Antibiotic Use Assessment in Paediatric Ward of Jimma University Teaching Hospital, Southwest Ethiopia

BY:
HAFTE KAHSAY KEBEDE (B.Pharm)

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Jimma University
Collage of Public Health and Medical Sciences
Department of Pharmacy

BY:

Hafte Kahsay Kebede (B.pharm)

ADVISORS:

1. Kabaye Kumela (B.pharm, MSc in Clinical Pharmacy)
2. Hailay Abrha (BSc, MPHE)

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ABSTRACT

Background*: The issues of antibiotics availability, selection, and proper use are of critical importance to the global community. Despite their importance, the continued efficacy of antibiotic therapies is threatened by the emergence of resistance. Inappropriate use of antibiotics is one of the major contributing factors for the development of antibiotic resistance.*

Objective*: To assess the pattern of antibiotic use and predictors in the pediatric ward of Jimma University Teaching Hospital, Jimma, south-west Ethiopia, 2014.*

Methods*: A retrospective cross-sectional study was used to assess antibiotic use using Gyssens et al. checklist and SPS manual "antimicrobial use investigation" in the pediatric ward of Jimma University Teaching Hospital. Six hundred fourteen patient files were selected by simple random sampling method. The data obtained were analyzed using Statistical Package for Social Sciences for windows version 20, and logistic regression method was used and P value of less than 0.05 was considered as statistically significant in the final model.*

Results: *Of the total 471patient files were assessed. Most of the participants were males (58.81%), and rural residents (57.11%). The Percentage of hospitalized patients with one or more antibiotics prescribed was 86.41%. Of the total of 812 antibiotics prescribed; crystalline penicillin G was the most frequently prescribed166 (20.44%). A total of 126(30.96%) patients were deemed to be used antibiotics inappropriately. Inappropriate use of antibiotics was associated with being between age category of 5-14 years (AOR: 2.40 (1.17-4.91)), >10 days duration of hospital stay (AOR: 3.06 (CI=1.70-5.53)), and using >= 2 antibiotics per encounter (AOR: 3.50 (CI=1.77-6.93)).*

Conclusion: *This study has identified the presence of significant antibiotic use in Pediatric patients admitted to JUTH. Percentage of hospitalizations with one or more antibiotics prescribed and inappropriate use of antibiotics were a considerable number. Being between age category of 5-14 years, >10 days duration of hospital stay, and using >= 2 antibiotics per encounter were the independent predictors of inappropriate antibiotic use. Therefore, measures needs to be taken by the responsible body to reduce inappropriate antibiotic use to the possible level and against the independent predictors*

Key Words: *Antibiotic use, Assessment, Retrospective, predictors*

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LIST OF ACRONOMYS AND ABBREVIATIONS

ADRs	Adverse Drug Reactions
AMR	Antimicrobial Resistance
CAI	Community Acquired Infections
CI	Confidence Interval
CSA	Central Statistical Agency
DACA	Drug Administration and Control Authority
ECDC	European Center for Disease Prevention and Control
EDL	Essential Drug List
FMHACA	Food Medicine and Health Administration and Control Authority
FMOH	Federal Ministry of Health
HAI	Hospital Acquired Infections
ICU	Intensive Care Unit
IRB	Institutional Review Board
JU	Jimma University
JUTH	Jimma University Teaching Hospital
LDDH	List of Drugs for District Hospitals
MOH	Ministry of Health
NICUs	Non Intensive Care Units
PFSA	Pharmaceuticals Fund and Supply Agency
PI	Principal Investigator
PICU	Pediatric Intensive Care Units
SPSS	Statistical Package for Social Sciences
URTIs	Upper Respiratory Tract Infections
UTI	Urinary Tract Infections
WHO	World Health Organization

1 INTRODUCTION

1.1 Background

Antibiotics are defined as substances produced by microorganisms (bacteria, fungi, actinomycetes), which suppress the proliferation of other (pathogenic) microorganisms and can eventually destroy these. The term "antibiotics" now includes synthetic antibacterials such as the sulfonamides and quinolones, which are not actually synthesized by microbes [1]. The issues of their availability, selection, and proper use are of critical importance to the global community. They are among the most commonly used medications worldwide and are of tremendous value to public health [2]. Antibiotics can interact with other drugs patients take, making antibiotics less effective. Some drug combinations can worsen the side effects of the antibiotic or other drug [3].

Antibiotics are among the most commonly prescribed pediatric therapeutic agents [4]. As a result, several key considerations must be incorporated in decisions about the appropriate empirical use of antibacterial agents in infants and children. It is important to know the age-appropriate differential diagnosis with respect to likely pathogens. This affects the choice of antimicrobial agent and also the dose, dosing interval, and route of administration [**5**]. Antibiotic use is considered inappropriate if the dosage, intervals, routes of administration, duration, effectiveness, indication and completeness of records or any one of the criteria's goes wrong [6].

Despite their importance, the continued use of antibiotic therapies is threatened by the emergence of resistance due to their inappropriate use. Inappropriate antibiotic use, including overuse and misuse, is a serious global problem [7]. The inappropriate use of antibiotics is the key driver of antimicrobial resistance (AMR). The epidemic of AMR is changing the way antibiotics are used, increasing mortality and morbidity, and greatly increasing the cost of health care [7]. An extra burden is likely to hit resource-poor countries [8], as inappropriate use leads to resistance, treatment failure, and waste of scarce resources [9]. A combination of underuse, often for financial reasons, leading to incompletion of treatment courses, overuse particularly for minor infections, and misuse due to lack of access to appropriate treatment of antibiotics have increased the prevalence of multidrug resistant pathogens leading some to even speculate that we are nearing the end of the antibiotic era [10, 11]. Thus, the main aim of this research was to assess antibiotic use and associated factors.

1.2 Statement of Problem

Antibiotics are frequently used in the therapy of numerous infectious diseases in children and neonates. Children differ from adults in a physiological, psychological and developmental sense, so the use of drugs in this population, including antibiotics, requires special knowledge and skill. Therefore, from the aspect of safety, neonates and children comprise a particular, so-called risk or vulnerable, patient group. The lack of pharmacokinetic and pharmacodynamics data for drugs used in children increases the risk of overdose and sub dose, adverse effects and inefficacy of a generally efficient drug [12]

Established and newly emerging infectious diseases are increasingly threatening the health of populations. In many countries, antimicrobials are the most frequently prescribed therapeutic agents, accounting for 30 to 50 percent of prescriptions for medicines [7]. Worldwide, it is estimated that over half of all medicines are prescribed, dispensed or sold inappropriately. Inappropriate use may take many different forms, for example, polypharmacy, over-use of antibiotics and injections, failure to prescribe in accordance with clinical guidelines [13]. Though inappropriate use of antibiotics has been found to be common in various parts of the world, but there have been few studies in developing countries [14]. A survey conducted in three European countries (UK, Italy, Greece) in 2009, showed that antibiotics were used at un registered dose in more than 5% of the prescriptions in children admitted to ICU & pediatric wards, in 4.1% outside the registered age range in the neonatal age group and 1.7% in the pediatric wards, and for an off label indication in more than 5% of the prescriptions in at least one of the centers in the patients admitted to the NICUs [15]. Similarly Studies from Turkey, Brazil, India, Mangalore, Tehran, Pakistan, Kenya and Arba-minch of Ethiopia reported that the inappropriate use of antibiotics were (47.30%, 50%, 20%, 32.03%, 42.7%, 39%, 64.70%, and 17.1%) respectively [11, 16-21].

On the other hand, a nationwide drug use study conducted by MOH of Ethiopia 2003 revealed that the percentage of antibiotic use was 58% [22]. World health leaders have described antibiotic-resistant microorganisms as “nightmare bacteria” that “pose a catastrophic threat” to people in every country in the world [3]. This results in the emergence of drug resistant bacteria, adverse drug events, death drug interactions, increased risk of side effects, and serious clinical and financial consequences. The consequences of inappropriate antibiotic use in turn lead to

therapy failure [23], ineffective and unsafe treatment, exacerbation or prolongation of illnesses, distress and harm to the patient, and higher costs, increased cost of treatment, increase in risk, and the patient becomes less rewarding [24], increased consumption of antibiotics, frequent emergency department visits, complications secondary to antibiotic resistant infections, decreased effect of the antibiotic/other drug or worsening of the side effects of the antibiotic/ other drug [25], prolonged hospitalization, spread of resistant clones, termination of antibiotic therapy immaturely [26], and wastage of drugs.

Ethiopian hospitals consume about 50% of the national drug budget [27], which are considered to have high drug budget compared to the population segment using these health facilities. However, very little is known how drugs (particularly antibiotics) are used in hospitalized patients. An attempt was made to assess the pattern of drug use in children in JUTH; but, there was no research done in JUTH that assess antibiotic use in hospitalized pediatric patients as to the investigators knowledge. Therefore, the main objective of this research was to assess antibiotic use in the pediatric ward of JUTH, southwest Ethiopia.

2 LITERATURE REVIEW

2.1 Overview

Although bacteria naturally adapt to outsmart antibiotics, human actions accelerate the development and spread of resistance [11]. Here below is the literature review of the prevalence and factors contributing to inappropriate use of antibiotics.

2.2 Pattern of Antibiotic Use

Studies regarding irrational use of antibiotics among pediatric patients were conducted in many areas around the world. A cross-sectional study done to assess the appropriateness of usage of antimicrobials and associated factors influencing their use on patients hospitalized in 12 different children's hospitals in Turkey revealed that the antimicrobial prescription rate was highest in pediatric intensive care (75.7%) and lowest in the surgery wards (37.0%)[28]. This study also reported that respiratory tract infection was the most common indication for antimicrobial use (29.4 %). Similar study from Italy reported that of the total hospitalized children evaluated antibiotics were prescribed for 43.9% of them [29].

Another point prevalence survey done by the European Centre for Disease Prevention and Control (ECDC) reported that of the total admitted pediatric patients 30.30% received antibiotics; and as per hospital admission rate: <1 year 181 (24.30%), 1-4 years 135 (50.60%), and 5-14 years 148 (37.70%) [30].

A case control study conducted in a pediatric intensivist in the University of Iowa Hospitals and Clinics' USA, reported that in the pediatric intensive care units (PICU), 134 (92.40%) patients receive antimicrobial treatment, 48 (33.1%) received one antimicrobial agent, and 86 (59.3%) received two or more antimicrobial agents. Median duration of stay in the PICU was 4 days. The mean age of patients who received antimicrobials was (5.7 years). Overall, gentamicin, cefazolin, and vancomycin were the three most commonly used antimicrobials, accounting for 60.3% of the total antimicrobial prescriptions during the study period. Neonates received more antimicrobial prescriptions per patient (mean: 5.17 antimicrobial prescriptions per patient) [31].

A prospective cross sectional study carried out in Navodaya Medical College Hospital & Research Center, Raichur, India reported that the average number of drugs prescribed per encounter was 2.99, percentage of drugs prescribed by generic name was 14.83%.

