



RATIONAL USE OF ANTIBIOTICS IN THE TREATMENT OF DIARRHEAL DISEASES IN THE PEDIATRIC POPULATION IN THE AGE GROUP (0-6) YRS

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ABSTRACT

To check whether the use of antibiotics are rational in Acute Diarrhoeal Diseases in the paediatric age group (0 – 6 yrs) A retrospective study was conducted on total of 100 patients using patient profile sheets as data collection tool at Pediatrics Department, Government District Headquarters Hospital, Tiruppur. In the age group 1-3 years, the number of patients was found to be significantly less (37%) when compared to the number of patients in the age group 3-6 years (63%). Acute diarrheal diseases in children presented with various symptoms, the most being Loose Stools (85%) and vomiting in 65% of the patients. The most commonly prescribed antibiotic was Ceftriaxone

55%, followed by Amikacin (48%) and Cefotaxime (39%), anaerobic antibiotic – Metronidazole (21%), Ciprofloxacin (14%) and Gentamicin (4%). 94% of patients received antibiotics, out of which 12% received 1 antibiotic each and 82% were prescribed more than 1 antibiotic. The index of antibiotic prescribing is found to be 0.31. The mean value of IRDP was 3.103 close to the WHO optimal value of 5. Protocol of management strategy of acute diarrheal diseases in the concerned hospital was not optimal but found near to standard recommended guidelines. Educational programs with emphasis on Home management and Prevention of Diarrheal Diseases are necessary to create awareness among mothers.

KEYWORDS: Antibiotics, Rational Use, Dehydration, ORS.

INTRODUCTION

WHO defined **Rational use of drugs** as patients receiving 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 both to them and the community. Irrational use of medicines include the use of too many medicines (poly pharmacy); use of antibiotics for non- bacterial infections; inadequate dosage of antibiotics; use of injections when oral medication is appropriate; prescribing medicines that contravene clinical guidelines; and patient self-mediations.

WHO and the **International Network of Rational Use of Drugs (INRUD)** have developed a set of drug prescribing indicators to be used as measures of prescribing performance.

- Average number of drugs prescribed per encounter.
- Percentage of drugs prescribed by generic name.
- Percentage of patient encounters with an antibiotic prescribed.
- Percentage of patient encounters with an injection prescribed.
- Percentage of drugs prescribed from the national EDL or the facility's formulary.

Antibiotics are one of the most commonly prescribed drugs today. Rational use of antibiotics is extremely important as its use can adversely affect the patient, cause emergence of antibiotic resistance and increase the cost of health care.

Diarrhea is defined as a change in consistency and frequency of stools, I.e., liquid or watery stools, that occur >3 times a day. If there is associated blood in stools, it is termed as dysentery. In the vast majority of cases, these acute episodes subside within 7 days. Acute diarrhea may persist for >2 weeks in 5-15% cases, which is labeled as persistent diarrhea.

Diarrheal illnesses accounted for about 4-6 million deaths from around 1 billion episodes of diarrhea every year in children younger than 5 years. Most recent estimates suggest the number of deaths is closer to 2.5 million. Diarrhea, however, remains a prolific killer of children.^[6-14]

Diarrhea is the major cause of malnutrition and mortality in children younger than 5 years of age, especially in developing countries so that 80% of mortalities occurs in the first two years of life.^[1,2] Persistent diarrhea is followed by death in 35% of cases. Malnutrition along with diarrhea leads in persistent diarrhea and further negative impact on mortality rate.^[3]

In developed countries, over-prescription of antibiotics for AGE was reported, and physician responses to patients' treatment expectations was an important cause of inappropriate antibiotic use.^[15] However, in as many as 10% of children admitted to hospital, unnecessary antimicrobial therapy is prescribed because of a "probable bacterial cause".^[16]

Diarrhea control programme needs to be reinforced and the mothers made aware to improve the existing practices regarding the management of acute diarrhea in children.

