



Original Research Article

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Irrational Use of Antibiotics in Management of Acute Watery Diarrhea in Children under 5 years

Samah Omer Abdallah Ibrahim ^{1*}, Mutaz Abdallah Gamaledin²,
Omer Saeed Magzoub ³ and Isam Eldin H. A. Magid⁴

¹*Pediatric, Faculty of Medicine, Dongla University, Sudan*

²*Consultant Pediatrician, Head Department of Pediatric, Faculty of Medicine, Ribat University, Khartoum, Sudan*

³*Specialist General Pediatric, AinAl-Khaleej Hospital, UAE*

⁴*Pediatric and Child Health, Faculty of Medicine and Health Science, National University, Sudan*

**Corresponding author*

ABSTRACT

Diarrheal disease is the second leading cause of death in children under five years. It's responsible for around 525, 000 deaths of children every year. The use of antibiotics for treatment of pediatric diarrhea has been observed in spite of World Health Organization guidelines which discourage the use of antibiotics for treating acute diarrhea. Here we assess the extent of irrational use of antibiotics in management of acute watery diarrhea among under-five children both at home and health setting. Children under 5 years of age ($n = 147$) presenting at Mohammed Al-Amin Hamed Hospital with acute watery diarrhea were included in the study. Background information on the children was collected by questionnaire, including home treatments, and clinical information including symptoms and treatment were provided at hospital. Data were collected and analyzed for associations between variables and use of antibiotics using Chi-square statistic (X^2). Among the 147 patients, 87 (59.3%) were males and 60 (40.7%) were females. The mean age of the children was 12 ± 12.1 months. 119(80.9%) were treated as in patient, while 28(19.1%) were treated as outpatient. 61(53%) were admitted because of ongoing losses, (24.3%) admitted because they were malnourished children, 25(21.7%) had some dehydration. (63.7%) didn't have stool analysis done and only 36.3% had stool analysis done. 110 (76%) received antibiotics, which prescribed by health care provider. Regarding antibiotics, 82(63.4%) were third generation cephalosporin in form of Ceftriaxone, cefotaxime and cefixime, followed by benzyl penicillin and gentamycin injection for 72 (55%), and 24 (18.6%) metronidazole. Use of antibiotics was not influenced by age of the child, reason of admission or stool analysis. The only variable positively associated with antibiotic prescription was diarrhea from one to three days at admission. It is clear that young children presenting with acute watery diarrhea to Mohammed Al-Amin Hamed Hospital are likely to be treated with antibiotics, despite there is being no obvious reason that this treatment is appropriate. The present study results support the need for institution-based antimicrobial stewardship to be implemented to decrease antimicrobial resistance.

Keywords

Watery diarrhea in children, irrational use of antibiotics

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Introduction

Diarrhea is the passage of loose or watery stools at least three times in a 24 hour period. Diarrhea is usually a symptom of intestinal infection, which caused by a variety of viral, bacterial, and parasitic organisms. Infection is spread through contaminated food or water, or from person to person as a result of poor hygiene. Diarrhea could be associated with vomiting, or systemic manifestations, such as fever and abdominal cramps (<https://www.who.int/en/news-room/fact-sheets/detail/diarrhoeal-disease>).

Diarrheal disease is a leading cause of child mortality and morbidity in the world. Worldwide, 780 million individuals lack access to improved drinking water and 2.5 billion lack improved sanitation. Diarrhea due to infection is widespread throughout developing countries. In low-income countries, children under three years old experience on average three episodes of diarrhea every year. Each episode deprives the child of the nutrition necessary for growth. As a result, diarrhea is a major cause of malnutrition, and malnourished children are more likely to fall ill from diarrhea (<https://www.who.int/en/news-room/fact-sheets/detail/diarrhoeal-disease>).

Diarrheal disease is the second leading cause of death in children under five years of age and was responsible for the deaths of 370,000 children in 2019 (https://www.who.int/health-topics/diarrhoea#tab=tab_1). Each year there have been about 2.5 billion diarrheal cases has been reported in children under the age of five, out of which approximately 1,400 end up in death every day (Sanyaolu *et al.*, 2020).

