ORIGINAL PAPER

https://dx.doi.org/10.4314/njpr.v17i2.11

Nig. J. Pharm. Res. 2021, 17 (2) pp 257-265

Available online at http://www.nigjpharmres.com

The Prescription of Medicines for Childhood Acute Diarrhoea: A Retrospective Study at Four Secondary Healthcare Facilities in Lagos State, Nigeria

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Abstract

Background: Diarrhoea remains the second leading cause of mortality in children, with an estimated 205 children under the age of 5 dying daily in Nigeria. Combination therapy of ORS with zinc tablets is the cornerstone for its management. Secondary healthcare facilities (SHFs) represent the second level of contact for patients requiring professional care; hence an appropriate prescription for diarrhoea is crucial for the survival of under-fives.

Objectives To evaluate the prescription of medicines in the management of acute watery diarrhoea (AWD) in under-fives at SHFs, and determine the appropriateness of the prescriptions.

Method A descriptive cross-sectional study was done at four randomly selected SHFs in Lagos State. A retrospective review of prescriptions for diarrhoea cases totaling 480, was done using records from the General Out-Patient Department from September 2018 to August 2019. A descriptive analysis was performed.

Results: All cases reviewed were diagnosed as AWD occurring either alone (352; 73.3%) or in combination with malaria/fever (55; 11.5%), cough/URTI (23; 4.8%), and other conditions (50; 10.4%). Of the 352 AWD only cases, there were 121 (34.4%) prescriptions for ORS/Zinc as combined therapy without addition of antibiotics, 120 (34.1%) for antibiotics, and 134 (38.1%) for probiotics. Other prescriptions include analgesics (18.2%), injectables (9.7%) and antimalarials (8.8%).

Conclusion: The study revealed suboptimal prescriptions of ORS/Zinc with the appropriateness of prescription at 34.4%. The prescription of antibiotics and other medicines which have no rehydration benefits was high.

Keywords: Diarrhoea, Under-fives, Prescription, Secondary healthcare facilities

INTRODUCTION

Diarrhoea is defined as the frequent passage of watery/loose stools three or more times within 24 hours (WHO, 2017). Acute diarrhoea, which starts suddenly and lasts for a few hours or days, but usually less than 14 days, is the most occurring type of diarrhoea in children. It occurs mainly due to infective and non-infective origin such as mal absorption. The most implicated infective organisms for diarrhoea in children in low and middle-income countries (LMIC) are rotavirus and *E. Coli* (Platts-Mills *et al.*, 2015). The loss of fluids during diarrhoea inadvertently leads to life-threatening dehydration if not replaced promptly and appropriately.

Diarrhoea has remained the second leading cause of mortality in under-five children worldwide, with an estimated 205 deaths occurring daily in Nigeria (UN-IGCME, 2018). The goal of therapy therefore is fluid replacement to curb dehydration, which is the main cause of death. Since the inception of oral rehydration therapy (ORT) consisting of oral rehydration salts (ORS), increased fluid intake and continued feeding, global annual mortality due to diarrhoea in under-fives

has remarkably reduced from about 5 million in the early 80s to less than 500,000 in 2018 (Snyder and Merson, 1982; Nalin and Cash, 2018). However, the decline seems to be uneven as some developing countries like Nigeria, India and Senegal still experience significant loss of under-fives due to diarrhoea and therefore bear the brunt of the global number of deaths (De *et al.*, 2015; Morakinyo and Fagbamigbe, 2017; Sreeramareddy, Low and Forsberg, 2017).

In 2004, World Health Organization (WHO) and United Nations Children's Fund (UNICEF), in a joint statement, approved ORS and zinc supplementation as combined therapy for the treatment of childhood diarrhoea both at home and in the health facility (WHO/UNICEF, 2004). This simple, effective, evidence-based and approved treatment has been adopted and included in treatment guidelines in many countries including Nigeria and it is expected to be the first-line treatment for diarrhoea in children (FMoH, 2016). The use of antimicrobials, antidiarrhoeals, antiemetics and other medicines that provide no benefits for rehydration is not recommended. Antibiotics are reserved for suspected cases of cholera, persistent diarrhoea and acute bloody diarrhoea (dysentery) (WHO, 2005). The use of probiotics has also become part of diarrhoea treatment in recent years. Although probiotics have been found to reduce the risk and duration of diarrhoea, it is recommended that they be used in conjunction with rehydration therapy (Allen *et al.*, 2010; Islam, 2016).

