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# Inappropriate use of antibiotics in the management of diarrhoea in children under five years admitted with acute diarrhoea in four provinces of Mozambique 2014–2019

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## Abstract

**Background** Even with a great reduction in the last years, diarrhoea continues to be one of the leading causes of hospital admission and mortality in children less than five years of age globally. The success of diarrhoeal disease management relies on the rapid recognition of the symptoms and adequate treatment, with World Health Organization (WHO) guidelines, limiting the use of antibiotics for all diarrhoea cases being reserved to specific circumstances. Therefore, this study aimed to evaluate the frequency of antibiotics use in diarrhoea management in children aged 0–59 months admitted with acute diarrhoea in four provinces of Mozambique, from 2014 to 2019.

**Methods** A cross-sectional hospital-based surveillance was conducted from January 2014 to December 2019 in six sentinel sites located in four provinces. Socio-demographic, epidemiological and clinical data were obtained by interviewing the child's caregivers and by accessing the child's medical records and children's vaccination card. Data collected through National Surveillance of Diarrhoea (ViNaDia) was double-entered in Epi Info™3.5.1. (Centers for Disease Control and Prevention, Atlanta 2008), followed by data comparison. IBM SPSS software was used to conduct the data analysis.

**Results** During the study period 2014–2019 a total of 2382 children presenting at one of the designated health facilities were enrolled via ViNaDia surveillance. Of these 85.1% (2028/2382) provided data of antibiotics (ATB) usage and thus included in the present analysis. The majority was male with 59.3% (1203/2028), with infants aged 0–11 months composing the largest age group with 49.4% (1002/2028). Nutritional assessment revealed that 28.8% (585/2028) were underweight and 15.2% (308/2028) faced wasting. The comorbidities included human immunodeficiency virus (HIV) 7.8% (159/2028), malaria 7.0% (141/2028), and pneumonia 2.1% (42/2028). The rates of bloody diarrhoea and “rice-water” were reported in 1.5% (10/1664) and 2% (29/1664) respectively. Antibiotics use was reported in 93.2% of the children [95% CI: 92.0–94.2; 1890/2028], with 49.1% [95% CI: 47.0–51.5; 930/1890] received

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more than one ATB. The most prescribed antibiotics were Ampicillin (46.2%), Gentamicin (38.4%) and Cotrimoxazole (30.5%).

**Conclusions** The results of this study indicate inappropriate use of antibiotics in the management of acute diarrhoea in children attended in four provinces of Mozambique. The study suggests the drawing of a local guideline for the efficient management of acute diarrhoea, and the need for education on adherence of WHO recommendations on antibiotics use in acute diarrhoea.

**Keywords** Acute diarrhoea, Children under five, Antibiotics, Diarrhoea management, Mozambique

## Introduction

Diarrhoeal diseases remain one of the skyrocketing causes of morbidity and mortality worldwide, notwithstanding its great reduction in the last years, diarrhoea continues as an important cause of hospital admission and mortality in children less than five years of age globally [1]. In 2019, 9.9% of childhood deaths due to diarrhoea were reported in children under the age of five [2], and sub-Saharan African countries (including Mozambique) contributed with more than 80% of these deaths [3]. In spite of the global decrease in the total number of deaths in children under five from 2009 to 2018, sub-Saharan Africa remains the major contributor to this morbidity rate [4].

In Mozambique, diarrhoea has been reported as the 3rd leading cause of mortality [5] and considered to be responsible for 21% of deaths in children under 5 years old between 2019 and 2020 [5]. Even with the implemented strategies in the last decades, the country still reports one of the highest prevalences of diarrhoea in the region reports more than 7.340 deaths in children under five years annually, contributing with 13% of deaths in Sub-Saharan Africa [6, 7].

