estimated proportion of the inappropriate antibiotic prescription in Mengo and Lubaga hospitals.

A 75.1% prevalence of inappropriate antibiotic prescription from a study among 229 children whose records were reviewed and analysed in Bwizibwera Health center IV was assumed (Abeja et al., 2022). A sample size of 288 was calculated. Twenty percent missing data was anticipated in the calculation of the sample size. Hence, the final sample size was 346. But due to clustering at the health facility level, the sample size was adjusted using a design effect of 2.

Hence the estimated sample size was 346*2 which gave a sample size of 692 participants.

Objective 3

For this objective, the sample size was calculated using the formula for comparison of proportions in two groups that is;

$$N = \frac{[Z_{\alpha/2}\sqrt{p(1-p)(1/q_1 + 1/q_2)} + Z_{\beta}\sqrt{p_1(1-p_1)\,1/q_1 + p_2(1-p_2)\,1/q_2}]^2}{(p_1 - p_2)^2}$$

Where N was the required number of participants, q1 - proportion of subjects in group 1, q2 - proportion of subjects in group 2, p1 - proportion in group 1 that had the outcome of interest, p2 - proportion in group 2 that had the outcome of interest, p = p1q1 + p2q2, Zα – standard normal value corresponding to level of significance, Zβ - standard normal value corresponding to power of the study. Age was used as the independent variable.

According to a study by Launay, (Launay et al., 2016), q1 was obtained at 17% and q2 at 83% as proportions for age categorized at less than one year and greater than one year in that study respectively. Proportions p1=71% and p2=43% were the proportions of children less than one year and children with one year and above respectively in the same study that had inappropriate antibiotic prescriptions while Zα and Zβ were 1.96 (5% level of significance) and 0.84 (80% power of the study) respectively.

This gave a sample size of 169 participants. After adjusting for 10% missing data, a sample of 186 participants was obtained.

Clustering at the health facility level was expected therefore a design effect of 2 was used to adjust for this clustering. Hence the sample size estimate was 186*2 which gave a sample size of 372.

A sample size of 692 participants, which was the largest estimated sample size was utilized for this study.

3.6 Sampling procedure

The records to be sampled from Lubaga hospital were expected to be 404, and 288 participant records were expected to be selected from Mengo hospital.

Simple random sampling technique was used to select the 692 records of study participants from both Mengo and Lubaga hospitals. To select individual records for study participants, identification numbers were first assigned to the inpatient files of children aged under five years diagnosed with pneumonia. A list of all inpatient numbers for children admitted with pneumonia at the paediatric wards during the year 2022 was compiled for both Mengo and Lubaga hospitals. Random numbers were generated using a computer and patient files corresponding to these generated random numbers were selected.

In order to account for files that might not meet the eligibility criteria as the files were reviewed, 716 files and 412 were selected from Lubaga and Mengo hospitals respectively. This ensured that enough eligible files would remain after the review process using the eligibility criteria in order to meet the minimum of 404 and 288 files required from Lubaga and Mengo hospital respectively.

Each selected file was reviewed in detail to confirm eligibility by the research assistants. Files that did not meet the eligibility criteria were excluded.

3.7 Study Variables

3.7.1 Dependent variable

- ✓ Inappropriate antibiotic prescription among children under 5 years admitted with pneumonia at Mengo and Lubaga hospitals' pediatric wards.

3.7.2 Independent variables

- Sociodemographic factors (sex of the child, age of the child, weight)
- Length of stay in hospital

- Sex of the health worker
- Comorbidity indicated
- Antibacterial use prior to hospital visit
- Prescription based on laboratory or radiology diagnosis.

3.8 Data Collection

The data abstraction form was developed in Epidata manager in reference to the UCG, Mengo hospital treatment protocol for pneumonia and the Lubaga hospital treatment protocol for pneumonia. Data was collected by two registered nurses and the principal investigator who abstracted data from the files on the child's social demographics, and hospital-related factors. The research assistants were trained on how to use the data abstraction tool for three days by the principal investigator. They further took part in the pretesting of the data abstraction tool.

The files were further assessed if the child received any treatment before admission and any antibiotic treatment given to the child which were assessed for appropriateness based on name of the antibiotic, the dosage, the treatment duration and if the drugs were prescribed using the generic name.

3.9 Data management

Data abstracted from the files was checked for any missing data every day after data collection. In case of any missing data found, the file was retrieved using the unique identifier code assigned during data collection and then filled with the help of the inpatient files' custodian. The hard copies of the abstracted data from the pediatric patient files were stored in lockable cabinets that were only accessed by the principal investigator. This data was double entered into Epidata for cleaning and the raw data was stored on a password protected computer.

3.10 Data analysis

Data were analyzed using STATA version 14.0. At univariate analysis, continuous variables were summarized using medians and ranges, while categorical variables were summarized using frequencies, and percentages.