Since the mortality of under-fives in Nigeria due to diarrhoea remains high, researchers have inquired into the utilization of the evidence-based treatment identified in ORS/Zinc. These enquiries have shown poor prescription and recommendation of ORS/Zinc, and high use of antimicrobials and other inappropriate medicines for acute diarrhoea in primary health facilities, community pharmacies and proprietary and patent medicine stores (Aguwa, Aniebue and Obi, 2010; Ogbo, Aina and Aderemi-Williams, 2014; Ogbo *et al.*, 2019). Beyond poor prescription and recommendation of ORS/Zinc, is failure of health providers to deliver effective care commonly referred to as unwarranted variation in effective care and patient safety (Wennberg, McPherson and Goodman, 2015). While failure to deliver effective care has been identified in the aforementioned health settings, studies on prescription of medicines for childhood acute diarrhoea is scarce in secondary health care settings. Although referral is needed from the primary care to secondary and then to tertiary care, the process is not yet well established in Nigeria. Consequently, many attendees of the secondary healthcare facilities have no referrals or have self-referred themselves (Akande, 2004; Aguwa *et al.*, 2010; Okoli *et al.*, 2017). Therefore, caregivers of under-five children access care directly at the SHFs for any illness that could have been managed efficiently by primary healthcare providers. To this end it became important to evaluate the prescription of medicines for acute diarrhoea in the secondary healthcare setting to add to the body of knowledge as well as define the difference compared to previous findings from the primary care setting.

The objective of the study was to evaluate the prescription of medicines for childhood acute diarrhea, determine the appropriateness of the prescriptions and check the availability of any form of treatment guideline in the facilities.

METHODOLOGY

Study setting

The study was carried out in Lagos State, Nigeria with latitude and longitude coordinates of 6.5236ºN and 3.6006ºE. The state is the smallest in the country but it has the highest urban population of approximately 25 million and it is the commercial hub of the country (Lagos State 2021). Lagos State has 3 tertiary, 27 secondary, 248 primary public healthcare facilities in addition to other private facilities such as community pharmacies, hospitals and patent and proprietary medicine vendors. This study was carried out at four public secondary healthcare facilities located in the metropolis — two on the Island and two on the Mainland.

Study design

The study was a descriptive retrospective review of prescriptions for diarrhoea in under-five children from September 2018 – August 2019.

Study population

The study population included under-five children who were treated for diarrhoea in these facilities within the study period.

Sample size

A minimum sample size of 368 was calculated using the formula $n=Z^2pq/d^2$ (where z = 1.96, p = 0.4, q = 0.6, d= 0.05). P was the prevalence of appropriateness of prescription from a previous study (Ogbo *et al.*, 2019). However, a sample size of 480 was used to make up for attrition, and allow for at least 10 prescriptions monthly for the one year period.

Sampling technique

The study area was stratified into two — Mainland and Island. Then, using a sampling frame, two secondary healthcare facilities were randomly selected from each stratum. Four facilities were chosen to have a substantial number of prescriptions per facility to make up the sample size. Onikan Health centre and Massey Street Children's Hospital were selected from Lagos Island, and Ebute Meta Health Centre and Ajeromi Health Centre were chosen from Mainland.

Data collection

Information was collected from the general outpatient department register, which had all information of patients who visited the facility together with prescriptions and laboratory tests done. Records for under-five diarrhoea cases were first of all identified for each month of the year, and then 10 cases were selected for assessment through simple random sampling technique, totaling 120 per facility. The information collected from the register were date of prescription, age and sex of child, presented complaints, diagnosis, and medicines prescribed. An adapted pro forma from WHO was used to input data (World Health Organization, 1993). Availability of any form of treatment guideline was checked and recorded as Yes or No after observation.

Data analysis

Data were coded and entered into SPSS version 23.0. Descriptive analyses were carried out and results presented in charts and tables. Chi square was used to test for relationships in the prescribing of medicines among the health facilities with statistical significance set at $p < 0.05$.