Percentage of prescribed injections was 11.03% and that of prescribed antibiotics was 41.99%. The percentage of drugs prescribed from essential drug list (EDL) was 70.26% [32]. Additional retrospective studies conducted in China, Indonesia, and Nepal revealed that of the total hospitalized pediatric patients 93.90%, 50.0% and 93.00% patients received antibiotics respectively [33-35].

A hospital-based retrospective cross-sectional study was conducted over a 12-month period at the San Fernando General Hospital, southern part of Trinidad, showed that the mean age and length of hospital stay were 5.52 years and 6.71 days, respectively. The mean number of drugs prescribed per child on admission was 3. Respiratory tract illnesses were the most common complaints. Antimicrobial agents were the most frequently used drugs (36.4%). Almost 60% of the antimicrobials belong to the β-lactam group of antimicrobials with cefotaxime (18.9%) being the most commonly prescribed followed by ceftriaxone (16.0%), ampicillin (14.5%), gentamicin (12.4%) and amoxicillin-clavulanic acid (8.9%). The other antimicrobials each accounted for less than 6% of the total [36].

On the other hand, a study conducted in Malaysia to assess the Pattern of Antibiotic Usage in hospitals reported that purpose of prescribing antibiotic was therapeutic in 1263 (66%) prescription and in 614 (32%) the intension was prophylaxis, and 41 prescriptions the purpose was unknown. It also revealed that 1063 (55%) were single antibiotic prescriptions and 855 (45%) combination antibiotics. It also reported that the most common reason for antibiotic prescription was lower respiratory infection, accounting for 390 (31%) therapeutic prescriptions. Skin and soft tissue infection (19%) ranked 2nd, followed by UTIs (8%) [37].

A longitudinal surveillance of antibiotic use done in Israel, Iran and KSA showed that percentage of pediatric patients receiving antibiotic were 72 $\pm$12, 79.40%, and 39.2% respectively [38-40].

A study conducted to assess pattern of Parenteral Antimicrobial Prescription among Paediatric patients in Al-Watani Governmental Hospital in Palestine reported that among all the patients who received antimicrobials 61.8% of them had received parenteral anti-microbial therapy and cefuroxime was the most commonly used (31%patients). The most frequent used combined parenteral antibiotics were ceftriaxone + aminoglycoside in 2.2%, followed by cefazolin + metronidazole in 1.5% and cefotaxime + ampicillin in 1.2% of the treated patients [41].

A study done in china shows (70.8%) had received antibiotics and (63.4%) of them were treated with antibiotic combinations. The average length of stay was 7.5 days. The intravenous (IV) route was used for administration of 93.9% (1475/1571) of the antibiotics prescribed in the PICU. In addition, a total of 33 different antibiotics were used in 957 prescriptions of which the top ten antibiotics accounted for 83.2% and they were: cefotaxime (20.2%), amikacin (15.7%), cefuroxime (9.5%), metronidazole (9.2%), penicillin G (8.5%), 98 vancomycin (6.8%), cloxacillin (4.3%), imipenem (4.1%), co-amoxiclav (2.5%) and gentamicin (2.5%). The most common diagnoses were pneumonia, septicaemia and UTI [42]. Studies conducted to assess antibiotic use in Botswana and Sudan reported that (92%, 65%) respectively was used [43, 44].

Different studies conducted in many parts of Ethiopia: Harari region hospitals and Mizan hospital, reported that antibiotic use was (57.0%, 64%) respectively [45-47]. A retrospective cross sectional study conducted in Mekelle general hospital to assess irrational use of antibiotics in children attending in the hospital showed that Prescriptions containing one or more antibiotics constituted 73.68% of all prescriptions. The percentage of encounters with antibiotic injections prescribed was 95.2%. The number of antibiotics prescribed from the Essential Drug List in this study was 74.8% [48].

In addition, the study from Mekelle revealed that the majority, 36.7% of outpatient and inpatient antibiotic prescriptions were issued to infants 1month to 12 month of age whilst only 1.2% of prescriptions were for new born in between 0-72 hours of age. The average number of antibiotics per encounter was 1 for inpatient, the number of antibiotics prescribed from the Essential Drug List was 96.53. The list of drugs for district hospitals (LDDH) was 76.1% of inpatient antibiotic prescriptions were for drugs included on the list as developed by the former Drug administration and control authority (DACA) of Ethiopia and current Food Medicines Health Administration and Control Authority of Ethiopia (FMHACA). This is higher than the percentage of drugs prescribed from the EDL of Ethiopia [48].

2.3 Factors That Contribute to Inappropriate Use of Antibiotics:

2.3.1 Socio Demographic factors

In appropriate use of antibiotics is associated with different socio-demographic and economic characteristics. A cross sectional study done in Italy showed that out of 181 children who were treated with antibiotics, 78 (43.8%) received more than one antibiotics and the prevalence of antibiotic use was higher in older children, ranging from 33.7% in 0-6-month-old infants to 42.4% in children aged from seven months to five years and 49.1% in children older than five years (chi-square for trend: p=0.049) [29]. This study also depicted that there is no statistically significant differences by sex. But, a study conducted in many European countries by European Center for Disease Control (ECDC) revealed that antibiotic use was independently associated with age (highest adjusted odds ratio in the age category 1–4 years, p<0.001), male sex (p<0.001) [30].

A study done to assess prescribing pattern of antibiotics among pediatric patients in a teaching hospital in western Nepal, reported that out of the total admitted pediatric patients (75%) of them received antibiotics and a single antibiotic was prescribed in 147 admissions (41.3%). One hundred two (28.70%), of them were prescribed with two or greater than two antibiotics. It also revealed that of the total prescribed drugs, 789 (48.9%) were by the parenteral route [49]. Similarly, in a retrospective study conducted in Nepal in 2003, infants received antibiotics more frequently than 15 and 5-12 years age children i.e. 40%, 31% and 29% respectively, (P<0.001, P=0.000) [35].

A cross-sectional study done in Bahir-Dar, Ethiopia, showed that patients at pediatric age group were more likely to receive an antibacterial drug than adult counter parts (70.3% vs. 62.8%, p = 0.038, OR = 1.33) [46].

2.3.2 Patient Related factors

Similarly patient related factors were associated with irrational use of antibiotics. Pilot point prevalence survey done In Europe in 2010 showed that antimicrobial use was independently associated with the number of invasive devices (urinary catheter and intubation, p <0.001), length of stay in the hospital (p <0.05) and surgery since admission (p<0.001) [28]. In addition, study employed in Turkey also revealed that the most frequent causes of irrational antibiotic

use were short treatment period (2.1%), unnecessary use (1.5%), and recommendation of a more effective antibiotic (3.5%) [50].

2.3.3 Disease related factors

A cross-sectional study done to assess the appropriateness of usage of antimicrobials and associated factors influencing their use on patients hospitalized in 12 different children's hospitals in Turkey revealed that, of the total patients receiving antimicrobials, (46.7%) were found to be receiving at least one inappropriately prescribed drug. Inappropriate use was most frequent in surgery wards (80.2%), while it was less common in oncology wards (31.8%; $p < 0.001$). Inappropriate use was more common in deep seated infections (54.7%) and respiratory infections (56.5%) [28].

Another study conducted in the Children's Hospital of Winnipeg, showed that unnecessary prophylaxis was the reason for therapeutic error in a large proportion (46%) of the surgical patients who were treated. Lower respiratory tract infections appeared to be treated erroneously 37% of the time, either with unnecessary antibiotic therapy in conditions such as bronchiolitis, or with inappropriate combination therapy. Serious infections, such as meningitis, were handled appropriately, although one patient received an unnecessarily prolonged course with a combination of antibiotics [51].

A base line survey of antibiotic use in Tanzania showed that antibiotics were indiscriminately used for about 44% of diarrhea cases in children and up to 90% of non-pneumonia acute respiratory infections whilst 42% of all patients received antibiotics [52].

2.3.4 Prescribing related factors

A retrospective study reported from Chinese university hospital, Wuhan, P.R.China, revealed that among the 797 patients, 357 cases (44.8%) were prescribed one antibiotic, 250 cases (31.4%) two types of antibiotics, 125 cases (15.7%) three types of antibiotics and 65 cases (8.2%) four or more types. Antibiotics were prescribed to treat infections in 466 cases (58.5%). Perioperative antibiotics were prescribed in 239 cases (30.0%); antibiotics were used before or during an operation in 20% of these cases, and after operation in 80%. The duration of perioperative antibiotic prophylaxis was less than or equal to seven days in 42.7% of patients, 8±13 days in 31%, and 14 days or more in 26.3%. [33]. A cross sectional study done in Italy

showed that out of 181 children who were treated with antibiotics, 78 (43.8%) received more than one antibiotics [29].

A cross-sectional study done to assess the appropriateness of usage of antimicrobials and associated factors influencing their use on patients hospitalized in 12 different children's hospitals in Turkey reported that fluoroquinolones were used inappropriately more than any other drugs (81.8%, $p = 0.021$) [32]. A prospective study conducted to determine misuse of antibiotics in the Pediatric patients in India in 2007 found that misuse of antibiotics was documented in 36.8% patients (no indication in 35.3%, improper selection in 17.9% and incorrect dosage in 7.7%) [58]. A longitudinal surveillance of antibiotic use done in Israel also reported that the in appropriate antibiotic use was 8% [37].

A retrospective cross sectional study conducted in Mekelle general hospital to assess irrational use of antibiotics in children attending in the hospital reported that around 5.9% of encounters were treated without any diagnosis [48].

