Drug Prescribing Pattern among Hospitalized Children in Selected Hospitals at Addis Ababa

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DRUG PRESCRIBING PATTERN AMONG HOSPITALIZED CHILDREN IN SELECTED HOSPITALS AT ADDIS ABABA

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ABSTRACT

Background: One of the most pressing problem facing public health providers and administrators in many countries is ensuring the rational use of drugs. Children constitute the large proportion of the population in most developing countries sharing significant health care cost. In Ethiopia, studies on drug use pattern in these special groups of populations are rare.

Objective: To assess the drug prescribing pattern among hospitalized children in selected hospitals at Addis Ababa.

Method: A prospective cross sectional study was conducted in pediatric wards of two randomly selected hospitals (St. Paul General Specialized Hospital and Zewditu Memorial Hospital) from 06 March to 06 May, 2011. All hospitalized children who were volunteers to participate were enrolled. Inpatient cards of the study subjects were reviewed on daily basis from time of admission to discharge. Relevant details such as demographic variables, clinical and medication data were collected. The data collected were analysed using SPSS version 16 and descriptive analysis was undertaken.

Result: During the study period a total of 155 Children were admitted at both hospitals. The mean numbers of medicines prescribed per admission was2.92.Antibacterials accounted for 59.3% of the drugs prescribed. The dose, duration of therapy and drug selection was inappropriate for 54(15.65%), 50(15.43%) and 47(12.1%) of the medicines evaluated for dose, duration of therapy and indication respectively. More than half (53%) of the diseases diagnosed were treated in accordance to the Standard treatment guideline of Ethiopia while 29% of the cases were not. On average, 0.3 potential drug-drug interaction was observed per patient most of which were minor in their severity followed by moderate and major.

Conclusion and recommendation: Antimicrobials and analgesics/antipyretics were the most common groups of medicines for prescription. Significant amounts of medicines were prescribed inappropriately in both wards. All major, moderate and minor level Potential drug-drug interactions were observed in a total of 30(19.3%) of the studied subjects. Involvement of clinical pharmacy in medication management, preparation of pediatric specific formulary and medicine list may help in the process of providing more rational medication therapy.

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ACRONYMS AND ABBREVATIONS

CNS	Central Nervous System
DACA	Drug Administration and Control Authority
DDI	Drug-Drug Interaction
FDA	Food and Drug Administration
FMHACA	Food, Medicine and health care Administration and Control Authority
FMOH	Federal Ministry of Health
JUSH	Jimma University Specialized Hospital
NLEM	National List of Essential Medicines
pDDI	Potential drug-drug interaction
RPM	Rational Pharmaceutical Management
RVI	Retroviral Infection
SPGSH	Saint Paul's General Specialized Hospital
STG	Standard Treatment Guideline
TB	Tuberculosis
WHO	World Health Organization
ZMH	Zewditu Memorial Hospital

OPERATIONAL DEFINITION OF TERMS

Antimicrobials shall mean antibacteria including anti TB agents.

Average number of medicines per hospitalization: Total number of medicines prescribed during hospitalization divided by total number of hospitalizations.

Compliance to standard treatment guideline: The practice is considered compliant when either first or second line medicines stated in the standard treatment guideline of the country prepared for general hospitals is used to manage the case.

Duration of hospitalization: The time gap between time of admission and discharge/death.

Number of medicines per admission: The total number of medicines the child took during her/his hospital stay. For the purpose of this study, fixed dose combination drugs and a drug prescribed in different dosage forms will be considered as a single medicine.

Standard Treatment Guideline (STG) shall mean the Standard Treatment Guideline for general hospital 2nd ed (2010), developed by FMHACA of Ethiopia.

Appropriate dose shall mean the dose prescribed is in accordance to weight or age based as specified by the references used.

Inappropriate dose shall mean the dose prescribed is either above or below the recommended weight or age based dose as specified by the references used.

Appropriate route of administration shall mean the route used to administer the drug is as described by the references used.

Inappropriate route of administration shall mean the route used to administer the drug to treat a particular disease is out of alternatives specified in the references used.

Appropriate frequency of drug administration shall mean the frequency of actual drug administration is in accordance to the recommendations by the references used.

Inappropriate frequency of drug administration shall mean a drug is administered in a more frequent or less frequent manner compared to the one specified by the references used.

Appropriate duration of drug therapy shall mean the duration of drug therapy is in accordance to the one described in the references used.

Inappropriate duration of drug therapy shall mean the duration of drug therapy is either for shorter or longer than the recommended duration described by the references use.

Co-morbid condition: A medical condition existing simultaneously but independently with the current reason for hospital admission

Potential drug-drug interaction: The interaction which is expected from pharmacoepidemiologic evidences.

Medicine utilization pattern: Extent and profiles of drug use together with quality of actual use compared to current recommendations.

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1. INTRODUCTION

1.1. Background

The potential inappropriate uses of medicines are becoming a concern worldwide with their increament in quantity and variety. Inappropriate use is associated with health risks to the patient and financial crisis to the health facilities and patients. As a result, numerous articles, conferences and studies try to address the issue and design strategies to identify, resolve and prevent inappropriate medicine use (WHO, 1998).

The rational use of medicines requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time and at the lowest cost to them and their community. However, ensuring the rational use of medicines remains a challenge for public health providers and administrators in many countries (Moore *et al*., 1997). Health professional's limited basic training or continuing education on medicines, influences from socio-cultural factors on medicine prescribing and dispensing patterns, prescriber's attitude towards risk, previous prescribing experience and drug promotions are some of the reasons behind irrational or inappropriate use of medicines (Vans, 1995).

Inappropriate use of antimicrobials, over-use of injections when oral formulations would be more appropriate, the use of too many medicines per patient (polypharmacy), failure to prescribe in accordance with clinical guidelines, inappropriate self-medication (often of prescription only medicines) are some of the forms of irrational medicine use as described by numerous studies from developed and developing countries (Vans, 1995 and WHO, 2002).

