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Retrospective Study of the Pattern of Antibiotic Use in Hawassa University Referral Hospital Pediatric Ward, Southern Ethiopia

Minyahil A. Woldu*, Sultan Suleman, Netsanet Workneh and Haftay Berhane
Department of Pharmacy, College of Public Health and Medical Sciences, Jimma University; Jimma Ethiopia

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ABSTRACT

Paediatric antibiotic prescription is a major concern in terms of public health, since infections are the most frequent cause of childhood disease. The aim of this a hospital-based cross sectional study was to assess the pattern of antibiotic use in the Paediatric ward of Hawassa University referral hospital, southern-Ethiopia. Data was entered into a computer and statistical analysis was done using SPSS for windows version16. From the result of the study, the frequency and percentage of antibiotic prescriptions identified was 1381 (74.7%); (Wald test, $p < 0.01$), and the frequency and percentage of Injectable prescription was 1729 (93.6%); (Wald test, $p < 0.01$). The mean number of drugs prescribed per-prescription was 1.58±0.743. The mean of antibiotics prescriptions in preschool children was relatively higher (1.26; 95% C.I b/n 1.03-1.29) compared to other pediatric age groups. The use of antibiotic by pediatric age category was found to be significant (Pearson Chi-Square P= 0.037). Very strong positive correlation of antibiotic use was observed with generics prescriptions and injection prescriptions (0.740 and 0.731 with p-value < 0.01) respectively. The potential Drug-Drug Interactions (DDIs) identified in the study area was 66% (Fisher's Exact Test, P< 0.01). The availability of a set of key antimicrobial drugs in the hospital stores on the day of the study was 90.1%. The most frequently prescribed single antibiotic was penicillin G crystalline 146 (28.4%), While the most commonly prescribed multiple antibiotic prescriptions was 'Ampicillin inj plus Gentamicin inj' 113 (27%) followed by 'Chloramphenicol inj plus Cloxacillin inj' 60 (14.4%). From the result we can conclude that, there was a significant oral and injectable antibiotic utilization in the study area compared to similar studies conducted in other part of the world.

INTRODUCTION

Antibiotics are powerful and effective drugs in the fight against infectious diseases caused by bacteria and have been frequently used for decades worldwide for effective treatment of a variety of bacterial infections (Jayakar *et al*., 2011; FDA, 2012). Antibiotics have saved millions of lives since their first appearance about fifty years ago (CDC, 2012; Jayakar *et al*., 2011). Yet, more and more people are dying from infectious disease that were curable but for which we no longer have the right treatment. This is because certain bacteria are transforming themselves and developing resistance to antibiotics (Jayakar *et al.*, 2011; Ramanan, 2012).

Antibiotics are an essential part of modern medicine and play a major role both in the prophylaxis and treatment of infectious diseases (Abula *et al*., 2004; Coates and Y Hu, 2007) and are among the drugs most commonly prescribed for children (Marta *et al*., 2008).

The issues of their availability, selection, and proper use are of critical importance to the global community (Abula *et al*., 2004; MacDougall and Polk, 2005). Prudent use of antibiotics will curtail health care costs and potential adverse effects to the individual taking them and also diminishes the wide ecologic effects leading to selection of antibiotic resistant pathogenic Organisms (Abula *et al*., 2004).

Problem Statement

Worldwide, it is estimated that over 50% of all medicines are prescribed, dispensed or sold inappropriately (Holloway, 2011). Though Inappropriate use of antimicrobial agents has been found to be common in various parts of the world, but there have been few studies in developing countries (Aswapokee *et al*., 1989).

* *Corresponding Author*
Department of Pharmacy College of Health Sciences, Mekelle University, Ayder referral hospital P.O.Box: 1871, Mekelle, Ethiopia. Tel. (Mobile): +251911571337.

Antimicrobial agents are the most commonly used and misused of all the drugs (Jimoh, 2011). Bacteria are becoming resistant to the point where none of the available antibiotics work for some of the infections that confront patients and physicians in hospitals around the world. "For these patients we are slipping back in time to a pre-antibiotic era where we have little to offer but comfort for diseases which we have been easily able to cure over the last 50 years" (Shlaes, 2010).