2.4 Conceptual Framework

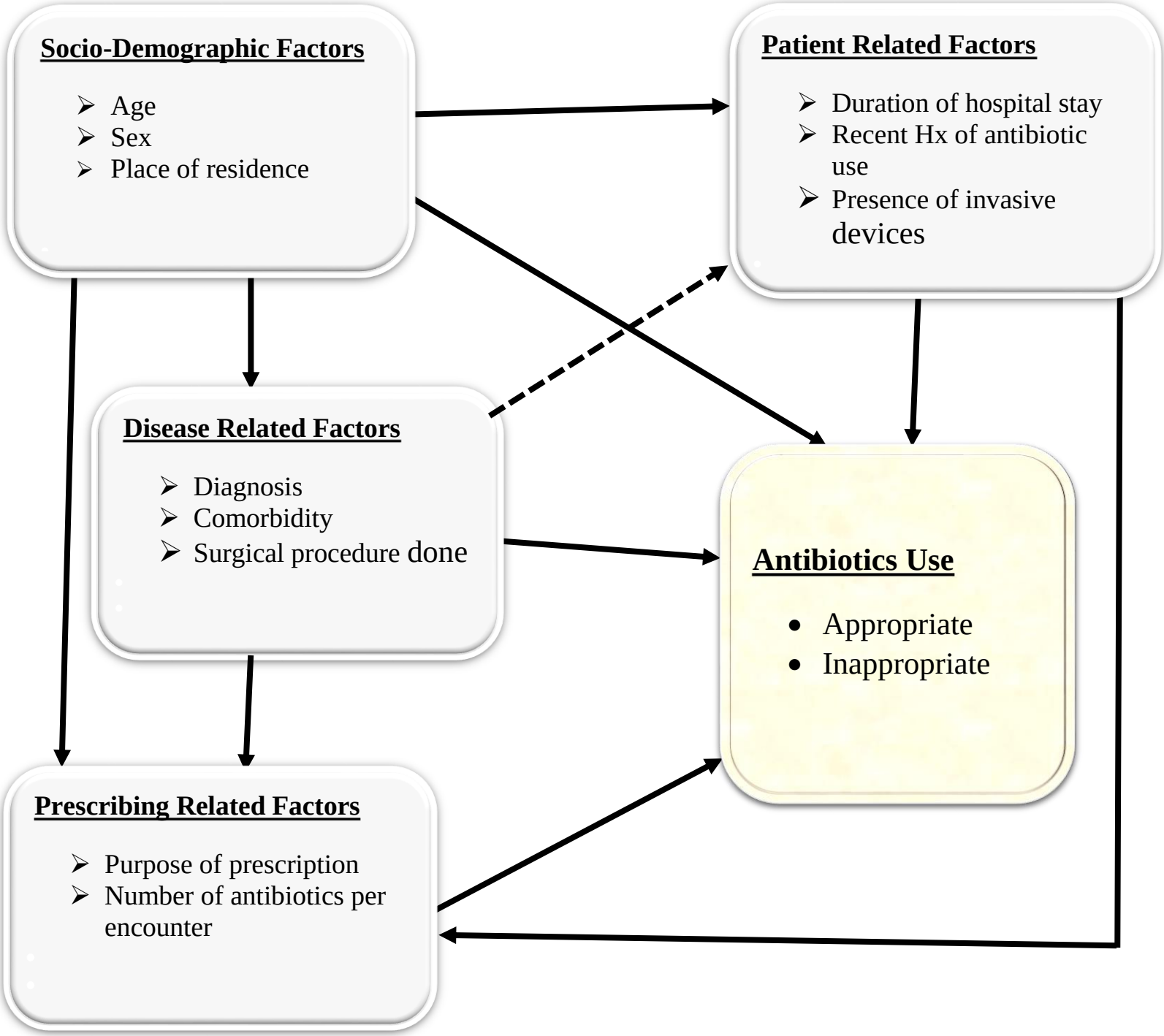

Figure 1: Conceptual framework showing factors associated with antibiotics use in patients admitted to the pediatric, 2014.

2.5 Significance of the Study:

Currently, there is very limited research conducted in this important issue especially in pediatrics and it was necessary to conduct a study to determine the utilization of antibiotics and correlation between antibiotics use and different factors. The aim of this study was to assess antibiotics use in children under the age of 14 years in JUTH, South West Ethiopia.

The findings of the study may in general help the health management at a higher level and in particular those looking after Jimma University Teaching Hospital to understand the extent of the problem in pediatric ward of JUTH. The study will enhance the capacity to look for possible alternative solutions to appropriateness of antibiotic use with regard to associated factors with inappropriate use of antibiotics in collaboration with the hospital, pediatric and child health department and relevant stake holders. It will also contribute to increase in the knowledge about associated factors with inappropriate use of antibiotics in pediatric patients in the ward by concerned bodies including the hospital administration and JUTH pediatric ward staffs so as to develop strategies to alleviate this problem.

In addition, the paper may be useful to other researchers as springboard while conducting further studies on similar problems. Identification of associated factors with inappropriate use of antibiotics is also essential in order to guide program planning, and organizing appropriate use for antibiotics. Exploring the inappropriate use of antibiotics in pediatric patients will help to design reliable and effective interventions to improve the use of antibiotics so as to improve the health outcome of the pediatric population and use the resources effectively and efficiently. Moreover, to identify areas for improvement in antibiotic handling and using in the paediatric ward of JUTH.

3 STUDY OBJECTIVES

3.1 General Objective:

- To assess the pattern of antibiotic use and predictors of inappropriate antibiotic use in the pediatric ward of Jimma University Teaching Hospital, Jimma, south-west Ethiopia, 2014.

3.2 Specific Objectives:

- To determine the magnitude and pattern of antibiotic use among pediatrics patients in JUTH, south-west Ethiopia
- To determine level of inappropriate antibiotic use in pediatrics ward of JUTH
- To identify predictors of inappropriate antibiotic use in JUTH

4 METHODS AND PARTICIPANTS

4.1 Study area and Period

This study was conducted by reviewing selected sample files of patients admitted to the pediatric ward of Jimma University Teaching Hospital (JUTH) during the period February 2012 and January 2014. JUTH is a teaching hospital located in Jimma town, Oromia Region, south west Ethiopia, 336 km from Addis Ababa. It is the only teaching hospital in South west part of Ethiopia, with 558 health professionals, administrative and supporting staff, and 450 beds where a multi-disciplinary team of diverse professionals provides a range of health services for approximately 9000 inpatients and 80,000 outpatients each year. [54].

It provides both medical and teaching services in different health and medical departments. According to the data obtained from the Human Resource Information Office of the hospital in January 2014. In addition the Hospital has nine departments' (wards): Surgical, Paediatrics, Genecology and obstetrics, Ophthalmology, psychiatry, Medical ward, anaesthesia, dentistry, radiology. The total number of children admitted to pediatric ward of JUTH is around 2000 annually. The study period was from March 20 up to April 20, 2014.

4.2 Study Design

A hospital based retrospective cross sectional study design was used.

4.3 Source of Population

All the records of pediatric patients, who were admitted to JUTH pediatric ward from February 2012 up to January 2014

4.4 Study/Sample Population

Patient records which were randomly selected out of files of pediatric patients admitted to JUTH from February 2012 to January 2014 and which fulfills the inclusion criteria**.**

4.5 Inclusion and Exclusion Criteria

4.5.1 Inclusion Criteria:-

- ☞ All the records of Paediatric patients who were admitted to JUTH pediatric ward from February 2012 to January 2014.

4.5.2 Exclusion criteria

- ☞ Who have no drug prescription
- ☞ Records who have no antibiotic prescription
- ☞ Based on the WHO criteria the following drugs were not be considered as antibiotics and therefore excluded from being considered as antibiotics. These are: Ant tuberculosis, antiretroviral dugs used for HIV, Ant leprosy drugs, Antifungal drugs, Ant amoebic and ant giardiasis drugs, antileishmaniasis drugs.
- ☞ Self-discharge
- ☞ Incomplete files
- ☞ Death

4.6 Sample Size Determination and Sampling technique

All the records of paediatric patients that were admitted to JUTH from February 2012 to January 2014 were enrolled in the sample drawing. Computer method sample drawing was used to select the sample. According to the RPM/SPS manual Sample Size for a retrospective study conducted in one hospital should be at least 100 or more considering all the cards were complete [7]. But, Considering the Gyssens et al. criteria that was used to assess antibiotic use, the incompleteness and missing of patient fillies in the pre-test; estimating a population proportion with specified relative precision was done

$$n = \frac{Z^2_{1-\alpha/2} P(1-P)}{d^2} \quad \ldots\ldots [55]$$

Where:-

- Confidence level (%), 1-α = 95% =1.96
- Population proportion P= 0.58……...[22]
- Marginal error=0.04
- Sample size, n = 585
- Additional in complete and missing files will be 5%, = 29
- Sample size considering missing and incomplete files was = 585+29=614

4.6.1 *Sampling Technique*:

Simple random sampling technique was used for selection of study participants and data collection technique. Since the total number of pediatric patients admitted to JUTH during the study period (from February 2012 up to January 2014) was 4121. The data was entered in to SPSS and ordered to select 614 numbers randomly.

4.7 Variables in the Study

4.7.1 Dependent variables

Antibiotic use (appropriate, inappropriate)

4.7.2 Independent variables

- **Socio-demographic factors**
  - ✓ Age
  - ✓ Sex
  - ✓ Area of residence
- **Patient related factors**
  - ✓ Duration of hospital stay
  - ✓ Recent history of antibiotic use
  - ✓ Invasive devises used

- ***Disease related factors***
  - ✓ Diagnosis
  - ✓ Comorbidity
  - ✓ Surgical procedures done
- ***Prescribing related factors***
  - ✓ Purpose of prescription
  - ✓ Number of antibiotics prescribed per encounter

4.8 Data Collection Procedures

A total of 4121 patient records of those who were admitted to the paediatric ward of JUTH from February 2012 up to January 2014 were identified. The hospital discharge numbers for these patient records were used to access the patient records in the hospital's records department. A data extraction tool (Annex I-III) was completed for each sampled patient record. The data captured included:

- **Patient Information**: information on admission, date of admission and discharge, the referral source, age, gender, weight, invasive devices, underlying diseases, diagnoses include problems on admission and complications, surgical procedures performed during the stay in the paediatric ward of JUTH and the outcome were recorded.
- **Drug Information:** antibiotics initiated before admission to the paediatric ward of JUTH, antibiotic use during admission to JUTH (including where antibiotic therapy was stopped and changed), duration of each antibiotic used, route of administration of antibiotics, antibiotics used, drug allergies and concurrent medicine used were recorded.

The availability of the information recorded on the datasheet and missing records was proven by undertaking a pilot study of ten patient records, i.e. ten files from February 2012 to January 2014. The establishment of drug and therapeutics committee, existence of standard treatment guidelines and existence of formulary list and/or essential drug list was explored by asking JUTH pharmacy department head using manual developed by the Rational Pharmaceutical Management Plus (RPM Plus) Program of Management Sciences for Health and revised by the Strengthening Pharmaceutical Systems (SPS) Program check lists [7].

Three hospital pharmacists were selected for the data collection position and one pharmacist for supervision position. They were trained for 2 days on how to collect the data and use the instruments and were recruited based up on their availability and their interest to be involved in the study. Both the data collectors and supervisors were trained through the provision of a detailed explanation on how to complete the standardized tool. That was done using sample cards of patients which was not included in the study period and sample. The supervisor was a pharmacist who works on the pediatric ward of JUTH and had supervised the data collectors in daily bases.

Additionally, the principal investigator had worked and observed the data collection process and communicated with the supervisor and data collectors as frequent as possible and worked closely with these personnel until they had finalized their assignments.

Pretested structured data extraction tools were used to extract data from the selected patient files and each data were assed using the manual developed under the Rational Pharmaceutical Management Plus (RPM Plus) Program of Management Sciences for Health and revised under the Strengthening Pharmaceutical Systems (SPS) Program [7] and the appropriateness of

antibiotic therapy was assessed using a standardized checklist developed by Gyssens et al. The following classifications are used: correct decision, incorrect decision, incorrect choice, incorrect use, or insufficient data. The tool used to assess appropriateness of antibiotic use was pediatric hospital care: Ethiopian (Democratic Republic of Ethiopia
Ministry of Health, World Health Organization**.** Guidelines for the Management of Common Illnesses in Hospitals. First Edition, 2010) [56]. Whenever, the national guideline did not address specific diagnosis, pediatrics standard books [57-61] was used to categorize treatments as appropriate and inappropriate.