Prescribing practices are a reflection of health professionals abilities to discriminate among the various choices of drugs and determine the ones that will most benefit their patient (Gujar *et al*, 2008). To conform to the criteria for rational drug use, prescribers and dispensers should display a high quality of professionalism as well as unity of purpose in their respective activity, as important members of the therapeutic management team. This is because, the actions of the

consumers and the outcomes of therapy will be highly dependent on the quality, level of commitment and professionalism displayed by these care providers (Chukwani *et al*., 2002).
There are some concerns on medications utilized in children. For example, safe and effective use of medications is challenging because of the lack of FDA-approved indications (Koda-Kimble *et al*, 2009). Only one fourth of the marketed drugs approved by FDA and used by pediatric patients have indications specific for use in these group of population. Identifying optimal dosage regimen is another area of concern in pediatric populations. Dosage regimens cannot be based simply on body weight or surface area of a pediatric patient extrapolated from adult data. Bioavailability, pharmacokinetics, efficacy, and adverse-effects information can differ markedly between pediatric and adult patients, as well as among pediatric patients, because of differences in age, organ function and disease state (Milap *et al*, 2008).

Drug utilization research which was defined as "the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences" remains an important tool in the processes of improving the rationality of medicine use at different levels of health institutions (WHO, 2003). The study of prescribing pattern in particular, seeks to monitor, evaluate and if necessary, suggest modifications in prescribing practices (Gujar *et al*, 2008).

1.2. Statement of the problem

About 30 – 40% of the limited health sector budget in developing countries is spent on drugs (WHO, 1993). Despite this, drugs are often managed and used inefficiently and irrationally. Inappropriate use and over-use of medicines results in significant patient harm in terms of poor patient outcomes and adverse drug reactions. Overuse of antimicrobials is leading to increased antimicrobial resistance. Overuse of medicines can stimulate inappropriate patient demand, and lead to reduced access and attendance rates due to medicine stock-outs and loss of patient confidence in the health system. It also wastes resources often out of pocket payment form patient side (WHO, 2002).

Worldwide, more than 50% of all medicines are prescribed, dispensed, or sold inappropriately (Vans, 1995). It is estimated that significant percentage of antibiotic prescriptions in teaching hospitals are inappropriate and half of the world's 15 billion injections are unsafe (Beggs *et al*., 2005). Many of the antibiotics are unnecessarily prescribed for viral infections such as common cold. It has been reported that 20-50% of antimicrobial usage is questionable or inappropriate. It has also been reported that the incidence of bacterial resistance to commonly used antibiotics in pediatric patients is rising, requiring the assurance of judicious antibiotics use in these special group of patients (Hecker *et al*., 2003).

There are certain unique set of challenges to the prescribers as to the use of medicines in infants and children is concerned. It is obvious that the actions, effectiveness and safety of medicines are influenced significantly by physiological variances between children and adults, including the ontogeny of organ maturity and body composition. However, most pharmacokinetic and pharmacodynamic studies provide little, if any, information on drug action in infants and children, because they are usually conducted in adults (WHO, 2010).

The 'Better Medicine for Children' slogan of 2007, World Health Assembly, recognized the need for research and development on medicines for children including better dosage forms, better evidence and better information about how to ensure that medicines for treating the common childhood diseases are given at the right dose for children of all ages (WHO, 2007).

There is inadequate formal pharmacoepidemiologic study in the pediatric population when compared to the rest of the population, or even with the specific range such as the elderly. Children are all the more forgotten or seen as strangers when referring to rational use of drugs and have been “an almost hidden reality” in the medical literature (Bonati, 1994).

Thus, this study aims to asses drug utilization pattern in hospitalized pediatric patients as determined by prescribing practice in two selected hospitals in Addis Ababa, Ethiopia.

2. LITERATURE REVIEW

A one month prospective study was done in one governmental hospital found in Palestine to evaluate and therapeutically analyze the pattern of parenteral antimicrobial prescriptions among admitted pediatric patients. Accordingly, 61.8% of the studied subjects received their antibiotic drugs parentrally. A single antimicrobial medicine was prescribed for 50.6% of the patients studied. Cefuroxime appeared to be the main single antimicrobial agent prescribed and was administered to 31% of patients. It was also concluded that treatment patterns for most patients studied were nearly according to empiric and therapeutic recommendations active at the time of study (Sawalha *et al*, 2006). Similarly, one study was done at one hospital found in Kathmandu Valley, capital of Nepal. The study focuses on antibiotic prescribing practice and reported that about 75% of the antibiotics prescribed were for parentral administration. On average, 2.41antibiotics were prescribed for each study subject and cephalosporin groups of antibiotics were the common one for prescription (Palik he, 2004). These two results showed difference as to prescription rate of parentral antibiotics is concerned.

A prospective study on prescribing patterns among pediatric inpatients in one tertiary teaching hospital from Nepal showed that the use of medicines was not appropriate for the clinical diagnosis in 93(26.1%) patients (Shankar *et al*., 2006). The problems observed were use of antibiotics in viral infections and in fever under investigation the mean number of drugs prescribed per admission was 4.5. Less than half of the drugs prescribed (44.8%) were from the essential drug list of Nepal while 738 (45.7%) were prescribed from the WHO list of essential drugs. Prescription by generic name was practiced for 938 (58.1%) drugs. Antibiotics were most commonly- prescribed, followed by antipyretic and anti-inflammatory drugs and intravenous fluids. Ampicillin and paracetamol were most commonly used individual medicines. Almost half of the drugs prescribed (48.9%) were administered by the parenteral route, 38.2% of the drugs were prescribed by the intravenous route and 112 drugs (6.9%) were fixed-dose combinations (FDCs). (Shankar *et al*., 2006).

According to a retrospective drug use study conducted in a regional hospital in Trinidad, antimicrobials and antipyretic-anti-inflammatory drugs were the most frequently prescribed

drugs for hospitalized pediatric patients. Sixty percent of the antimicrobial drugs prescribed belong to β-lactam antibiotics with cefotaxime being the most commonly prescribed followed by ceftriaxone, ampilcillin, gentamycin and amoxicillin-clavulanic acid (Fitzroy *et al*., 2010).

