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Retrospective assessment of irrational use of antibiotics to children attending in Mekelle general hospital

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Abstract: Background**:** In the last decades, there has been an escalating consumption of antibiotics with the number of antibiotic prescriptions increasing worldwide. Since children are more vulnerable to infectious disease than adults, more antibiotics are prescribed for them. Inappropriate use of antibiotics has resulted in a major increase in the development of multi-drug resistant pathogens with great implication in terms of morbidity, mortality and costs. The objective of this study was to determine the irrational use of antibiotics prescribed for children under the age of 15 years in Mekelle general hospital. Methods: A retrospective cross sectional study was conducted. Four hundred three children's prescriptions and corresponding cards which were recorded by the year 2012 were selected by systematic random sampling proportionally from each month in the year. Results: Of all antibiotic prescriptions reviewed, the numbers of outpatient antibiotic prescriptions were 222 (55.1%) while inpatient prescriptions were 181 (44.9%).The predefined antibiotics indicators like percentage of antibiotics prescribed, frequency of route of administration, antibiotics prescribed from Standard treatment guideline, proportion of antibiotics, cost of antibiotics per antibiotics days, incidence and antibiotics utilization ratio were determined and 141(35.1%) were treated with different antibiotics irrationally. Conclusion: The finding of this study indicated that antibiotics were prescribed irrationally. Prescriptions containing one or more antibiotics constituted 73.68% of all prescriptions and around 5.9% of encounters were treated without any diagnosis. T he study has revealed that third generation cephalosporin (ceftriaxone) has been highly prescribed in the study hospital.

Keywords: Antibiotics, Children, Cross sectional, Irrational, Mekelle, Retrospective

1. Introduction

The discovery of antibiotics has brought about a dramatic turning point in the treatment of infectious disease in the 20th century [1]. In the last decades there has been an increase in consumption of antibiotics with the number of antibiotic prescriptions increasing worldwide, although recently, some stabilization or decrease in this trend is evident in some countries [2]. More than 50% of all medicine worldwide are prescribed, dispensed, or sold inappropriately and not in the principle of rational drug use. More than 50% of patient fails to take them correctly. This inappropriate dose results in increasing morbidity and mortality particularly for childhood infectious disease and chronic disease [3]. Various studies conducted in developed as well as developing countries regarding the safe and effective use of antibiotics showed that, irrational antibiotics use is a global problem and about 75% of antibiotics are prescribed inappropriately [4].

The increased and inappropriate consumption of antibiotics has been related to the development of microbial resistance to many agents. Increased levels of microbial resistance are a global concern and some countries have implemented strategies to decrease unnecessary antibiotic prescription. Since 1993 World Health Organization (WHO) in collaboration with international network for rational use of drug introduce asset of indicators called "drug use indicators" which includes prescribing indicators, patient care indicators and facility indicators [5]. WHO also recommends different strategies to decrease inappropriate antibiotics prescription and for the containment of antimicrobial resistance.

A quarter of world's population is concentrated in developing countries and has access only to small proportion of world's drug product [6]. Health budget in these country are generally small when compared to the

developed countries and 30-40% of the total health budget is spent on drug [7]. However, studies carried out in these countries have a significant degree of inappropriate utilization of drug in their health facility [8].

Inappropriate use of antibiotics results in Antimicrobial resistance, which also results in waste of resources and serious financial consequences. Mortality and morbidity are increased by delays in administering effective treatment for infections caused by resistant microbes. This can result in costly prolonged illness and hospitalization, and the use of other than first line drugs may also increase costs 100 fold making it unaffordable for many governments and patients especially in developing countries. As an example, in the United States, more than half of the 2 million nosocomial infections occurring annually are as a result of antibiotic resistant organisms. This has an estimated impact of more than 70,000 lives, $5 to $10 billion dollars annually [9, 10]. It also results patient harm in terms of poor patient outcome and adverse drug reaction. Non sterile injection is increasing the transmission of hepatitis, HIV/AIDS, and other blood born disease [11].

As microbial resistance is not limited by borders this problem is also the problem of Ethiopia. Infectious diseases are major causes of morbidity and mortality in the country, and together with nutritional problems account for 60-80% of the health problems. Less large scale studies done on the extent of antimicrobial resistance in Ethiopia, but existing reports indicate that it is a growing problem and irrational use of antibiotics was identified as one of the major problems contributing to antimicrobial resistance [12].