The most stereotypical cause of all diarrheal diseases around the world is bacteria. *V. cholerae*, *C. botulinum*, *Shigella*, *C. jejuni*, *E. coli*, *Salmonella*, and *S. aureus* are the most common causes of diarrhea amongst children under the age of five. Water sources that have been contaminated, bacterial infections, malnourishment, poor personal hygiene and poor living conditions all contribute towards acute diarrhea in children under the age of five years (Sanyaolu *et al.*, 2020).

The WHO guidelines recommend the use of oral rehydration solution or an intravenous electrolyte solution in cases of severe dehydration as well as zinc supplementation and continued on breast feeding as

treatment for diarrhea, nutrient rich diet Vitamin A. The routine use of antimicrobials for diarrhea in children is not recommended by the World Health Organization (WHO) except for clinically recognizable severe cases. Antibiotic is indicated for cholera, shigellosis, dysenteric presentation of campylobacteriosis and non-typhoid salmonellosis when they cause persistent diarrhea and when host immune status is compromised (WHO, 2017). Over use and misuse of antibiotics adds to the cost of treatment, risks adverse reactions and enhances the development of resistant pathogens.

According to a recent report on global antimicrobial resistance by the World Health Organization (WHO), antimicrobial resistance among pathogens responsible for common infections is alarmingly high. In order to combat pressing public health concerns of antimicrobial resistance, a global action plan was adopted by the World Health Assembly in 2015 (WHO, 2015).

Inappropriate antibiotic use in diarrhea is a potential driver of resistance development, and could worsen the course of disease especially when broad spectrum agents are used due to their effects on the gut micro flora.

In our analysis, we aimed to measure the prevalence of irrational antibiotic prescription for childhood diarrhea management, to determine factors associated with antibiotic over- prescription and to recommend suggestion to improve management of diarrhea.

Materials and Methods

This is a cross sectional hospital-based descriptive study. The Study was conducted in Mohammed Al-Amin Hospital for children, which is the main referral hospital for children in Omdurman City, Khartoum State, Sudan. It accommodates huge number of cases per day. This study was carried out during the period from December 2021 to April 2022.

The objectives:

- To identify the irrational use of antibiotics in management of acute watery diarrhea.
- To assess the management practices for acute watery diarrhea at home and in health care setting.

The population consisted of children between 3 months and 5 years with acute watery diarrhea admitted to hospital or as outpatient clinic in the same study period.

Children older than 5 years and seriously ill children were excluded. The number of children included was 147.

Interview administered questionnaire was administered by the researcher to mothers or care-givers of children under 5 years who came as an outpatient and those who were admitted to short stay ward after meeting the doctors, stabilization and prescribed management plan.

The obtained data was entered into the Statistical Package of Social Sciences (SPSS) program version 26 to be organized, coded, and checked for errors. Descriptive analysis was performed using SPSS software, and Means and Standard Deviation (SD) were used for numerical (continuous) data, while percentages and frequencies were used for categorical data. Chi-square tests were used to examine association between categorical variables, and results were reported and interpreted using P-values, and Chi-square statistic (X^2). A P-value of less than or equal to 0.05 was considered significant for all purposes. Written ethical clearance for conducting this research was obtained from the caregivers and concerned authorities.

Results and Discussion

A total of 147 children under 5-years having acute watery diarrhea were included in the study. 86 (59.3%) were male and 59 (40.7%) were females. The average age of children under 5 years was 16 months (SD 12.1), with the highest frequency between 12 and 36 months (50.7%, n =74), less than 12 months (40.4%, n=59), and lowest frequency more than 36 months (8.9%, n=13) Figure (1).

The mean age of caregivers was 26 years, (SD 5) about one half of the study participants (n = 70, 47.9%) were 25–31 years of age and one third (n =54, 37%) were 18-24 years and reminder (19, 13%) were more than 32 years Table (1).

A big number of the caregivers (67/147, 47.2%) had primary education, while 43(30.3%) had secondary school education, 19(13.4%) had no formal education and the remainder (13, 9. 2%) had tertiary education Table (2).

Of 147 participant; 119(80.9%) were treated as in patient, while 28(19.1%) were treated as outpatient). The majority of the inpatient 61(53%) were admitted because

of ongoing losses, 28(24.3%) admitted because they were malnourished children, 25(21.7%) had some dehydration, and one child had severe dehydration Figure (2).