The majority of hospitalized patients receive antibiotics for therapy or prophylaxis during their inpatient stay. It has been estimated that at least 50% of patients receive antibiotics without clear indications (Rehm *et al*., 2009). Over prescribing not only increases the costs of health care, but may result in super-infection due to antibiotic-resistant bacteria, as well as opportunistic fungi, and may increase the likelihood of an adverse drug reaction. The frequent use of antibiotics is considered to be one of the main reasons for the high prevalence of antimicrobial resistance observed in hospitals (Rehm *et al*., 2009; Marta L. *et al*., 2008).

Compared to adult medicine, drug use in Paediatric is not extensively researched and the range of licensed drugs in appropriate dosage form is limited (Palikhe, 2004). Paediatric antibiotic prescription is a major concern in terms of public health (Lusini *et al*., 2009). Infants and children are among the most vulnerable population groups to contract illnesses because of this the use of antimicrobial agents, especially antibiotics has become a routine practice for the treatment of Paediatric illness (Arulmoli *et al*., 2009).

Ethiopian hospitals consume about 50% of the national drug budget, 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 hospitals like in other health facilities (Abula *et al*., 2004).

OBJECTIVES

General Objective

To assess the pattern of Antibiotic Use in the Paediatric ward of Hawassa University Referral Hospital, Southern Ethiopia

Specific Objectives

- *To assess antibiotics prescribing practice of prescribers* in terms of age and sex difference, percentage of prescription from the drug information resources, percentage of generics prescription, percentage injectables prescription and percentage of potential drug-drug interactions.
- *To evaluate the hospital service facilities* by assessing the availability of key antimicrobials, antibiotic sensitivity tested conducted, existence of drug information resources [like Essential Drug List of Ethiopia (EDL), Standard Treatment Guidelines (STGs), and List of Drugs for Referral Hospitals of Ethiopia (LDRH)], expenditure on antibiotics as a percentage of total hospital medicine costs and Average number of days that a set of key antibiotics is out of stock.

METHODS AND PARTICIPANTS

Study Area

Hawassa University Referral Hospital (HURH) located in the south central part of Ethiopia, in Hawassa city. It is found 275km away from Addis Ababa, the capital city of Ethiopia towards south direction. It is believed that HURH provides medical services for more than 500 patients per day.

Study Period

The study was conducted from February 20, 2012 up to March 20, 2012.

Study Design

A hospital-based retrospective cross sectional study.

Source Population

Paediatric population, age < 14 years

Study Population

Pediatric Population admitted at HURH within one year period and who fulfills the inclusion criteria.

Inclusion and Exclusion Criteria

- Inclusion Criteria for the Study Population:-
- All Paediatric population admitted to HURH
- Inclusion Criteria for the Study Population:-
- who have no drug prescription
- Inclusion Criteria for Drug-Drug Interaction Data:-
- Patient's record with multiple drug therapy; with a minimum of two drugs out of which one is at least an antimicrobial agent

Data Collection and Management

Sample Size

The Sample size considering non-response rate for the retrospective study was 1169.

Source of Data

Patient chart, laboratory results and prescription orders.

Sampling Technique

Systematic sampling technique was followed for data collection technique.

Data Analysis Procedures

The collected data was entered to and analyzed by using SPSS for windows version 16. Descriptive statistics were used to determine the prevalence and incidences of the dependent variables, correlation and chi-square tests were used to determine

any association. A 95% CI and p-value of < 0.05 was considered to be statistically significant.

RESULTS

Demographic Data

Of the total (n=1169) pediatric patients who were admitted to pediatric ward of Hawassa University Referral Hospital (HURH) during 2011/2012, 768 (65.7%) were male and 401 (34.3%) were females. 616 (52.7%) were came from areas outside Hawassa city and 553 (47.3%) were from the city.

Two hundred sixty (22.2%) of the admitted children were Toddlers (age in between 1 and 3) followed by school children (age in between 6 and 10) 239 (20.4%), and adolescents (age in between 11 and 14) 187 (16%), [Fig.1].

