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Abstract

Inappropriate use of antibiotics can potentially lead to antimicrobial resistance and increase the necessity to use more expensive antibiotics to treat common and life threatening infections. The major goal of this research was to determine antibiotics utilization and their cost among in-patients treated in Ayder Referral Hospital. An institution based cross-sectional study was conducted in medical, gynecology and obstetrics, and surgical wards from September to December, 2012. The prevalence of antibiotics use was 35.5

Index terms— irrational drug use, antibiotics, ayder referral hospital, cost, inpatients.

1 Introduction

ntimicrobials are agents that can suppress the growth of pathogens or destroy them. Use of these drugs in clini¬cal practice has changed the natural course and improved the prognosis of infectious diseases. Appropriate antibiotic use is one of the main goals of the medical community.1, 2 They can be used as prophylactic and therapeutic agents, but their increasing and in¬discriminate uses are the main contributors to the emergence of resistant microbial strains. 2 The issues of antimicrobial misuse are of global concern, not only because of the development and spreading of antimicrobial antibiotics resistant bacteria, but also due to escalating health care costs that cause severe financial hardship for the poor in developing countries. 3 The primary objective of drug utilization studies is to enhance the rational use of drugs in populations. For the individual patient, the rational use of antibiotics implies the use of the right drug with the right dose at the right interval and at the right duration together with the correct information, at an affordable price. 4 When the use of drugs is not in accordance with the above definition, there are often undesirable health and/or economic problems, such as insufficient therapeutic effect, adverse drug reactions, preventable side effects, interactions of drugs and the worst of all is increasing resistance of bacteria to antimicrobial medicines which in turn results in increased, prolonged and expensive hospital admission. 5 Hence, drug utilization research can increase our understanding of how drugs are being used and pave the way to manage undesirable health and/or economic problems resulted from inappropriate use. Several reports have investigated the antibiotic utilization pattern in various hospitals around the world.1-5 These studies have reported concern about the continuous, indiscriminate, and excessive use of antimicrobial agents that promote the emergence of antibioticresistant organisms.6 More than 80% of the most common bacteria, Staphylococcus aureus are now resistant to penicillin such as ampicillin.7 Given the fact that the rule and regulation of drug control in developing courtiers is not as firm as developed countries, high level and irrational antimicrobial use, in fact, would aggravate the emergency of antimicrobial resistance. 8 Monitoring antimicrobial use as well as evaluating prescription habits are among the strategies recommended to contain resistance to antimicrobials in hospitalized patients. Antimicrobial resistance substantially raises already-rising health care costs and ultimately increases patient morbidity and mortality. 9 Hence, the present study was conducted to determine antibiotic utilization among inpatients at ARH in Mekelle, Ethiopia.

2 II.

3 Methodology a) Study Area

The study was conducted in Ayder referral and teaching hospital (ARH), in Mekelle town which is located 783 km away from Addis Ababa, capital city of Ethiopia. ARH provides its medical services to around 8 million populations in its catchment areas of Tigray, Afar and South-eastern parts of the Amhara Regional States. It has

a total capacity of 500 beds in four major departments and other specialty units along with six other affiliated hospitals in the Tigray regional state. The hospital has more than 45 specialists in the various areas of medical specializations and adequate number of other health professionals which constitute the health care team. b) Study design, study population and sampling An institution based cross-sectional study was conducted in medical, gynecology and obstetrics, and surgical wards from September to December, 2012. The study population was all admitted patients in the aforementioned wards within the study period. The sample size was calculated by considering 95% confidence interval, 5% margin of error and 10% contingency for loss. The calculated sample size was 170. Samples were selected using simple random sampling within their respective wards and the samples were allocated to each ward proportionally.

4 c) Data collection and analysis

The medical record (chart) of each patient was reviewed and information pertinent to the objective of the study was collected. Medication data including name of the antibiotics prescribed, dosage regimen (dosage form, dose, route, frequency and duration of administration) and use of antibiotic combination were noted.