An assessment of the pharmaceutical sector in Ethiopia by the Federal Ministry of Health (FMOH) in collaboration with World Health Organization showed a high rate of antibiotic prescriptions (55.43%) contained one or more antibiotics [13]. Another study in health care facilities in North West Ethiopia showed that antibiotics account for 60% of all prescriptions [14] while a South West Ethiopia study indicated that 25.6% of prescriptions include an antibiotic which is closer to the WHO recommendation of less than 25 % [13,15].

Generally, the development of antimicrobial resistance, antibiotic consumption in hospital and non-hospital settings and the economic impact of antibiotic prescription in un-indicated situation are due to the rise and inappropriate consumption of antibiotics [16-19].

Observation of prescription patterns in Mekelle general hospital indicates that antibiotics might be inappropriately prescribed. It would appear that there is a trend to give most outpatients and hospitalized patients antibiotics with general practitioners and other prescribers prescribing antibiotics as an empiric treatment. Observations also suggest that the number of prescriptions for the previously reserved classes of antibiotics like 3rd generation cephalosporin have recently been increasing. This could be either due to increased availability of these classes of antibiotics or it could be increased microbial resistance to other antibiotics.

Currently, there is very limited research conducted in this important issue especially in pediatrics and it was necessary to conduct a study to determine the utilization of antibiotics and correlation between diagnosis of infectious disease and prescribed antibiotics. The aim of this study was to determine the irrational use of antibiotics prescribed for children under the age of 15 years in Mekelle general hospital in Tigray, Northern part of Ethiopia.

2. Methods

2.1. Ethical Approval

After thorough revision of the paper approval letter was obtained from Mekelle University College of Health Science research & community service Ethical review committee and Tigray regional health bureau. The hospital administrators and staffs were briefed about the objectives of the study and the patients name was kept anonymously by using identification number to refer each study participants.

2.2. Study Area

The study was conducted in Mekelle general hospital from 5/01/2013 to 10/01/2013. The hospital has pediatrics, internal medicine, surgical and obstetrics and gynecology unit. There were four pharmacies used for inpatient and outpatient and seven specialists, but no pediatrician and 6 general practitioners, 47 nurses, 3 pharmacists and 5 pharmacy technicians.

2.3. Study Participants and Sampling Techniques

This study used a retrospective cross sectional study design and the source populations were all children below the age of 15 years. Children who took anti Tuberculosis drugs, topical antibiotics, antifungal and antiviral drugs were excluded from the study. The sample size was calculated using single population proportion formula and by considering a 50% prevalence of irrational antibiotics prescription, 95% Confidence Interval and 5% non-response rate gives the final sample size of 403. To select the study subjects, all antibiotics prescribed from 01/01/2012 to 30/12/2012 for children less than 15 years were identified, categorized and listed on monthly bases and used as a sample frame. Then the sample was proportionally allocated for each month and finally simple random sampling technique was used to select study subjects. Data were collected using two structured checklist. The first checklist was used to collect necessary information from the prescribed paper such as Age, sex, prescribed type of antibiotics, preparation, duration and route of administration and the second check list used to collect the type and number of infectious diseases diagnosed. The cost of antibiotics prescribed was calculated based on the cost from a government owned pharmaceutical importer and Distributor Company that supplies drug for hospitals in the country.

Invoices of pharmaceuticals purchases made from this company were used to determine the cost of a given antibiotic. In cases where an antibiotic was not commonly supplied by Pharmaceutical importer and Distributor Company (PHARMID) other costs from the providing companies used to calculate the costs. Two pharmacy technicians were selected and trained to collect the data using standardized tool. Finally the collected data were entered to EPINFO 3.5.1 and transferred to SPSS 16 for further analysis.

3. Result

3.1. Percentage of Prescription with Antibiotics

Of all antibiotic prescriptions reviewed, the numbers of outpatient antibiotic prescriptions were 222 (55.1%) while inpatient prescriptions were 181 (44.9%).

3.2. Distribution by Age Group

The majority, 148 (36.7%), of outpatient and inpatient antibiotic prescriptions were issued to infants 1month to 12 month of age whilst only 5(1.2%) of prescriptions were for new born in between 0-72 hours of age (table1).

Table 1. *Age distribution of children below 15 years who took antibiotics in Mekelle General Hospital, 2012*

Age	Frequency	Percent
0-72hrs	5	1.2
72hrs-28days	43	10.7
1mon-12month	148	36.7
1year-5yers	69	17.1
Greterthan5years	138	34.2
Total	403	100.0
Sex		
Male	254	63
Female	149	37

3.3. Average Number of Antibiotics per Prescription

The average number of antibiotics per encounter was identified for both inpatient and outpatient prescriptions. According to this the average number of antibiotics per encounter was 1 and 1.05 for inpatient and outpatient, respectively.