Causes of Acute Diarrhea	
Bacterial	<i>E.coli (ETEC, EIEC, EHEC), Shigella, Vibrio cholera, Salmonella typhi and paratyphi, Campylobacter species, Bacillus cereus, Clostridium perfringens, C. difficile, Staphylococcus aureus, Yersinia enterocolitica</i>
Viral	<i>Rotavirus, Astrovirus, Coronavirus, Enteric adenovirus</i>
Parasitic	<i>Giardia lamblia, Cryptosporidium parvum, Entamoeba histolytica, Cyclospora, Isospora belli</i>

Clinical features: Child is thirsty, irritable, pinched look, abdominal pain, weight loss, vomiting, fever, breathing becomes deep and rapid (Kussmaul breathing), Signs of dehydration can be seen like depressed fontanel, sunken eyes, tongue and inner side of cheeks appear dry, distended abdomen in hypokalemia, weak and thread pulses, low blood pressure and reduced urine output, Affected children may present with abdominal distension, paralytic ileus and muscle hypotonia.

Assessment of child with Acute Diarrhoea: It is important to differentiate whether this is a persistent diarrhea following an acute dehydrating diarrheal episode, so clinical settings may require additional specialized treatment.^[4] The need for any specialized investigation and treatment will depend on the clinical picture of the patient and would usually include stool MC&S to exclude parasites, stool reducing substances and elastase, and possibly sweat test or coeliac serology.^[5] **History:** This should include information on onset of diarrhea; duration and number of stools per day, blood in stools, number of episodes of vomiting, presence of fever, cough or other significant symptoms, type and amount of fluids and food taken during the illness and preillness feeding practices, drugs or other local remedies taken like loperamide and immunization history. **Clinical Examination:** Dehydration is assessed by general conditions like: - Alertness, Irritability, Consciousness, Skin turgor, Urine output.

Lab investigations: Stool microscopy, Stool culture, Urine routine estimation, Blood gas estimation, Serum electrolytes, Complete blood count, RFT.

Antimicrobial agents used frequently for the treatment of acute infectious diarrhea

- Ampicillin 50-100 mg/Kg/day in four doses if weight under 20 Kg, 250-500 mg four times a day if weight above 20 Kg.
- TMP-SMX 10/50 mg/Kg/day in 2 doses.
- Chloramphenicol 50-100 mg/Kg/day in 4 doses.
- Tetracycline 20-50 mg/Kg/day in 4 doses.
- Doxycycline 2-4 mg/Kg/day in 1-2 doses (adult dosing 100mg BD may be used if wt above 45kg).
- Ciprofloxacin 20-30 mg/Kg/day in 2 doses.
- Ceftriaxone 50-100 mg/Kg/day in 1-2 doses.
- Cefixime 7.5-10 mg/Kg/day in 1-2 doses.
- Metronidazole 20-40 mg/Kg/day in 3 doses

METHODOLOGY

Study Site: The study was carried out at the Department of Pediatrics, Govt. District Hospital, Tiruppur.

Study Design: This is a retrospective study.

Study Period: This study was carried out for a period of six months, January 2018- June 2018.

Sample Size: A total of 100 patients.

Study Population: Pediatric population aged 0-6yrs on treatment for diarrheal diseases who attended the Pediatric In Patient Department of Govt. District Headquarters Hospital, Tiruppur were included in the study. The patients were selected on the basis of inclusion and exclusion criteria.

Inclusion Criteria: Pediatric population aged 0-6yrs with risk factors and symptoms of diarrheal diseases. Patients who attended IPD with diarrheal episodes, vomiting, fever, dehydration, reduced urine output and reduced food and water intake.

Exclusion criteria: Infants less than 1 year old, children with obvious malformations/ congenital anomalies, Immunocompromised/ HIV patients, children who were on any other treatment with steroids, anticancer drugs, antimetabolites, immunosuppressants, etc, mentally

ill patients on treatment with antipsychotics, antidepressants, etc, patients who were on any other treatment follow-up or after surgeries.