Data were coded, checked for completeness and consistency. Data processing and analyzing were done by using statistical package for social sciences (SPSS) version 20 and Microsoft excel 2010. Descriptive statistics such as frequency and proportion for categorical variables including cross-tabulations were used for data summarization. The local prices of antibiotics were based on the respective hospital's pharmacy prices. All p values were two tailed with the significance level set at 0.05. Use of antibiotics was measured based on the standard treatment guideline (STGs) prepared by FMOH and distributed to different hospitals including ARH.

5 d) Ethical consideration

The study was approved by the health research ethics review committee (HRERC) of college of health sciences, Mekelle University. The purpose of the study was explained to respective departments and letter of permeation was sought from the heads of departments of Internal medicine, Surgery and Gynecology and obstetrics.

III.

6 Results

7 a) Demographic and clinical characteristics of inpatients

Medical records of 722 patients were reviewed in order to identify the use of antibiotics during their hospital stay. Among these, 170 patient's medical records with complete information were found to be eligible for further study. The demographic characteristics of the patients are shown in Table 1. About 53.3% of them were female, and three quarter of patients belonged to the 53-92 year age group. The patients were admitted in three different wards i.e. surgical, internal medicine and gynecology and obstetrics ward with gynecology being the highest with 87 (51.2%) admissions. Among the total, 255 patients received antibiotics and the percentage of antibiotics utilization was calculated to be 35.6%. Patients admitted in three wards with antibiotics regimens included infections of different organ systems. Most patients were diagnosed with respiratory tract infections (RTI) 69(37.1%), followed by genitourinary infections (GUTI) 45(24.2%) (Figure 1). 2). Among these, 100(32.7%) antibiotics were prescribed from cephalosporins followed by 48(15.7%) from nitro immidazoles (metronidazole) and 46(15%) from penicillins. Surprisingly, only 2(0.7%) aminoglycosides was prescribed during the study period. From the total single antibiotics, the majority of the antibiotics were given intravenously 171(55.9%) followed by oral administration 134(43.8%) (Figure 3). Antibiotic therapy was found to be inappropriate in 137 patients (80.6%). The most common reason for inappropriateness was improper duration of treatment (DOT) 65(47.4%) followed by improper drug regimen 52(38%) and unjustified use 20(14.6%) (Table 4). All of the reasons for inappropriateness were found to be statistically significant.

8 Discussion

Appropriate antibiotic use has both clinical and economic significance to any health system and should be given adequate attention. Inappropriate use of antibiotics can potentially lead to antimicrobial resistance and increase the necessity to use more expensive antibiotics to treat common and life threatening infections. 10 The finding of the present study revealed the presence of high levels (80.6%) of the inappropriate use of antibiotics in the study area. This result is more or less similar to the findings of studies done in Thailand (80.9%) 11 and Japan (73.3%) 6; higher than study conducted in Sudan (60%) 3 and Gondar, Ethiopia (70.8%) 12; and much higher than the study conducted in Canada (13.8%) 13 and Turkey (35.6%) 14. From this trend it can easily be understood that the principles of rational use of antimicrobial have been well established in developed countries whereas their inappropriate use is still out of control, in developing countries. For that matter, a selective restriction policy of antibiotic use with the aid of agreed guidelines can lower the rate of inappropriate use of antibiotics in developing country including Ethiopia. Besides, using an antibiotic order form for restricted antibiotics and audited by pharmacists could enhance a more appropriate use of the antibiotics.