4.9 Data Processing and Analysis

The collected data were checked for completeness, entered into a computer using Epi-Data version 3.1 and Exported into SPSS version- 20 statistical software for analysis. A descriptive analysis was conducted to check for outliers, consistencies and to identify missed values for independent variables. Bivariate logistic regression analysis was employed to see the crude association between each exposure versus outcome variables. To control the effect of confounding factors or to get independently associated factors, each variables that were statistically significant at p –value <0.25 in bivariate analysis was entered in to backward stepwise multiple logistic regression model as the independent variables and antibiotic use being a dependent variable. Odds ratio with its 95% CI was calculated and $P < 0.05$ was considered as statistically significant for all the independent variables in the final model. The antibiotic use indicators: prescribing indicators, patient care indicators and hospital indicators were assessed using the given formulas.

4.10 Data Quality Management

The availability of the information recorded on the datasheet was proven by undertaking a pilot study of patient records. Ten files of patients who were admitted during the period February 2012 and January 2014 were taken and necessary modifications made on the instrument. Patient files involved in the pre-test were excluded in the actual study analysis. The collected data were compiled daily before the next day of data collection.

4.11 Ethical Consideration

The proposal of this thesis was approved by ethical clearance committee of College of Public Health and Medical Sciences of JU, JU Institution Review Board (IRB) prior to the start of data collection. Permission was taken from clinical director JUTH.

4.12 Dissemination Plan

The result of this study will be presented and submitted to Jimma University, College of Public Health and Medical Sciences, post graduate school as part of MSc partial fulfillment. The final report will be communicated through Local and international organizations, through formal presentation of the findings at the appropriate conferences, meetings, seminars, workshops; and by publishing the result in a scientific journal.

4.13 Limitations of the Study

Comprehensive data of all the factors that affect antibiotic use and its information were not included because of nature of the study design. We couldn't determine whether such factors local antibiotic resistance may have affected the physician's choice of a second- or third-line antibiotic. Beside this, incompleteness and missing of records. Relative small sample size was the other limitation.

4.14 Operational Definitions

Antibiotic: include all antimicrobial agents excluding anti-tuberculosis, all antiviral dugs, anti-leprosy drugs, antifungal drugs, anti-amoebic and anti-giardiasis drugs, anti-leishmaniasis drugs.
An antibiotic course is defined as an episode in which one or more antibiotic agents were prescribed, either consecutively or in combination for prophylaxis or to treat a suspected or documented infection that labelled as ***appropriate*** or ***inappropriate*** use.

Appropriateness of the Therapy: right medication, right patient, right dose, right frequency for the right duration of treatment.

Inappropriate antibiotic use: Inappropriate prescribing includes use of antibiotics without proof of infection or to treat viral infections or noninfectious diarrhea. The wrong medicine may be prescribed or taken for a particular infection or, if the correct medicine is used, it may be prescribed or taken at the wrong dosage or by an inappropriate route of administration. Perhaps the greatest misuse of antibiotics is failing to follow the indicated full course of therapy.

Assessment: A systematic review and appraisal of the patient's drug-related needs
Combination antibiotics: Two or more antibiotics that are prescribed for a given health condition.

Co-morbidity: This refers to the disease which had occurred with diagnosis during the time of admission and which doesn't require antibiotic treatment as per the guide lines used.

Diagnosis: the disease Identified by the practicing physician by considering the patient's signs and symptoms, history, laboratory findings, and physical examination and that require antibiotic use as per the guide lines used.

Dosage: The total amount of antibiotic that a patient takes during his/her hospital stay and discharge. It includes the dose of the antibiotic, the method of administration, the frequency, and the duration of treatment.

Dose: The amount of antibiotic administered to the patient as a single event

Dosing interval: Frequency of doses over a 24 hours

Effectiveness of antibiotic therapy: Ability of the antibiotic therapy to produce the desired or intended beneficial result (outcome) in a specific patient.

Formulary: A list of medicines approved for use in the health care system by authorized body.

Hospitalizations: This is defined as a ≥24 hour's admission to an inpatient hospital ward and are captured among both discharged patients.

Incomplete records: if the patients' medical record had missed parts like duration of treatment, dose, frequency etc.

Medication history: A record of past uses of medications and preventive pharmacotherapies. Includes prescription medications, alternative therapies, and nutritional supplements.

Patient: An individual who is admitted to pediatric ward of JUSU and receives or requires health care services.

Pediatrics: are neonates, infants, children, and adolescents who are aged <=14.

Prophylactic antibiotic use: is defined as antibiotic is initiated when (1) the patient had no evidence of infection and the patient was immunocompromised, had an anatomical defect, had recurrent infections, or had an indwelling device or (2) the patient was scheduled for a surgical procedure and antibiotic was given to prevent surgical site infections, but not for a neonate who had an infectious abscess.

Reason for admission: Refers to the diagnosis given to the illness of the patient by the physician when the patient is admitted.

Therapeutic use of antibiotic: is defined as antibiotic is initiated when there is a known identified infection by the practicing physician.

5 RESULTS

Characteristics of Study Participants

A total of 4121 patients were admitted to pediatric ward of JUTH between February 2012 and January 2014 and 614 patient's files were selected randomly. Of which 143 files were missed/ incomplete. Therefore, 471 files were assessed. Most of the participants were males (58.81%), and rural residents (57.11%). Table-1

Summary of study participants

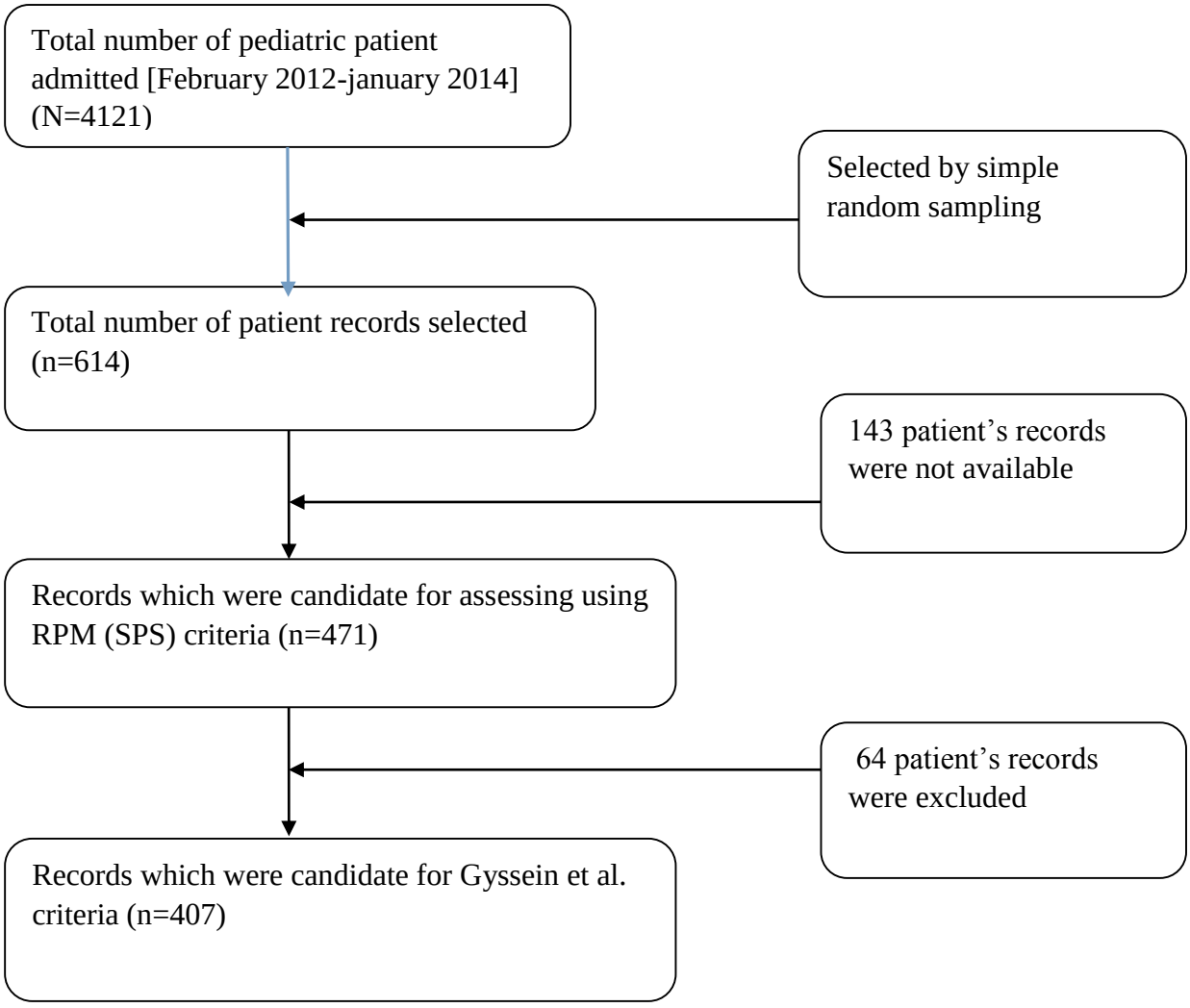

Figure 2: Summary of study participant's flow chart for pediatric patients admitted at JUTH pediatric ward, from February 2012 - January 2014

Pattern of Antibiotic use

The mean age of the study participants was 2.74±3.43 years and majority of them were toddlers and pre-school children accounting (35.46%) followed by infants (33.33%), children and adolescents (18.68%) and neonates (12.53%). The median duration of hospitalization was five days (with IQR =8.2 days) and the maximum duration of hospital stay was 58 days. The majority of patients, 207 (50.90%), were hospitalized for duration of less than or equal to five days.

Pattern of antibiotics use

A total of 1241 (90.18%) parenteral medicines were prescribed followed by oral 110 (8%). The maximum number of drugs per prescription was 8 while the maximum number of antibiotic prescribed per-prescription was 5. The maximum number of injectables prescribed per prescription was 6 while the maximum number of generics prescribed per prescription was 8. The median number of drugs prescribed per-prescription was 3 (IQR=7). One hundred sixty six (12.06%) of the total drugs prescribed were mono drug prescriptions; from which 131(16.13%) of the total prescribed antibiotics were prescribed as single antibiotic prescriptions and the rest 35(6.21%) were non antibiotic single drug prescriptions. (Table: 2)

Table 1: characteristics of study participants who were on antibiotics use Feb 2012-jan 2014

Patient Characteristics		Frequency	Percent
Sex	Female	175	43.0
	Male	232	57.0
	Total	407	100.0
Age	0-27 days	56	13.8
	1month- 1year	137	33.7
	>1yr-5yrs	144	35.4
	>5yrs-14yrs	70	17.2
	Total	407	100
Place of residence	Urban	169	41.5
	Rural	238	58.5
	Total	407	100
Diagnosis	1	270	68.2
	≥2	126	31.8
	Total	396	100.0
Duration of hospital stay (days)	≤5	207	50.9
	>5-10	86	21.1
	>10	114	28.0
	Total	407	100
Co-morbidity	No	202	49.6
	yes	205	50.4
	total	407	100.0
Purpose of antibiotic order	therapy	364	89.43
	prophylaxis	26	6.39
	Prophylaxis + therapy	5	1.23
	Unknown ant. use	12	2.95
	Total	407	100
Antibiotics ordered per encounter	1 antibiotic	131	32.2
	≥2 antibiotics	276	67.8
	Total	407	100.0
Surgical procedure done	yes	48	11.8
	no	359	88.2
	total	407	100
other medications concomitantly used	no	171	42.0
	yes	236	58.0
	total	407	100.0
Chief compliant	cough	127	31.2
	vomiting	47	11.5
	diarrhea	31	7.6
	fever	45	11.1
	swelling	82	20.1
	SOB & others	75	18.4
	total	407	100

Prescribing and Patient Care Indicators

Of the total patient files assessed (471), antibiotics were prescribed for 407(86.41%) and from this 232(57.00%) were males. Majority of patients, 276 (67.8%), had received more than one antibiotic per encounter.