Important descriptions for the purpose of the study

- Appropriate prescription for AWD cases without comorbid conditions was defined as the prescription of ORS/Zinc without addition of antibiotics, injections and antimalarials.
- Inappropriate prescription for AWD cases without comorbid conditions was defined as prescriptions other than appropriate as defined.
- Oral rehydration salts and zinc tablets prescribed together as combined treatment were counted as one medicine.

RESULTS AND DISCUSSION

Availability of treatment guidelines

Only one facility (Ebute-Metta) out of the four surveyed had treatment guidelines available for sighting at the time of data collection.

Diagnosis of diarrhoea cases

A total of 480 diarrhoea cases in under-fives were randomly selected for assessment from the four facilities — 120 cases from each facility. All the cases were acute watery diarrhoea (AWD) occurring alone in 352 cases (73.3%) or in combination with malaria/fever (55; 11.5%), cough/URTI (23; 4.8%) and others (50; 10.4%). 'Others' represented conditions such as boils, sepsis and rash. There were no cases of dysentery (Fig. 1).

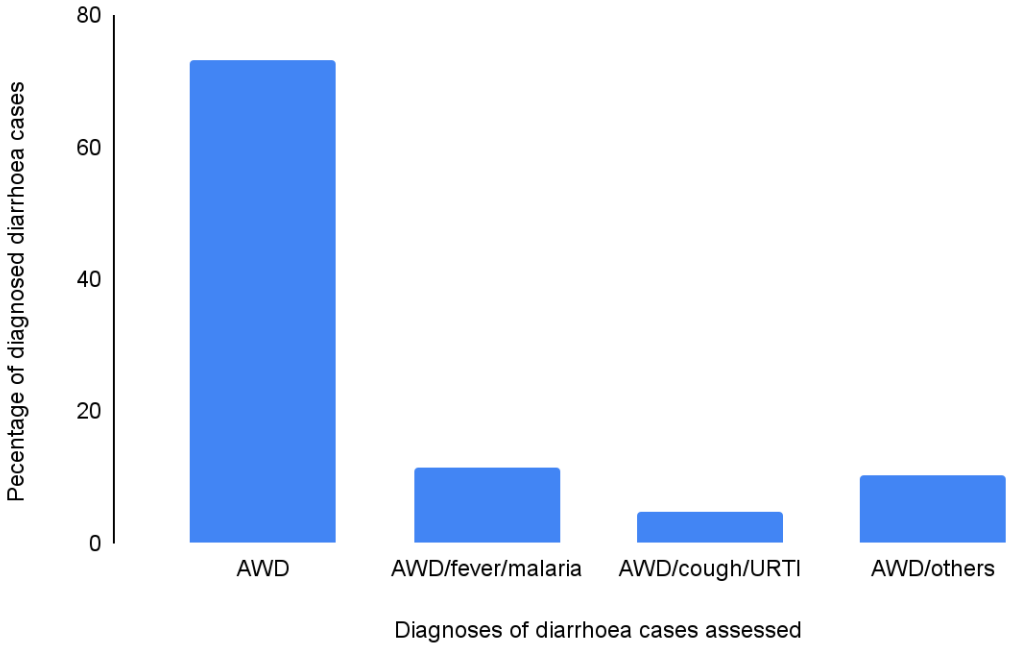

Figure 1: Diagnoses of diarrhoea cases surveyed

The assessment of prescription of medicines was done for acute watery diarrhoea cases only (n = 352), to remove bias of prescriptions for the other conditions.

Socio demographic characteristics of sample population: There were 193 (54.8%) male and 159 (45.2%) female children treated for acute watery diarrhoea. Majority (32.4%) of the cases occurred in children 12-23 months (Table 1). Mean age was 16.44 ± 12.610, median was 12 and the mode was 12.

Table 1: Socio demographic data for children who were treated for AWD cases only

Variable	Characteristics	Frequency (n-352)	Percent
Sex	Male	193	54.8
	Female	159	45.2
Age categories (months)	0-5	46	13.1
	6-11	102	29.0
	12-23	114	32.4
	24-35	36	10.2
	36-47	33	9.4
	48-59	21	6.0

Medicines prescribed for AWD only A total of 574 medicines from seven drug classes were contained in 352 prescriptions for AWD, ranging from 0 (no medicine) in 23 cases to 4 in 5 cases. Average number of medicines was 1.63 ± 0.837**,** median was 2 and mode was 2. These medicines were prescribed in various combinations. The prescriptions also contained 34 injections (Table 2).