There are inadequate studies done on drug use pattern among Ethiopian hospitalized children, despite their importance in the development of pediatric specific prescribing practices, in pharmaceutical service planning and in the identification of problems of drug supply and administration.

A prospective study on patterns of drug utilization in inpatient departments of jimma University Specialized Hospital (JUSH) showed that mean of 2.9 medicines were given for pediatric patients during their hospital stay. Antimicrobials, vitamins and minerals and CNS acting drugs were among the most frequently prescribed agents. Among antimicrobials, crystalline penicillin was the most common. The maximum number of drugs used per pediatric patients was eight. According to the result, 76% (189) of the total (including adult and pediatric inpatients) prescriptions were appropriate i.e. the right drug was ordered for the given disease condition and 24% of the order was inappropriate. One (0.4%) drug was prescribed although it was contraindicated drug for the patient given. From total medicines examined for dose appropriateness, 53 (61%) were appropriate and 11(12.6 %) of the medicines prescribed were below the recommended dose. Over dosing was observed for 3(3.4%) of medicines examined for appropriateness of doses. The route, interval and duration of administration were appropriate in 77 (58%), 92 (77%) and 55 (53%) of the prescriptions evaluated for route, frequency and duration of drug administrations, respectively (Amare 2005).

A retrospective study done in North-West Ethiopia to assess prescribing pattern of drugs in pediatric wards of three hospitals (Gondar, Bahirdar and Debretabor) showed that Penicillin and Chloramphenicol were the top-two most frequently prescribed drugs in the hospitals. The mean number of medicines prescribed per patient was 4.0±2.76 in Gondar Hospital, 3.2 ±1.8 in Bahirdar Hospital and 3.3 ± 1.9 in Debretabor Hospital. A high percentage of patients, (80% in Gondar, 79% in Bahirdar and 96% in Debretabor) were prescribed at least one antibacterial drug (Abulla *et al*., 1999). According to the study, Prescriptions were largely on empiric base.

3. SIGNIFICANCE OF THE STUDY

Appropriate drug utilizations are essential to assure that drugs are correctly used in terms of medical, social and economic aspects. Having seen the problems associated with irrational use of drugs it will be reasonable to understand the situation in Ethiopia. There are inadequate published research papers regarding the utilization of drugs in pediatric patients in Ethiopia and hence little is known about the prescribing pattern of drugs in hospitals. Specifically, as to the researcher's knowledge, there is no published study in the hospitals selected addressing the medicine utilization pattern in relation to prescribing in these special groups of patients. The outcome of this study is will,

- Provide useful information regarding drug utilization pattern in hospitalized children in the selected health facilities within the study period
- Generate tangible data for possible interventions and corrective measure
- Serves as baseline information for further assessment of drug related problems in this group of patients.

4. OBJECTIVES

4.1. General objective

- To assess the medicine utilization patterns as described by prescribing practice for hospitalized Children in selected hospitals at Addis Ababa, Ethiopia.

4.2. Specific objectives

- To assess and characterize the profiles of medicines used in hospitalized children at St. Paul's General Specialized Hospital (SPGSH) and Zewditu Memorial Hospital (ZMH) during the study period.
- To evaluate the appropriateness of medicines prescribed against current recommendations of standard guidelines.
- To assess the incidence and frequency of potential drug-drug interaction occurred in the two pediatric wards during the study period.

5. PATIENTS AND METHODS

5.1. Study area and period

The study was conducted in pediatric wards of two hospitals found in Addis Ababa, Ethiopia; SPGSH and ZMH from March 6-May 6, 2011. In the region, there are 11 governmental hospitals and two were selected by lottery method.

St. Paul's specialized hospital is a referral hospital in Addis Ababa under the Ethiopian Federal Ministry of Health (FMOH). It is the second largest public hospital in the nation, built by the Emperor Haile Selassie in 1961 with the help of the German Evangelical Church. It became a medical college in 2007 and its core services include the provision of medical care, teaching and research. It is providing medical speciaity services to an estimated 110,000 people annually who are referred from all over the country. Among 8 departments present in the hospital, Pediatric is one with 28 beds capacity. On the other hand, Zewditu memorial hospital was built by the Seventh Day Adventist Church during the first years of Emperor Haile silasie. Now it is a general referral hospital under Addis Ababa Regional Health Bureau. It is giving both inpatient and outpatient services for a total of 150 patients per day excluding those attending ART clinic. It has about 6 departments, pediatric being one with a total of 42 beds capacity.

5.2. Study design

A cross-sectional prospective study was conducted in the pediatric wards of the two hospitals on two months data.

5.3. Population

Source population

All patients who were admitted in pediatric wards of SPGSH and ZMH.

Study population

All hospitalized children who were admitted in the pediatric wards of the respective hospitals during the study period.

5.4. Inclusion and exclusion criteria

Inclusion criteria

- ☞ Pediatric patients who stayed hospitalized in the ward for more than 24 hours
- ☞ Patients between one and fourteen years of age
- ☞ Patients who were volunteers to participate in the study.

Exclusion criteria

- ☞ Patients who were managed none pharmacologically

5.5. Sample size and sampling technique

The Joint Commission on Accreditation of Health Care Organizations (JCAHO) provides a sampling technique for medication use evaluation. It states that, if the average number of cases per quarter is fewer than 600, at least 30 cases should be reviewed (JCAHO). According to the information from record offices of the respective hospitals, about 40-50 patients were expected to be admitted per month in each hospital which implies that about a total of 300 (less than 600) patients are expected to be admitted per quarter. In this study, all patients who were admitted in the ward within the study period and fulfil the inclusion criteria were enrolled.

5.6. Data collection process

Four BSc. Nurses working in the two hospitals studied (two from each) were recruited as data collectors. Training was given to them for one day on how to collect information from patient charts.