Diarrhoea is commonly caused by virus, bacteria and parasites, with Rotavirus A being the most important etiology linked with severe acute diarrhoea in children under five years [8]. However, bacterial infections also play a critical role in the burden of bloody acute diarrhoea among the identified pathogens, *Shigella* is the most common worldwide, accounting for over 60% of associated mortality, followed by other notable bacterial contributors as, enterotoxigenic *Escherichia coli* (ETEC), *Salmonella*, *Campylobacter*, *Entamoeba histolytica*, and *Giardia lamblia* are also significant pathogens associated with bloody acute diarrhoea, particularly in children under the age of five [8, 9]. Studies including Global Enteric Multicenter Study (GEMS), and others conducted in Mozambique have reported enterotoxigenic *Escherichia coli* producing heatstable toxin (ST-ETEC; with or without co-expression of heat-labile enterotoxin) and *Shigella* as the primary pathogens associated with diarrhoea [7, 10]. In fact, the clinical presentation typically begins with fever, followed by headache, malaise, anorexia and vomiting, then, the bloody diarrhoea; in

severe illness, the number of stools can reach 20 per day [10]. One of the life threatening complication of bacterial infection in acute diarrhoea is the hemolytic-uremic syndrome (HUS), characterized by hemolytic anemia, thrombocytopenia and acute kidney injury. This condition is directly related to the Shiga toxin produced by some bacterial strains including type 1 *Shigella dysenteriae*, entero-hemorrhagic *Escherichia coli* and shiga producer *Escherichia coli*, which are commonly associated with use of antibiotics as well [11, 12].

In the last decades, an increasing trend of multidrug resistant diarrhoeagenic bacteria has been reported worldwide [13–16]. Recent studies show a growing trend towards of emerging multidrug-resistant health care associated bacteria such as *Achromobacter xylosoxidans* and *Acinetobacter baumannii* which are described as being associated with high mortality rates in some countries [17, 18]. In Mozambique, studies have shown important rates of resistance in the most common diarrhoeagenic bacteria (*E. coli*, *Shigella* and *Salmonella*) [19, 20]. Data from Manhica district, Southern of Mozambique, showed a high frequency of resistance of *Shigella* to Trimethoprim-Sulfamethoxazole (92.5%), Chloramphenicol (53.7%) and Ampicillin (50.7%), multidrug resistance (MDR) was observed in 55.2% of *shigella* strains in children with diarrhoea [19]. Furthermore, an analysis of *E. coli* strains isolated from children with acute diarrhoea in four Mozambican provinces, revealed high resistance rates to Ampicillin and Tetracycline, reaching 97.0% and 68.0% respectively [21]. This finding highlights the urgent need to optimize local antibiotic consumption, including diarrhoeal management recommendations [22].

The World Health Organization (WHO) and World Gastroenterology Organization Global Guidelines (WGOGG), admonishes an acute diarrhoea treatment based on the clinical presentation, with a display of lower cost interventions such as oral rehydration solution, intravenous fluids, breastfeeding, probiotics, supplementation with zinc, vitamin A, and community-based management practices by parents or guardians, depending on severity level presented [23, 24]. The WHO does not recommend the routine use of antibiotics for diarrhoea management, even if the bacterial infection is confirmed [23]. Withal, the antibiotic therapy can be considered in

some specific clinical situations such as severe diarrhoea with septic presentations, bloody stools or diarrhoea associated with another acute infection (e.g. pneumonia, urinary tract infection); cholera, shigellosis, dysenteric presentation of campylobacteriosis and non-typhoidal salmonellosis in case of causing persistent diarrhoea, when host immune status is compromised including severe acute malnutrition chronic disease, or lymph proliferative disorders; traveler's diarrhoea or diarrhoea accompanied by fever [25–28].

Due to high burden of diarrhoea in the country, the *Instituto Nacional de Saúde* implemented the National surveillance of Diarrhoea (ViNaDia) since 2014, aiming to assess the etiology, the magnitude, and risk factors associated with diarrhoeal diseases in pediatric patients ( $\leq 14$ -year-old) [29]. In Mozambique, there is a lack of data on antibiotic use specifically in the management of acute diarrhoea in children under five years particularly in relation to WHO recommendations. Therefore, the present analysis aimed to evaluate the frequency of antibiotics use in management of acute diarrhea in children aged 0–59 months admitted across four provinces of Mozambique, between 2014 and 2019 as well as compliance with WHO guidelines.