The outcome variable, inappropriate antibiotic prescription was dichotomized as Yes = 1 if the prescription was inappropriate, and No = 0 if the prescription was not inappropriate. In determining this proportion, the numerator was the number of files for the study participants with their prescriptions not conforming to the recommendations of the UCG, Mengo treatment protocols for pneumonia and Lubaga treatment protocol for pneumonia while the denominator was the total number of the files that met the eligibility criteria. The antibiotic agents prescribed for treatment of pneumonia in children under five years admitted in Mengo and Lubaga hospitals were summarized and reported as percentages. Bivariate and multivariate analyses were performed with a generalized linear model (modified Poisson) using robust standard errors since the prevalence of inappropriate antibiotic prescription was more than 10%. A multivariate regression was performed to determine how the independent variables were associated with inappropriate antibiotic prescription. Variables with a P-value of ≤ 0.2 at bivariate analysis were to be considered for the multivariate regression analysis. However, the sample size was adequate for all variables to be considered for multivariate analysis. Data was assessed for outliers and collinearity. Interaction terms were formed between all the independent variables to form a full model. The reduced model (without interaction terms) was preferred having been compared to the full model (with interaction terms) using the chunk test.

The variables dropped at assessment of interaction were assessed for confounding. Confounding was considered at a difference of $\geq 10\%$ between the crude and adjusted measure of effect (prevalence ratio) for the variables that were dropped. The level of

significance was set at 0.05.

3.11 Quality Control

Ten data abstraction forms from each study site; Lubaga and Mengo hospitals were pretested before being used for the actual data collection. The principal investigator cross checked with all the filled data abstraction forms for completeness at each end of the data collection day. These forms were further be cross referenced with the patient files to ensure complete data abstraction. The research assistants received a three-days training about the data abstraction form and how to pick out the data from the patient files. This data was double entered into Epidata for cleaning before being imported into STATA for analysis.

3.12 Ethical considerations

Permission to conduct the study was sought from the Clinical Epidemiology unit and approval of the research protocols to be used to conduct the study was sought from the Makerere University School of Medicine Research and Ethics Committee, SOMREC with REC reference number Mak-SOMREC-2023-613.

On receipt of approval from SOMREC, administrative clearance was sought from the management of both Mengo Hospital and Lubaga hospitals. Additional permission to collectdata was sought from the heads of paediatric departments and the in-charges of the records offices at Mengo and Lubaga hospitals.

Informed Consent waiver was sought from SOMREC since abstracted data from files of children admitted with pneumonia in the year 2022 was used in this study.

In order to ensure confidentiality, identification data of research participants on the files were assigned unique serial numbers instead of their identification credentials when abstracting data.