Study Methods

Methods for calculating prescription indicators: This indicator is aimed at assessing the extent of poly-pharmacy. The WHO proposes that optimally, this should be <2 . This indicator is obtained by first counting the total clinical encounters for which data was collected (x). Subsequently, the total number of medicines prescribed for the total encounters is determined (y). By dividing the total number of medicines prescribed (y) by the number of encounters (x) yields the average number of medicines per encounter (p). This is expressed mathematically as follows: $(p) = y/x$

Percentage of encounters with an antibiotic prescribed: This indicator assesses the frequency of antibiotic prescribing. The percentage of encounters with antibiotic prescribed (b) is calculated by dividing the number of clinical encounters in which one or more antibiotic was prescribed (f) by the total number of encounters (x) and expressed as a percentage. The WHO indicates that optimally, this value should be $<30\%$. Mathematical expression is provided below: $(b) = f/x * 100\%$

Percentage of encounters with an injection prescribed: This indicator describes the frequency with which injectable forms of medicines are prescribed. This indicator (j) is calculated by dividing the number of clinical or drug use encounters in which an injectable form of medicine was prescribed (t) by the total number of encounters studied (x) and expressed as a percentage. The WHO optimal value for this indicator is $<20\%$. Mathematical expression is presented as follows: $(j) = t/x * 100\%$

Percentage of medicines prescribed by generic name: This indicator is aimed at measuring prescriber's tendency to prescribe medicines using generic or international nonproprietary name (INN). This indicator (g) is calculated by dividing the total number of medicines prescribed in the INN format (d) by the total number of medicines prescribed (y) and expressed as a percentage. The WHO proposes that optimally, all medicines (100%) should be prescribed by generic names. The calculation of this indicator is expressed mathematically as follows: $(g) = d/y * 100\%$

Percentage of medicines prescribed from the EDL/ Formulary: The main focus of this indicator is to assess whether prescribing practices conform to drug use policy as pertaining to the use of EDL. The percentage of medicines prescribed from EDL (k) is calculated by dividing the number of medicines prescribed from the EDL (m) by the total number of medicines prescribed (y) and expressed as a percentage. Ideally, all medicines prescribed at PHC facilities should be from the EDL, hence the optimal value for this indicator is 100%.

$$(K) = m/y * 100\%$$

Index of Rational Drug Prescribing (Irdp)

Zhang and Zhi developed an index system to gauge the performance of a healthcare system in terms of drug utilization. For the calculation of non- poly pharmacy, rational antibiotic and injection safety indices, the following formula was used.

$$\text{INDEX} = \text{optimal value} / \text{observed value}$$

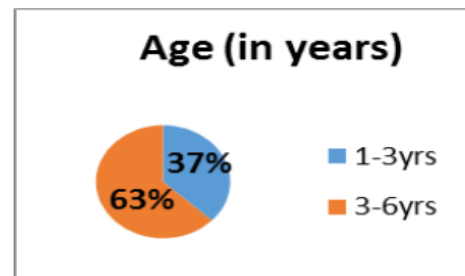
All other indices (index of generic name, index of EDL) were calculated by the following formula: $\text{INDEX} = \text{observed value} / \text{optimal value}$

OBSERVATION AND RESULTS

Age Wise Distribution

Table. 1.

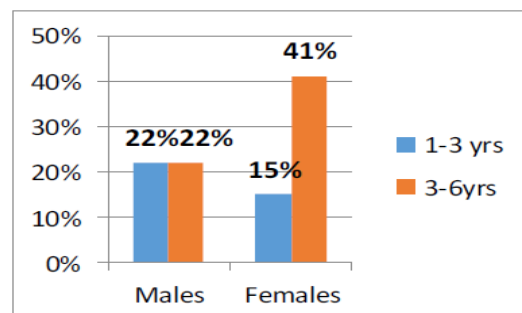
Age (in yrs)	Percentage
1-3	37%
3-6	63%
Total	100



Gender Wise Distribution

Table. 2.