3.4. Percentage of Encounters with Injectable Antibiotics

The number of encounters that received one or more injectable antibiotics was determined. Out of all antibiotics prescribed, 172 (42.7%) for inpatient and 148 (36.7%) for outpatient encounters involved injectable antibiotics (Intra Venous or Intra Muscular). The oral liquid (syrup) formulations were the most frequently prescribed antibiotic dosage form 199(49.4%), followed by 160 (39.7%) intravenously (Fig 1).

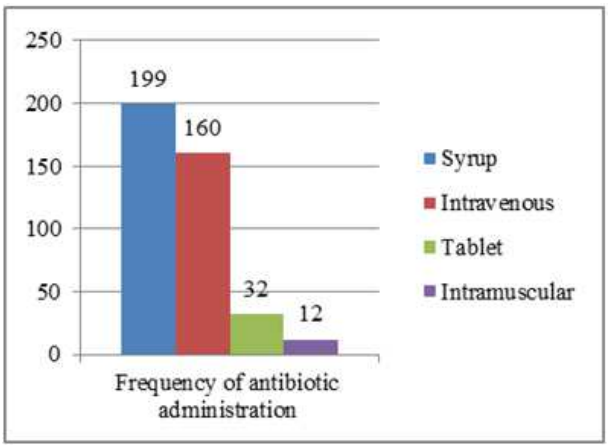

Figure 1. *Frequency of antibiotic administration in Mekelle general hospital, 2012*

3.5. Aggregate Antibiotics Use Indicators

3.5.1. Antibiotic Days Prescribed by Study Period

A total of 2000 antibiotic days was prescribed in the sampled antibiotics. Outpatients accounted for 55.1% of the antibiotic days prescribed when compared with the inpatient which accounts 44.9%. Amoxicillin was the most frequently prescribed antibiotic which account for 165(40.9%) of the prescription (table 2).

3.5.2. Antibiotic Days Prescribed by Dosage Form

About 9(2.2%) of different antibiotics prescription did not mention the strength of antibiotics or the dose was not known.

3.5.3. Antibiotic Utilization Ratio

The antibiotic utilization ratio is the ratio of the number of antibiotic days to the number of Inhabitants. In Mekelle general hospital the number of antibiotic days by 2012 was 71489.36 for both inpatients and outpatients for pediatrics department. The target population that is being served by the hospital is 100,000. Therefore, the antibiotic utilization ratio for the year was 0.71(0.71 antibiotics days per person per year) indicated in table 2.

3.5.4. Incidence of Antibiotic Use

The incidence of antibiotic use, the number of antibiotic prescriptions per 1000 inhabitants, for the hospital was aggregated based on the number of inhabitants and prescriptions encountered in the study period. The number of antibiotic prescriptions encountered in the hospital was 15,120 for both outpatients and inpatients and 6,789 for inpatient and 8,331 for outpatient. This incidence of antibiotic use for outpatients was 8.331 (8.331 antibiotic prescriptions per 1000 inhabitants per year). The incidence of antibiotic use for inpatients was calculated i.e. the number of antibiotic prescriptions per 100 beds/ day. The number of hospital beds and the occupancy rate was taken into account. The inpatient incidence of antibiotic use was 65 antibiotic prescriptions per 100 beds per day in pediatrics department (table 2).

3.5.5. Cost of Antibiotics

A total of 3,000,000 (three million) Ethiopian Birr (ETB) which is equivalent to 168,539.33$ was spent to purchase pharmaceuticals in the hospital. Of this the pediatrics antibiotic expenditure alone was 219,718.73 ETB ($12,343.43) which constituted 7.32% of all drug expenditure. The expenditure on amoxicillin alone was 68,096 ETB ($3,825.23), which accounted for 30.99% of all antibiotic expenditure. Ceftriaxone was the second followed by Penicillin, cloxacillin, Augmentin (amoxicillin + clavulanic acid) and ampicillin and gentamycin are most prescribed from combined antibiotics followed by ceftriaxone and gentamycin. These agents accounted for 86.2% of all the costs of antibiotics dispensed in the study period. The cost of ceftriaxone, penicillin, cloxacillin, ampicillin and gentamycin, and ceftriaxone and gentamycin accounts for about 96% of all inpatient antibiotic expenditures (table 2).

3.5.6. Cost per Antibiotic Day

Cost per antibiotic day was calculated by dividing the total antibiotic expenditure in the hospital pediatrics department of both outpatient and inpatients in the year by the total number of Antibiotic days prescribed in the year. Based on this the cost per antibiotic day for the hospital pediatrics department was 219,718/71,489.36=3.07 ETB ($0.17 USD).