Duration of diarrhea ranging from 1 to 10 days, with mean of 3 days (SD 2.2), 50% had diarrhea from 1 to 3 days, 26% from 4 to 7 days, and 22.4% had diarrhea for one day, and 0.7% and 1.4% for hours and more than 7 days respectively. 136(94.4%) had 3-6 motion per day, 7 of them (4.9%) had motion more than 6 times per day and only one child (0.7%) had less than 3 motion per day Table (3).

Of participants, 94(63.7%) didn't do stool analysis, while 53(36,3%) had stool analysis done, over those 75% had pus cell in stool,65.9% had mucus and 31.7% had RBCS in their stool, while 36.6% had *Giardia cyst* and *Entamoeba histolytica* and 9% had unspecified bacteria Figure (3).

92.4% of caregivers go to doctor immediately after their children became ill, 18.2% give traditional medicine like baobab and custard. With 10.6% gave their children un-prescribed antibiotic like metronidazole and Co-Trimoxazole Figure (4).

Of the 147 children under five, 112 (76%) were on breast feeding and only 35(24%) were weaned. (99.1 %) of mothers didn't stop breast feeding during episode of diarrhea which is a good practice.

Of all study subjects 84(57.9%) received intra venous fluid, 38(26%) received ORS and 10 (6.9%) received Resomal. As to zinc supplementation 103 (70%) children received it. Of participant, 9 (6.2%) children received folic acid and 8 of them received multivitamin syrup. Antibiotics were prescribed by health care provider to 128(88.3%) of children, and only 22(15%) received anti emetic (Ondansetron and one received Domperidone), and only one child received anti-diarrheal treatment Table (4).

Of antibiotics used, 82 (63.4%) received third generation cephalosporin in form of Ceftriaxone, Cefotaxime and Cefixime, followed by Benzyl Penicillin and Gentamycin injectionfor 72 (55%), and 24 (18.6%) Metronidazole, one child received Amoxicillin/Clavulanic and another child received Co-Trimoxazole Table (5).

Duration of diarrhea (from 1 to 3 days) was significantly associated with antibiotic prescription with (p 0.04)

Table (6). Although for most variables investigated, there was no difference in use of antibiotics, the proportion of children receiving antibiotics was statistically higher among children with diarrhea from 1 to 3 days than among children with less frequent diarrhea at presentation.

Diarrhea is the passage of loose or watery stools at least three times in a 24 hour period. Diarrheal disease is the second leading cause of death in children under five years old, and was responsible for the deaths of 370,000 children in 2019 (<https://www.who.int/en/news-room/fact-sheets/detail/diarrhoeal-disease>).

In our study we found that over half of participants were males, this finding is similar to study conducted in Southeast Nigeria state by [Ekwochi et al., \(2013\)](#) where 59% of participants were males ([Ekwochi et al., 2013](#)). Only high frequency of diarrhoea (from 1 to 3 days) at presentation was statistically significantly associated with the use of antibiotics. This is similar to study done in Abakaliki, Nigeria by [Efunshile et al., \(2019\)](#) which showed positive association with antibiotic prescription and diarrhoea more than three times per 24 hours at admission ([Efunshile et al., 2019](#)).

Our study identified zinc supplementation to children with diarrhea as 103 (71%). This result is comparative to the finding from study done at Addis Ababa Health centers (43.8%) and much higher than report of study from health centers of Tanzania by [Gwimile et al., \(2012\)](#) and Iraq by [Lafta et al., \(2014\)](#) which were 1.25% and 28% respectively ([Gwimile et al., 2012](#); [Lafta et al., 2014](#)). However, this finding is in consistent with the WHO recommendations in the management of acute diarrhea to include zinc usage in combination with the supplementation of ORS ([Simpson et al., 2013](#)). This zinc supplementation found essential as the WHO and UNICEF brought attention to the impact of zinc in reducing the severity of the diarrheal episode and the number of subsequent acute diarrheal disease episodes in children younger than 5 years ([Huluka and Dessiso, 2020](#)).