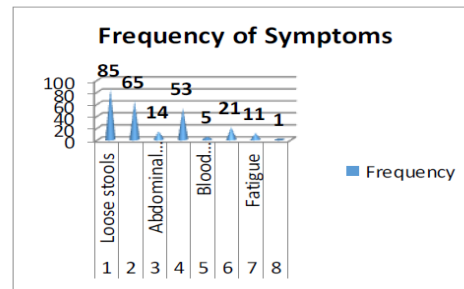
% of Males		% of Females		Total
1-3yrs	22	1-3yrs	15	100
3-6yrs	22	3-6yrs	41	
Total	44%	Total	56%	



Distribution of Symptoms

Table. 3.

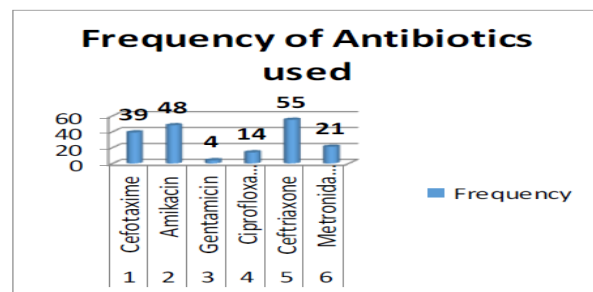
Serial No.	Symptoms	Frequency
I.	Loose stools	85
II.	Vomiting	65
III.	Abdominal pain	14
IV.	Fever	53
V.	Blood stained stools	5
VI.	Reduced urine output (dehydration)	21
VII.	Fatigue	11
VIII.	Hematemesis	1



Antibiotic Usage

Table. 4.

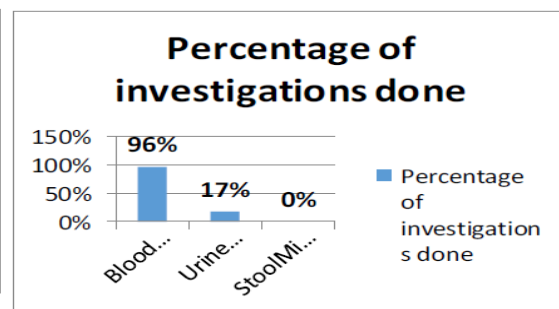
Serial No.	Antibiotics administered	Frequency
I.	Cefotaxime	39
II.	Amikacin	48
III.	Gentamicin	4
IV.	Ciprofloxacin	14
V.	Ceftriaxone	55
VI.	Metronidazole	21



Distribution on Routine Investigations

Table. 5.

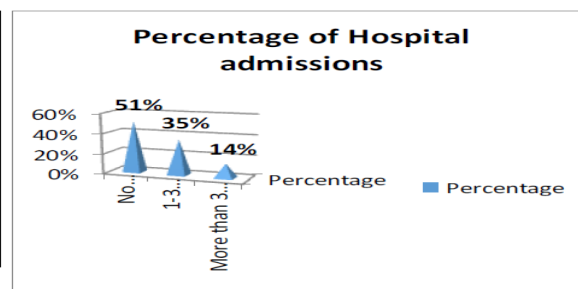
Routine Investigations	Percentage of investigations done
Blood routine examination	96%
Urine routine examination	17%
Stool Microscopy and culture	Not done
Total	100



Frequency of Hospital Admissions With Loose Stools

Table. 6.

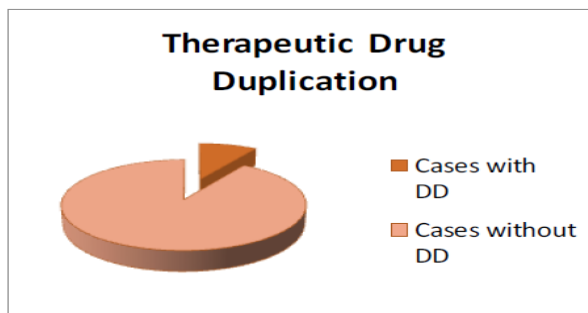
No. of Hospital admissions/month	Percentage
No admissions yet	51%
1-3 admissions/month	35%
More than 3 admissions/month	14%
Total	100



Therapeutic Drug Duplication Per Encounter.