CHAPTER FOUR: RESULTS

4.1 Description of study participants

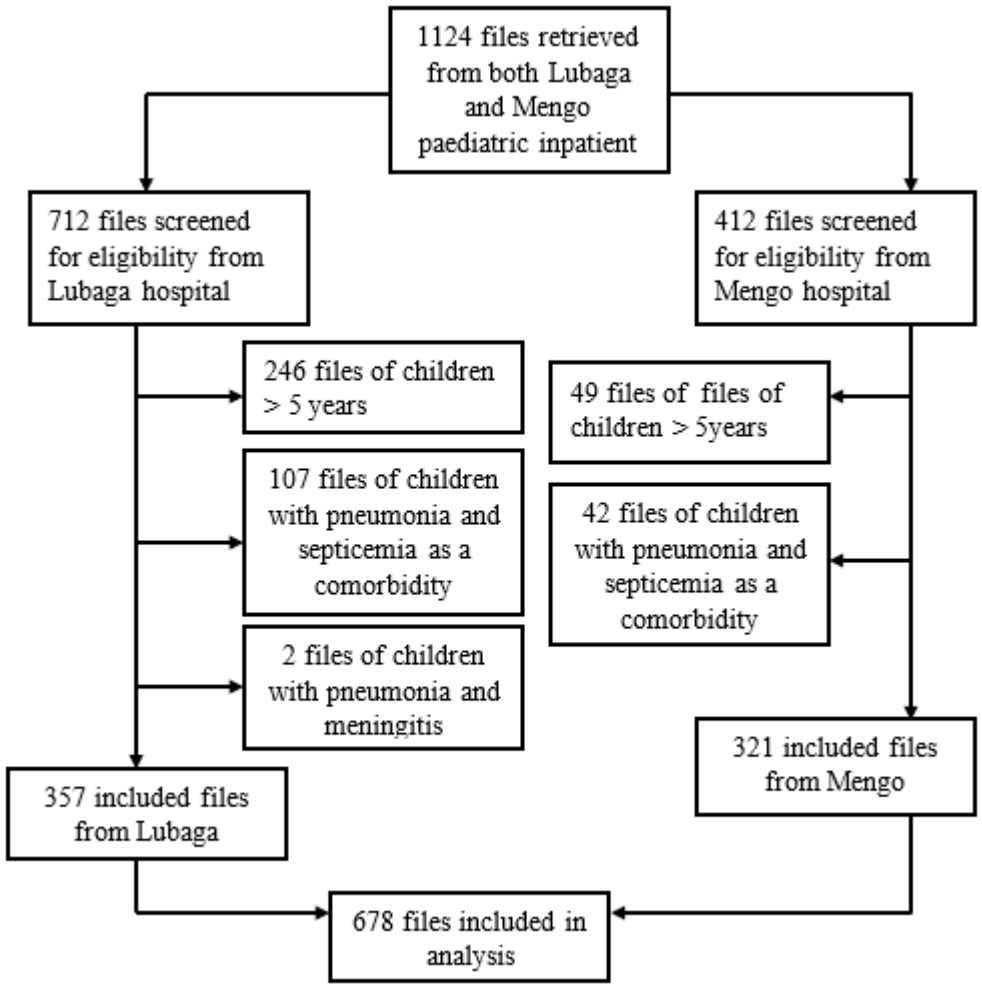

Figure 2: Study profile of files of children under five years admitted with pneumonia in Mengo and Lubaga hospitals

4.1.1 Sociodemographic and hospital-related characteristics

There were 678 files from which data was abstracted which were assessed for inappropriate antibiotic prescription. Files of male children constituted the majority of the abstracted data (n=375, 55.3%). The median age from the abstracted files was 15 (6, 33) months. The data on weight from the abstracted files had a median of 9.8 (7,12) Kgs. The majority of the files had a pneumonia diagnosis confirmed after utilization of both the Complete Blood Count and chest X-ray results (n=676, 99.7%).The socio-demographic and hospital related characteristics are summarized

in table 1 below.

Table 1: Socio-demographic and health worker- and hospital-related characteristics of 678 files of children under five years admitted with pneumonia in Mengo and Lubaga hospitals

Variable	Variable description	Median (IQR)	n (%)
Age (in months)		15 (6, 33)	
Duration of stay in hospital*(n=668)		4 (3, 5)	
Weight (in Kgs) * (n=658)		9.8 (7, 12)	
Sex of the child			
	Male		375 (55.3)
	Female		303 (44.7)
Comorbidity indicated			
	Yes		406 (59.9)
	No		272 (40.1)
Prescription based on laboratory or radiology diagnosis			
	Yes		676 (99.7)
	No		2 (0.3)
Sex of the prescriber			
	Male		402 (59.3)
	Female		276 (40.7)
Antibacterial use prior to hospital visit			
	No		574 (84.7)
	Yes		104 (15.3)

**missing data IQR- Interquartile range n- Number of files of children*

4.2 Antibiotic agents prescribed for the management of pneumonia

The majority of the files had two antibiotics (n=556, 82.0%) prescribed for the management of pneumonia during their admission. The most prescribed antibiotics were a combination of ceftriaxone and gentamicin (n=194, 28.6%) and ceftriaxone was the most singly prescribed antibiotic (n=97, 14.3%) prescribed alone (Table 2).

Table 2: Antibiotic agents prescribed for management of pneumonia in 678 files of children under five years admitted in Mengo and Lubaga hospitals

Antibiotics	n (%)
Ceftriaxone and Gentamicin	194 (28.6)
Ceftriaxone and Amikacin	183 (27.0)
Ceftriaxone Only	100 (14.7)
Cefotaxime and Amikacin	42 (6.2)
Ampicillin and Gentamicin	32 (4.7)
Other antibiotics prescribed singly	26 (3.8)
Ceftazidime and Amikacin	24 (3.5)
Flucloxacillin and Amikacin	24 (3.5)
Other antibiotics prescribed in combination*	21 (3.1)
Piperacin, Tazobactam and Amikacin	10 (1.5)
Ceftazidime and Gentamicin	9 (1.3)
Cefuroxime and Gentamicin	8 (1.1)
Ceftriaxone and Flucloxacillin	5 (0.7)

*n-frequency *(Ampicillin and Amikacin, Flucloxacillin and Gentamicin, Meropenem and Amikacin, Cefotaxime and Gentamicin, Cefixime and Gentamicin, Flucloxacillin and Meropenem, and Cefuroxime and Amikacin)*

4.3 Prevalence of inappropriate antibiotic prescription among files of children admitted with pneumonia in Mengo and Lubaga hospitals.

The prevalence of inappropriate antibiotic prescription was 39.7% (95% CI: 36.1-43.4) based on recommendations from the UCG, Lubaga hospital protocol for treatment of pneumonia and Mengo hospital protocol for treatment of pneumonia. The prevalence of antibiotic prescription inappropriate based on recommendations by the UCG was 95.3% (95% CI: 93.4-96.7), based on the Lubaga hospital protocol for treatment of pneumonia, it was 48.7% (95% CI: 43.6-53.9), and 40.5%(95% CI: 35.2-45.9) based on the Mengo hospital protocol for treatment of pneumonia (Table 3).