## Materials and methods

### Study design, site, population

A cross-sectional, hospital-based surveillance was conducted from January 2014 to December 2019 in six sentinel sites located in four provinces. *Hospital Central de Maputo* (HCM), *Hospital Geral de Mavalane* (HGM) and *Hospital Geral José Macamo* (HGJM) all located in Maputo City; *Hospital Central da Beira* (HCB) located in Sofala Province; *Hospital Geral de Quelimane* (HGQ) located in Zambézia Province and *Hospital Central de Nampula* (HCN) located in Nampula Province. Maputo City is in southern region of Mozambique and is the country capital, *Sofala* and *Zambézia* provinces are located in the center region while *Nampula* is in the northern region. Children aged up to 59 months admitted with diarrhoea as defined by WHO, to one of the specified healthcare facility were recruited into the ViNaDia surveillance [1, 26] after obtaining signed informed consent from their caregivers. Children with nosocomial diarrhoea, without ATB information or those whose caregivers denied participating, were excluded from the analysis.

### Data collection

Socio-demographic, epidemiological and clinical data, were collected through interviews with the children's caregivers, by reviewing the children's medical records and vaccination card. Trained health professionals of the ViNaDia, filled all information in a semi-structured data

collection form [30]. Data regarding ATB use and type were collected from the children medical record files. Inappropriate use of antibiotics is defined as prescription when unnecessary or not indicated [31, 32].

### Sample size

As far as we know, this is the first study in Mozambique reporting the use of ATB in children admitted with diarrhoea, so we considered the expected prevalence of 50% to estimate the maximum sample size. Convenience sampling was performed, considering antibiotic information availability. Considering a 95% Confidence Interval (CI) and assuming an acceptable error of 0.03, a minimum of 1068 children is required to respond the hypothesis of this analysis. We increased the sample size assuming a 20% of non-response compensation rate. Thus, at least 1282 children with diarrhoea are required in the present analysis. The sample size was calculated using EpiTools [33] (available from: <http://epitools.ausvet.com.au>).

### Data management and statistical analysis

Data collected through ViNaDia was double entered in Epi Info™3.5.1. (Centers for Disease Control and Prevention, Atlanta, 2008), followed by data comparison. IBM SPSS [34] software was used to conduct the data analysis.

Secondary data from ViNaDia surveillance was used for this specific analysis. Descriptive statistics and chi-square comparison or Fisher's Exact test for small sample sizes was used to identify socio-demographic and clinical factors related to antibiotics use in children aged up to 59 months.

Clinical factors related to antibiotic use were accessed by cross-tabulation followed by the chi-square test or Fisher's Exact test if assumptions were not met. All analyses were performed considering a 95% confidence interval and a p-value  $< 0.05$  was considered statistically significant.

### Ethical statement

This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki [35]. The study protocol was approved by the National Bioethics Committee for Health in Mozambique (IRB00002657, reference 348/CNBS/13). Parents or legal guardians of the children signed or provided their fingerprints in the informed consent form, which described the study objectives and clarified that participation was voluntary.

## Results

During the study period 2014–2019, a total of 2382 children presenting with diarrhoea at one of the designated health facilities were enrolled via ViNaDia surveillance. Of these, 85.1% (2028/2382) provided data on ATB usage and were thus included in the present analysis.

### Sociodemographics and clinical characteristics

The majority of children were male (59.3%). Nearly half (49.4%) of the children were aged from 0 to 11 months, 29.4% were enrolled at HGM sentinel site and 31.8% were enrolled 2015 (Table 1).

Regarding the clinical characteristics, in addition to the diarrhoea, other concurrent symptoms such as vomiting and fever was reported in 62.2% (1262/2028) and 17% (282/1678) children respectively. Three quarters (841/1129) of children presented with moderated dehydration while less than 1% (10/1129) experienced shock. Bloody diarrhoea and “rice water” diarrhoea stool were reported in 1.5% (10/1664) and 2% (29/1664) respectively.

In terms of nutritional status, roughly one third were underweight (28.8%), followed by stunting (16.8%) and wasting (15.2%). The most common comorbidities observed were HIV (7.8%), malaria (7.0%) and pneumonia (2.1%). Most children with diarrhoea were discharged (63.9%) (Table 1).

### Overall and yearly antibiotics use in four province

Antibiotics use was observed in 93.2% [95% CI: 92.0–94.2; 1890/2028] and the administration of multiple antibiotics in 49.1% [95% CI: 47.0–51.5; 930/1890]. The most prescribed antibiotics were Ampicillin (46.2%), Gentamicin (38.4%), Cotrimoxazole (30.5%), Metronidazole (11.1%) and Ceftriaxone (8.8%) (Fig. 1).