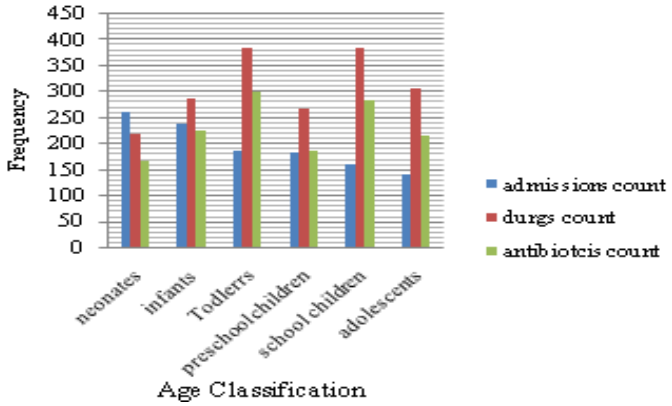

Fig. 1: Percentage of Admissions from all cause, Drugs and Antibiotics prescription among different Age Categories of Pediatric Pediatric patients during 2011/2012 Year at HURH, Hawassa - Ethiopia.

Prescribing Indicators

The maximum drug prescription and antibiotics use was observed in May. The minimum admission rate, drug and antibiotic use was observed on April. And while from May to August with most admissions and drug prescriptions observed. However, antibiotic use by month was not statistically significant (Pearson Chi-Square P= 0.582), [Fig. 2]. Antibiotics were prescribed for 933 (79.8 %) pediatric patients and from this 616 (52.7%) were male and 316 (27%) were females. 486 (52.3%) of them came from areas outside Hawassa city and while 444 (37.7 %) came from the city. Injectables were prescribed for 1112 pediatric patients (95.12%). Of all injectables prescribed pediatric patients 63.2% were male and the rest 31.9% were females. 1381 (74.7%) prescriptions were antibiotic prescriptions [Table-1]. The percentage of antibiotics prescribed from EDL and LDRH of Ethiopia was 1251 (90.6%) and 1381 (100%), respectively.

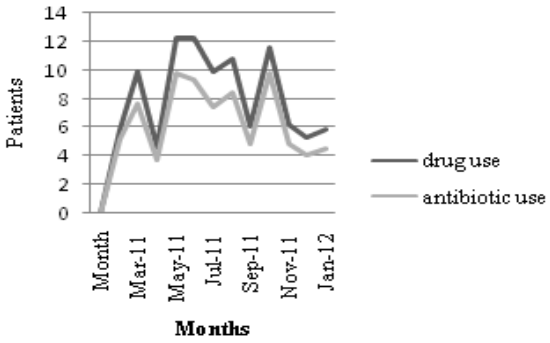

Fig. 2: The Pattern of Drugs and Antibiotics Use across the Different Months of Year 2011/12 at HURH, Hawassa – Ethiopia.

The maximum number of drugs per prescription was 6 while the maximum number of antibiotic prescribed per-prescription was 3. The maximum number of injectables prescribed per prescription was 5 while the maximum number of generics per prescription was 6. The maximum number of antibiotics prescribed from either EDL or LDRH per prescription was 3.

The mean number of drugs prescribed per-prescription was 1.58±0.743. The mean number of antibiotics prescribed per-prescription was 1.18±0.813. The mean number of injection prescribed per-prescription was 1.48±0.766. The mean number of generics prescribed per-prescription was also1.48±0.766. The mean of antibiotics prescribed from EDL of Ethiopia was 1.07±0.893. The mean number of Antibiotics from LDRH was 1.18±0.813.

The mean of antibiotics prescriptions in preschool children is relatively higher (1.26; 95% C.I b/n 1.03-1.29) compared to infants (1.24; 95% C.I b/n 1.14-1.35), neonates (1.19; 95% C.I b/n 1.05-1.32), school children (1.19; 95% C.I b/n 1.09-1.30), adolescent (1.16; 95% C.I b/n 1.02-1.29) and Toddlers (1.16; 95% C.I b/n 1.06-1.25).

Seven hundred fifty (64.2%) of the prescriptions were mono drug prescriptions from which 517 prescriptions (44.2 %) were single antibiotic prescriptions and the rest 233 (19.93%) were non antibiotic single drug prescriptions. The most frequently prescribed single antibiotic was penicillin G crystalline 146 (28.4%), followed by cefrtiaxone 128 (24.9%), cloxacillin inj 66 (12.84%), ampicillin inj. 58 (11.28%), genatmicin 51 (9.92%) and chloramphenicol inj. 28 (5.45%), [Figure 3].

Table. 1: Frequency and Percentage of All Drugs, Antibiotics only, Injectables and Generics among Pediatric Pediatric patients Admitted to Pediatric Ward of HURH during 2011/2012 Year.