Table 3: Prevalence of inappropriate antibiotic prescription among 678 files of children under 5 years admitted with pneumonia at Mengo and Lubaga hospitals

Reference guideline	Inappropriate antibiotic prescription	n (%)	95% CI
UCG, Lubaga protocols and Mengo treatment protocols			
	Yes	269 (39.7)	36.1 - 43.4
UCG			
	Yes	646 (95.3)	93.4 - 96.7
Lubaga treatment protocols*(n=357)			
	Yes	174 (48.7)	43.6 - 53.9
Mengo treatment protocols*(n=321)			
	Yes	130 (40.5)	35.2 - 46.0

4.4 Factors associated with inappropriate antibiotic prescription among children under five years admitted with pneumonia at Mengo and Lubaga hospitals

The proportion of inappropriate antibiotic prescription was high (39.7%), bivariate and multivariate analyses were performed with a generalized linear model (modified Poisson) using robust standard errors. A p value of 0.2 was used to select for variables to include in the multivariate analysis

4.4.1 Bivariate analysis of the socio-demographic and hospital-related factors associated with inappropriate antibiotic prescription of 678 files of children under five years admitted with pneumonia in Mengo and Lubaga hospitals

At bivariate analysis, age of the child (PR – 0.996, 95% CI: 0.994 0.999), weight of the child [PR – 0.981, 95% CI: 0.953 1.009], and duration of stay in hospital (PR – 0.964, 95% CI: 0.917 1.012), had a P value less than 0.2 (Table 4).

Table 4: Bivariate analysis for socio-demographic and hospital-related factors of 678 files of children under five years admitted with pneumonia in Mengo and Lubaga hospitals

Variable	Inappropriate Antibiotic prescription		cPR	95% CI	P value
	No, n (%)	Yes, n (%)			
Sex of the child					
Male	224 (59.7)	151 (40.3)	Reference		
Female	185 (61.1)	118 (38.9)	0.967	0.832 - 1.125	0.218
Age			0.996	0.994 - 0.999	0.031
Weight of the child			0.981	0.953 - 1.009	0.075
Duration of stay in hospital			0.964	0.917 - 1.012	0.067
Comorbidity indicated					
Yes	248 (61.1)	158 (38.9)	Reference		
No	161 (59.2)	111 (40.8)	1.049	0.315 - 3.496	0.704
Antibacterial use prior to hospital visit					
No	346 (60.3)	228(39.7)	Reference		
Yes	63 (60.6)	42 (39.4)	0.992	0.004 - 247.515	0.989
Sex of prescriber					
Male	237 (62.3)	165 (37.7)	Reference		
Female	172 (59.0)	104 (41.0)	0.918	0.299 - 2.813	0.51

cPR- crude prevalence ratio CI-confidence interval

4.4.2 Multivariate analysis of factors associated with inappropriate antibiotic prescription among 678 children under 5 years admitted with pneumonia at Mengo and Lubaga hospitals

At multivariate analysis, weight of the child (aPR: 0.979, 95% CI: 0.968 0.990),and duration of stay in hospital (aPR:0.959, 95% CI: 0.915 0.992) were significantly associated with inappropriate antibiotic prescription (Table 5).

Table 5: Multivariate analysis of factors associated with inappropriate antibiotic prescription among 678 files of children under 5 years admitted with pneumonia at Mengo and Lubaga hospitals

Variable	aPR	95% CI	p-value
Weight of the child	0.979	0.968 - 0.990	0.027
Duration of stay in hospital	0.959	0.915 - 0.992	0.049

aPR- adjusted prevalence ratio

CHAPTER FIVE: DISCUSSION

5.1 Antibiotic agents prescribed for the management of pneumonia

In this cross-sectional study, both single and a combination of two antibiotics were used in the treatment of pneumonia. The proportion of antibiotics prescribed singly ranged between 3.8% and 14.7% and the antibiotics prescribed in double combination ranged from 0.3% to 28.6%. This follows the recommendations by the UCG, Lubaga and Mengo hospitals' treatment protocols for pneumonia. The guidelines and protocols recommend at least two antibiotic regimens for the treatment of pneumonia.

All the regimens that were identified in this study are categorized in the list of essential medicines for children under the Access and Watch categories (World Health Organization, 2023). The Access category includes antibiotics that are active against a wide range of common susceptible microorganisms with a lower resistance. Some Access category antibiotics are recommended as essential first- or second-line treatment options for infectious diseases. They are required to be widely available, affordable and quality assured. The Watch category includes antibiotics with higher resistance potential. These medicines are key targets of stewardship programs and monitoring. Some Watch category antibiotics are recommended as essential first- or second-line treatment options for a limited number of specific infectious diseases (World Health Organization, 2023).