The possible reasons for irrational use of antibiotics were also assessed in this study. Duration of treatment (47.4%), regimen (38%), and unjustified use (14.6%) were found to be significantly associated with inappropriate

use of antibiotics in this hospital ($p<0.05$). Similar reasons were also forwarded in the results of the study done by Baktygul K and his co-workers. 6 Besides, drug that did not follow the specified indications, no dosage adjustment in patients with renal impairment, improper dose, improper dosing interval were reported as reasons for irrational antibiotics use in the study conducted in teaching hospital, Thailand.11 The group of drugs mostly used in the study site included cephalosporins , nitro immidazoles and penicillins. The same group of antibiotics but different in proportion with the current study was also reported by **??**atakam P et al., 2012.9 In addition, penicillins, aminoglycosides, and cephalosporins were demonstrated as the most frequently used antibiotic group in the result of the study done in Japan. 6 From the preceding it is understood that penicillins and cephalosporins have been continued to be a mainstay of therapy in hospitals because of their broad spectrum of activity, clinical efficacy and favorable tolerability profiles.6 However, studies in hospitals of Jordan15 and Estonia16 reported different groups of antibiotics as compared to the aforementioned studies. For instance, fluoroquinolones, penicillins, and aminoglycosides were the most commonly used antibiotics in Jordan whereas tetracyclines and aminoglycosides were the antibiotics used most commonly in Tartu hospital, Estonia. In general, the wards of similar medical specialties used similar groups of antibiotics.

The most frequently used single antibiotics in the current hospital were ceftriaxone (28.7%), followed by metronidazole (15.7%), anti-TB drugs and clarithromycin (7.1%), whereas study conducted in Libya 9 reported amoxicillin+clavulanic, ceftriaxone and metronidazole were the commonly utilized antibiotics with proportion of 31.3, 26.6 and 13.3%, respectively. Another study from Japan indicated that penicillin G , gentamicin and metronidazole were the most frequently used antibiotics of which Penicillin G was the most prevalent with 24.5% as opposed to 15.9 % for gentamicin and 15.4% for metronidazole6.The variation observed could be due to differences in disease pattern and drug availability in different countries.

It is generally preferable to keep the number of antibiotics per prescription as low as possible to minimize the risk of drug interaction, development of bacterial resistance and hospital cost, and to enhance patient compliance. 17 In this study, a considerable number of patients received as many as 3 to 4 antibiotics in a single encounter, whereas majority received only 1 or 2 antibiotics. The average number of antibiotics used per encounter in this study was more or less similar to what was obtained in teaching hospitals of Southern Nigeria 4 and northwest Ethiopia. 12 However, there was polypharmacy in more than half of (59.8%) the encounters which is far from WHO recommended value **??**1.6-1.8) in this study. This might be due to empirical use of antibiotics as infectious diseases are prevalent in Ethiopia.

Respiratory tract infections (37.1%), genitourinary infection (24.2%), infections related to pregnancy and childbirth (7.5%), gastrointestinal infections (6.9%), cancer (4.3%) and parasitic diseases (3.2%) were the conditions for which patients were admitted with antibiotics regimens in the hospital. These findings are in agreement with other local studies 12 as well as studies in Africa 9 and Asia. 6, 11 However, recent survey in South Nigeria found that the conditions for which antibiotics were prescribed included trauma (14.3%), malaria fever (14.1%), cardiovascular diseases (13.5%), retroviral disease (11.8%), and central nervous system disorders (6.1%).17

Administering antibiotics using intravenous (IV) route is appropriate when oral route is not effective, rapid response is needed, and large doses are required which is not feasible with the oral route. 18 In this study, 55.9% of the antibiotics were administered through IV route while 43.8% were administered orally. Similar findings were also revealed in the studies conducted in hospitals of Nigeria 17 and Japan 6.

Changing route of administration from intravenous to oral route has been studied and shown to save costs, shorten the length of hospital stays, and decrease the adverse reactions of intravenous administration, all with equal therapeutic outcome. 6 The cost of antibiotics used by the patients during the study period was also investigated in the current study. A total of 3243 USD (55125 ETB) was spent by the patients for antibiotics which is 0.5% of the annual budget of the hospital for medications. This finding is in accordance with the study done by Erah PO and his co-workers in Nigeria. 17 In their result, the authors pointed out that many antibiotics in Nigeria are too expensive for the patients to purchase and the possible reasons mentioned by the authors includes high cost of transportation and many local taxes. All in all, where possible, nearly all patients would prefer to receive treatment with minimum cost. However, due to irrational drug use and high resistance of many microorganisms to many other antibiotics, the prices being paid by patients for medicines are major concern in health care delivery in developing countries. In our setting, for instance, there was a high use of intravenous antibiotic. This could be raised as one reason for high cost incurred by the patients in the study period as intravenous antibiotics account for the most expensive category of antibiotics in hospitalized patients.19