In our study; Oral Rehydration Solution (ORS) was prescribed to only 38 (26.2%). This finding showed poor practice with regard to ORS prescription when it is contrary to WHO estimates which showed among children with acute diarrhea in developing Countries, less than 60% of them received ORS ([Mahapatra et al., 2015](#)) and study done in Kenya reported by [Simpson et al.,](#)

(2013) showed ORS prescription rate by healthcare workers to be as high as 90 % ([Simpson et al., 2013](#)). Malpractices like Antiemetic and Anti-diarrheal agents' prescription were 15.2% and 0.7% respectively. This is much lower than study done in Baghdad by [Lafta et al., \(2014\)](#) which showed 33.2% and 12.8% prescription of Antiemetic and Anti-diarrheal agents respectively ([Lafta et al., 2014](#)). It is closer to finding of study from Addis Ababa health center by [Gashaw \(2015\)](#) showing only 7% of children were given Antiemetic with null Anti-diarrheal prescription ([Gashaw, 2015](#)).

As to the antibiotics prescription rate, our study distinguished about (76%) of children have received antibiotics. These findings are even higher than WHO estimate that more than 40% of the children with acute diarrhea in developing countries received antibiotics ([Mahapatra et al., 2015](#)). However, this result is significant as similar study conducted in Tanzania and Addis Ababa which shown 80% and 73% of children with acute diarrhea were given antibiotics respectively ([Gwimile et al., 2012](#); [Gashaw, 2015](#)).

Although irrational prescription of antibiotics by clinicians is a well-recognized global problem ([WHO, 2018](#); [Kmietowicz, 2018](#)), we consider that the rate of use (76%) in watery pediatric diarrhea observed in this study to be impressively high and unacceptable, as it appeared that it was probably largely unreasoned.

However, other studies from different African countries have shown similar results. In a Burkina Faso teaching hospital, febrile children under five-years of age presenting with diarrhea were treated with antibiotic in 90.9% of cases ([Savadogo et al., 2014](#)), in Ethiopia, antibiotic prescription for childhood diarrhea was reported to be over 86% ([Tekleab et al., 2017](#)) and around 80% in Tanzania ([Gwimile et al., 2012](#)). Thus, use of antibiotics in Africa clearly merits more focus. A study among physicians in India indicated that less than 20% had good overall knowledge of diarrheal disease and its management, and that around only 17% prescribe antibiotics on the basis of appropriate clinical investigation ([Mahapatra et al., 2015](#)).

Furthermore, a recent study of antibiotic prescription patterns among Nigerian doctors showed that 97% prescribe antibiotics frequently and mostly without laboratory support, and that institutional policies or guidelines regarding antimicrobial therapy are generally lacking ([Ogunleye et al., 2018](#)).

Table.1 Caregivers distribution according to age in years (n=147)

Age	Number	Percentage
Less than 18	3	2.1%
18 – 24	55	37.0%
25 – 31	70	47.9%
32 – 38	17	11.6%
More than 39	2	1.4%

Table.2 Distribution of caregivers according to level of education (n=147)

Educational level	Number	Percentage
Primary school	69	47.2%
Secondary school	45	30.3%
University and above	14	9.5%
Illiterate/Non-formal education	19	13.4%

Table.3 Distribution of participants according to frequency of diarrhea per 24 hours (n=147)

Frequency	Number	Percent
Less than 3	1	0.7%
3-6	139	94.5%
More than 6	7	4.9%

Table.4 Distribution of participants according to treatment received at hospital (n=147)

Type of treatment	Number	Percent
Antibiotics prescribed	128	88.3%
Anti-diarrheal	1	0.7%
Antiemetic	22	15.2%
Folic acid	9	6.2%
Intravenous fluids	84	57.9%
Multivitamin	8	5.5%
ORS	38	26.2%
Resomal	10	6.9%
Vitamin A	0	0.0%
Vitamin D	2	1.4%
Zinc sulphate	103	71.0%

Table.5 Distribution according to type of antibiotic used in hospital (n=128)

Type of antibiotic	Number	Percent
Benzyl penicillin+ gentamycin	41	31.8%
Benzyl penicillin alone	1	0.8%
Ceftriaxone	59	45.7%
Cefixime	19	14.7%
Metronidazole	23	18.6%
Amoxicillin/Clavulanic acid	1	0.8%
Cefotaxime+ vancomycin	4	3.1%
Co-trimoxazole	1	0.8%