Percentage of hospitalizations with one or more antibiotics prescribed was 86.41% and the average number of antibiotics prescribed per hospitalized patient in which antibiotics were prescribed was 2. The percentage of patients with pneumonia who are prescribed antibiotic in accordance with standard treatment guidelines was 82.14%, percentage of antibiotics prescribed by generic name 98.64%, and average duration of hospital stay of patients who receive antibiotics were 8 days with min 2 and max 58 days. In addition, the average duration of prescribed antibiotic treatment was 7 days with minimum 1 day and maximum 43 days.

Antibiotics prescribed from EDL was (95.75%). The maximum number of antibiotics prescribed from EDL per prescription was 5. The mean number of antibiotics prescribed per-prescription was 2.00$\pm$0.91. The mean number of antibiotic injections prescribed per-prescription was 1.6904$\pm$1.08391. The mean number of antibiotics prescribed by generic name per-prescription was also 1.9705$\pm$0.93330. The mean of antibiotics prescribed from EDL of Ethiopia is 1.75$\pm$0.83. The drug and antibiotic utilization pattern of the study population during the retrospective period is presented in (table-2).

Table 2: Frequency of all Drugs, Antibiotics only, Injectables and Generics among Pediatric Subjects Admitted to Pediatric Ward of JUTH b/n Feb 2012 and Jan 2014

Number per encounter	**All Drugs**		**Antibiotics**		**Injectable antibiotics prescribed**		**Antibiotics prescribed by Generic name**	
	count	%	Count	%	count	%	Count	%
1	135	28.66	131	32.19	163	40.85	120	30.30
2	80	16.98	181	44.47	176	44.11	181	45.71
3	71	15.07	65	15.97	57	14.29	65	16.42
4	79	16.77	26	6.39	3	0.75	26	6.56
5	87	18.47	4	0.98	0	0.00	4	1.01
>6	19	4.03	---	---	---	---	---	---
Total	471	100	407	100.00	399	100.00	396	100.00

A total of 812 antibiotics were prescribed for the 407 patients; and 721(88.79%) were for therapy, 70 (8.62%) for prophylaxis, and 21 (2.59%) were for patients with no known infection. Among the 407 patients, 131 (32.19%) cases were prescribed one antibiotic, 181 (44.47%) cases two types of antibiotics, and 95 (23.34%) cases three or more types of antibiotics during their hospital stay. Three patients had a history of antibiotic use in the last three months before their admission. One patient was found to be sensitive to cloxacillin.

Hospital Care and Supplemental Indicators

As to the WHO hospital indicators there was an already established drug and therapeutics committee but it is in active. In addition, there was no STGs, drug formulary or essential drug list exist. All antibiotics were prescribed without any microbiological evidence.

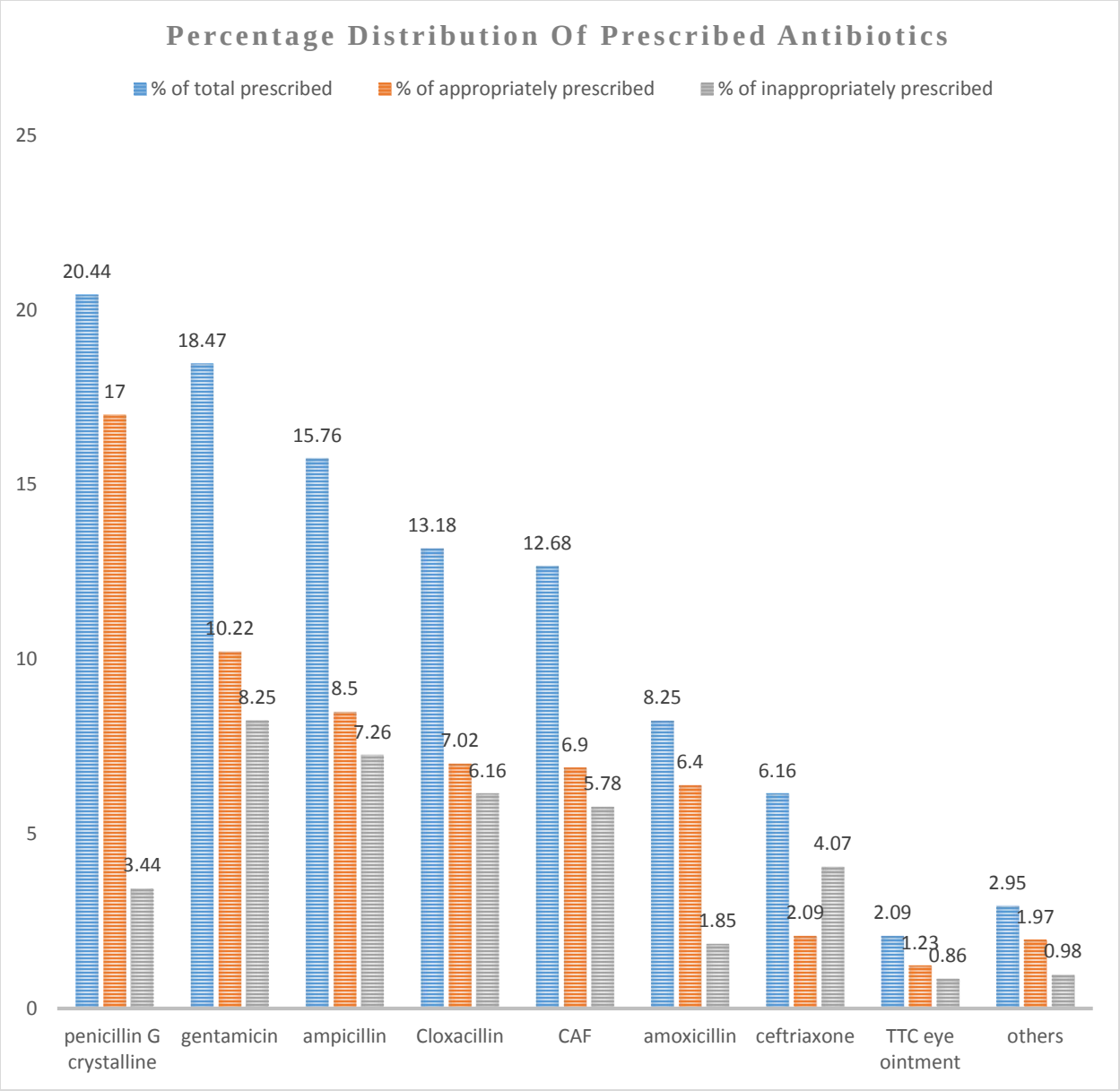

Figure 3: The percentage and characteristics of prescribed Antibiotics in Pediatric Ward of JUTH b/n Feb 2012/Jan 2014.

From the total of 812 antibiotics prescribed; penicillin G crystalline was the most frequently prescribed 166 (20.44%), followed by gentamicin 150 (18.47%), ampicillin 128(15.76%), Cloxacillin 107(13.18%) and chloramphenicol 103 (12.68%). (Figure: 1) Out of the total prescribed antibiotics, 698(85.96%) were injectables, 97(11.95%) were oral formulations, and 17 (2.09%) were topical formulations. Eight hundred and one (98.6%4) were prescribed in generics and 11(1.36%) were in brand.

The Percentage of antibiotics prescription was higher in Toddlers and pre-school children [1-5 years] 286(35.22%). But, considering hospital admissions rates there was high use of antibiotic in neonates [27 days] and infants [1month-1year] with 94.92%. The mean of antibiotics prescriptions in neonates was relatively higher (2.32; 95% C.I b/n 2.12-2.51±0.72) compared to other age groups. (Table 3)

Table 3: Characteristics of antibiotic used among different age groups admitted to Pediatric Ward of JUTH b/n Feb 2012 and Jan 2014.

Age category	**Number who received antibiotics**	**Number of antibiotic prescriptions among patients who received antibiotics (mean per patient and 95% CI)**	**median duration of antibiotic therapy in days [interquartile range, IQR]**
<1 month	56 (13.80)	2.32 (2.12- 2.51±0.72)	9.50 (13.75)
1month - 1 year	137 (33.70)	1.90 (1.74-2.06±0.94)	4.00 (6.00)
>1year - 5 years	144 (35.40)	1.99 (1.83-2.14±0.95)	5.00 (9.00)
>5 years	70 (17.20)	1.96 (1.76-2.16±0.84)	7.00 (9.00)
All	407	2.00 (1.91-2.09±0.91)	5.00 (9.00)

Of the total prescriptions which had multiple antibiotics prescribed concomitantly (259), the combination of 'Ampicillin and Gentamicin' took the largest portion with 79 (30.50%) followed by 'Chloramphenicol and Cloxacillin 50 (19.30%), Ceftriaxone and gentamicin 29 (11.20%), and 'Ampicillin, Cloxacillin and Gentamicin' 28 0.81%). (Table: 4)

Table 4: The Frequency and Percentage of Multiple Antibiotic prescriptions in Pediatric Ward of JUTH, from Feb 2012- Jan 2014 Year.

S.No	Antibiotics	Frequency	Percent
1	Ampicillin + Gentamicin	79	30.50
2	Chloramphenicol + Cloxacillin	50	19.30
3	Gentamicin + Ceftriaxone	29	11.20
4	Cloxacillin + Ampicillin + Gentamicin	28	10.81
5	Chloramphenicol + Crystalline penicillin G	18	6.95
6	Chloramphenicol + Ampicillin + Gentamicin	10	3.86
7	Cloxacillin + Ceftriaxone + gentamicin	8	3.09
8	CAF + Cloxacillin +Crystalline Penicillin G	8	3.09
9	Crystalline Penicillin G + Gentamicin	5	1.93
10	Chloramphenicol + Ceftriaxone + Gentamicin	3	1.16
11	CAF+ Cloxacillin + Cry. Penicillin G + Gentamicin	3	1.16
12	CAF + Cloxacillin + Ceftriaxone	3	1.16
13	Cloxacillin + Gentamicin	2	0.77
14	CAF + Cry. Penicillin G +TTC eye ointment	2	0.77
15	CAF + Cloxacillin + TTC eye ointment	2	0.77
16	Amoxicillin + TTC eye ointment	2	0.77
17	CAF + Cloxacillin + Gentamicin + Ampicillin + TTC ointment	2	0.77
18	Cloxacillin + Crystalline Penicillin G	1	0.39
19	Ampicillin + Gentamicin + TTC eye ointment	1	0.39
20	CAF + Cry. penicillin G + Gentamicin	1	0.39
21	Ampicillin + Gentamicin + TTC eye ointment	1	0.39
22	Crystalline Penicillin G + TTC eye ointment	1	0.39

Reason for antibiotic prescription

Antibiotics were prescribed to treat infections in 363 cases (98.20%), 26 (6.40%) for prophylaxis, 12 (2.90%) for therapy + prophylaxis, and 6 (1.50%) were unknown.