Table 7

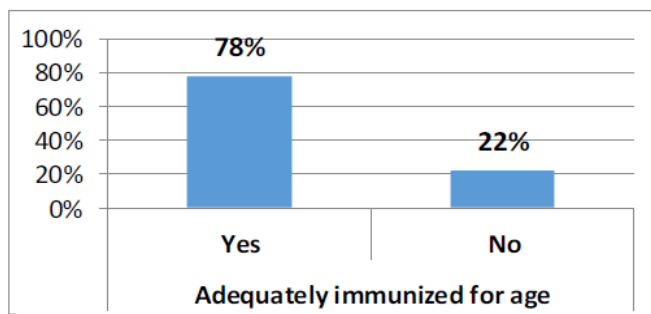
Therapeutic Drug Duplication	Percentage
Cases with DD	9%
Cases without DD	91%
Total No. of Prescriptions	100



Distribution Based on Adequate Immunization for Age

Table. 8.

Adequately immunized for age	
Yes	No
78%	22%
Total	100



Therapeutic Drug Duplication encountered in the Govt. Hospital

Average Number of Drugs Per Prescribing Encounters (degree of poly pharmacy).

Table. 9.

No. of drugs per patient	Frequency	Percentage%	Average	WHO Standard
1 or less	2	2%	4.14	1.6-1.8 (2 or less)
2	11	11%		
3	22	22%		
4	30	30%		
5	13	13%		
6 or more	22	22%		
Total no. of Drugs	414			

Percentage of Encounters With Antibiotics.

Table. 10.

Total no. of antibiotic encounters out of 100	% of encounters in which one antibiotic was prescribed	% of encounters in which more than one antibiotics were prescribed	WHO Standard
	12%	82%	<30% (20-26.8%)
	94%		

Percentage of Encounters With Injections Prescribed.**Table. 11.**

Total No. of encounters	% of encounters with an injection prescribed	WHO Standard
100	97%	<20%

Percentage of Drugs Prescribed By Generic Name**Table. 12.**

Total No. of drugs prescribed	No. of drugs prescribed by generic name	% of drugs prescribed by generic name	WHO Standard
414	402	97.1%	100%

Percentage of Drugs Prescribed from EDL/Formulary.**Table. 13.**

Total No. of drugs prescribed	No. of drugs prescribed from EDL/Formulary	% of drugs prescribed from EDL/Formulary	WHO Standard
414	414	100%	100%

Assessment of Prescribing Indicators**Table. 14.**

Prescribing indicators assessed	Average/ percentage	WHO Standard
Average number of drugs per encounter	4.14	2 or less
Percentage of encounter with antibiotics	94%	<30%
Percentage of encounter with injections	97%	<20%
Percentage of drugs prescribed by generic name	97.1%	100%
Percentage of drugs from essential drug list	100%	100%

Index of Rational Use of Medicines**Table. 15.**

Prescription indicators	Optimal Value	Observed Value	Individual Index (Optimal Index= 1)	IRDU (maximum IRDP = 5)
Average no. of drugs/ encounter	<3	4.14	0.72	3.103
Antibiotic prescribing	<30%	94%	0.31	
Injection prescribing	<10%	97%	0.103	
Generic name prescribing	100%	97.1%	0.97	
EDL/ Formulary prescribing	100%	100%	1	