9 V. Conclusions and Recommendations

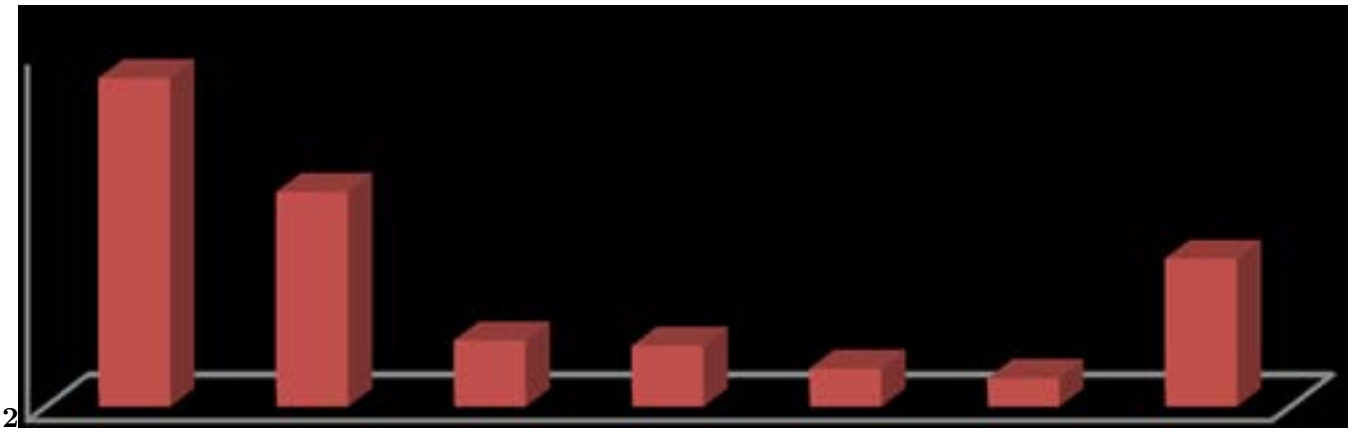
The prevalence of inappropriate use of antibiotics in Ayder referral hospital was 80.6%. The major reasons for inappropriate use of antibiotics were found to be duration of treatment, regimen and unjustified use. Respiratory tract infections (RTI) and genitourinary infection (GUTI) were the two most commonly reported diagnosis for which patients received antibiotics in the current study. Cephalosporins , nitro immidazoles, and penicillins were mostly used groups of drugs, whereas ceftriaxone, metronidazole and anti-TB drugs were the most frequently used single antibiotics in the hospital. Parenteral route of administration was the most common route of administration. Moreover, relatively large amount of money (3243 USD) was spent by the patients for antibiotics.

Hence, the following specific recommendations have been made based on the finding of the study in order

to give a clue about the possible direction to follow and focus to alleviate the problems of antibiotics resistance occurred due to drug misuse. It is known that cost is an important factor governing access to and use of medicines in developing countries and irrational use of antibiotics could significant results in an increased cost. Therefore, many healthcare institutions should introduce programmmes aiming at reducing the expenditure by improving rational antibiotic use, initiating education campaigns, regulating drug auditing practices, restricting dispensing techniques and controls. Furthermore, patients on intravenous therapy often has prolonged hospital stay to complete antibiotic treatment, a switch from intravenous to oral therapy could favor an earlier discharge and directly save health care costs. [1]

1

Figure 1: Figure 1 :



2

Figure 2: Figure 2 :