The majority of the prescribed antibiotic were third generation cephalosporins. Ceftriaxone, prescribed singly or in double combination was the most prescribed cephalosporin. A study in Bangladesh also reported closely related findings with ceftriaxone (50%) being the most prescribed antibiotic (Rashid et al., 2017).This difference in the amount of ceftriaxone prescribed could be due the difference brought about by the study site. This study was conducted in private not for profit hospitals yet the study in Bangladesh was conducted in a teaching hospital. The findings of this study are relatable to the results conducted at a tertiary

private not for profit hospital in Uganda which reported a 50.6% use of ceftriaxone among in-patients (Kizito et al., 2021). This reported prevalence of ceftriaxone use was lower than the prevalence reported in this study and this could be attributed to the difference in study population with this study focusing on children under five years and the other study focusing on participants with a mean age of 56.2. Other studies done in other public healthcare facilities in Uganda have also shown a relatively high extent of ceftriaxone prescription; for instance, in a study from a tertiary care hospital in Kampala, the ceftriaxone prescription rate was 43% (Kiguba, Karamagi and Bird, 2017) and 66% (Kiguba, Karamagi and Bird, 2016). Similar studies conducted in public healthcare facilities in other parts of Uganda such as Mbarara (Kemigisha et al., 2018), and Bwindi (Rudd, Tutaryebwa and West, 2017) reported high ceftriaxone prescription rates of 77.7% and 45%, respectively. This could be attributed to the choice of drugs delivered at public health facilities in Uganda by the National Medical Stores and Joint medical sores to private not for profit hospitals.

The high use of ceftriaxone-based regimens indicates a reliance on this third-generation cephalosporin for its broad spectrum coverage. The addition of Gentamicin or Amikacin enhances gram-negative bacterial coverage, crucial in severe cases with drug resistance. The lower use of Ampicillin-based combinations (e.g., Ampicillin and Gentamicin at 4.72%) may reflect resistance patterns observed by sensitivity culture tests conducted at the hospitals (Ampaire et al., 2016).

5.2 Prevalence of inappropriate antibiotic prescription among study participants admitted with pneumonia in Mengo and Lubaga hospitals.

The reported prevalence of inappropriate antibiotic prescription in this study is 39.7% (95% CI: 36.1-43.4). This high prevalence aligns with global concerns about antimicrobial resistance (AMR), highlighting a significant issue within the healthcare system (Michael,

Dominey-Howes and Labbate, 2014). The reported inappropriate prescription may be attributed to the presence of specialist care at private hospitals who are more likely to adhere to evidence-based practices and may be better equipped to make nuanced clinical decisions, that may deviate from the recommended regimens.

The absence of similar studies on inappropriate antibiotic prescriptions among children under five years admitted with pneumonia in private not-for-profit hospitals in Uganda makes direct comparisons challenging. However, insights can be drawn from similar research conducted in public health facilities.

Two studies conducted in public health facilities in western Uganda revealed a higher prevalence of inappropriate antibiotic prescriptions, of 75.1% (Abeja et al., 2022) and 65.8% (Nantongo et al., 2022). These studies were based on the Uganda Clinical Guidelines (UCG) (Ministry of Health Uganda, 2022), which provides standardized treatment protocols aimed at optimizing clinical outcomes and minimizing inappropriate prescriptions in health facilities in Uganda.The higher prevalence rates observed in these public facilities may be attributed to factors like differences in the types of healthcare facilities. The difference may additionally be due to the fact that the private hospitals have local treatment protocols that can be enforced and overseen by therapeutic committees within the private hospitals. Furthermore, public hospitals in Uganda may face severe resource constraints, including drug shortages that can lead to deviations from guidelines, contributing to inappropriate prescriptions.

5.3 Factors associated with inappropriate antibiotic prescription among study participants admitted with pneumonia at Mengo and Lubaga hospitals

5.3.1 Weight of the child

Inappropriate antibiotic prescription was significantly associated, p = 0.027, with weight of the child. This finding could be explained by the consideration of weight when calculating the dose to be administered to the child yet dose is one of the factors considered when determining rationality of a prescription. The adjusted prevalence ratio (aPR) of 0.979 suggests that for each unit increase in the child's weight, the likelihood of inappropriate antibiotic prescription decreases by 2%. A study conducted in Tanzania noted that factors such as the child's age and weight were often not adequately considered when prescribing antibiotics for children, leading to inappropriate dosing and treatment durations, which could potentially contribute to inappropriate antibiotic prescription (Nkinda et al., 2022). The significant association between a child's weight and inappropriate antibiotic prescriptions highlights the necessity for precise dosing calculations in paediatric care. This association could be attributed to the fact that prescribers assume doses in younger children whose weights may vary considerably. Proper dosing based on weight is essential to ensure therapeutic efficacy and avoid underdosing or overdosing, which can lead to treatment failure or adverse drug reactions, respectively.