For each pediatric patient admitted during the study period, the age, sex, height, weight, reason for admission, date of admission and discharge was collected from patient cards and nurse's registry book depending on the completeness of the data. In addition, the prescribed medicines together with their, indication for use, dose, route and frequency of administrations as well as duration of therapy were noted from patient's medication chart. History of allergy to any medicines used previously, medication history and comorbid conditions were also extracted from the medical records when they are available. Structured data collection format was used to collect the relevant details needed and each patient's medication chart was reviewed on daily

basis (Monday – Friday). Any regimens change at the weekend times were retrived at the beginning of the working day (Monday).

5.7. Variables used

- Age of the child
- Sex of the child
- Weight of the child
- Diagnoses
- Medications prescribed
- Medication history
- Comorbidity
- Presence of potential drug-drug interaction
- Dosage regimens (dose, Route of administration, frequency and duration of therapy)
- Compliance to Standard Treatment Guideline of Ethiopia

5.8. Data analysis

Drug data and patient characteristic data were computed using SPSS statistical package. Descriptive statistics was used to describe age, sex, diagnosis, pattern of drug utilization and treatment outcomes. WHO model formulary for children (WHO, 2010), Standard treatment guideline of the country (DACA, 2010), Pocket book of hospital care for children (WHO, 2005), Ethiopian National Drug Formulary (DACA, 2008), Standard text books (E. Braunwald *et, al,* 2007, Dipiro J.S *et al*, 2008) were used as a reference to evaluate the appropriateness of the prescription order.

The drug interaction section was evaluated separately using Micromedex® Health care series Database Description software in collaboration with Drug Information Center of School of Pharmacy, Jimma University.

Severity of DDI was classified as major, moderate, or minor.

- Major DDI refers to an interaction which may be life threatening and medical intervention may be necessary to minimize or prevent serious adverse effect.

- Moderate DDI refers to an interaction which may result in an exacerbation of the patient's condition and may require an alteration in therapy.
- Minor DDI refers to an interaction which has limited clinical effect

The onset of potential DDIs was classified as rapid, delayed or not specified

- Rapid onset DDIs are those interactions in which case the clinical effect is expected within 24 hours of drug administration
- Delayed onset DDIs are those interactions in which case the clinical effect is not expected within 24 hour following drug administration.

The documentation status of the potential DDI was also classified as Excellent, Good, Fair, poor or unlikely.

- Excellent: Controlled Studies have clearly established the existence of the drug interaction
- Good: The documentation strongly suggests that a drug interaction exists, but well-controlled studies are lacking.
- Fair: Available documentation is poor, but pharmacological considerations may lead clinicians to suspect the existence of a drug interaction; or documentation may be good for pharmacologically similar drug.

5.9. Data quality control

The data collection format was pre-tested for its accuracy and consistency prior to actual collection of data on case notes of admitted patients. The pre-test was done by the principal investigator on total of 20 admitted children at Zewditu Memorial Hospital before a week (10% of the assumed total study subjects) and necessary adjustment was made prior to actual data collection process. Furthermore, the principal investigator had assigned two supervisors to closely follow the data collection process in both hospitals. The completeness, accuracy, and clarity of the collected data was checked before data entry.

5.10. Ethical considerations

Letter of ethical clearance were obtained from Research Ethics Committee of Jimma University and official letter was written to each of the hospitals from Pharmacy Department of Jimma

University prior to data collection. Written consent was obtained from patient care givers before reviewing patient charts after explaining about the objectives of the study. During the investigation, the confidentiality of all patient records was kept in such a way that each patient was identified by code. Neither their name nor residential address was noted during data extraction from patient chart. The right of the patient not to participate or to withdraw at any time from the study was respected. Completed data collection forms were taken by the assigned supervisors each time patients are discharged to maintain the confidentiality of patient information.

5.11. Communication of results

The result of the study will be disseminated to relevant bodies including the study hospitals and Addis Ababa city Administration Health Bureau and Federal Ministry Of Health (FMOH) for corrective action and/or follow-up to improve the practice. Finally, the findings from this study will be sent for publication to make it accessible for the scientific world.

6. RESULTS

During the two month study period, the drug utilization pattern for a total of 155 hospitalized children was studied (66 from SPGSH and from 89 ZMH). Children of age less than 10 years constituted 78 % of the studied populations. The mean age was 85.68 months. Admission rate for female patients was lower as compared to their male counter parts. The mean length of hospital stay was 8.32 ± 6.737days. Information about Co-morbid conditions was recorded for seven children six of which were Retroviral Infection (RVI) cases and one epilepsy case. Information about allergy history was not obtained for the studied subjects during the study period.

Table 1: Age and sex distribution of studied subjects at SPGH and ZMH, March – May, 2011

Age (years)	SPGSH Number of admissions (%)			ZMH Number of admissions (%)		
	Female	Male	Total	Female	Male	Total
1 - 5	10(15.15)	17(25.75)	27(40.9)	17(19.1)	21(23.60)	38(42.7)
5 - 10	7(10.60)	20(30.30)	27(40.9)	12(13.48)	17(19.1)	29 (32.58)
10 - 14	5(7.58)	7(10.60)	12(18.18)	12(13.48)	10(11.2)	22(24.7)
Total	22(33.33)	44(66.68)	66 (100)	41(46.06)	48(53.94)	89(100)

Pneumonia, acute appendicitis, pulmonary tuberculosis, anaemia and severe acute malnutrition were the reasons for admission of more than half (51.3%) of studied subjects (Table 2).

A total of 452 medicines were prescribed for 155 children admitted at the studied wards during the study period which gives an average number of medicines per admission of 2.92 ± 2.051 with 1 and 13 being the minimum and maximum medicines prescribed per admission. Antimicrobial medicines were the most frequently prescribed groups of medicines in both hospitals followed by analgesics and antipyretics. At least one antibiotic was prescribed for 89.6 % of the studied subjects during the study period and 75% of the antibiotics prescribed were parentrals. Most of the medicines prescribed (94.25 %) were from the list of essential medicines for Ethiopian. Prescription by generic name was noted for 382 (84.5%) of medicines prescribed.