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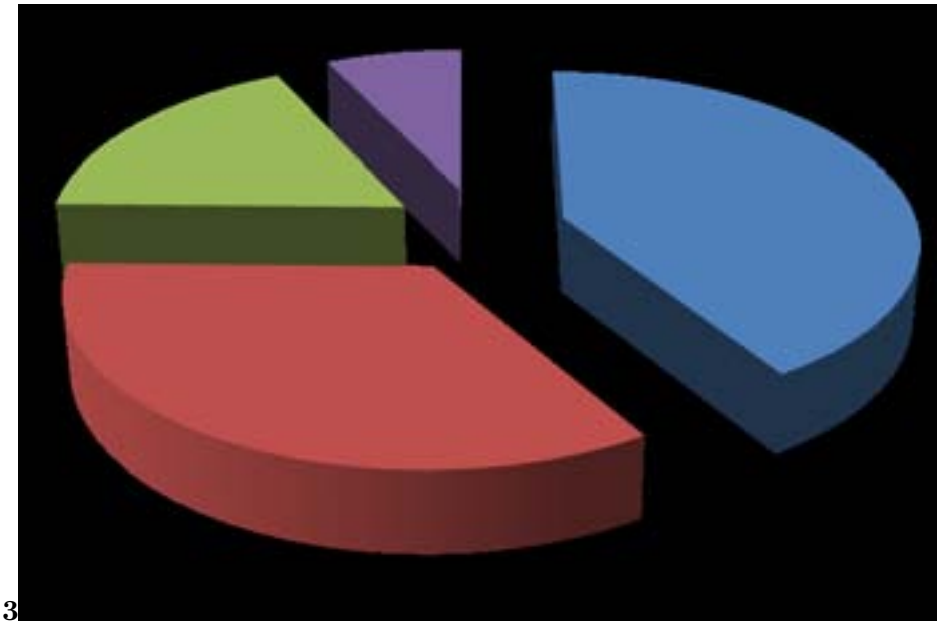

Figure 3: Figure 3 :

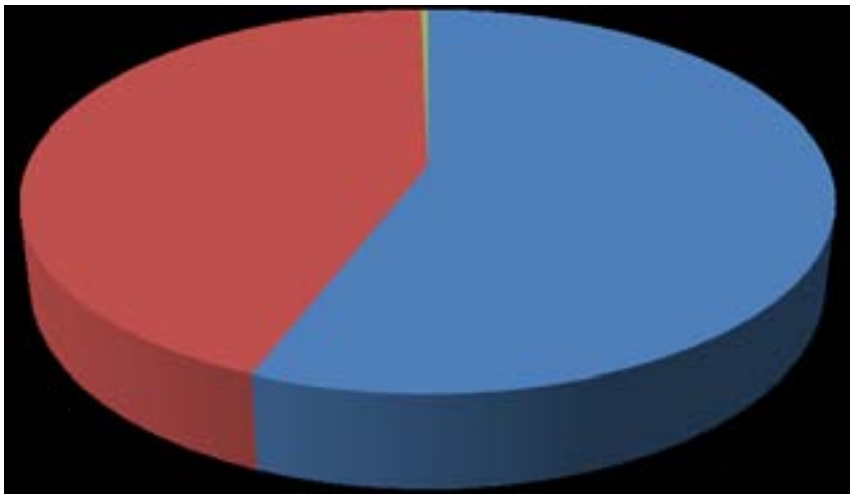

Figure 4: Antibiotics

1

Variables	(n=170) Frequency	Percentage (%)
Gender		
Male	79	46.5
Female	91	53.5
Age group		
19-52	127	74.7
53-92	43	25.3
Ward		
Internal Medicine	87	51.2
Surgery	47	27.6
Gynecology and obstetrics	36	21.2

Figure 5: Table 1 :

2

Antibiotics Group a	Frequency	Percentage (%)
Cephalosporins	100	32.7
Nitro immidazoles	48	15.7
Penicillins	46	15
Anti-TB b	32	10.4
Quinolones	31	10.1
Macrolides	26	8.5
Tetracyclines	18	5.9
Aminoglycosides	2	0.7
Other antibiotics c	3	1

[Note: a Grouping was based on 'Anatomical Therapeutic Chemical Classification System' b Isoniazid, ethambutal, rifampicin, streptomycin c Other antibiotics Included Clindamycin, VancomycinThe frequency of single antibiotics use is shown in]

Figure 6: Table 2 :

3

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Figure 7: Table 3 .