Between 2014 and 2019, antibiotics use has increased in all sentinel sites, being surprisingly administrated in 100% of children admitted in 2018 and 2019 (Table 2). Comparing the use of antibiotics per year, Ampicillin was the most prescribed antibiotic in 2014 (36.8% – 28/76), 2015 (34.2% – 364/1063), 2018 (36.3% – 165/455) and 2019 (28.4% – 63/222). While in 2016, Cotrimoxazole was the most prescribed antibiotic (30.5% – 181/594) and gentamicin in 2017 (33.0% – 199/603) (Table 3).

### Clinical and sociodemographic factors related with antibiotics use

Antibiotic use was reported in the equal proportions among male and female (93.2%) and were prescribed to more than 90% of children across all age groups, with the highest frequency observed among of children across all age groups, with the highest frequency observed among children aged 12–23 months with the highest frequency (95.3%) and the lowest among children under one year (91.2%). Two of the six sentinel sites (HCM and HGM) prescribed antibiotics to less than 90% of the children with diarrhoea, while HGJM had the highest frequency ATB administration (99.45%) (Table 4).

In children with co-morbidities antibiotics were most frequently prescribed for those who were HIV positive (95.0% – 151/159) followed by those with Malaria (94.3% – 133/141), underweight status (93.8% – 549/585),

stunting with 89.4% (305/341) and, pneumonia (85.7% – 36/42). Fever (97.9% – 276/282) and vomiting (92.6% – 1169/1262) were the most common clinical characteristics related to ATB use. Children with bloody diarrhoea received fewer antibiotics (86.7% – 26/30) compared those without bloody diarrhoea (98.7% – 376/381). Regardless of the outcome, antibiotics prescription exceeded 90%, with the highest frequency observed among children who were discharged (Table 3).

### Discussion

In this analysis, we provided evidence on the extent of antibiotic use in children with acute diarrhoea admitted in six hospitals from four provinces of Mozambique. Our results demonstrated that the majority of children were treated with at least one antibiotic regardless of their clinical presentation or laboratorial evidence of bacterial infection.

The antibiotics use in children under five years with diarrhoea reported in this study (93.2%) is notably higher than those from previous studies from other African countries such as Nigeria (85%) and Tanzania (68,9%). A possible explanation for this discrepancy is that those studies were conducted in outpatients and the clinicians had access to the diagnostic test results before the prescribing antibiotic [36, 37]. Additionally, similar studies conducted in Low and Middle-Income Countries (LMIC) reported even lower rates of antibiotics prescription for managing acute diarrhoea in children [38]. These lower rates are often linked to specific enteric pathogens such as *Shigella* and rotavirus which are identified as the primary causes of diarrhoea in such settings [32]. The availability of diagnostic tools and pathogen-specific management approaches may explain antibiotic variations across studies and regions. Moreover, the rate of inappropriate antibiotic prescription has thrived over the years in these six sentinel sites, consequently increasing the treatment costs and contributing to the emergence of resistant bacterial strains over these years, as reported previously in several countries, demonstrating a direct impact in children mortality rate [39, 40].

The empirical antibiotics inappropriate use by clinicians may be driven by the limitations faced in microbiology facilities at the hospitals, considering that similar studies have reported inappropriate antibiotic prescription for childhood diarrhoea management in rural and urban sites of LMIC [19, 41]. Although ViNaDia is based in all hospitals collecting and testing samples, it does not provide real-time results for the clinician to make decisions. Since the objective is to produce scientific evidence for research purposes, and contribute to the country's health policy changes by providing data about acute diarrhoea burden in children from 0 to 14 years and the