Table.6 Association between antibiotic prescription and duration of diarrhea

Duration of diarrhea		Antibiotics prescribed				p (X ²)
		yes		No		
		N	N%	N	N%	
Hours	yes	1	100.0%	0	0.0%	0.75 (0.1)
	no	126	90.6%	13	9.4%	
1 day	yes	27	93.1%	2	6.9%	0.61 (0.26)
	No	99	90.0%	11	10.0%	
1-3 days	yes	59	85.5%	10	14.5%	0.04* (4.2)
	no	67	95.7%	3	4.3%	
4-7 days	yes	37	97.4%	1	2.6%	0.095 (2.8)
	no	89	88.1%	12	11.9%	
More than 7 days	yes	2	100.0%	0	0.0%	0.65 (0.2)
	no	124	90.5%	13	9.5%	

Figure.1 Distribution of participants according to the age (n=147)

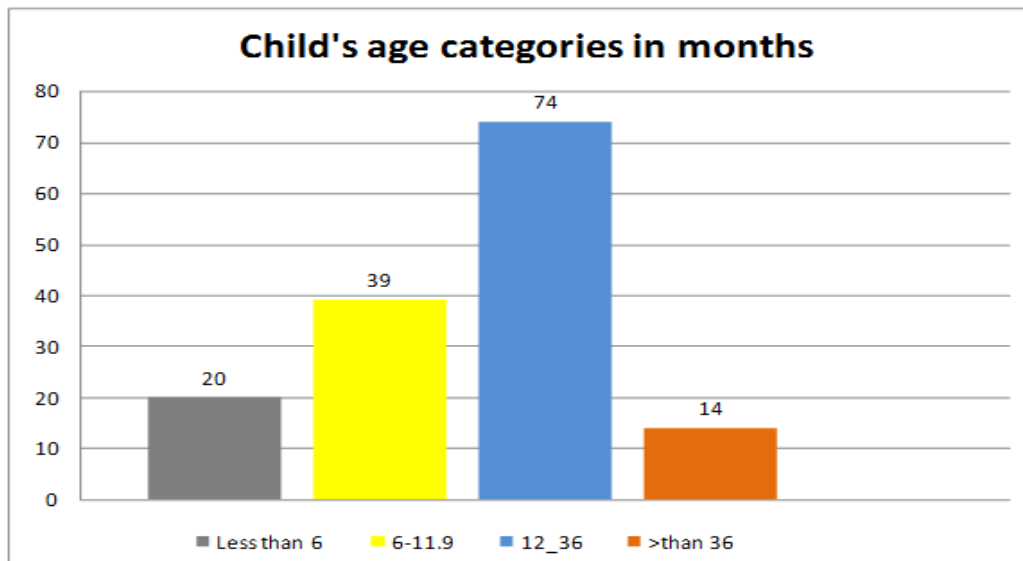


Figure.2 Distribution according to reason of admission (n =119)

