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Antimicrobial abuse in treatment of acute diarrhea.

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Abstract

Background: Diarrheal disorders in childhood account for large proportion of deaths. They may have significant impact on psychomotor and cognitive development in young children. In a community with high incidence of diarrhea (like the Iraqi one), proper management is expected to reduce morbidity and mortality.

Aim of the study: To see how common antimicrobials were used at home for diarrhea, what type of antimicrobials?

Patients and Methods: The mothers (or the accompanying relatives) of children admitted for acute diarrhea (*i.e.*, <2 weeks) in Al-Zahraa maternity and children hospital, Al-Najaf filled for the period March 2019 to October, 2020 information about 100 children was obtained. The accompanying relatives were interviewed about the causes of diarrhea before admission, what antimicrobials were given at home? Prescribed by whom? Finally, what was the diagnosis their child labeled with in the hospital?

Results: Acute gastroenteritis was the most frequent 'pre-hospital' diagnosis (26%), followed by "cold" (21 and "teething" (15%). Seventy-eight percent of the 'total' and 88% of those with pre-hospital diagnosis of 'gastroenteritis' received antimicrobials. Metronidazole (58%) followed by cephalosporins (30%) and co-trimoxazole (29%) were the most frequent agents used. Two or more antimicrobials were prescribed for the 'same' child in 40% of cases.

Conclusion: Antimicrobial abuse in acute diarrhea was obvious in this study because more than 75% of the total cases (regardless of the pre-hospital diagnosis) and most of those with the diagnosis of gastroenteritis were given antimicrobials (most commonly metronidazole). Two antimicrobials were given in a high percent of cases (about 40%).

Keywords: Diarrhea, Acute gastroenteritis, Antimicrobial abuse, Antibiotics.

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Introduction

Definition and physiology

Diarrhea, defined as increased total daily stool output, is usually associated with increased stool water content. For infants and children, this would result in 'stool output >10 g/kg/24 hr, or more than the adult limit of 200 g/24 hd When diarrhea lasts >2 wk, it is considered 'chronic'. The term 'gastroenteritis' denotes infections of the gastrointestinal tract caused by bacterial, viral, or parasitic pathogens [1].

Diarrheal disorders in childhood account for a large proportion (1.8%) of childhood deaths, with an estimated 1.8 million deaths per year globally. The World Health Organization (WHO) suspects that there are >700 million episodes of diarrhea annually in children <5 years of age in developing countries [1].

In developing countries, children may have an average of 2-3 episodes per year, with an annual death of 3-4 million [2]. This means that (1%-4%) of the billion episodes of diarrhea worldwide each year is fatal [3]. In developed countries like USA and Canada, the death from diarrhea is estimated to be 325-425 a year [4]. An estimated hospital admission for diarrhea in USA is almost 50 per 10,000 children every year and approximately (9%) of all hospitalization of children under 5 years of age was because of diarrhea. This makes a direct loss of 2 billion dollars a year.

In Iraq after the first Gulf War and during economic sanctions, the death from diarrhea increased from 1950 in 1989 to 21000 in 1998 *i.e.*, 14-fold increase. Among the reasons were unsafe water supply, defective sanitation and malnutrition (Table 1).

	Infancy	childhood	Adolescent
Carmon causes	GE	Food poisoning	GE
	Systemic infection	Systemic infection	Food poisoning
	Antibiotics associated diarrhea	Antibiotics associated diarrhea	Antibiotics associated diarrhea
	Over feeding		
Other causes	Primary disaccharidase def.	Toxic ingestion	Hyperthyroidism
	Hirschsprung's disease		
	Adrenogenital syndrome		
	Neonatal opiate withdrawal		

Table 1. Etiology of acute diarrhea.

Aim of the study

To see how common antimicrobials were used at home in acute diarrheal episodes and what type of antimicrobials were used.

Patients and Methods

The mothers (or the accompanying relatives) of children admitted for acute diarrhea (*i.e.*, <2 weeks) in Al-Zahraa maternity and children hospital, Al-Najaf filled for the period March 2010 to October 2020 information about 100 children was obtained with age ranging between 2 months to 5 years.

The accompanying relatives were interviewed about the causes of diarrhea before admission, what antimicrobials were given at home, prescribed by whom, finally what was the diagnosis their child labeled with in the hospital?

Results

The patients studied were 100, 56 (56%) were males; 44 (44%) females. The male: female ratio was 1:0.79. The age of children ranged from 2 months to 5 years. Seventy six (76%) cases were infants and the remaining 24 (24%) were 1-5 years.

Pre-hospital diagnosis as an acute gastroenteritis was the most common (26%) followed by cold (21%) and teething (15%). Pre-hospital diagnoses are shown in Table 2.