Table 2: The ten most common reasons for admission of children at the studied wards, March-May, 2011

HMIS code	Diagnoses	No. of admissions (%)
1105	Acute appendicitis	30(17.9)
0125	Pneumonia	26(15.5)
0123	Pulmonary Tuberculosis	12(7.1)
0301	Anaemia	9(5.4)
0404	SAM	9(5.4)
0106	Gastro-enteritis	7(4.2)
1802	Burn	6(3.6)
0999	CHF	4(2.4)
0105	Diarrhoea	4(2.4)
0107	Meningitis	4(2.4)

Key: SAM- Severe acute malnutrition, HIMS-Health Information Management System (FMOH, 2008)

The five most common groups of drugs prescribed constituted 86.4 % of total medicines prescribed (Table 3).

Table 3: Top five drug classes prescribed among hospitalized children at SPGSH and ZMH pediatric ward, March-May, 2011

Ser.No.	Drug Class	No. Prescriptions (%)
1.	Antibacterial	254(59.5%)
2.	Analgesics/antipyretics	80(18.7)
3.	Diuretics	17(4.0)
4.	Anticonvulsant/antiepileptic agents	9(2.1)
5.	Vitamins and Minerals	9(2.1)

Table 4: The top ten most frequently prescribed medicines for hospitalized children at SPSGH and ZMH, March-May, 2011.

Ser. No	Medicine	Frequency of prescription (%)
1.	Ceftriaxone	77 (18.0)
2.	Diclofenac	32 (7.5)
3.	Crystalline Penicillin	25 (5.9)
4.	Metronidazole	25 (5.9)
5.	Cloxacillin	21(4.9)
6.	Paracetamol	20(4.7)
7.	Amoxacillin	19(4.4)
8.	Co-trimoxazole	18 (4.2)
9.	Ampicillin	15(3.5)
10.	Furosemide	15 (3.5)

In appropriate dose, inappropriate duration of drug therapy and selection of inappropriate medicines to treat a particular diagnosis made were the three most problematic areas observed. They accounted for 54(15.65%), 50(15.43%) and 47(12.1%) of medicines evaluated for dose, duration and indication respectively. Similarly, the frequency and route of drug administration were inappropriate for 3(0.78%), 33(8.7%) medicines evaluated for frequency and route of administration respectively during the study period (Table 5).

Table 5: Appropriateness of regimens of medicines utilized in hospitalized children at SPSGH and ZMH, March-May 2011.

Indicators		Frequency
Drug selection	Appropriate	343(80.3)
	Not appropriate	43(10.1)
	Contra indicated	4(0.94)
	Incomplete information	38 (8.9)
Drug dose	Appropriate	291 (68.1)
	Over dose	33 (7.7)
	Under dose	21 (4.9)
	Incomplete information	82 (19.2)
Route of administration	Appropriate	381 (89.2)
	Not appropriate	3 (0.7)
	Incomplete information	43 (10.1)
Frequency of drug administration	Appropriate	345(80.8)
	More frequent than recommended	16 (3.7)
	Less frequent than recommended	17 (4.0)
	Incomplete information	49 (11.5)
Duration of drug administration	Appropriate	274 (64.2)
	For longer than recommended	20 (4.7)
	For shorter than recommended	30 (7.0)
	Incomplete information	103(24.1)

Clinically significant potential drug-drug interactions were observed from prescriptions of 30 (19.35%) hospitalized children at the two studied wards. On average, 0.3 pDDI was observed per patient. With respect to the severity of the pDDI occurred, 8 (17%) were major, 17 (36%) were moderate, and 22(46.8%) were minor (Table 6).

Table 6: Profile of potential drug-drug interactions detected from medicines prescribed for hospitalized children at the studied wards, March – May, 2011.

PDDI	Frequency (%)	Severity of DDI	Onset of effect	Documentation
Ampicillin + Gentamicin	8(17.1)	Minor	Rapid	Good
Penicillin G + Chloramphenicol	7(14.9)	Minor	Delayed	Good
Penicillin G + Gentamicin	3(6.4)	Minor	Rapid	Good
Cimetidine + Diazepam	2(4.3)	Minor	Rapid	Good
Co-trimoxazole + Fluconazole	2(4.3)	Major	Not specified	Fair
Dexamethasone + Phenobarbitone	2(4.3)	Moderate	Delayed	Good
Diazepam + Phenobarbitone	2(4.3)	Major	Not specified	Good
Phenytoin + Diazepam	2(4.3)	Moderate	Delayed	Good
Aspirin + Dexamethasone	1(2.1)	Moderate	Delayed	Good
Aspirin + Diclofenac	1(2.1)	Moderate	Delayed	Fair
Aspirin + Warfarin	1(2.1)	Major	Delayed	Excellent
Chloramphenicol + Warfarin	1(2.1)	Moderate	Delayed	Fair
Cimetidine + Metoclopramide	1(2.1)	Minor	Delayed	Good
Cimetidine + Phenytoin	1(2.1)	Moderate	Delayed	Good
Dexamethasone + Phenytoin	1(2.1)	Moderate	Delayed	Good
Dexamethasone + Warfarin	1(2.1)	Moderate	Not specified	Good
Digoxin + Spironolactone	1(2.1)	Major	Delayed	Good
Fluconazole + Cimetidine	1(2.1)	Moderate	Delayed	Good
Furosemide + Aspirin	1(2.1)	Moderate	Rapid	Good
Furosemide + Diclofenac	1(2.1)	Moderate	Delayed	Good
Furosemide + Digoxin	1(2.1)	Moderate	Delayed	Good
NVP + Rifampicin	1(2.1)	Major	Delayed	Excellent
Phenytoin + Metronidazole	1(2.1)	Moderate	Delayed	Fair
Phenytoin + Phenobarbitone	1(2.1)	Minor	Delayed	Good
Potassium chloride + Spironolactone	1(2.1)	Major	Delayed	Fair
Rifampicin + Dexamethasone	1(2.1)	Moderate	Delayed	Good

Assessment of compliance to the Standard Treatment Guideline of the country when treating a particular case yields that, 90 (53.3 %) of the cases at both wards studied were managed in compliance with STG, while 49 (29 %) were not. For the remaining 29 (17.2 %) cases, management protocols were not described in the STG of the country.