Number per encounter	All Drugs		Antibiotics		injectables		Generics	
	count	%	count	%	count	%	count	%
1	644	34.8	545	29.5	623	33.7	618	33.4
2	392	21.2	650	35.2	744	40.3	346	18.7
3	116	6.28	186	10.1	321	17.4	312	16.9
4	14	0.76	0	0	36	1.95	44	2.38
5	2	0.11	0	0	5	0.27	5	0.27
6	1	0.05	0	0	0	0	6	0.32
Total	1848	100	1381	74.7	1729	93.6	1731	93.7

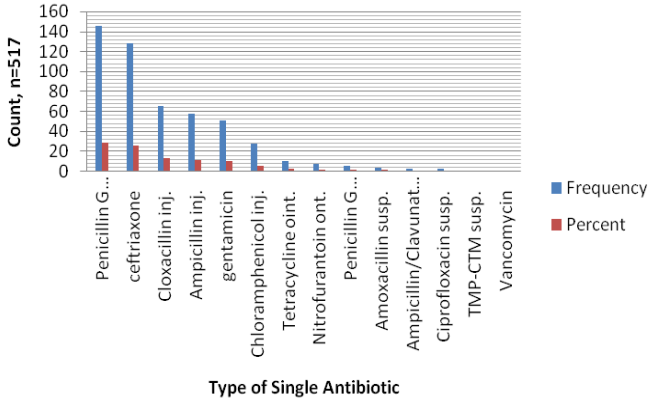

Fig. 3: The Frequency and Percentage of single prescribed Antibiotics in Pediatric Ward of HURH during 2011/2012 Years, Hawassa - Ethiopia.

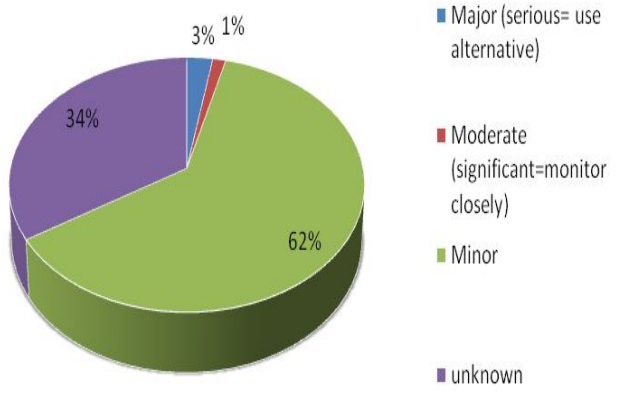

Fig. 4: The Frequency and Percentage of *Potential drug interactions* in Pediatric Ward of HURH during 2011/2012 Years, Hawassa – Ethiopia.

Four hundred sixteen (35.6 %) of the prescriptions were multiple antibiotic prescriptions and from these the combination of 'Ampicillin inj and Gentamicin' took the largest portion with 113 (27%), followed by 'Chloramphenicol inj and Cloxacillin inj' 60 (14.4%), 'Ceftriaxone and Cloxacillin' 47 (11.3%), and 'Ampicillin, chloraphenicol and Gentamicin' 45 (10.8%), [Table 2]. There were only 3 (0.3%) prescrptions which identified as combination of drugs with no antibiotics.

All the data (N=525) which have the potential of drug interactions were used for identification of potential drug-drug interactions. DDI identified was 66% (Fisher's Exact Test, P< 0.01). The most common type DDIs identified in the study area was 'Minor' Drug-drug Interaction 326 (62%) [Fig. 4].

Table. 2: The Frequency and Percentage of Multiple Antibiotic prescriptions in Pediatric Ward of HURH, during 2011/2012 Years, Hawassa – Ethiopia.