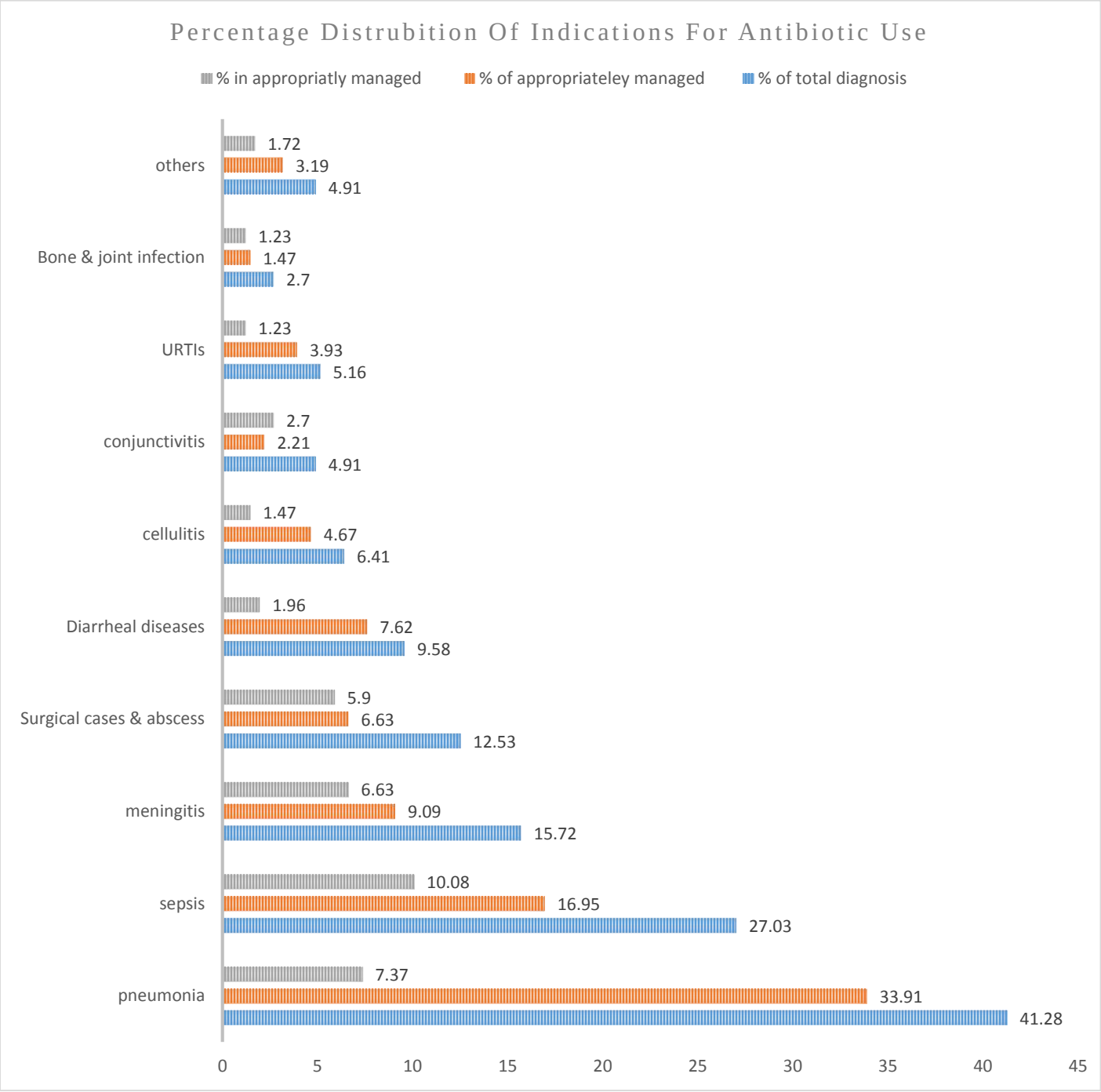

Figure 4: The percentage and characteristics of reasons for antibiotic use in Pediatric Ward of JUTH b/n Feb 2012/Jan 2014 Years

Reasons for antibiotics prescription (diagnosis): pneumonia was the most frequent (n = 168, 31.76%) followed by sepsis (n = 110, 20.79%) **(figure2)**. About 202 (49.6%) of patients did not have co-morbid illness, whereas 205 (50.4 %) patients had one or more co-morbidity while they were admitted. About 381 (93.61%) of patients have had IV line.

Appropriateness of Antibiotic Therapy and Prophylaxis

A total of 126 (30.96%) patients were deemed to be used antibiotics inappropriately. More specifically: in 51 patients (40.5%) incorrect application, in 50 patients (39.7%) an incorrect choice was made, in 16 patients (12.7%) was unjustified use (could not be judged because of insufficient information), in 5 patients (4.0%) antibiotic use was not indicated, and in 4 patients (3.2%) divergence from guidelines. (Table 5)

Table 5: Antibiotics used among pediatric patients admitted to JUTH from Feb 2012-jan 2014

Antibiotic Characteristics		Frequency	Percent
Purpose of prescription	therapy	722	88.9
	prophylaxis	70	8.6
	unknown	20	2.5
	total	812	100
Antibiotic use	appropriate	281	69.0
	inappropriate	126	31.0
	total	407	100
Type of in appropriate use	indication	5	4.0
	choice	50	39.7
	Application	51	40.5
	Divergence from guide line	4	3.2
	Insufficient data	16	12.7
	total	126	100.0
Reasons for inappropriate use	Does not need antibiotic use	4	3.2
	Too broad spectrum	13	10.5
	Too narrow spectrum	19	15.3
	Entirely wrong	17	13.7
	Inappropriate toxicity profile	1	0.8
	Inappropriate dosing	21	16.9
	Inappropriate timing	3	2.4
	Inappropriate duration	27	21.8
	unclassified	21	15.3
	total	124	100.0

Prophylaxes were more frequently inappropriate than therapies (42.31% versus27.47 %). In the various age groups there were remarkable differences in the patterns of inappropriate prescribing. An incorrect prescription of antibiotics for prophylaxis was found in 30 (42.86%) antibiotics prescribed per encounter; 11 (36.67%) antibiotic ordered did not cover the antibiotic spectrum to be expected, 16(53.33%) inappropriate application, and 3 (10.0%) divergence from local guide lines. (Table 6)

Table 6: prevalence of inappropriate antibiotic use among pediatric admitted to JUTH between Feb 2012- Jan 2014

Patient characteristics		IA use (%)	AP use (%)
Sex	Female	52 (41.27)	123 (43.77)
	Male	74 (58.73)	158 (56.23)
Age	<1 month	23 (18.25)	33 (11.74)
	1month- 1year	33 (26.19)	104 (37.01)
	>1yr-5yrs	36 (28.57)	108 (38.43)
	>5yrs-14yrs	34 (26.98)	36 (12.81)
Place of residence	Urban	43 (34.13)	126 (44.84)
	Rural	83 (65.87)	155 (55.16)
Diagnosis	1	72 (57.14)	198 (70.46)
	≥2	43 34.13)	83 (29.54)
Duration of hospital stay (days)	≤5	40 (31.75)	167 (59.43)
	>5-10	28 (22.22)	58 (20.64)
	>10	58 (46.03)	56 (19.93)
Co-morbidity	No	57 (45.24)	145 (51.60)
	yes	69 (54.76)	136 (48.40)
Purpose of antibiotic order	therapy	101 (80.16)	264 (93.95)
	prophylaxis	11 (8.73)	15 (5.34)
	Prop + therapeutic	3 (2.38)	2 (0.71)
	Unknown ant. use	11 (8.73)	0 (0.00)
Surgical procedure done	yes	22 (17.46)	26 (9.25)
	No	104 (82.54)	255 (90.75)
Antibiotics ordered/encounter	1	19 (15.08)	112 (39.86)
	≥2	107 (84.92)	169 (60.14)
medications concomitantly used	No	55 (43.65)	116 (41.28)
	yes	71 (56.35)	165 (58.72)
Chief compliant	cough	28 (22.22)	99 (35.23)
	vomiting	16 (12.70)	31 (11.03)
	diarrhea	10 (7.94)	21 (7.47)
	fever	10 (7.94)	35 (12.46)
	swelling	35 (27.78)	47 (16.73)
	SOB & others	27 (21.43)	48 (17.08)

IA- Inappropriate AP- Appropriate

Result of bivariable logistic regression analysis of inappropriate antibiotic use among pediatric patients admitted to JUTH from February 2012 to January 2014

In the bivariable analysis, the socio-demographic characteristics: age and place of residence were statistically significantly associated with more frequent inappropriate use of antibiotics. As a result they are candidates for the multivariable model (Table 7).

Table 7: Result of bivariable logistic regression analysis of socio-demographic characteristics' for inappropriate antibiotic use among pediatric patients admitted to JUTH from February 2012 to January 2014

Socio-demographic Characteristic		**IA use (%)**	**AP use (%)**	**COR[95% CI]**	**p-value**
Sex	Female	52 (41.27)	123 (43.77)	1	
	Male	74 (58.73)	158 (56.23)	0.905 (0.58-1.41)	0.637
Age	<1 month	23 (18.25)	33 (11.74)	2.09 (1.09-4.02)	0.027
	1month-1year	33 (26.19)	104 (37.01)	0.95 (0.55-1.64)	0.859
	>1yr-5yrs	36 (28.57)	108 (38.43)	1	
	>5yrs-14yrs	34 (26.98)	36 (12.81)	2.83 (1.55-5.17)	0.001
Place of residence	Urban	43 (34.13)	126 (44.84)	1	
	Rural	83 (65.87)	155 (55.16)	1.57 (1.01-2.43)	0.043

IA-Inappropriate, AP- Appropriate, COR- crude odds ratio, P- p value, 1-Reference

The use of antibiotics based on different clinical characteristics of the patient in the bivariate logistic regression analysis: diagnosis per encounter, duration of hospital stay (days), co-morbidity, surgical procedure done, antibiotics used per encounter, purpose of antibiotic order, other medications used concomitantly, and chief compliant were proved to be statistically significantly associated with more frequent inappropriate use. (Table 8). The overall model to predict the association of inappropriate antibiotic was found as fit.