Pre-hospital diagnosis	N	%
Gastroenteritis	26	26
Cold	21	21
Teething	15	15
Unknown-diagnosis	14	14
Contaminated-food and/or water	12	12
cow's milk allergy	6	6
Changing formula	1	1
Drug induced	1	1
Measles	1	1
Post-vaccination	1	1
Hospital acquired	1	1
total	100	100

Table 2. Pre-hospital diagnosis of the children with diarrhea.

Two or more antimicrobials are prescribed in 40 (40%) cases. The types of antimicrobials prescribed and the person who prescribe them are shown in Tables 3 and 4. Two or more antimicrobials may be used for the same child Tables 5 and 6.

Antimicrobials prescribed	Number of children received antimicrobials	%
Metronidazole	58	58
Cephalosporin	30	30
Co-trimoxazole	29	29
Gentamicin	17	17
Ampicillin	5	5
Unknown antibiotic	4	4
Erythromycin	1	1
Lincomycin	1	1
Nalidixic acid	1	1

Table 3. Types of antimicrobials prescribed.

Source of prescribing the antimicrobials	No. of children received them	%
Private clinic doctor GP	53	53
Relatives	16	16
Primary care center doctor GP	14	14
specialist	11	11
Friend	3	3
Pharmacist	3	3

Table 4. Source of prescribing the antimicrobials.

Hospital diagnosis	No. of cases	%
Gastroenteritis	74	74
Urinary tract infection	7	7
secondary lactose intolerance	5	5
Sepsis	6	6
Pneumonia	4	4
Hepatitis	1	1
Nosocomial	1	1
Typhoid	1	1
Unknown	1	1
Total	100	100

Table 5. Hospital diagnosis.

Pre-hospital diagnosis		Hospital diagnosis		
Cause	No. of cases	No. of cases	Percent%	Cause
Gastroenteritis	26	22	84.6	Gastroenteritis
		2	7.7	UTI
		1	3.8	Typhoid
		1	3.8	Pneumonia

Cold	21	14	66.6	Gastroenteritis
		3	14.28	UTI
		2	9.5	Pneumonia
		2	9.5	2n lactose intolerance
Teething	15	13	86.6	Gastroenteritis
		2	13.2	unknown
Don't know	14	9	64.2	Gastroenteritis
		4	28.57	sepsis
		1	7.1	Pneumonia
Contaminated food	12	9	75	Gastroenteritis
		2	16.6	UTI
		1	8.3	hepatitis
Cow's milk allergy	6	3	50	Gastroenteritis
		3	50	2 lactose intolerance
Changing formula	1	1	100	Gastroenteritis
Drug induced	1	1	100	Gastroenteritis
Hospital acquired	1	1	100	nosocomial
Post-measles	1	1	100	Gastroenteritis
Postvaccination	1	1	100	Gastroenteritis
Breast milk allergy	1	1	100	sepsis

Table 6. Pre-hospital versus hospital diagnosis.

Discussion

An acute gastroenteritis was the most frequent pre-hospital diagnosis and found in 27 cases (27%); 84.6% (22 cases) of them were labeled as acute gastroenteritis in the hospital;7.7% (2 cases) as urinary tract infection; 3.8% (1 case) as pneumonia and the last 3.8% (1 case) as typhoid. In lauys study, pre-hospital diagnosis as "gastroenteritis" was found in 58% of cases [5]. Cold was the 2nd most frequent pre-hospital diagnosis and found in 21 cases (21%). Cold environment exposure is "not a cause" of diarrhea; in fact, moderate hypothermia may lead to intestinal hypomotility [6]. Many families in our community are advised to keep the child warm when having diarrhea which may lead to increased fluid loss from skin, make the child uncomfortable, fretful& may possibly delay seeking medical advice. In fact, 66.6% (14 cases) of those with pre-hospital diagnosis as cold were labeled in the hospital as gastroenteritis; 14.28% (3 cases) as urinary tract infection; 9.5% (2 cases) as secondary lactose intolerance; 9.5% (2 cases) as pneumonia in Lauy's study cold was the 3rd most frequent diagnosis and found in 8% of cases [5].

Teething was the 3rd most frequent pre-hospital diagnosis and found in 15 cases (15%). Teething is not a cause of diarrhea and this may be a reason for delaying proper management [7]. 86.6% (13 cases) of those having teething as pre-hospital diagnoses were regarded as gastroenteritis in the hospital 6.6% (one case) was of unknown diagnosis. In lauys study, teething was the 4th most frequent and found in 6% of cases. In 14 cases the mothers (or the accompanying relatives) didn't know the diagnosis. It might represent: (i) The relatives had sought medical advice directly and came to hospital (*i.e*., they didn't see a doctor before), (ii) They were not told the diagnosis by their doctors, (iii) Their doctors didn't know the diagnosis and had been send them to the hospital for further investigations and treatment, (iv) Lack of knowledge and awareness by the relatives towards the cause of their children illness (simply they didn't know). 64.2% (9 cases) were regarded as gastroenteritis in the hospital; 28.57% (4 cases) as sepsis and 7.1% as pneumonia.