5.3.2 Duration of hospital stay

The study found an adjusted prevalence ratio (aPR) of 0.959 for antibiotic treatment duration in admission. This indicates that for each additional day of hospital admission, the likelihood of inappropriate antibiotic prescription decreases by 4%. Although this finding is on the border of statistical significance (p = 0.049), it suggests a trend where longer hospital stays are associated with more inappropriate antibiotic prescriptions. The findings of this study

are similar to a study conducted in Pakistan which found that the long length of stay in admission is associated with inappropriate antibiotic use. This study reported that the odds of experiencing inappropriate use were 12.5 times higher in patients with long length of hospital stay LOS, compared to patients with a short length of hospital stay (Iftikhar et al., 2019) .

5.4 Factors not associated with inappropriate antibiotic prescription among study participants admitted with pneumonia at Mengo and Lubaga hospitals

5.4.1 Age of the Child

In this study, age of the child was not found to be a significant factor associated with inappropriate antibiotic prescription. This is reassuring as it indicates that healthcare providers are likely considering age-appropriate guidelines for antibiotic use. Nonetheless, given that children's pharmacokinetics and disease presentations can vary significantly with age, continuous education on age-specific antibiotic guidelines remains essential.

5.5 Strength of the study

The study sought to determine whether antibiotics were utilized appropriately in children under five years admitted with pneumonia. The sample size was large and representative and offered a great chance to contrast antimicrobial therapy with established treatment protocols at private tertiary hospitals in Uganda.

5.6 Limitation of the study

A secondary patient chart review was used for this study and this limited the variables whose data was already recorded. The principle investigator was not able to ascertain the inappropriateness of the antibiotics from the hospital itself.

There was a possibility of recording the same patient more than once since patients are assigned new patient numbers with each visit to the hospital.

The private not for profit hospital-based nature of the study may also not be generalized to public health centers and health institutions due to the different mix of health professionals and availability of drugs

The retrospective nature of the study could not assure the cause-effect relationship of the significantly associated factors linked to inappropriate antimicrobial use.

There were other factors that could not be investigated such as influence from pharmaceutical and health insurance companies, cadre of health workers intention of prescribers and the medication that the person had received before admission to the two study sites.

Some patients may have received longer duration of antibiotics for the right indications which could not be established by the study tool.

The clinical impact of inappropriate prescription could not be evaluated, including treatment failures and adverse drug events.

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1 Conclusion

- The study found that combination antibiotic therapy was widely used in treating pneumonia in children under five, with a preference for dual-agent regimens. This approach likely reflects an effort to broaden antimicrobial coverage and improve treatment outcomes for severe pneumonia cases, addressing both common bacterial pathogens and potential resistance issues in the local context.
- Among the combination treatments, ceftriaxone and gentamicin emerged as the most frequently prescribed agents. This preference aligns with the broad-spectrum efficacy of these antibiotics against key pneumonia pathogens in children and may indicate their availability and cost-effectiveness in private not-for-profit hospital settings. The popularity of this combination suggests a standardized approach to first-line treatment in line with clinical expectations for managing pediatric pneumonia.
- Most of the prescriptions observed in this study conformed to both national and local treatment guidelines. This alignment indicates a strong adherence to recommended practices, which is crucial in standardizing care and minimizing the misuse of antibiotics. Such compliance suggests that hospitals are prioritizing evidence-based protocols, potentially contributing to better health outcomes and a reduction in antimicrobial resistance.
- The study identified child weight and length of hospital stay as factors significantly associated with inappropriate prescriptions. This finding points to specific areas where targeted interventions, such as weight-adjusted dosing protocols and periodic prescription reviews during extended hospital stays, could improve prescribing accuracy. Addressing these factors could enhance antibiotic stewardship and minimize

the risk of inappropriate antibiotic use, thereby safeguarding pediatric patient health and reducing the risk of developing resistance.

6.2 Recommendations

Continuous Monitoring and Review of Antibacterial Prescriptions

To ensure appropriate antibacterial use and mitigate resistance, hospitals must establish robust, continuous monitoring systems for evaluating antibacterial prescriptions. These systems should be designed to align prescribing practices with current antimicrobial stewardship guidelines.

Regular Training Programs for Healthcare Workers on Antimicrobial Stewardship

Hospitals must prioritize ongoing education for all healthcare providers on antimicrobial stewardship principles. Regularly implemented training programs will reinforce appropriate prescribing practices, enhance awareness of antimicrobial resistance, and empower informed clinical decision-making.

Strengthening the Operations of Medicines and Therapeutic Committees

Hospitals should allocate resources to strengthen the capacity and influence of their Medicines and Therapeutic Committees. Empowered MTCs can provide more effective oversight of antimicrobial utilization, establish clear prescribing guidelines, and implement a framework for ongoing evaluation and policy adaptation based on emerging data.