Table 2: Prescription of medicines

Characteristics	Variable	Frequency	Percent*
Medicines prescribed	ORS	12	3.4
	ORS/Zinc	172	48.9
	Antibiotics	120	34.1
	Analgesics	64	18.2
	Probiotics	134	38.1
	Injections	34	9.7
	Antimalarials	31	8.8
	Multivitamins	7	2.0
Number of medicines per case (n = 352)	0	23	6.5
	1	138	39.2
	2	142	40.3
	3	44	12.5
	4	5	1.4

***Percentage was calculated based on number of cases (n = 352)**

ORS/Zinc was prescribed in 172 cases but further analysis showed that only 121 (34.4%) prescriptions were appropriate and had no addition of antibiotics, antimalarials or injections (Fig. 2).

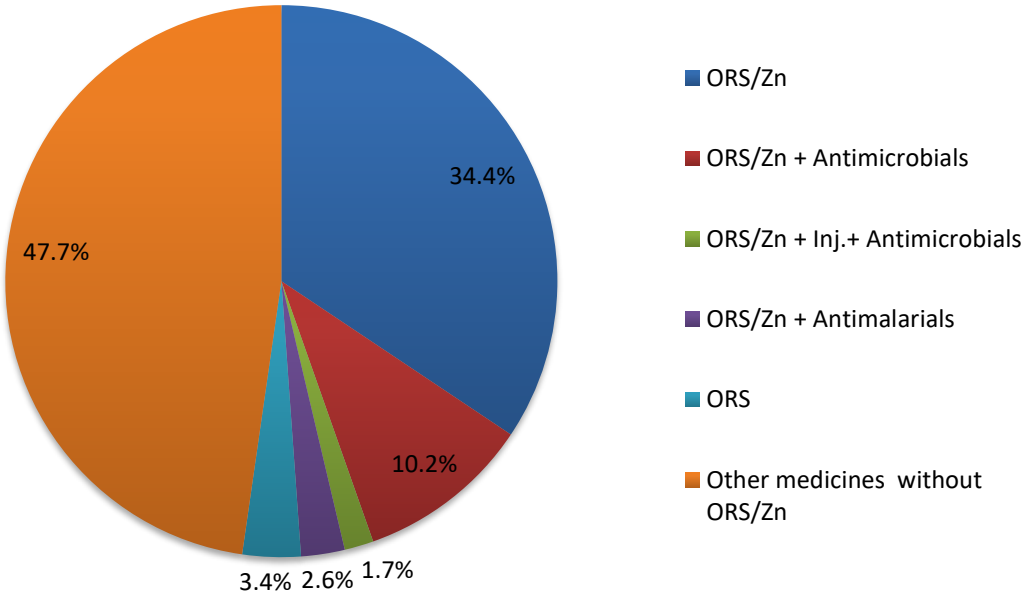

Figure 2: Prescription of medicines

Classes of antibiotics

Four classes of antibiotics were prescribed: Penicillins (16; 13.3%), Cephalosporins (84; 70.0%), Nitro-imidazoles (9;7.5%) and Macrolides (11; 9.2%).

Prescription of selected medicines per SHF

The prescription of medicines varied from one SHF to another. Chi square tests showed there were statistically significant differences in the prescription of ORS/Zinc (p = 0.000), antibiotics (p = 0.007), injections (p =0.000) and probiotics (p = 0.000) among the health facilities. There was no statistically significant difference in the prescription of antimalarials (p =0.438) (Table 3).