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Figure 8: 10.0% 20.0% 30.0% 40.0% 37.1% 24.2% 7.5% 6.9% 4.3% 3.2% 16.8% 41.2% 34.1% 17.6% 7.1% Single antibiotics Two antibiotics Three antibiotics Four antibiotics

3

Single Antibiotics	Frequency	Percentage (%)
Ceftriaxone	88	28.7
Metronidazole	48	15.7
Anti-TB a	32	10.4
Clarithromycin	22	7.1
Ciprofloxacin	19	6.2
Ampicillin	18	5.9
Doxycycline	17	6
Amoxicillin	12	3.9
Cloxacillin	12	3.9
Norfloxacillin	12	3.9
Cephalexin	10	3.2
Other antibiotics b	16	5.2

[Note: a Isoniazid, ethambutal, rifampicin, streptomycin b Included Erythromycin, Gentamicin, Vancomycin, Augmentin, C.penicillin, Clindamycin, Azythromycin, Ceftazidime, Cefuroxime, TTCeyeointment]

Figure 9: Table 3 :

4

Reason for inappropriateness	Frequency	Percentage (%)	p-value	OR (95% CI)
DOT	65	47.4	0.011	4.725 (1.425-15.671)
Regimen *	52	38	0.009	15.900 (2.025-124.850)
Unjustified use	20	14.6	0.024	3.814 (1.198-12.148)

Improper dose and frequency

d) Cost of antibiotics

The local price and total cost expenditure of antibiotics during the study period is shown in Table 5. A total of 55125 (3243 USD) Ethiopian birr was spent to purchase 306 antibiotics during the study period.

Figure 10: Table 4 :

5

Antibiotics prescribed	Unit	Frequency	Average DOT a	Total Qty prescribed	Unit price		Total cost		Percent (%)
					Br	Ce	Br	Ce	
Ceftriaxone	Vial	Bid	9 days	88	9	90	15681	60	28.4
Metronidazole	Vial	Tid	11 days	48	18	00	28512	00	51.7
Clarithromycin	Tab	Bid	9 days	22	5	40	2138	40	3.88
Ciprofloxacin	Tab	Bid	8 days	19	1	00	304	00	0.55
Ampicillin	vial	Qid	7 days	18	1	56	786	24	1.4
Doxycycline	Cap	Bid	8 days	17	0	28	76	16	0.14
Amoxicillin	Cap	Tid	13 days	12	0	88	411	84	0.7
Cloxacillin	Vial	Qid	9 days	12	2	90	1252	80	2.27
Norfloxacin	Tab	Bid	8 days	12	0	59	113	28	0.21
Cephalexin	Cap	Qid	7 days	10	2	50	700	00	1.27
Erythromycin	Tab	Qid	12 days	2	0	80	76	80	0.14
Vancomycin	vial	Bid	5 days	2	142	00	2840	00	5.15
Gentamycin	Amp	Bid	7 days	2	1	56	43	68	0.08
Augmentin	Tab	Tid	9 days	3	3	70	299	70	0.54
C.penicillin	Vial	Q4hr	19 days	2	4	40	1003	20	1.82
Clindamycin	Tab	Tid	11 days	1	9	40	310	20	0.56
Azithromycin	Tab	Qd	3 days	1	26	13	78	39	0.14
Ceftazidime	Vial	bid	10 days	1	7	00	140	00	0.25
Cefuroxime	cap	Bid	7 days	1	23	20	324	80	0.59
TTCeyeoint	tube	bid	5 days	1	3	25	32	50	0.06
		Total					55125	59	

*[Note: *The local prices of antibiotics were based on the respective hospital pharmacy's prices *1USD=17 ETB (exchange rate when the study was conducted) a DOT: duration of treatment IV.]*

Figure 11: Table 5 :

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