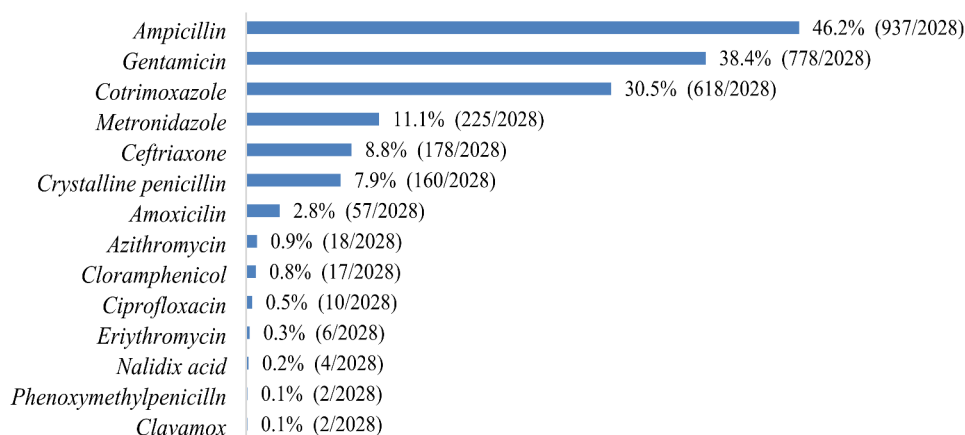
**Table 1** Sociodemographic and clinical characteristics of children with diarrhoea, May 2014 to December 2019, Mozambique

Characteristics	N=2028	%
Sex		
Male	1203	59.3
Female	825	40.7
Age categorized (in months)		
0–11	1002	49.4
12–23	730	36.0
24–59	296	14.6
Year		
2014	91	4.5
2015	645	31.8
2016	397	19.6
2017	416	20.5
2018	318	15.7
2019	161	7.9
Sentinel site		
HCM	200	9.9
HGM	597	29.4
HGJM	344	17.0
HCB	103	5.1
HCN	639	31.5
HGQ	145	7.1
Malaria		
No	1715	84.6
Yes	141	7.0
Unknown/missing	172	8.5
Pneumonia		
No	1812	89.3
Yes	42	2.1
Unknown/missing	174	8.6
Stunting		
No	573	28.3
Yes	341	16.8
Unknown/missing	1114	54.9
Wasting		
No	650	32.1
Yes	308	15.2
Unknown/missing	1070	52.8
Underweight		
No	1279	63.1
Yes	585	28.8
Unknown/missing	164	8.1
HIV		
Negative	1341	66.1
Positive	159	7.8
Unknown/missing	528	26.0
Fever ( $\geq 38^{\circ}\text{C}$ )		
No	1396	68.8
Yes	282	13.9
Unknown/missing	350	17.3
Vomit		
No	722	35.6
Yes	1262	62.2
Unknown/missing	44	2.2

**Table 1** (continued)

Characteristics	N = 2028	%
Bloody diarrhoea		
No	381	18.8
Yes	30	1.5
Unknown/missing	1617	79.7
Outcome		
Discharged	1296	63.9
Death	18	0.8
Transferred/abandonment	50	2.5
Unknown/missing	664	32.7

#### Antibiotics administered in children hospitalized with diarrhoea

**Fig. 1** Types of antibiotics used in children with diarrhoea, May 2014–December 2019, Mozambique

etiology associated to four provinces of Mozambique [6, 42–44].

According to the WHO management guidelines for an acute diarrhoea treatment in children, antibiotics are not routinely indicated, being recommended in specific situations such as bloody diarrhoea, co-infections, malnutrition, and other special conditions. The first choice of recommended antibiotic is Ciprofloxacin specially in bloody diarrhoea and Ceftriaxone as an alternative [23, 45]. These WHO guidelines were designed based on the clinical presentation, feces characteristics and considering laboratory diagnosis limitations of LMIC [23].

The magnitude of antibiotics over-prescription is unjustifiable, given that the present analysis reported a low number of children with bloody diarrhoea (less than 10 children), as observed in co-infection and co-morbidities, conditions which indicate the use of antibiotics for its treatment, underlying the inappropriate prescription and use of antibiotics in acute watery diarrhoea [46], suggesting that clinicians perceive acute diarrhoeal illness as an indication for antibiotic use, despite the WHO recommendations.

Taking into account the diarrhoeal etiologic aspects, previous studies described high rates of viral and parasitic infections on the children included in the present

analysis showcasing that not all diarrhoea manifestations are caused by bacterial infection, instilling the need for careful usage of ATB in Mozambique [42, 44, 47].