With respect to therapeutic outcome, 133 (85.8%) of the studied subjects got improved from their illness or discharged while 18 (11.6%) had been referred and 4(2.6%) death has been recorded during the study period at the studied wards.

7. DISCUSSION

The immunity status of pediatric population exposes them to various disease conditions majorly being infectious in nature (Steinberg I., 2009). Correct diagnosis of a disease and its management with medicines particularly antibiotics, constitute important aspects of patients care. For this it is very prudent to study the prescribing practice in pediatric patients in order to find out lacunae, if any, and suggest remedial measures to overcome it.

A relatively wide spectrum of clinical diagnoses had been observed in the two wards studied. Majority of these diagnoses are infectious in nature and hence are responsible for high consumption of antimicrobial drugs at the two hospitals.

It is important to choose the right medicine(s) for a patient and in an appropriate manner in order to achieve the best results of medicine therapy. In the present study, 38 (8.87%) of the medicines prescription orders lack clear information about indication while 82(19.2%) of the medicines prescription orders were not evaluated for dose appropriateness as weight and/ or information about dose was lacking. This may result in over dose or under dose treatment of the patient which inturn affects the health of the patient negatively. Similarly, significant numbers of medicines lack information regarding the route, frequency and duration of therapy which may result administration of the medicines prescribed through wrong route and frequency for wrong duration of time.

It was good news to note that out of 384 medicines with complete information about route of administration, 99.22% were prescribed for administration through the right route. Amare (2005), showed appropriateness for 58 % of the medicines evaluated for route. However, from 324 medicines with information about the duration of therapy 15.43% were inappropriate. In other words about 1 out of 7 of medicines were inappropriate as to duration of drug treatment is concerned. The problem was worst at SPGSH (teaching hospital) which shares 9.25% of inappropriateness. A possible reason for this observation could be due to the fact that in a teaching hospital all prescriptions are not written by senior physicians but some are written by post graduate students and interns who are in a formative period of training. This aspect of medicine use certainly needs correction as duration of drug therapy affects both the health and economy of patients. Treatment of a clinical condition for shorter than a recommended duration

will lead to therapeutic failure and also emergency of drug resistant microbes. On the other hand, Treatment of a clinical condition for longer than recommended duration will expose the patient for undesired drug toxicity and unnecessary cost to the patient or health facility. However, compared to a report from South-West Ethiopia (Amare, 2005) which had reported appropriateness for 53% of medicines evaluated for duration, the present result is better.

From a total of 390 medicines evaluated for appropriateness of indication, 47(12.1%) of the medicines prescribed were not indicated for the disease diagnosed or had no clear benefit to the patient. Amare (2005) reported inappropriateness for 24% of medicines prescribed as indication is concerned. The probable reasons for the differences in the two findings could be attributed to one or more of the following reasons. First, the present study excludes neonates and infants who are at higher risk for medication errors than older age pediatric patients. Secondly a report from South-West Ethiopia includes prescriptions for adult inpatients too, in whom case multiple co-morbidity and multiple medication orders may put these groups of patients at higher risk for prescription errors than hospitalized children.

Evaluation of the quality of prescription with respect to dosing also showed that 54 (15.65%) of the medicines evaluated were inappropriate. Amare (2005) also reported problem of dosing for 16% of medicines evaluated for dose appropriateness which is similar to the present finding. However, compared to a finding from Crotia, Zagreb, which documented an incidence of incorrect dose for 3.4% of medicines for hospitalized patients (Basic, *et al*., 2005), the present finding is almost four times higher. Similarly, the evaluation of frequency of medicine administration had yielded appropriateness for 345 (91.27%) of medicines evaluated. Compared to a result from South-West Ethiopia which documented appropriateness for 77% of medicines (Amare, 2005), the present one is better. However, the present study indicates higher figure of inappropriateness (8.73%) compared to crotian study which reported only 2.7% ((Basic, V., *et al*., 2005).Differences in socio-economic status may explain the differences partially. Additionally, the latter study was done in adult inpatients in which case dose calculation may not be a problem. However, it is important to remember that both under dosing and overdosing of medicines affect the health of patients negatively. When it happens in children who have less developed organ for medicines excretion, overdosing may be fatal. Antibiotics, common groups

of medicines for prescription, when given in under dose, may lead to therapeutic failure. They may even favour the emergency of antibiotic resistant microbes.

Development of standard treatment guidelines for commonly encountered diseases and assurance of its acceptance by prescribers is also one of the important step in the processes of provision of rational medicine use. Evaluation for compliance to STG of the country (DACA, 2010) when choosing medicines to treat a particular disease indicates that 90 (53.3%) of the cases were managed as per STG recommendation while 29.0 % of cases were not. The remaining 17.8 % of cases could not be evaluated as their management was not described in the STG.

There are also measures being undertaken by many countries to improve the rationality of medicine use in health facilities. Promotion of generic prescription, prescription from the national essential drug lists etc. The national list of essential medicine avails the most cost effective medicine which can satisfy priority health care needs of the population (FMHACAE, 2010). With this regard, there were practices observed to be encouraged in the process of assuring rational use of drugs in the studied wards. Most of the medicines prescribed (94.25%) were from the national list of essential medicines. Shankar, *et al,* 2006 reported prescription from NLEM of Nepal to be 44.8%. WHO recommends 100% practice as prescription from the national list of essential medicine is concerned. However, compared to studies from Nepal, the present study documented a figure closer to WHO recommendation.