Table 3: Prescription of selected medicines per secondary healthcare facility

Medicines	SHF 1 n (%)	SHF 2 n (%)	SHF 3 n (%)	SHF 4 n (%)	Total n (%)	*P* value
ORS/Zn	20 (11.6)	72 (41.9)	36 (20.9)	44 (25.5)	172 (100)	0.000
Antibiotics	46 (38.3)	23 (19.2)	25 (20.8)	26 (21.7)	120 (100)	0.007
Antimalarials	8 (25.8)	5 (16.1)	9 (29.0)	9 (29.0)	31 (100)	0.438
Injections	10 (29.4)	0 (0)	18 (52.9)	6 (17.6)	34 (100)	0.000
Probiotics	15 (11.2)	75 (56.0)	21 (15.7)	23 (17.2)	134 (100)	0.000

key
SFH 1 — Onikan Health Centre
SFH 2 — Massey Street Children's Hospital
SFH 3 — Ebute Meta Health Centre
SFH 4 — Ajeromi Health Centre

DISCUSSION

This study evaluates the prescription of medicines in the management of acute diarrhoea in children under five years old at four secondary healthcare facilities (SHFs) in Lagos State. The prescription of medications from seven drug classes confirms the use of unnecessary drugs, polypharmacy, and demonstrates failure to deliver effective care for acute diarrhoea using the first-line and cornerstone treatment – ORS/Zinc. The study also shows statistically significant variation of prescription of medicines for the treatment of acute diarrhoea in under-fives from one secondary healthcare facility to another. This significant difference in prescription indicates variations in outcomes in the management of acute diarrhoea by the same level of healthcare which are supposed to have a synchronized system. Variation in outcomes signifies slow adoption of the use of ORS/Zinc for the management of acute diarrhoea in under-fives and explains the slow progress in tackling under-five deaths due to diarrhoea and achieving the Sustainable Development Goals (NHS Confederation 2004). Majority (74.5%) of the cases assessed in this study, occurred in children under 24 months confirming the more vulnerability of this age group to diarrhoea (Platts-Mills *et al.*, 2015).

All 480 cases of diarrhoea randomly selected for this study were diagnosed as acute watery diarrhoea (AWD) with 73.3% occurring alone without comorbidities. This result is close to findings of a study done at primary healthcare centers (PHCs) in Lagos, Nigeria where 97.5% of all diarrhoea cases presented within one year were AWD; and occurring alone in 64.4% of the cases (Ogbo *et al.*, 2019). The prescribing implication of this diagnosis is an expected 100% prescription of ORS/Zinc without unnecessary addition of other medicines which are not beneficial to achieving the treatment goal.

Prescriptions for AWD contained a variety of medicines prescribed in a combination of two (40.3%) to four (1.4%) medications. This observation is lower than that found in the PHC study where up to seven medicines were prescribed (Ogbo *et al.*, 2019). The clinical implications of unnecessary polypharmacy include exposure of children to unnecessary medicines and features of drug therapy problems.

The prescriptions of antibiotics (34.1%) found in this study is similar to that found in the PHC study (30.4%) but lower than identified in similar studies carried out in other locations: Punjab, India (78.0%), Addis-Ababa (86.6%) and Abakaliki, Nigeria (86.9%) (Devi *et al.*, 2015; Tekleab *et al.*, 2017; Efunshile *et al.*, 2019; Ogbo *et al.*, 2019). The clinical implication of unnecessary and inappropriate use of antibiotics remains the risk of antibacterial resistance which has been declared a public health crisis and threat to national security (WHO, 2013). In addition, there is unnecessary exposure of the child to drug therapy problems including adverse effects. There is therefore a need for the initiation, implementation and sustenance of antimicrobial stewardship programs in healthcare facilities to improve prescribing of antimicrobials (File, Srinivasan and Bartlett, 2014; Nathwani *et al.*, 2019). Of the four classes of antibiotics prescribed in this study, cephalosporins were the most prescribed (70.0%). Prescription and recommendation of antibiotics for AWD seems to vary from one health setting to the other probably due to the fact that they are not indicated for AWD. Previous

studies have shown penicillins to be the most prescribed in PHCs, and nitroimidazoles, the most recommended in community pharmacy and patent medicine vendor settings (WHO, 2013; Ogbo, Aina and Aderemi-Williams, 2014; Uzochukwu *et al.*, 2014; Ogbo *et al.*, 2019). These have implications for antimicrobial resistance and consolidate the need for antimicrobial stewardship programs in different healthcare settings.

In this study, antimalarials and injections, basically gentamicin injections were also among the prescribed medicines. These are unnecessary and have no benefits for AWD since the goal of therapy of AWD is rehydration. Other studies have also identified the use of these unnecessary medicines (Devi *et al.*, 2015; Meremikwu *et al.*, 2015; Efunshile *et al.*, 2019).