Regarding the commonly prescribed ATBs, it was observed that Ampicillin is the first choice, making it the most used with a rate of 46.2% over the five years of analysis, followed by Gentamicin with 38.4%. In 2016, in this analysis, Cotrimoxazole was rated as the third most used antibiotic reaching 30.5%, although it is no longer used routinely to treat patients with acute diarrhoea in Mozambique, however, it is used for the prevention of opportunistic infections in HIV-positive and exposed children, suggesting that the high rate of consumption is due to the high prevalence of HIV infections in Mozambique [48].

The consumption of cephalosporin increased from less than 3% in 2014 to 18% in 2019, possibly due to the antibiotic availability at the moment of the treatment [49]. The barrier to accessing antibiotics remains global, especially in LMIC, where some settings have to endure with less than 60% of essential listed medicines available. The most significant challenges are associated with the low availability of essential medicines, weak health systems, poor quality control and inadequate government funding [49].

**Table 2** Antibiotic use in children with diarrhoea by site, in each year, May 2014–December 2019, Mozambique

Site	2014		2015		2016		2017		2018		2019	
	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%
HCM	-	-	0/46	0.0	43/46	93.5	48/49	98.0	28/28	100.0	31/31	100.0
HGM	50/91	54.9	175/181	96.7	59/59	100.0	85/85	100.0	121/121	100.0	60/60	100.0
HJM	-	-	140/142	98.6	21/21	100.0	102/102	100.0	74/74	100.0	5/5	100.0
HCB	-	-	11/18	61.1	32/32	100.0	27/27	100.0	26/26	100.0	-	-
HGQ	-	-	22/37	59.5	48/49	98.0	25/26	96.2	19/19	100.0	14/14	100.0
HCN	-	-	207/221	93.7	189/190	99.5	127/127	100.0	50/50	100.0	51/51	100.0
Total	50/91	54.9	555/645	86.0	392/397	98.7	414/416	99.5	318/318	100.0	161/161	100.0

HCM – Hospital Central de Maputo; HGM – Hospital Geral de Mavalane; HJM – Hospital José Macamo; HCM – Hospital Central da Beira; HGQ – Hospital Geral de Quelimane; HCN – Hospital de Nampula

Previous studies in Mozambique found that clinical condition (severity) and age under 5 years were the main determinants for antibiotic prescription in children with different pathologies including diarrhoea, and beta-lactams being the most used antibiotic class [50].

The findings shows a strong evidence of high levels of over-prescription of antibiotics and a weak adherence of antibiotic guidelines in children with acute diarrhoea, resulting in an urgent need of education on antibiotic use, development of local guidelines and antibiotic stewardship implementation programs [51, 52].

The study had limitations such as the missing data for some clinical variables, which disables the overall screen of the study settings. All collected relief on medical records, and thus unable to observe further antibiotic management for example dispensed antibiotics. All the hospitals are quaternary and located in urban areas, which does not allow having the whole scenario of populations living in rural areas as well as, patients assisted on health centers or other type of health services that provides primary care. Despite the limitations, we were able to produce important information about ATB use in children with diarrhoea in four provinces of Mozambique.

## Conclusions

The results of this study indicate inappropriate use of antibiotics in the management of acute diarrhoea in children attended in four provinces of Mozambique. Clinicians should consider the epidemiology, the etiology, and the clinical presentation of acute diarrhoea, as well as consult the approved guidelines on the management of acute diarrhoea and empirical antibiotic therapy. Mozambique has produced sufficient epidemiologic data to draw a local guideline on the management of acute diarrhoea to improve the care given to children with diarrhoea, and likewise to define policies that will reduce the overuse of antibiotics, as a preventable measure for antibiotic resistance emergence.