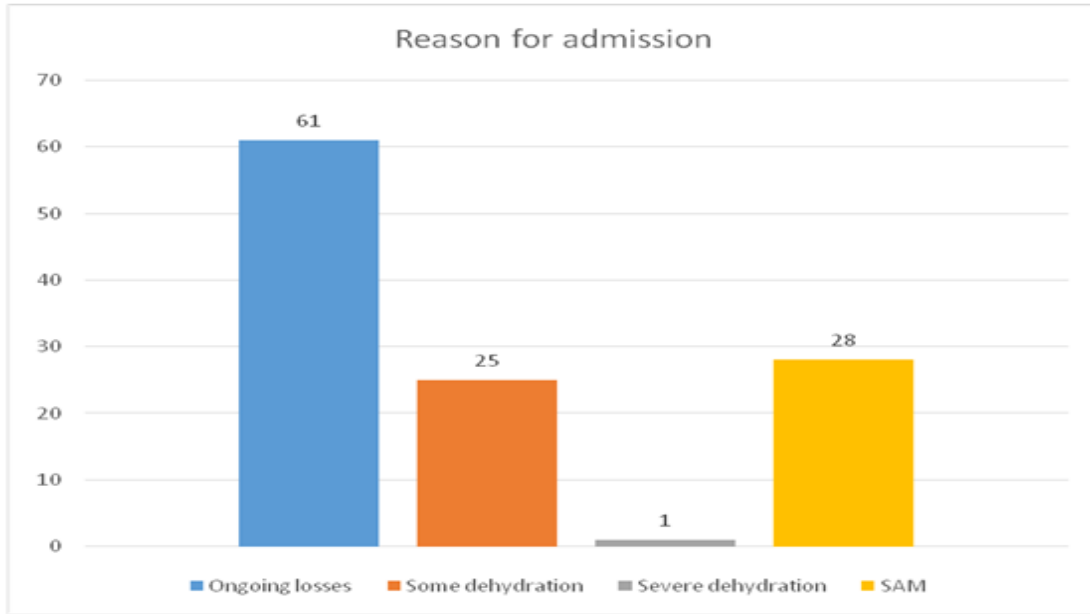


Figure.3 Distribution of participants according to stool analysis finding (53)

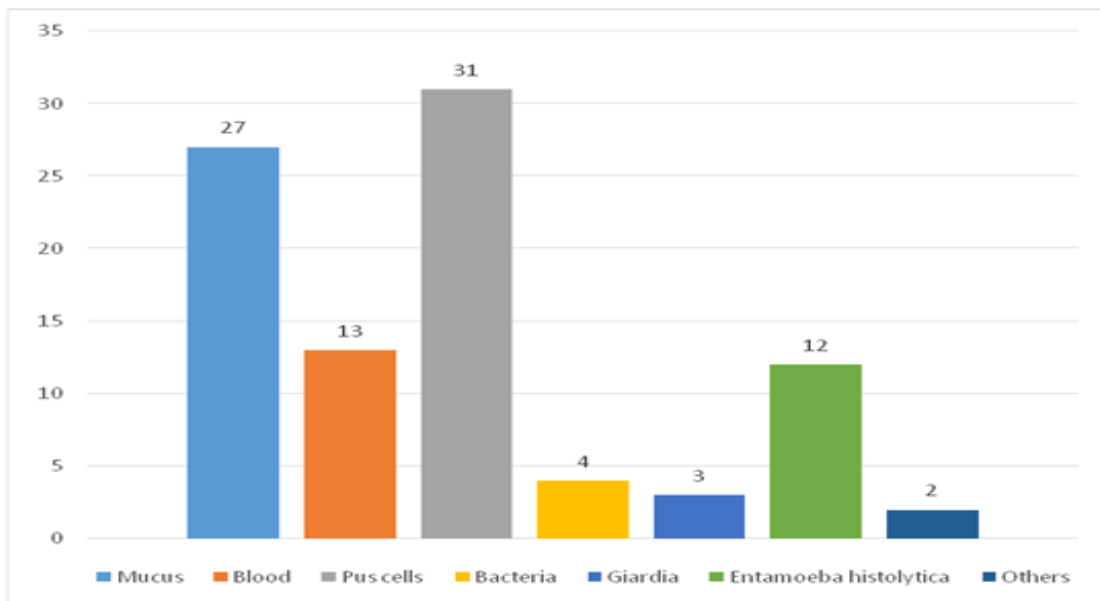
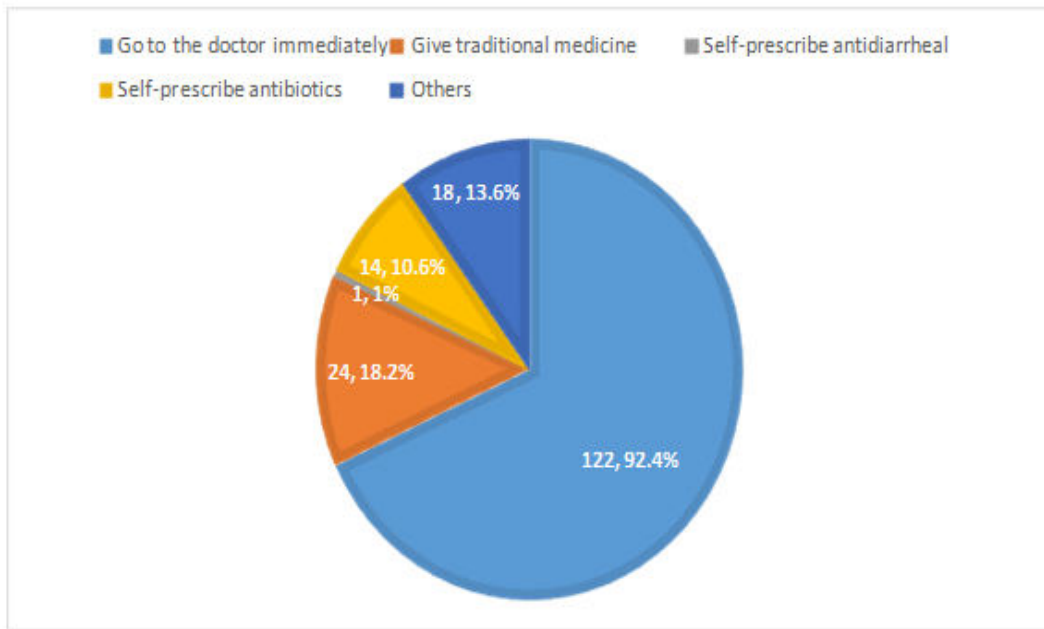