Antibiotics	frequency	percent
Ampicillin inj.+ Gentamicin	113	27.2
Chloramphenicol inj + Cloxacillin inj	60	14.4
Ceftriaxone + Cloxacillin inj	47	11.3
Ampicillin inj + chloraphenicol inj + Gentamicin	45	10.8
Chloramphenicol inj. +Penicillin-G crystallin	35	8.41
Ceftriaxone + Metronidazole inj	25	6.01
Ampicillin inj + Chloramphenicol inj	18	4.33
Cloxacillin inj + Gentamicin	15	3.61
Ampicillin inj + Cloxacillin inj	11	2.64
Chloraphenicol inj. + Gentamicin	6	1.44
Ampicillin inj + Cloxacillin inj + Gentamicin	6	1.44
Cloxacillin inj + Penicillin-G crystallin	4	0.96
Ceftriaxone + Chloramphenicol inj	4	0.96
Cloxacillin inj + Ceftriaxone + Chloramphenicol inj	4	0.96
Ampicillin inj + ceftriaxone + Gentamicin	3	0.72
Ampicillin inj + Ceftriaxone	3	0.72
Ampicillin inj + Gentamicin + Metronidazole inj	3	0.72
Cloxacillin inj + Ceftriaxone + Metronidazole inj	2	0.48
ceftriaxone + Gentamicin	2	0.48
Cloxacillin inj + Metronidazole inj	1	0.24
Amoxicillin inj + Tetracycline eye ointment	1	0.24
Ceftriaxone +Vancomycin	1	0.24
Ampicillin inj + Penicillin-G crystallin	1	0.24
Cloxacillin inj + Nitrofurantoin	1	0.24
Gentamicin + Penicillin-G crystallin	1	0.24
Metronidazole inj + Penicillin-G crystallin	1	0.24
Ampicillin inj + Chloramphenicol + Vancomycin	1	0.24
Ampcillin inj + ceftriaxone + metronidazole inj	1	0.24
Ampicillin inj + Ceftriaxone + Cloxacillin inj	1	0.24
Total	416	100

Hospital facility Indicators

HURH has its own formulary list that was revised within the last 12 months and is intended for use by physicians, nurses, and the pharmacy professionals. But there is no STGs exist which serves for the paediatric service and no identified microbial sensitivity test done during the study period.

Availability of a set of key antimicrobial drugs in the hospital stores on the day of the study was 90.1%. The estimated annual budget on drugs was 8.3 million birr of which the cost of antimicrobials was around 2.8 million birr. Therefore, the Expenditure on antimicrobial drugs as percentage of total hospital drug budget was around 33.7%. The Average number of days that a set of key antimicrobial drugs is out of stock in a 12-month period was 15- 45 days.

DISCUSSION

Antibiotics represent one of the most commonly used drugs (Donkor *et al*., 2012). Their irrational use leads to a number of consequences in term of cost, drug interactions, hospital stay and bacterial resistance (Brahma *et al*., 2012). In this study, it was found that there was higher incidence of antibiotic and injectables prescription compared to similar studies conducted in other part of the world. The percentage of antibiotic in prescriptions containing one or more antibiotic in the study area was consistent with the study conducted in Ethiopia (Abula *et al*., 2004) and lower than the one in Botswana (Fisher *et al*., 2009), but the result was generally higher compared to other studies (Marta *et al*., 2008; Husni *et al*., Niemat *et al*., 2008) and the WHO guideline (28). The frequency and percenatge of Injectables prescription in the study area was higher compared to other similar studies (Palikhe, 2004; Sawalha *et al*., 2006; and Shankar *et al*., 2006) and WHO guideline (WHO, 1993). The Percentage of antibiotics prescription in Toddlers was relatively higher, but considering admission rate high percentage of antibiotics was prescribed for school children and adolescents. The minimum percentage of antibiotic use was in Neonates. Therefore, the mean of antibiotics prescriptions in preschool children is relatively higher compared to the other pediatric age groups. This could be due to physician behavior in

ordering medication in association with age; diagnostic and clinical investigation factors, and variability in patient complaints. This result was consistent with the study conducted in Italy (Marta *et al*., 2008).

Very strong positive correlation of antibiotic use was observed with generics prescriptions and injection prescriptions (0.740 and 0.731 with p-value < 0.01) respectively, shows that good generic prescription behaviors in physician and the high burden of parenteral medication administration for hospital admitted children, which may be due to the more seriousness of the infection.