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Appendices

Appendix 1: Waiver of Consent Request

18th January 2023

The Chairperson,

School of Medicine Research and Ethics Committee

Makerere University

College of Health Sciences

P.O. Box 7072

Kampala, Uganda

Dear Sir,

RE: REQUEST FOR A WAIVER OF CONSENT FOR A PROPOSED STUDY TITLED "**ANTIBIOTIC PRESCRIPTION PRACTICES AND ASSOCIATED FACTORS AMONG CHILDREN UNDER FIVE YEARS ADMITTED WITH PNEUMONIA AT MENGO AND LUBAGA HOSPITALS**"

I am writing to request a consent waiver for my proposed research on antibiotic prescription practices and associated factors among children under five years admitted with pneumonia at Mengo and Lubaga hospitals. I am requesting a waiver because I will be collecting and analysing abstracted data for this study, and therefore the individual participants will not be identifiable in the data we collect. This data will be for children that were admitted with pneumonia at the paediatric wards of Mengo and Lubaga hospitals and were discharged prior to the time of data collection.

My research aims to understand and document the prevalence of irrational antibiotic prescription practices and their associated factors. As part of this study, I will be collecting and analysing abstracted data on antibiotic prescription practices from inpatient files for 2022 at the paediatric wards in Mengo and Lubaga Hospitals. I will be collecting and analysing this data in an anonymous form, meaning that individual participant information will not be linked to the data collected.

Steps will be taken to ensure that that the data collected and analysed will be kept confidential and will not be shared with anyone outside the research team. Additionally, appropriate measures to protect the privacy and confidentiality of the data will be taken throughout the course of the study.

I believe this study has the potential to contribute important insights into rational antibiotic prescription practices and I hope that you will consider grating a consent waiver for this research study.

Thank you for considering my request.

Sincerely

Kamoga Gonzaga Cena

Appendix 2: Eligibility assessment table

Participant's file unique code			
Inclusion criteria		Yes	No
	Aged under 5 years		
	Admitted with pneumonia at Mengo hospital between January and December 2022		
	Admitted with pneumonia at Lubaga hospital between January and December 2022		
Exclusion criteria			
	File with a diagnosis of pneumonia and septicemia and meningitis as other co-morbidities indicated		

Appendix 3: Data abstraction form

Study title: **Antibiotics prescription practices and associated factors among children under five years with pneumonia at Mengo hospital**

1	Abstraction tool Number	□……
2	Unique Patient File Serial No.	
	Section A: Data collector information	
3	Study staff initials	
4	Date of data abstraction	
	Section B: Participation information	
5	Unique patient code	
6	Sex	Male
		Female
7	Age (in months)	
8	Referral	Yes
		No
	Section C: Clinical information	
9	Date of diagnosis/admission	
10	Medication given prior to admission into the paediatric ward in case of a referral	
11	Were laboratory tests done to assist diagnosis of pneumonia	Yes
		No
12		Yes

	Was pneumonia indicated as the diagnosis and reason of admission?				No		
13	Any other comorbidity indicated during diagnosis and admission of patient?				Yes:		
					No:		
14	Duration of stay in admission						
15	Antibiotics prescribed						
16	Antibiotic	Route of administration	Dose/Units	Frequency	Duration	Appropriate	
						Yes	
						No	
						Yes	
						No	
						Yes	
						No	
						Yes	
						No	
17	Were the drugs prescribed using the generic name?				Yes		
					No		
Section D: Health worker related Information							
18	Sex of prescribing health worker				Male		

		Female
Section E: Disease related Information		
19	Nature of Disease	Community acquired
		Hospital acquired

Appendix 4: Approval letter from MAK SOMREC

MAKERERE UNIVERSITY
P.O. Box 7072 Kampala, Uganda
E-mail: rresearch9@gmail.com
Phone: 256 414 533541
Fax: 256 414 541036/0414 532204
COLLEGE OF HEALTH SCIENCES
SCHOOL OF MEDICINE
RESEARCH ETHICS COMMITTEE

03/07/2023
To: Gonzaga Kamoga

+256705276226

Type: Initial Review

Re: Mak-SOMREC-2023-613: ANTIBIOTIC PRESCRIPTION PRACTICES AND ASSOCIATED FACTORS AMONG CHILDREN UNDER FIVE YEARS ADMITTED WITH PNEUMONIA AT MENGO AND RUBAGA HOSPITALS

I am pleased to inform you that at the **147** convened meeting on **18/05/2023**, the MAK School of Medicine REC (Mak-SOMREC) meeting voted to approve the above referenced application.
Approval of the research is for the period of **03/07/2023** to **03/07/2024.**

As Principal Investigator of the research, you are responsible for fulfilling the following requirements of approval:

1. All co-investigators must be kept informed of the status of the research.
2. Changes, amendments, and addenda to the protocol or the consent form must be submitted to the REC for re- review and approval **prior** to the activation of the changes.
3. Reports of unanticipated problems involving risks to participants or any new information which could change the risk benefit: ratio must be submitted to the REC.
4. Only approved consent forms are to be used in the enrollment of participants. All consent forms signed by participants and/or witnesses should be retained on file. The REC may conduct audits of all study records, and consent documentation may be part of such audits.
5. Continuing review application must be submitted to the REC **eight weeks** prior to the expiration date of **03/07/2024** in order to continue the study beyond the approved period. Failure to submit a continuing review application in a timely fashion may result in suspension or termination of the study.
6. The REC application number assigned to the research should be cited in any correspondence with the REC of record.
7. You are required to register the research protocol with the Uganda National Council for Science and Technology (UNCST) for final clearance to undertake the study in Uganda.