DISCUSSION

The drug utilization study is being conducted widely and it is being carried out in different health care sectors. Such studies are helpful to determine the behavior of the use of medicines

most importantly antibiotics in a society. A survey based on prescription is considered to be one of the most effective methods to determine the prescribing approach of physicians. Pediatric patients in the age group 1-6 years were considered. In the age group 1-3 years, the number of patients was found to be significantly less (37%) when compared to the number of patients in the age group 3-6 years (63%). As far as the gender factor is concerned, the number of male patients was found to be equal (22%) in both age groups, whereas the number of female patients differed as 15% in the age group 1-3 years and 41% in the age group 3-6 years. Acute diarrheal diseases in children presented with various symptoms, the most being Loose Stools with a frequency of 85% followed by vomiting in 65% of the patients. There were also accompanied complaints of fever (53%), reduced urine output showing signs of dehydration (21%), abdominal pain (14%), blood stained stools (5%), fatigue (11%) and hematemesis in 1% of the patients. Such patients were prescribed antibiotics as a part of both out patient and in patient treatment setup. In our study, the most commonly prescribed antibiotic was Ceftriaxone 55%, followed by Amikacin (48%) and Cefotaxime (39%) for the treatment of ADD in children despite their side effects. Anaerobic antibiotic – Metronidazole (21%), Ciprofloxacin (14%) and Gentamicin (4%) were also prescribed by the physicians.

Commonly Used Antibiotics in District Headquarters Hospital, Tiruppur In the Treatment of Diarrhea in Children

Sr. No.	Name of Antibiotic	Mech. of Action	Adverse effects	Other Uses	Contra-indications
1.	Cephalosporins- Ceftriaxone	Inhibit bacterial cell wall synthesis- bactericidal	Pain at the site of injection, bleeding, nephrotoxicity, neutropenia, thrombocytopenia, disulfiram like reaction.	Enteric fever, RTI, UTI, septicemia, meningitis, alternative to penicillin	h/o penicillin allergy, h/o gastrointestinal diseases especially colitis, renal impairment
3.	Nitroimidazole- Metronidazole	Inhibit protein synthesis	Metallic taste, vomiting, peripheral neuritis, stomatitis, glossitis	H. pylori infections, amoebiasis, giardiasis, dysentery	In pregnancy, convulsive seizures, encephalopathy, aseptic meningitis, leucopenia
4.	Fluoroquinolones - Ciprofloxacin	Inhibit DNA gyrase & Topoisomerase 4	Reversible arthritis, arthropathy, tenosynovitis, tendon rupture	UTI, Typhoid, RTI, Gonorrhoea	h/o tendinitis, tendon rupture, Not used in children below 18yrs & in pregnancy,

					hypoglycemia, convulsions
5.	Aminoglycosides- Amikacin, Gentamicin	Bactericidal	Nephro, ototoxicity, neuromuscular blockade, super infection	Cholera, atypical pneumonia, malaria, rickettsia	Hearing impairment, preexisting renal Impairment.

Routine Investigations were done on the selected patients and the treatment provided. Blood Routine Examinations were done on 96% of the patients and appropriate antibiotics given. Urine routine examinations were done on 17% of the patients whereas Stool Microscopy and culture was not carried out in any of the patients with diarrhea. Thus the lack of necessary investigations poses a major problem in irrational drug use. Out of 100 children with diarrheal diseases selected for the study, 51% of the patients had no history of hospital admissions due to diarrhoea since birth. 35% were admitted to hospital 1-3 times in a month and 14% had history of more than 3 hospital admissions in a month due to diarrhea. In this study, 78% of the patients who reported with complaints of loose stools were adequately immunized for age. Rest of 22% of patients were not adequately immunized or unimmunized for age which calls for a need for public awareness regarding the importance of adequate immunizations and vaccine preventable diseases. Out of the 100 prescriptions, 9 prescriptions were found to have therapeutic drug duplication and 91 without drug duplication. Antibiotics are predominant among the prescriptions encountered with therapeutic drug duplication. The maximum number of drugs to be concurrently used is 2, but in a single prescription 3 to 4 drugs of the same class were prescribed.