**Table 3** Antibiotic use by type within the years in children with diarrhoea, May 2014-December 2019, Mozambique

Antibiotic type	2014		2015		2016		2017		2018		2019	
	n	%	n	%	n	%	n	%	n	%	n	%
Ampicillin	28	36.8	364	34.2	144	24.2	173	28.7	165	36.3	63	28.4
Gentamicin	12	15.8	261	24.6	112	18.9	199	33.0	144	31.6	50	22.5
Cotrimoxazole	20	26.3	227	21.4	181	30.5	108	17.9	48	10.5	34	15.3
Metronidazole	2	2.6	78	7.3	59	9.9	35	5.8	39	8.6	12	5.4
Ceftriaxone	0	0.0	33	3.1	57	9.6	32	5.3	16	3.5	40	18.0
Crystalline penicillin	4	5.3	62	5.8	14	2.4	38	6.3	26	5.7	16	7.2
Amoxicillin	5	6.6	25	2.4	12	2.0	9	1.5	5	1.1	1	0.5
Azithromycin	1	1.3	2	0.2	3	0.5	2	0.3	5	1.1	5	2.3
Cloramphenicol	0	0.0	5	0.5	8	1.3	3	0.5	1	0.2	0	0.0
Ciprofloxacin	3	3.9	3	0.3	2	0.3	1	0.2	1	0.2	0	0.0
Erythromycin	0	0.0	2	0.2	0	0.0	2	0.3	2	0.4	0	0.0
Nalidix acid	0	0.0	1	0.1	0	0.0	1	0.2	2	0.4	0	0.0
Phenoxymethylpenicillin	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.5
Clavamox	1	1.3	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
Cefaclor	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
Total	76	100.0	1063	100.0	594	100.0	603	100.0	455	100.0	222	100.0

**Table 4** Clinical and sociodemographic factors related to antibiotic use in children with diarrhoea, May 2014-December 2019, Mozambique

Characteristics	Antibiotics use	Column1	p-value
	n/N	%	
Sex			0.976
Male	1120/1202	93.2	
Female	769/825	93.2	
Age categorized (in months)			0.002
0–11	914/1002	91.2	
12–23	696/730	95.3	
24–59	280/296	94.6	
Does the child has comorbidities			< 0.001
No	1270/1339	94.8	
Yes	618/686	90.1	
Malaria			0.052
No	1672/1715	97.5	
Yes	133/141	94.3	
Pneumonia			0.001
No	1767/1812	97.5	
Yes	36/42	85.7	
Stunting			0.496
No	504/573	88.0	
Yes	305/341	89.4	
Wasting			0.393
No	572/650	88.0	
Yes	265/308	86.0	
Underweight			0.347
No	1185/1279	92.7	
Yes	549/585	93.8	
HIV			0.418
Positive	151/159	95.0	
Negative	1251/1341	93.3	
Fever			0.356
No	1352/1396	96.8	
Yes	276/282	97.9	
Vomit			0.338
No	677/722	93.8	
Yes	1169/1262	92.6	
Dehydration status			NA
None	21/21	100.0	
Moderate	841/841	100.0	
Severe	256/257	99.6	
Shock	10/10	100.0	
Stool characteristics			0.102
Watery	591/639	92.5	
Semi-pasty	359/359	100	
Pasty	592/627	94.4	
Bloody	10/10	100.0	
Rice water	25/29	86.2	
Mucuous	4/4	100.0	
Has the child bloody diarrhoea?			0.002
No	376/381	98.7	
Yes	26/30	86.7	
Has the child received rotavirus vaccine?			< 0.001
No	1108/1238	89.5	

**Table 4** (continued)

Characteristics	Antibiotics use	Column 1	p-value
	n/N	%	
Yes	782/790	99.0	0.030
Outcome			
Discharge	1267/1296	97.8	
Died	17/18	94.4	
Transferred/Abandoned	46/50	92.0	

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**Author contributions**

J.S.F., A.C., and N.dD - Designed the study. N.dD - principal investigator supervised the research and funding acquisition. J.S.F. and A.C. - analyzed data. J.S.F., and A.C. - wrote the manuscript first draft. J.S.F., A.C., M.C., N.dD - Methodology. J.S.F., A.C., A.K., L.M. and N.dD - Writing review and editing. N.dD - funding acquisition. All authors reviewed and approved the final manuscript.

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**Data availability**

The raw data are available upon reasonable request from the corresponding author.

**Declarations****Ethics approval and consent to participate**

The ViNaDia Protocol was approved by the National Health Bioethics Committee of Mozambique (CNBS) under number (IRB00002657, reference Nr: 348 / CNBS / 13). The participant's documents were stored in a secure and access-restricted location in the National Institute of Health. Parents or legal guardians of the children signed the informed consent form this document described the study objectives and clarified that participation in the study was voluntary and that refusal of participation would not result in any penalty or loss of medical care.

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare no competing interests.

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