The mean number of drugs received by study subjects during their hospital stay in the present study was 2.92 ± 2.051. Abulla, *et al* (1999) documented mean of drugs ranging 3.33-4.00 in three North-West Ethiopian hospitals. Shankar, *et al* (2006) also reported mean of 4.5. Compared to these two reports, the present study scores relatively lesser average number of medicines per hospitalization. The probable reason for this difference may be the former two studies were done for relatively longer period to account for seasonal variations in medicine prescribing trend as compared to the present one. Differences in morbidity pattern may also contribute for the differences observed between our present finding and the former two. However, it is comparable to a report from South-West Ethiopia (Amare, 2005) which reported mean of 2.9 medicines for pediatric inpatients. The result is a welcome trend as it reduces the risk for drug-drug interaction and medication errors occurring in polypharmacy and/or frequent alteration of medications. WHO recommends an average number of drugs per patient to be less than two. However, this

recommendation is applicable for outpatients. Hospitalized patients are exposed for more drugs compared to outpatients due to disease severity and complexity.

Anti bacterial groups of medicines rank highest to be prescribed frequently in the wards selected during the study period. They constitute 253 (59.3%) the prescribed medicines at the studied wards. This figure is almost similar to an average national level of antibiotics consumption which is 58.8 % of total medicines at health facilities. However, compared to reports from other studies, relatively higher percentages of prescriptions are antibiotics. For example, a report from similar study in Trinidad indicated that antibiotics accounts for 36.4% of total medicines prescribed for pediatric inpatients (Fitzroy, *et al, 2010*). Similarly, a study from Jimma, South-West Ethiopia, on drug utilization pattern in both pediatric and internal medicine ward showed that antibacterial medicines constitute 42.6 % of the medicines prescribed (Amare, 2005). The present study did not include infants and neonates, which were found to consume more antibiotics than their older age group pediatric patients in other studies (Palik , 2004,). However, antibiotics still remain high in percentage of medicines used. The probable reasons for the increased proportion of antibiotic utilization in the present finding includes increased incidence of infectious diseases during the study period, lack of antibiotic prescription protocol at the hospitals, ignorance of a risk of antibiotic resistance issue by the prescribers, and ignorance of prescribers to judge as to the importance of prophylactic use of antibiotics. A review article on antimicrobial drug use in hospitalized children stated that in one hospital at Netherland, out of 36% of hospitalized children receiving antibiotics; only 12.3% of them had proven bacteria (Gujar A, *et al*). From this result, one can say that not only in developing countries like Ethiopia where appropriate laboratory facilities are lacking, antibiotics are prescribed empirically for the majority of cases to address the most likely microbe(s) in developed countries too. However, it requires good judgement from prescribers side as to the importance of empiric antibiotic prescriptions.

Atleast one antimicrobial medicines was prescribed for 89.7% of hospitalized children at the studied wards during the study period. Reports from various previously done studies vary as to percentages of hospitalizations with one antimicrobial. For example, 84% was reported from western Nepal (Shankar, *et al*), 93% from Kathmandu Valley, Nepal (Palikhe, 2004) and 79-96 % from North West-Ethiopia at three hospitals (Abulla *et al*). All these results indicate that

antimicrobials are the main stay classes of medicines used commonly for therapeutic and prophylactic uses against various infectious diseases that are common in these age groups.

Unlike the study from South-West Ethiopia (Amare, 2005), North –West Ethiopia (Abulla, *et al*.,1999), and Western Nepal (Shankar, *et al*.,2006) where penicillins were reported to be the top most commonly prescribed medicines, the present study reveals that cephalosporins were the commonest to be prescribed at both hospitals followed by penicillins at both hospitals. This result may indicate the shift from first line antibiotics (penicillins) used for many infectious diseases described in the STG of the country to alternative ones. Ceftriaxone is being used as prophylactic agent for surgical site infection, especially pre and post appendectomy procedure in these wards. This practice needs a revision as to the appropriateness of the use of ceftriaxone as a drug of choice. Though ceftriaxone has broad spectrum activity against most microorganisms especially gram negative microbes, their poor anaerobic coverage and gram positive microbe activity in addition to their high cost discouraged their use as a prophylactic agents (Kanji, S. *et al* 2009). Literatures and guidelines recommend the use of cefotetan or cefoxitin as prophylactic antibiotic of choice for such procedures. Use of ceftriaxone in such cases may alter microbial flora, increasing the emergence of microbial resistance to these otherwise valuable agents (Thrion, *et al* 2009, STG, 2010).

Prescription of analgesic and antipyretic groups of medicines are also common in both hospitals, accounting for 80 (18.7%) of total medicine prescribed during the study period. Over prescribing of analgesic seems to be a problem at ZMH where 25(10.1%) and 14(5.6%) of total medicines prescribed at the ward calls for diclofenac and tramadol respectively. Diclofenac, although not recommended in children (Burke, *et al* 2005)), is widely used in this hospital. Paracetamol could be a good alternative to diclofenac with less toxicity and similar efficacy. For more severe pain, intravenous narcotic analgesics (e.g. morphine sulphate) are good alternatives recommended in some guidelines (WHO, 2005).

Now a day, there is a tendency to consider potentially serious drug-drug interactions as an indicator for appropriateness of prescribing practice. Because, these interactions has both clinical and economic implications (Williams, *et al* 2000).

Evaluation of prevalence of potential drug-drug interaction in the present study reveals that atleast one pDDI was documented in 30(19.35%) of the total study population. The current result is much lower compared to a report from Bartoli, *et al.* (2010), which documented pDDI for 62.5 % of adult study subjects. It is difficult to make a firm conlclusion from this differences as the two study groups are different in terms of age class, socioeconomic status etc. With respect to severity of pDDI occurred, most (46.8%) of the interactions happened to be minor followed by moderate (36%) and Major(17%). A similar profile of severity was observed by Bartoli, *et al.* (2010). A study from Brazil however, reported moderate level interaction to be predominant (Martinbiancho *et al*, 2007). However, the latter study was a retrospective analysis for discharged patients from one year data. Methodological differences could contribute to the differences observed. The present finding also indicated that, the number of moderate or Major DDI were 0.19 per patient which is much lower than a 0.75% report from 200 study subjects by Bartoli, *et al.* (2010).The present prescription pattern seems to provide a relatively safer therapy.