Average number of drugs per prescription was 4.14, double the average number recommended by WHO. However, this cannot be considered irrational poly-pharmacy practice as there is need of empirical therapy till definitive diagnosis becomes clear and secondly for management of acute life threatening conditions. Most of the patients would usually require more than two drugs. Different studies conducted in India have varied results, but all of them point to a higher incidence of irrational use of drugs namely antibiotics. Approximately, 94% of patients received antibiotics, out of which 12% received 1 antibiotic each and 82% were prescribed more than 1 antibiotic. In an acute condition, there is a need to give broad spectrum antibiotics as empirical therapy, which is essential to narrow down the therapy as soon as we have a sensitivity report of the infecting organism. Over estimation of the severity of illness may be the main reason for such an empirical use of antimicrobials in acute conditions. Appropriate antibiotic use has both clinical and economic significance to

any health systems 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 conditions in future. The WHO assembly in May 2005 warned that antimicrobial resistance was rapidly increasing, with resistance of upto 70-90% to original first line Antibiotics (Penicillin, Ampicillin, Cephalosporin) for dysentery (*shigella*), pneumonia, gonorrhoea and hospital infections (*Staphylococcus aureus*). The optimal value of Antibiotic prescribing is <30%, and the index of antibiotic prescribing is found to be 0.31. The overuse of antibiotics contributes significantly to an increase in antibiotic resistance and leads to increase in adverse drug reactions. Numbers of encounters with injectable was on the higher end (97%), which again was justifiable on account of need of immediate drug action. The index of injection prescribing (0.103) shows great variation from the optimal index value.

The percentage of drugs prescribed by generic name is 100% according to WHO standards, but in this study, out of 414 medicines prescribed, 402 were only prescribed in generic name (97.1%). There are several benefits of prescribing drugs as generic such as increased patient compliance and lower cost of drug therapy. By using generic names of prescription, chance of duplication of drug products is eliminated. Interventions are needed to raise the awareness of prescribers about the importance of generic prescribing which may also improve patient's medications adherence. The percentage of prescribing drugs from EDL/Formulary in the hospital was 100% as recommended by WHO. The mean value of IRDP was 3.103 close to the WHO optimal value of 5. The optimal index for all indicators was set as 1. The values closer to 1 indicated rational drug use and vice versa.

The index of poly pharmacy (0.72) shows variation from the WHO recommended standard which indicated that poly pharmacy had the most prominent effect on irrational drug prescribing in the government hospitals. Therefore action should be taken to raise the awareness of the prescribers about poly pharmacy as prescribing indicator and about the importance of rational prescribing of antibiotics and its effect on the patients. The medication error arises out mainly due to illegible prescription by the physicians including illegible handwriting, failure to mention the decimal points, dose and dosage forms.

CONCLUSION

- Protocol of management strategy of acute diarrheal diseases in the concerned hospital was found near to standard recommended guidelines.

- Similar studies with prospective view should be carried out frequently to collect more information on drug use pattern and to comment on rationality of the usage of antibiotics.
- During the analysis, the criteria of adequate immunization for age were found to be low among the patients and the frequency of previous hospital admissions due to diarrhea were high owing to the lack of knowledge among the mothers regarding active home management practices of ADD and the importance of adequate immunization for age.
- During assessment of rationality using WHO indicators, irrationality was found in prescribing antibiotics, injections and using generic names.
- The overuse of antibiotics contributes significantly to an increase in antibiotic resistance and leads to increase in adverse drug reactions.
- Prescribers should be encouraged to prescribe in generic names as it helps to prevent duplication of drugs and injections according to guidelines set by WHO. Preference should be given to oral route when patient is able to take the drug orally.
- The percentage of prescribing from EDL/Formulary in the hospital was 100% as recommended by WHO.
- The index of poly pharmacy showed great variation from the WHO recommended standards. Physician should be advised to prescribe lowest number of medicines needed and on the basis on routine baseline investigations to reduce the overuse of antibiotics.
- Educational programs with emphasis on Home management and Prevention of Diarrheal Diseases are necessary to create awareness among the general public especially mothers/caretakers.

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