Figure.4 Distribution according to the action of caregivers (mothers) when their child gets the disease



The problem of irrational antibiotic use is not limited to developing countries; it is also an issue in the developed countries as the USA where it has been reported that up to 47 million inappropriate antibiotic prescriptions are written in doctors' offices and emergency departments annually, for viral conditions that do not warrant antibiotic treatment (Fleming-Dutra *et al.*, 2016). In order to tackle the menace of antibiotic misuse in USA, the Centers for Disease Control and Prevention (CDC) has launched a program called "National Action Plan for Combating Antibiotic-Resistant Bacteria" with the goal that all hospitals will establish antibiotic stewardship programmes to help reduce inappropriate antibiotic prescriptions by 20% by the year 2020. One of the core elements of the program is continuous education of clinicians about antimicrobial resistance and optimal prescribing of antibiotics (CDC, 2017). It will be nice if such a program rolled out globally. Administration of Probiotics, instead of antibiotics, may be one approach to fulfilling patient/caretaker expectations of treatment when antibiotic treatment is not appropriate, and is part of the Probiotics/antibiotic debate (Nami *et al.*, 2015). Our study does not observe any child who received Probiotics.

It is clear that young children presenting with acute watery diarrhea to Mohammed Al-Amin Pediatric Hospital in Omdurman City, Khartoum State are likely to be treated with antibiotics despite there being no obvious

reason. Our study results support the need for institution-based antimicrobial stewardship being implemented with emphasis on continuous medical education for clinicians on rational antibiotic use.

Recommendation

- The health professional at the government hospitals should stick to the recommended guidelines in the management of diarrhea and use of oral rehydration solution as well as zinc supplementation, continued breast feeding as treatment for diarrhea and nutrient rich diet Vitamin A.
- Further studies should be done to identify whether this malpractice is knowledge or attitude gap and then should be acted accordingly.
- Increase awareness of caregivers (mothers) about self-using of antibiotics for diarrheal disease.

Ethical Considerations

1. Written ethical clearance and approval for conducting this research obtained from Sudan Medical Specialization Board, Ethical Committee, educational development center (EDC). Administrative authority of Mohammed Al-Amin Hammed Hospital, Khartoum State, Sudan.
2. Written informed consent from caregivers and assent

from children. Study information was used for research purpose only. Privacy and confidentiality by using coded questionnaire.

Author Contributions

Samah Omer Abdallah Ibrahim: Investigation, formal analysis, writing—original draft. Mutaz Abdallah Gamaledin: Validation, methodology, writing—reviewing. Omer Saeed Magzoub:—Formal analysis, writing—review and editing. Isam Eldin H. A. Magid: Investigation, writing—reviewing.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical Approval Not applicable.

Consent to Participate Not applicable.

Consent to Publish Not applicable.

Conflict of Interest The authors declare no competing interests.

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