Although the severity associated with the interaction between amino glycoside and penicillin groups of antibiotics is minor, it ranks first in its frequency of occurrence at both wards. This may be because of the fact that these two drugs are commonly prescribed together for their synergistic effect. However, the chemical inactivation of gentamicin by β-lactam antibiotics will reduce the effectiveness of gentamicin. Therefore, prescribers must be aware that atleast the concomitant administration of amino glycosides and penicillins through intravenous system should be avoided. Prescribers should give due emphasis during prescription of drugs which are known for their drug-drug interaction property. Anticonvulsant/anti-epileptic drugs are well known for their high profile drug interaction when given together with some other drugs. Cimetidine, a known drug metabolizing enzyme inhibitor, is also known for its interaction when given with some other drugs. The relatively high prescription rates of these groups of drugs at SPGSH may explain the relatively more drug-drug interaction profile seen as compared to results from ZMH.

8. Limitation of the study

The present study has its own limitations. First of all, being a prospective follow up study over two months, seasonal variations in disease pattern and drug utilization were not considered. Future studies should be designed to address this gap. Secondly, the number of study subjects in the present study and the number of health institutions selected in the area is limited and hence it presents challenge as to the extrapolation of results to other institutions in the region. Thirdly, because the categorization of therapy as appropriate or inappropriate was based solely on information available in the medical records, some appropriate regimens may have been misclassified as inappropriate due to inadequate documentation of the reasons for therapy. It is also possible that a greater number of inappropriate regimens might have been identified if we had interviewed and examined patients. Furthermore, qualitative study was not conducted to investigate the possible reasons behind the problems seen at the selected wards.

9. CONCLUSION AND RECOMMENDATIONS

9.1. Conclusion

Antibiotics and analgesics/antipyretics group of medicines were the two most common drug classess for prescription at the two wards studied during the study period. Most (94.25%) of the medicines prescribed were from the NLEM. Over prescription of analgesics/antipyretics seems to be a problem observed at ZMH. Ceftriaxone was the drug most frequently prescribed.

Lack of recommended medications used for prophylaxis of surgical site infections seems to be a reason for prescribers to depend on ceftriaxone leading to high prescription rate of this otherwise valuable antibiotic.

Inappropriate dose and inappropriate duration of therapy as well as inappropriate drug selection happened to be the three most problematic areas observed in the studied wards accounting for 15.65%, 15.43% and 12.1% of medicines evaluated for dose, duration and indication respectively. Wrong frequency of drug administration and wrong route was also observed in 8.73% and 0.78%of the medicines evaluated for frequency and route of administration.

As to adherence to Standard treatment guideline is concerned, 53% of the cases were managed as per the STG recommendation while 29.0% were not.

Problems of drug interaction was also observed in 30(19.35%) of the studied subjects most of which (46.8%) were minor in severity. On average, 0.35 pDDI was detected in each studied subject.

9.2. Recommendation

☞ To stakeholders

The development of a pediatric specific essential medicine list will increase the awareness of the need for pediatric specific medications and formulations and highlights areas of priority where medications or formulations are lacking.

Provision of first generation cephalosporins such as cefazolin and second generation cephalosporins such as cefotetan and cefoxitin will improve the rationality of perioperative medications.

☞ To the hospitals

Antimicrobial prescription protocol and guidelines; Preparation of Pediatric formulary; and involvement of clinical pharmacist in case management processes may provide a more rational antimicrobial pharmacotherapy.

Analgesic and antipyretic groups of drugs that are potentially harmful to the children are being utilized excessively at ZH compared to SPH. There is a need to provide analgesic prescription policy for prescribers.

Route conversion programmes should also be promoted as considerable number of patients took their medicine parentrally till discharge.

Continuous education and training of health professionals in the management of pediatric illnesses will improve the rationality of the overall management

☞ To researchers

The present study on drug utilization pattern in hospitalized children can provide a frame work for continuous prescription audit in the institutions.

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ANNEX

9.3. DATA COLLECTION FORM

PATIENT ADMISSION DATA

Name of the facility _____ Name of data collector_____

Date of admission _____

Patient chart No. _____ Patient case No. _____

Sex ☐M ☐ F | Height _____cm. | Weight _____Kg

Tentative diagnosis_____

Medication(s) to which the child were Allergic_____

_____

Co-morbid conditions _____

_____

MEDICATION HISTORY

Date	Medication (includes dose, route, frequency)	Indication	Duration

MEDICATIONS DURING HOSPITALIZATION

Date	Medication (s)	Direction (dose, route, frequency)	Indication	Comment
Therapeutic outcome ☐ Improved ☐ Transferred ☐ Dead				

MEDICATIONS DURING DISCHARGE (From discharge summary)

Date	Medications	Dose, route and frequency	Durations	Comment

LABORATORY RESULTS AVAILABLE

RENAL FUNCTION TEST (RFT)

JIMMA UNIVERSITY

COLLEGE OF PUBLIC HEALTH & MEDICAL SCIENCE

DEPARTMENT OF PHARMACY

PATIENT CARD REVIEW INFORMED CONSENT FORM FOR THE CLIENT

Greeting

Hello! My name is ----------I am working in research team of Jimma University College of Public health &Medical Science Post Graduate School. This is a study to be conducted with objective of assessing the medicine utilization patterns in hospitalized pediatric patients. As the study is directly related to pediatric inpatients seeking patient care in pediatric ward**, y**ou are one of the candidates who are selected to participate in this study. Therefore, your are kindly requested to allow me to extractor important information from your child's medical card.

Your participation in this study is completely on voluntary bases**.** I am going to extract informations relevant to me from your child's medical card and you have the right to refuse from participation. The data collected will be kept confidential and there will be no way of linking your individual medication data to the final result of the study findings.

I would like to inform you that your participation is very essential, not only, for the successful accomplishment of the study but also for producing relevant information which will be helpful in improving hospitalized patients care services.

Would you willing to participate in this study?

Yes ----------

No ----------.

If the patient says no, thank the patient and go to the next patient.

Name of care giver .....Sign..... Date of consent gained.....

Name of data collector---------- Sign ---------- Date of consent gained----------

Name of the supervisor ---------- Sign ---------- Date of consent gained----------