The following is the list of all documents approved in this application by MAK School of Medicine REC (Mak- SOMREC):

No.	Document Title	Language	Version Number	Version Date
1	Protocol revised and corrected with track changes accepted	English	2.0	2023-06-21
2	COVID-19 & EBOLA risk management plan for the study	English	Submission For review	2023-03-31
3	Data collection tools	English	Submission For review	2023-03-31
4	Application for waiver of informed consent if applicable to your study	English	Submission For review	2023-03-31

Yours Sincerely
Prof. Ponsiano Ocama
For: MAK School of Medicine REC (Mak-SOMREC)

Appendix 5: Administrative clearance from Lubaga hospital

LUBAGA HOSPITAL

Trustees of the Archdiocese of Kampala

21 July 2023

Lubaga Hospital
SCIENTIFIC COMMITTEE
21 JUL 2023
ADMIN APPROVAL
P.O. Box 14130, Kampala

REF: LHRRC/2023/56

Mr. Gonzaga Kamoga
Makerere University College of Health Sciences
School of Medicine
P.O Box 7072
Kampala, Uganda

Dear Mr Kamoga,

RE: LHSC PROTOCOL 2023/56 ADMINISTRATIVE APPROVAL OF: ANTIBIOTIC PRESCRIPTION PRACTICES AND ASSOCIATED FACTORS AMONG CHILDREN UNDER FIVE YEARS ADMITTED WITH PNEUMONIA AT MENGO AND LUBAGA HOSPITALS.

This is to acknowledge receipt of your proposal, introduction letter from Makerere University College of Health Sciences, Department of Medicine and letter of approval from Makerere University School of Medicine Research Ethics Committee. All that you require from the Lubaga Hospital Scientific Committee is an administrative clearance.
We hereby grant you the administrative approval, continued approval is conditional upon your compliance to the following requirements:

1. Significant changes to the study site and significant deviations from the research protocol and all unanticipated problems that may involve risks or affect the safety or welfare of subjects or others, or that may affect the integrity of the resercah must be promptly reported to the LHSC.
2. One of our staff would be a Co-investigator in your study.
3. Any problems or serious or unexpected adverse events, whether related to the study article or not must be reported to the LHSC in a timely manner as specified in the National Guidelines for Research involving Humans as Research Participants 2014 Edition.
4. Please send the report upon completion or termination of the study to the LHSC.The study cannot continue after 3 July 2024 until reapproved by the Makerere University School of Medicine Lubaga Hospital Scientific Committee.

Please call me if you have any questions about the terms of this approval.
Yours sincerely,

Sr Dr. Grace Nanyondo
MEDICAL DIRECTOR
For: CHAIRMAN LHSC

P.O. Box 14130, Kampala-Ug
0200244800
info@lubagahospital.org
www.lubagahospital.org
Toll Free: 0800 388 888
Service with love

Appendix 6: Administrative clearance from Mengo hospital

MENGO HOSPITAL

Christian Medical Witness

Our Ref : MH / 5021

RESEARCH ETHICS COMMITTEE

July 21, 2023

To: Kamoga Gonzaga Cena
Makerere University

Re: **MHREC Administrative Approval of Proposal Titled: "Antibiotic Prescription Practices and Associated Factors Among Children Under Five Years Admitted with Pneumonia at Mengo and Rubaga Hospitals." (Mak-SOMREC REF: 2023-613)**

This is to acknowledge receipt of your proposal, introduction letter and approval letter.
Since this protocol has been approved by the MAK School of Medicine Research and Ethics Committee (Mak-SOMREC), all that you require from the Mengo Hospital REC is an administrative approval.
We hereby grant you the administrative approval.

Continued approval is conditional upon your compliance with the following requirements:

1) Significant changes to the study site and significant deviations from the research protocol and all unanticipated problems that may involve risks or affect the safety or welfare of subjects or others, or that may affect the integrity of the research must be promptly reported to the MHREC.

2) Please send the report upon completion or termination of the study to the MHREC. The study cannot continue after 08/07/2024 until re-approved by MAK School of Medicine Research and Ethics Committee (Mak-SOMREC).

Please contact the MHREC office if you have any questions about the terms of this approval.

Yours Sincerely,

.....
Prof. Kawooya G. Michael
Chairman (MHREC)

08 JUL 2024

CC. Deputy Medical Director

Pioneer Hospital: Celebrating 125 years of Modern Medicine

Sir Albert Cook Road, Mengo • P.O. Box 7161 Kampala , Uganda • Tel: +256 (0)312 307100
Email: medicaldirector@mengohospital.org • www.mengohospital.org • Clients' Hotlines : 0771 370263 / 0771 370264