The mean number of drugs prescribed per-prescription was lower compared to studies conducted in Nepal (Palikhe, 2004; Kumar *et al*., 2010) and consistent with the WHO recommendations (WHO, 1993; WHO, 2001). The mean number of antibiotics prescribed per-prescription was lower than the one conducted in Ethiopia (Abula *et al*., 2004) and is consistent with the WHO recommendation (WHO, 1993). The mean number of injection prescribed per-prescription in the study area showed the burden of injectable prescription on pediatric population compared to the mean of antibiotics prescription in the same population. The mean number of generics prescribed per-prescription in the study area showed that not all drugs were prescribed by generic prescription. The WHO guidelines recommend 100% generic prescription (WHO, 1993). The mean of antibiotics prescribed from EDL of Ethiopia showed that not all antibiotics included from the EDLs of Ethiopia. Some of the antibiotics were frequently encountered for outpatient departments because of their dosage form (e.g. Chloramphenicol and gentamicin ophathalmic preparation) and some of the drugs like neomycin and streptomycin were not found in the hospital store due to drug stock out. A mono drug prescription in the retrospective study was found to be consistent with the study conducted in Nepal (Shankar *et al*., 2006) and the WHO guidelines (WHO, 1993; WHO, 2001; WHO, 2002). The frequently of single antibiotic prescription was consistent with other studies and the WHO guidelines (Lim *et al*., 1993; Abula *et al*., 2004; Sawalha *et al*., 2006). The frequency of multiple antibiotic prescriptions in the study area was consistent with other findings in which combination of ampicillin with gentamicin or chlorampheicol or both was the most frequent (Lim *et al*., 1993; Abula *et al*., 2004; Marta *et al*., 2008). Majority of antibiotic combinations were prescribed based on infectious disease guidelines even though some of the combinations were not justified.

The potential DDIs identified in the study area was higher compared to other study (Lal H.M & Lal U., 2008). The most common type DDIs identified in the study area was 'Minor' Drug-drug Interaction. The potential drug-drug interactions identified as 'major' was due to concurrent use of furosemide and gentamicin. Such type of combination may result in increased gentamicin plasma and tissue concentrations and additive ototoxicity and/or nephrotoxicity. Since such type of DDIs is life-threatening and/or require medical intervention to minimize or prevent serious adverse effects. The possible intervention may be one of these drugs should be substituted by other safer drug. Not many drugs were considered as possessing 'moderate' DDIs in the study area. The only identified combination drugs that result in moderate drug interaction was concurrent use of furosemide and digoxin, which may result in digoxin toxicity (nausea, vomiting, cardiac arrhythmias). Continuous monitoring of laboratory parameters is thus mandatory. Most of the multiple prescriptions were considered as producing minor drug interactions. Such drug interactions have only limited clinical effects. Manifestations may include an increase in the frequency or severity of the side effects but generally would not require a Major alteration in therapy. In the rest of the cases of multiple drug interaction, the interactions are considered unknown, but it does not mean that they have no drug interaction at all. The use of antibiotics in male pediatric patient was higher than the female pediatric patients. The use of antibiotics also found to be higher in patients who came from outside Hawassa city. However, the use of antibiotic use by address and sex was not found to be statistically significant (Chi square for trend: p > 0.5). In similar study conducted in Rome - Italy, no statistically significant differences by sex were noted (Marta *et al*., 2008). The use of antibiotic by pediatric age category was found to be significant in our study (Pearson Chi-Square P= 0.037). The Availability of a set of key antimicrobial drugs in the hospital stores on the day of the study was comparable to the study conducted in Nigeria (Li JZ *et al*., 2002).

CONCLUSION

This study gives an overview of the pattern of antibiotic use in the study area by age and sex distribution, frequency and percentage of single as well as combined drugs prescriptions, the potential of drug-drug interaction, and percentage of hospital stay with one or more antibiotics in pediatric population. Generally, we can conclude that there was:-

- High percentage of antibiotics and Injectables use
- High admission rate in neonates and high percentage of drug and antibiotic use in children beyond 5year of age considering admission rate.
- Penicillin G crystalline was the most frequently prescribed single antibiotic while 'Ampicillin.inj. + Gentamicin' was the most frequently prescribed combined antibiotics.

Overall there was good generic prescription as well as promising antibiotics prescriptions from EDL and LDRH of Ethiopia in the study area compared to other similar studies and the WHO guidelines.

RECOMMENDATIONS

The high percentage of prescriptions involving antibiotics observed in HURH requires rational use of antibiotics and judicious prescribing. It should be followed by the appropriate use of the selected medicine with frequent update of information. The establishment of antibiotic policy and treatment guidelines with periodic assessment of the sensitivity pattern of pathogenic

organisms is recommended. Recruiting clinical pharmacists in the study area is very important in order to monitor the clinical use of these medications and to tackle associated factors. The WHO should provide further updates and guidelines on the use of antibiotics in hospitals, specifically in admission wards and pediatric population.

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