3.5.7. Cost of antibiotics per patient care day

The cost of antibiotic per patient care day was calculated by dividing the total expenditure on antibiotics used in inpatients in the year by the total patient bed days in a year. The total cost of inpatient antibiotic expenditure at Mekelle general hospitals was 98,653.38 ($5542.32 USD). The number of patient care days in a year (i.e. occupied patient bed days in a year) was 5,398 for pediatrics department. The cost of antibiotic per patient care day in the study year was 18.27 ($1.03USD) (table 2).

Table 2. *Aggregate antibiotic use indicators at Mekelle general Hospital pediatrics department in 2012*

AB use indicators	Inpatient	Outpatient
Antibiotic utilization ratio, outpatient (antibiotic days/person/year)	5.75 days person year	0.75 days person year
Incidence of antibiotic Use	6789/5398/x100 =125.77	8331/250000x1000=33.32
% of Drug budget spent on antibiotics	7.32%	
Cost per Antibiotic day (ETB/USD)	3.07ETB ($0.17)	
Cost of Antibiotic per patient care day (ETB/USD)	18.27 ($1.03USD).	
Percentage of encounters with antibiotic prescribed	77.3%	
Average number of antibiotics per encounter	1.2	1
Percentage of encounters with antibiotics prescribed	104.49	
Percentage of encounters with injectable antibiotics prescribed	42.7	
Percentage of antibiotics prescribed from STG	93.4%	89.5%
Percentage of antibiotics dispensed	99.3%	100%
Proportion of antibiotics	0.73	
Number of patient (bed) days	31x48.4x365=547,646	

4. Discussion

Antimicrobial resistance has reached worrying levels for many common pathogens. It costs money, livelihoods and lives and threatens to undermine the effectiveness of health delivery programmers. For example, penicillin resistance in S. pneumonia ranges from 5.8% to 54% in different countries. The WHO Global Strategy for Containment of Antimicrobial Resistance attributes the growth of resistance to combination of overuse, misuse, and under-use (irrational use) of antimicrobials. It has been estimated that 50% of antibiotic use is by humans (of which 80% is outside of hospitals), and 20-50% of this is unnecessary [13, 15].

One of the commonly used drug use indicators in assessing rational prescribing practice is the percentage of prescriptions that contain one or more antibiotics. The review of prescriptions in this study showed that prescriptions containing one or more systemic antibiotics constituted 73.68% of all prescriptions. Which is significantly higher than the values observed in other public hospitals in Yemen (22.7%) and at Jimma University Hospital in South West Ethiopia (25.6%) , Harari region hospitals in east Ethiopia (57.0%), Mizan hospital (64%), Hosanna hospital (60%) and Dilla hospital 57% in Southern Ethiopia, ; in North West Ethiopia health centers 60% and a national average 55.43% of hospitals. When this result was compared to other developing countries it was again higher than Ikeja general hospital in Nigeria (54.8%) and two teaching hospitals in Sudan (65%), national figure for Uganda (61.9%) and Nigeria (59%), and 45% in Serbia [13, 15, 16, 20]. This result was almost three times higher than the WHO ideal value of less than 25 % and it showed that antibiotics were over prescribed in the Mekelle general hospital pediatrics department.

Moreover the correlation of antibiotic use and infectious diseases diagnosed in the hospital was a good indicator that there is over use or misuse of antibiotics. The number of infectious diseases diagnosed did not correspond to the number of antibiotic days prescribed in the department. Therefore, it indicated that there was significantly excess use of antibiotics irrationally for infections that do not require them or over use of antibiotics for infectious diseases that require them.

As the results of the study suggests the significant difference in the number of antibiotics required and antibiotic days prescribed could also be attributed to failure to follow the national treatment guidelines as developed by the Drug Administration and Control Authority of Ethiopia. According to this study for infectious diseases diagnosed and average number of antibiotic courses started was 1.3 at Mekelle Hospital for children. When overall antibiotic days prescribed and required were compared, there were 0.3 times more antibiotic days prescribed than were required for. The reasons for such variation in antibiotics prescribed and infectious diseases diagnosed might be related to the treatment guideline, the training and experience of prescribers, laboratory facility, absence of Drug and Therapeutic Committee to manage medicine use and lack of hospital specific formulary at this facility.

In this study the average number of antibiotics per encounter was 1 for outpatients and 1.11 for inpatients. This result was higher than the finding in Zimbabwe which was 0.72 among dispensing doctors and 0.54 for non-dispensing doctors [21]. As this finding was specific to antibiotics only it would not be accurate to compare with other research findings that were not limited to antibiotics.