Food poisoning is a common cause of diarrhea; nevertheless those 12 cases (12%) with pre-hospital diagnosis of food poisoning were labeled with gastroenteritis (9 cases or 75%), urinary tract infection (2 cases or 16.6%) and hepatitis (1 case or 8.3%). Children whose diarrhea was ascribed to unsuitable cow's milk formula (6 cases) were diagnosed in the hospital as gastroenteritis (3 cases or 50%) and sec. lactose intolerance (3 cases or 50%), While that single child (1%) whose diarrhea ascribed to unsuitable breast milk was found to have sepsis and the other one child (1%) with changing formula to have gastroenteritis in the hospital. Unsuitable formula was found in 3%of cases in Lauys study [5,7].

That single case (1%) with pre-hospital diagnosis of drug-induced diarrhea was labeled with gastroenteritis in the hospital, although drug-associated diarrhea is one of the common causes of diarrhea in pediatrics. In Lauys study, drug effect was found in 0.5% of cases. Another single case (1%) had a pre-hospital diagnosis of hospital-acquired infection (*i.e.,* nosocomial) which was also labeled in the hospital with that diagnosis. Diarrhea may commonly complicate nosocomial infection [8].

Although gastrointestinal symptoms (such as diarrhea and vomiting) are common in infants and small children with measles; that single case (1%) with pre-hospital diagnosis of measles, labeled as gastroenteritis in the hospital [9]. Vaccination may produce systemic reaction (like anaphylaxis or urticaria) [10]. Some adverse events, however, occur coincidentally in temporal association with vaccination and are not caused by the vaccine. Determination of causality of an adverse event in a single child may be difficult. However, that single case (1%) with pre-hospital diagnosis of vaccine-induced diarrhea was labeled as gastroenteritis in the hospital.

Most children with acute "infectious" diarrhea would not benefit from antimicrobial therapy; [11]. It is said that "polypharmacy is prosthesis for the physician's incompetence. The less he knows, the more prescriptions he gives two or more antimicrobials were prescribed in 40% of cases [12]. Seventy-four cases (74%) were attributed to a cause other than acute gastroenteritis before hospitalization; nevertheless 55 cases (74%) were given an antimicrobial which was unjustified and unacceptable practice. Patients with 'infectious' diarrhea associated with certain bacterial and protozoal agents may benefit from antimicrobial therapy.

Widespread indiscriminate use of antimicrobials can result in many problems including: development of resistance, the side effect of drugs, and super infection when normal flora is eradicated [13]. In addition, antimicrobials therapy with enterohemorrhagic *Escherichia coli* (*E. coli* 0157:H7) may be harmful, possibly because of induction of disease-producing bacteriophage and cytotoxin production by co-trimoxazole and quinolones [13]. Viral agents are the most common cause of acute gastroenteritis in childhood followed by bacteria then protozoal infection; nevertheless, metronidazole was the most common antimicrobial used (58 cases, *i.e*., 58%) although its main indications are antibiotic-associated colitis (*Clostridium difficile*) and protozoal infections *Entamoeba histolytica*, *Giardia lamblia* (symptomatic giardiasis in endemic areas), and *Blastocystis Hominis*.

Cephalosporin was the 2nd most frequent antimicrobial used (30%) followed by co-trimoxazole (29%). Metronidazole was the most frequent antimicrobial used in Luay's study (16.5%) followed by gentamicin (10.8%) and penicillin (6.9%) [5]. Four cases (4%) received antimicrobials, but their relatives didn't recall its name. Timely antimicrobial therapy in selected cases of diarrhea may reduce the duration and severity of diarrhea and prevent complications. While these agents are important to use in specific cases, their widespread and indiscriminate use leads to the development of antimicrobial resistance. Most of the antimicrobials were prescribed by private clinic doctors (GP) (53%), followed by relatives (16%), and then primary care center doctors (GP) (14%). Abuse of antimicrobials in acute diarrhea has been arisen by Najim's editorial in an Iraqi journal [14].

Conclusion

Abuse of antimicrobials in acute diarrhea was obvious, as more than three quarters of the cases whether diagnosed as gastroenteritis or not, received antimicrobials. Even more than two antimicrobials were prescribed in some. Metronidazole was the most common antimicrobial used; followed by cephalosporins and co-trimoxazole. Private clinic doctor (GP) was the major source of prescribing antimicrobials followed by relatives and then primary care center doctors (GP).

Recommendations

- Improve case management of diarrhea.
- Many of the pre-hospital diagnoses are arbitrary, wrong and should be avoided.
- Improve laboratory facilities.
- We should educate and encourage the medical and paramedical staffs as well as the community about the indication of antibiotics in diarrheal illness.
- Promotion of diarrhea preventive strategies.
- Promotion of exclusive breast feeding.
- Improved complementary feeding practices.
- Immunization.
- Improved water and sanitary facilities.
- Promotion of personal and domestic hygiene.

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