This study shows that 47.7% of the prescription did not contain ORS either alone or in combination with zinc. This is much higher than the study done at SHFs in Calabar where only 15.4% of the prescriptions did not contain ORS (Meremikwu *et al.*, 2015). This could be due to the fact that there were five other groups of medicines of competing interests thereby distracting from the use of ORS/Zinc. The risk of dehydration remains high when ORS/Zinc is not prescribed, since the goal of therapy in diarrhoea is rehydration. Although 48.9% of the prescription in our study contained ORS/Zinc, 14.5% also contained antibiotics, antimalarials and injections. This is in contrast with the aforementioned study done in Calabar where 70.5% of the prescriptions contained ORS together with antibiotics and other medicines. Overall, only 34.4% of the prescriptions in our study were appropriate. This is lower than the 80% target prescription of ORS/Zinc and therefore suboptimal (FRN, 2013). The suboptimal prescription of this cornerstone treatment, for which there is no other reasonable alternative, indicates failure to deliver effective care (Wennberg, McPherson and Goodman, 2015). This variation from standard care is a main factor for stalled or slow progress in combating under-five deaths due to diarrhoea (Sreeramareddy, Low and Forsberg, 2017).

The study showed statistically significant differences in the prescription of ORS/Zinc ($p = 0.000$), antibiotics ($p = 0.007$) and injections ($p = 0.000$) among the healthcare facilities. The inverse relationship between the prescription of ORS/Zinc and antibiotics, injections and antimalarials seen in this study demonstrates the distraction from the use of ORS/Zinc when other medicines are present. The use of probiotics was very prominent in this study as also seen in other studies (Devi *et al.*, 2015; Efunshile *et al.*, 2019). While probiotics are beneficial in reducing the risk and duration of diarrhoea, they are to be used with rehydration therapy. This study observed that the Massey Street Children's hospital (SFH 2) and Onikan healthcare center had contrasting prescribing behaviours for ORS/Zinc and antibiotics. SFH 2 had the highest prescription of ORS/Zinc and the lowest for antibiotics while SFH 1 had the highest prescription of antibiotics and lowest ORS/Zinc prescription (Table 3). This contrasting prescribing behaviours highlights the fact that ORS/Zinc and antibiotics are competing medications in the management of acute diarrhoea in children. This observation clearly shows the need for an intervention to promote the sole prescription of ORS/Zinc for AWD at the secondary level of healthcare.

Overall, this study highlights the prescription of several unnecessary medicines that seem to compete with the prescription of ORS/Zinc for the treatment of AWD in under-fives. It also accentuates the variation of prescribing from one healthcare facility to another irrespective of the gold standard treatment. The fact that only one facility had a source of

Treatment guidelines at the time of the survey could be the reason for poor prescriptions yet this might not be tenable as the facility with the most appropriate prescription for AWD did not have a treatment guideline at the time of the study.

The use of only four facilities is acknowledged as a limitation of this study. A larger study including more facilities is encouraged to have a more encompassing result.

CONCLUSION

This study has shown that the prescribing of ORS/Zinc for the treatment of acute diarrhoea in under-fives at the four secondary healthcare facilities surveyed is suboptimal. This is an indication of failure to deliver effective care to under-five children with diarrhoea. Of the 352 cases of acute diarrhoea cases occurring alone, only 121 (34.4%) received appropriate prescription of ORS/Zinc without unnecessary additions of antimicrobials, antimalarials, and injections. There is a need for an appropriate intervention to improve prescribing of ORS/Zinc for the treatment of diarrhoea at secondary health facilities in Lagos. An initiation of antibiotic stewardship program would ameliorate antibiotic prescribing. In addition, an establishment of audit and feedback through routine collection of prescription data would improve ORS/Zinc utilization in secondary health facilities.

ETHICAL APPROVAL

Ethical approval was obtained from the Ethics Committee of the Lagos University Teaching Hospital with the Health Research Committee assigned number: ADM/DCST/HREC/APP/3235. Approval to access records in secondary health facilities was obtained from the Lagos State Health Service Commission (HSC 378/Vol. V/47).

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Conflict of Interest: None declared

Received: 17 August, 2021

Accepted: 04 October, 2021