The percentage of encounters with antibiotic injections prescribed varied significantly between outpatient and inpatient departments. At inpatient departments 95.2%, 172 out of 181sampled antibiotic prescribed were parenteral formulations. This is higher than the finding of 79.4% in Sari Emam University Hospital in Iran [14]. In the outpatient departments however, the percentage of encounters with antibiotic injections prescribed was low (0.04%). This low rate of injections prescribed is important in minimizing the risk of diseases transmission like HIV/AIDS, hepatitis and other blood borne diseases [22]. The number of antibiotics prescribed from the Essential Drug List in this study was 74.8% in inpatient and 63.0% in outpatient departments. This result was lower than other studies such as Harar Region Hospitals in East Ethiopia which was 96.53% (14) and Lao PDR, 84% [23]; Northern Cape Province in South Africa, 92.5% [18]. However, this result is higher than the study result for the city of Kragujevac in Serbia, 21-65% [14]. This result suggests that the percentage of antibiotics prescribed from the EDL was low. The LDDH was 90.8% for outpatient and 76.1% of inpatient antibiotic prescriptions were for drugs included on the list as developed by the Drug administration and control authority (DACA) of Ethiopia. This is higher than the percentage of drugs prescribed from the EDL of Ethiopia. However, the percentage of antibiotics prescribed from the LDDH particularly for inpatients is low compared to what was supposed to be (100%), although it is better in outpatient departments (90.8%). As this drug list is developed to regulate the rational use of drugs by the various levels of health institutions it is of utmost importance that health facilities adhere to this drug list especially to minimize misuse and overuse of antibiotics. The possible reason for better compliance to LDDH than EDL could be related to the number and type of antibiotics that is included in the list. The LDDH contained more antibiotics than the EDL. All antibiotics that are in the EDL are also in the LDDH but there are antibiotics that are in the LDDL but not in EDL. For example cephalosporin among the most prescribed antibiotic class according to this study, were not included in the EDL while they are in the LDDL and STG [12].

The percentage of prescribed antibiotics actually dispensed in this study was 99.3% both for outpatients and inpatients. This finding was encouraging although the ideal value of 100 % was not attained. This result was higher than that of the Harar region which was 93.7% [13]. This is also higher than other studies, 39-68% in Serbia [14]. This suggests that the actual availability of antibiotics is adequate although it needs improvement to reach the ideal value of 100%. The cost of antibiotics calculated in this study showed that antibiotics accounted for 7.32% of all drug budgets. This figure showed that the antibiotic expenditure as compared to other medicine expenditure was high because it is only for pediatric patients. Of the expenditure on antibiotics a few antibiotics constituted the highest percentage.

The cost per antibiotic day at the Mekelle hospitals was 3.07 ETB ($0.17). If this was used for a full antibiotic course of about seven days the cost for treatment with a single antibiotic is about 13.03 ETB ($0.78). This is not an affordable cost for the majority of the population living in the districts assuming that there are also other drugs prescribed. This shows that there is need for interventions to minimize the cost of antibiotics particularly in the selection of cheaper but effective antibiotics. In general the study showed that indiscriminate use of antibiotics was common. This was evident in the high percentage of antibiotic encounters, the fact that antibiotic days prescribed were unreasonably high and a significant number of 787.89(5.9%) encounters are treated without any diagnosis.

5. Conclusion

This study indicated that antibiotics were over prescribed. Prescriptions containing one or more antibiotics constituted 73.68% of all prescriptions which is three fold of the standard developed by World health organization. It also showed that the average number of antibiotics per encounter was greater than one, for both inpatients which is an indicator of overuse of antibiotics. This study revealed that third generation cephalosporin was highly prescribed antibiotics and were prescribed without diagnosis and with non-infectious disease. This indicated that standard treatment guidelines and drug formularies were not closely followed in treating infectious diseases. This was also confirmed by the finding that the percentage of antibiotics prescribed from the STG was low.

The study showed that the number of antibiotic days prescribed does not correspond to the number of infectious

diseases diagnosed. The finding indicated that antibiotics constituted 7.32% of all drug budgets; the cost per antibiotic day was 3.07 ETB ($0.17).

List of Abbreviation

AIDS= Acquired immune deficiency syndrome
DACA= drug administration and control authority
DLDH= drug list for district hospital
EDL= essential drug list
PHARMID= pharmaceutical importer and distributer
STG= standard treatment guideline

Competing Interest

The author(s) declare that they have no competing interests.

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