Table 8: Result of bivariable logistic regression analysis of clinical characteris' for inappropriate antibiotic use in among pediatric patients admitted to JUTH from February 2012 to January 2014

Clinical Characteristics		**IA use (%)**	**AP use (%)**	**COR (95% CI)**	**p-value**
Diagnosis	1	72 (57.14)	198 (70.46)	1	
	≥2	43 (34.13)	83 (29.54)	1.42 (0.90-2.25)	0.129
Duration of hospital	≤5	40 (31.75)	167 (59.43)	1	
stay	>5-10	28 (22.22)	58 (20.64)	2.02 (1.14-3.56)	0.016
	>10	58 (46.03)	56 (19.93)	4.32 (2.61-7.16)	0.000
Co-morbidity	No	57 (45.24)	145 (51.60)	1	
	Yes	69 (54.76)	136 (48.40)	1.29 (0.85-1.97)	0.236
Surgical procedure	Yes	22 (17.46)	26 (9.25)	2.08 (1.12-3.82)	0.019
done	N0	104 (82.54	255 (90.75)	1	
Purpose of antibiotic	therapy	100 (79.37)	264 (93.95)	1	
order	Prophylaxis	14 (11.11)	17 (6.05)	2.17 (1.03-4.57)	0.043
	and other				
Antibiotics per	1	19 (15.08)	112 (39.86)	1	
encounter	≥2	107 (84.92)	169 (60.14)	3.73 (2.17-6.42)	0.000
medications	No	55 (43.65)	116 (41.28)	1	
concomitantly used	Yes	71 (56.35)	165 (58.72)	0.91(0.59-1.39)	0.654
Chief compliant	Cough	28 (22.22)	99 (35.23)	1	
	vomiting	16 (12.70)	31 (11.03)	1.82 (0.87-3.80)	0.109
	diarrhea	10 (7.94)	21 (7.47)	1.68 (0.71-3.99)	0.236
	Fever	10 (7.94)	35 (12.46)	1.01 (0.452.29)	0.981
	swelling	35 (27.78)	47 (16.73)	2.63 (1.44-4.83)	0.002
	Others	27 (21.43)	48 (17.08)	1.99 (1.06-3.74)	0.033

IA-Inappropriate, AP- Appropriate, COR- crude odds ratio, P- p value, 1-reference

Result of multi-variable logistic regression analysis

The multivariable analysis shows that; age, duration of hospital stay (days), and number of antibiotics used were statistically significant independent factors associated with inappropriate antibiotics use.

The odds of inappropriate antibiotics use was 2.4 times more likely in >5 years- 14 years (children and adolescents) age group than 1year -5 years age group [AOR=2.40, (CI=1.17-4.91), P=0.016*]. On the other hand, the probability of inappropriate antibiotic use was not statistically significant in the age groups of <1 month [AOR=1.74 (CI=0.77-3.95) P=0.182] and 1 month- 1 year [AOR=1.23 (CI=0.64-2.35) P=0.527].

The odds of inappropriate antibiotics use among patients with at least 10 days of hospital stay was about three times more likely to use antibiotics in appropriately than those who stayed for a maximum of five days [AOR=3.06 (CI=1.70-5.53)P=0.000*]. However, there was no statistically significant difference in the probability of inappropriate antibiotic use in patients who stayed for a maximum five days and those who stayed >5 days-10 days [AOR=1.14 (CI=0.58-2.23) P=0.700]. Similarly, the odds of inappropriate antibiotic use among patients who received at least two antibiotics during their hospital stay had probability of inappropriate antibiotic use 3.5 times more likely than those who had received one antibiotic [AOR=3.50 (CI=1.77-6.93) P=.000*]. (Table: 9)

Table 9: Result of multi-variable logistic regression of inappropriate antibiotic use among pediatric patients admitted to JUTH between Feb 2004 to Jan 2006 E.C (n=407)

Independent predictor variables		**IA use (%)**	**AP use (%)**	**AOR (95%CI)**	**P-value**
Age	<1 month	23	33	1.74 (0.77-3.95)	0.182
	1month- 1year	33	104	1.23 (0.64-2.35)	0.527
	>1yr-5yrs	36	108	1	
	>5yrs-14yrs	34	36	2.40 (1.17-4.91)	0.016*
Duration of hospital stay (days)	≤5	40	167	1	
	>5-10	28	58	1.14 (0.58-2.23)	0.700
	>10	58	56	3.06 (1.70-5.53)	0.001*
Antibiotics per encounter	1	19	112	1	
	>2	107	169	3.50 (1.77-6.93)	0.001*

IA-Inappropriate, AP- Appropriate, AOR- Adjusted odds ratio, P- p value, 1-reference

6 DISCUSSION

The inappropriate use of antimicrobials and the emerging problem of AMR require worldwide attention and urgent and intense actions. The use of antibiotics has greatly contributed to the decline in morbidity and mortality caused by infectious diseases, but these advances in treatment are being undermined by the rapidly increasing problems of AMR. Their inappropriate use leads to a number of consequences in term of cost, drug interactions, hospital stay and bacterial resistance. In this study, it was found that there was higher pattern of antibiotic prescription. [7]

One of the commonly used tools in assessing rational antibiotic prescribing is the antimicrobial use indicators and the data were analyzed accordingly [7].The review of different indicators in this retrospective study showed that percentage of hospitalizations with one or more antibiotics prescribed was 86.41%. This result is more or less in line with the works of other researchers from USA (92.40%) [31], China (93.90%) [42], Nepal (93.00%), Botswana, (92%) [44].

But, the above finding was not in agreement with studies done in Italy (43.9%) [29], India (41.99%) [32], Indonesia (50.0%) [34], Trinidad (36.4%) [36], KSA (39.2%) [40], which is significantly higher. This might be due to the absence of culture proven sensitivity results, relatively smaller sample size in this study as well as the poor implementation of antibiotic restriction policy in Ethiopia and unavailability of infectious disease guide lines contributes greatly to the high rate of antibiotic usage.

Similarly, when the above result was compared to other studies done in different African countries and different parts of Ethiopia: it was again higher than two teaching hospitals in Sudan (65%) [44], Uganda (61.9%) [44], as well as that of Harari region hospitals, Mizan hospital, and a national average of Ethiopia, Mekelle referral hospital (57.0%, 64%, 58%, and 36.7%) [45-47]. This may be due to the involvement of both outpatient, inpatient and/or the whole hospital in the other studies and the smaller sample size in this study relative to the studies.

Of all antibiotics prescribed 85.96%% were injectable antibiotics. This result is higher compared to the study done in Palestine (61.8%) [41]. But, in agreement with the studies done in Kathmandu Valley, Nepal (75%) [35] and Mekelle general hospital (93.6%) [48].

Average duration hospital stay for those patients who were on antibiotics were (7 days) which is consistent with the studies done in at the San Fernando General Hospital, southern part of Trinidad (6.71 days) [36], but not in agreement with the studies reported from USA (4 days) [31]. This could be as this study involves those who are admitted to both intensive care units and general pediatric wards, but the study done in USA involves only those who were admitted to PICU.

The percentage of antibiotics prescribed from EDL was (95.75%), which is promising according to the Ethiopian health policy which expects 100 % of the prescribed drugs to be included in the Essential Drug List. On the other hand, this is in agreement with the study reported from Botswana (92%) [43]. But the result was higher compared to the study conducted in Saudi Arabia (35.6%) [40], Italy (43.9%) [29], Indonesia (50%) [34] and Nepal (43.95%) [35].

The mean number of antibiotics prescribed per-prescription was 2.00±-0.91. This is higher than the study reported in Mekelle general hospital, Mekelle, Ethiopia, 1.18±0.813 [48]. This study involves pediatric patients only those who were admitted, who were critically ill and need more combination antibiotics and other additional medications. It is comparable to the one reported in Nepal 2.81 [49]. This is more or less consistent with the WHO recommendation, that antimicrobial drugs per hospitalization should be less than or equal to two. But, this is much lower result compared to the study reported from Kathmandu Valley, Nepal 5.01±1.36 [35].

The mean of antibiotics prescriptions in neonates was relatively higher compared to the other ages. This could be due to physician behavior in ordering medication in association with age, and variability in patient complaints. But, this is not in agreement when compared with the study conducted in USA (5.17) [31]. This is may be due to differences in diagnostic and clinical investigation factors, differences in sample size and the study conducted in USA involves only those patients who were admitted to pediatric intensive care unit.

In this study, there was an observed inappropriate antibiotic use (30.96%) differences compared to the study reported from Turkey (46.7%) [28], Israel 8% [38], but not from India (36.8%) [32]. This might be due to lack of sufficient diagnostic and laboratory equipment's, differences in technique and standards of care and the relatively smaller sample size.

In this study the use of antibiotic by age category was found to be significant (highest adjusted odds ratio in the age category >5yrs-14yrs AOR=2.40 (95% CI, 1.17-4.91), P<0.016*), which is similar to the findings in Mekelle, (Pearson Chi-Square P= 0.037) [48], in Italy (chi-square for trend: p=0.049) [29], and a multi-sited study conducted in Europe associated with age (highest adjusted odds ratio in the age category 1–4 years, p<0.001) [30]. This might be due to differences in Study duration and design and relatively smaller sample size and it needs further study.

Another variable that was found statistically significant in this study was, duration of hospital stay (highest in those who stayed > 10 days, AOR= 3.06 (95% CI= 1.70-5.53) p<0.001*) which is similar to the multi-sited study conducted in Europe, 2001 (p for trend<0.05) [30]. As length of hospital stay increases, there is a high chance of acquiring health care associated resistant microorganisms. Antibiotics per encounter**,** used during hospital admission was found statistically significant (with highest adjusted AOR in those who used >=2 antibiotics per encounter, AOR=3.50 (95% CI =1.77-6.93) P<0.001*). This may be because of the patient condition as critically ill patients are candidates for multiple antibiotics use.

However, this study was not without limitations. The presence of in complete records, nature of the study design and relatively small sample size were the limitations.

7 CONCLUSION AND RECOMMENDATIONS

7.1 Conclusion

The present study has established the presence of significant antibiotic and injectables use in Pediatric population compared to other similar studies. In addition, there was lower drug prescription from EDL. The Percentage of hospitalizations with one or more antibiotics prescribed was a considerable number. Of the total of antibiotics prescribed; penicillin G crystalline was the most frequently prescribed followed by gentamicin, ampicillin, Cloxacillin and chloramphenicol. Similarly, the prevalence of inappropriate antibiotics use was a considerable number. Inappropriate use of antibiotics was associated with being between age category of 5-14 years, >10 days duration of hospital stay, and using >= 2 antibiotics per encounter.

7.2 Recommendation

Based on the findings of the present work the following points are recommended:

- JUTH and JUTH pediatrics clinical staff need to give due emphasis on reducing inappropriate use of antibiotics. Therefore, developing effective interventions to reduce inappropriate antibiotic prescribing will require re-activation of drug and therapeutics committee, equip the hospital with necessary laboratory support microbiological tests, preparing standard treatment guide-lines, essential drug list and/or drug formulary and introducing antibiotic steward ship program in the hospital. This needs efforts from Jimma university teaching hospital and federal ministry of health of Ethiopia. In contrary, there was a promising generic prescribing and this needs to be continued.
- A larger scale prospective studies including sensitivity pattern: on hospital, health center, and community level to address inappropriateness and rationalize antibiotic use.
- Moreover, this study needs to be extended and repeated over time to maintain good quality health care in JUTH

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9 ANNEXES

9.1 Annex –I : Data Extraction Tools for the Quantitative Data

9.1.1 General information of the patient

Name of unit: _____ Data collector: _____ Date:_____

Subject/ study number		
Hospital registration number		
Age (yrs.)		
Sex		
Wt. (kg)		
Ht/length (cm)		
Place of residence		
Date of admission in a hospital		
Referred from		
Date of discharge from ward		
Discharge destination	Ward:	Home:

I. Diagnosis

1. chief compliant_____

   _____

2. Primary (diagnosis during admission)_____

   _____

3. Secondary (working diagnosis)_____

   _____

4. Type and site of infection _____

   _____

5. Underlying disease_____

   _____

6. Surgical procedures during stay in the hospital

   Procedure _____ Date:_____

7. Invasive devices

Endotracheal tube	
IV lines	
Urinary catheter	
Other catheter (type)	

8. Microbiology/laboratory

Date	Sample type/origin	Bacteria cultured	Sensitivity test results

9. Comorbidity: _____

II. Medication history

10. Antibiotics used before admission in ward and referred with

Antibiotic started (Name, strength, type, dose, frequency, rout, quantity)	Antibiotic class	Date		Indication
		Start	stop	
Other medications used during admission	Date			
Name of medicine	Stat	Stop		dose

6. Antibiotics used during admission

Antibiotic	Date		Dose	Frequency	Route	Evidence of therapy	Switched antibiotics? (Y/N)	If Y, Reason for switching antibiotic/s*					Purpose of antibiotic order*
	Start	stop						1	2	3	4	5	

* Purpose of order: 0. Curative 1. Prophylactic

*Evidence of therapy: empiric (with clinical S/S only) = 0, based on laboratory result =1*Antib. = antibioti

Antibiotic started	Antibiotic class	Date		Dose	Frequency	Rout	Indication
		Start	stop				

10. Other medications used during admission

Medication	Date		Dose
	Start	Stop	

9.2 Annex– II : Prescribing Indicator Form

Patient Care Indicators include the following data sources:

Average duration of hospital stay of patients who receive antibiotics

- The most frequent diseases treated with antibiotics
- Purpose of antibiotic therapy
    - Curative
    - Prophylaxis
- Average duration of prescribed antibiotic treatment
- Reason for antibiotics prescription
- Percentage of antibiotics prescribed by generic name

Prescribing indicators include the following data sources:

- Percentage of hospitalizations with one or more antimicrobials prescribed
- Antibiotic prescriptions by age group and gender
    - Distribution by age group
    - Distribution of Antibiotic encounters by gender
- Average number of antibiotics prescribed per hospitalization in which antibiotics were prescribed
- Percentage of Encounters with injectable antibiotics
- Percentage of antibiotics prescribed in generic
- Percentage antibiotics prescribed from the Essential Drug List and List of Ethiopia

1. Percentage of hospitalizations with one or more antibiotics Prescribed

$$= \frac{\text{Number of patient hospitalizations With one or more antibiotics prescribed}}{\text{Total number of hospitalizations studied}} \times 100$$

Percentage is calculated by dividing the number of patient hospitalizations during which one or more antibiotics are prescribed by the total number of hospitalizations studied and multiplying by 100**.**

2. Average number of antimicrobials prescribed per hospitalization in which antibiotic were prescribed

$$= \frac{\text{Number of antibiotics prescribed for all hospitalizations}}{\text{Total number of hospitalizations with antibiotics prescribed}}$$

The average is calculated by dividing the total number of antibiotics prescribed for all hospitalizations by the total number of hospitalizations studied in which antibiotics were prescribed. Different formulations of the same antibiotic should be counted as one.

3. Average duration of prescribed antibiotic treatment

$$= \frac{\text{Total number of days on antibiotic treatment}}{\text{Total number of antibiotics prescribed}}$$

The average duration is calculated by dividing the total number of days of antibiotics treatment by the total number of antibiotics prescribed. Different dosage forms of the same generic drug (i.e., ampicillin injection and ampicillin capsules) are counted as one.

4. Percentage of antibiotics prescribed by generic name

$$= \text{Total} \frac{\text{number of antibiotics prescribed by generic name}}{\text{Total number of antibiotics prescribed}} \times 100$$

5. Average duration of hospital stay of patients who receive antibiotics

$$= \text{Total} \frac{\text{number of days of hospitalization for patients receiving antibiotics}}{\text{Number of patients receiving antibiotics}}$$

Location: _____Data Collector: _____Date:_____

Table 3: Prescribing indicator form

Seq.#	Card #	Age (yr)	Sex (M/F)	# drugs	Antib (0/1)*	# Antib	Inject. (0/1)*	# inject.	# generics	Antib. sensitivity	Totaldaysof Rx	# on EDL	Diagnosis
		Total											
		Average											
		Percentage											

Footnotes: *0=No 1=yes = for PI only (not to be filled by data collector)

9.3 Annex – III Hospital Facility Data Collecting Questionnaire

Hospital indicators include the following data sources: -

- Existence of drug and therapeutics committee
- Existence of standard treatment guidelines (STGs) for infectious diseases
- Existence of an approved hospital formulary list or essential medicines list (EML

Instructions for Completing Instrument-V: Basic Information

This form is used for the following hospital indicators:

- ✓ Existence of standard treatment guidelines (STGs) for infectious diseases
- ✓ Existence of an approved hospital formulary list or essential medicines list (EML)

Name of unit: _____Data collector: _____

Date: _____

1. Does the hospital have a Drug and Therapeutics Committee?

➢ …….

2. If affirmative, when was the last meeting?

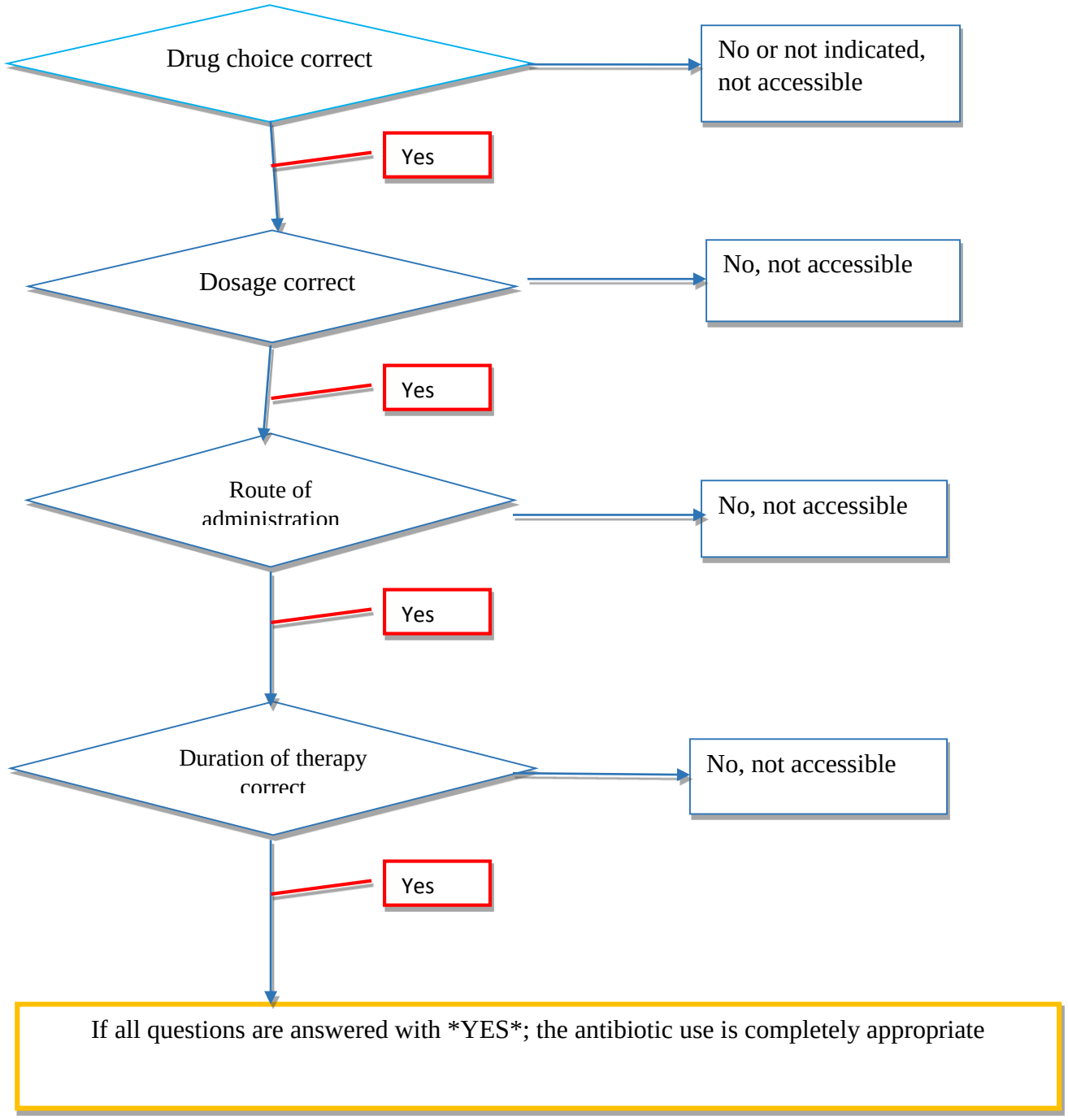
➢ …… [Review minutes, if any.]

3. Does the hospital have a formulary list or EML authorized for acquisition of medicines by the hospital?

➢ …….

4. Date of last revision of the formulary list or EML.....
5. If yes, how many antibiotics are on the formulary list or EML...? [Request a copy of the list.]
6. Are all of the medicines on the formulary list or EML identified by generic name (INN)...?
7. Are the formulary or EML medicines based on those recommended in the STG…?
8. Does the hospital have standard treatment guidelines for infectious diseases for the most prevalent conditions? ……..

Annex- IV. Data Assessment Tools **Description Action for the Appropriateness of Antibiotic Use Using a Standardized Method Developed By Gyssens et al**.



Score System and Description Action for the Appropriateness of Antibiotic Use Using a Standardized Method Developed By Gyssens et al.

- **Correct decision:**

  1. No antibiotic; no infection; no antibiotic needed
  2. No antibiotic; infection; no antibiotic needed
  3. Antibiotic; infection; appropriate choice; appropriate use

- **Incorrect decision**

  1. No antibiotic; infection; antibiotic needed
  2. Antibiotic; no infection; no prophylaxis; no antibiotic needed
  3. Antibiotic; no infection; prophylaxis; no antibiotic needed

- **Incorrect choice**

  1. Divergence from guideline

- **Incorrect use**

  1. Inappropriate dosage
  2. Inappropriate timing
  3. Inappropriate administration
  4. Inappropriate duration of therapy

- **Missing data**

  1. No antibiotic; not enough diagnostic information about infection
  2. Infection; not enough diagnostic information if antibiotic is needed
  3. Antibiotic; not enough diagnostic information about infection
  4. Infection; not enough information about antibiotic