

Prevalence and factors associated with acute diarrheal disease among under- five children in Southern Ethiopia: Community based cross sectional study

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Abstract

Background: Diarrheal disease remains the leading cause of morbidity and mortality among under-five children worldwide. It is one of the top leading causes of under-five morbidity & mortality in Ethiopia. Knowing the determinants of a disease enables us to design an effective intervention. The main objective of this study was to assess the prevalence and associated factors of acute diarrheal disease among under-five years of age.

Methods: Community-based cross-sectional study was carried out. Five hundred thirty mothers/care takers with under-five children were selected by using systematic random sampling from selected kebeles in the district. Data were collected using structured and pre-tested questionnaires. Data was cleaned and analyzed using SPSS version 20. Bivariate and multivariate analysis was done to assess factors affecting diarrhea.

Results: A total of 530 households with under- five children were involved in the study. The mean ages of the respondents and the index children were 33.30(±6.26SD) years and 22.75 (±12.79SD) months, respectively. Prevalence of diarrheal disease over a period of two weeks preceding the study was 21.3%. Water source [AOR: 4.476, 95% CI (1.962, 10.210)], distance to water source [AOR: 2.252, 95% (1.139, 4.451)], feces seen outside the pit hole of latrines [AOR: 2.943, 95% (1.347, 6.429)], mothers/care takers who feed adult food to the children [AOR: 6.985,95 %(1.074, 45,433)] and bottle feeding [AOR: 8.269,95%(1.086, 62.975)] were significantly associated variables on multivariate analyses.

Conclusions and recommendations: The magnitude of diarrhea among under -five children was relatively high. Improper use of latrines, source of water of for drinking, times to water source, types of food and methods of feeding were the factors associated with acute childhood diarrheal. The authors of the study recommend availing improved water sources for the community. The community is also advised to use latrine appropriately and use appropriate food and method of feeding to reduce the risk of diarrheal. Health education program should be given to the hygiene sanitation and behavioral practice of the households

Background

Diarrhea is defined as an increased in the frequency of stools over what is normal (at least three times per day or more) and stools are not formed (i.e. loose or watery(1). Severe dehydration caused by diarrhea is a major cause of morbidity and mortality among young children. Diarrhea predisposes children to malnutrition, which makes them highly susceptible to other infections and this has been found to be a major contributor to illness and death, particularly among children of under five years of age(2).

Diarrheal diseases have responsible for an estimated of 3–5 billion diarrheal illnesses and 5–10 million diarrhea-related deaths per year among under 5 children (3), the majority lives in Africa, specially Sub Sahara Africa, Asia and Latin America. In Africa diarrhea is responsible for 25–75% of all childhood diseases and about 14% of outpatient visits and 16% of hospital admission(4, 5, 6).

World health organization estimates that 88% of all diarrheal diseases are due to unsafe water supply, in adequate sanitation and poor hygienic practice. Globally, more than one billion people lacked access to

improved water sources (6). Although the condition can be easily treated with oral rehydration therapy(ORT), exposure to diarrhea-causing agents may results a severe form of acute diarrhea and it is frequently related to the use of contaminated water and to poor hygienic practices in food preparation and avoidance of excreta (7, 8). Severity is aggravated by many factors, including the agent and its pathogenicity and host characteristics ,such as immunodeficiency and age (9).

In Ethiopia, an acute diarrhea is one of the major causes of morbidity and mortality of under-five children that leads to severe dehydration and malnutrition end up with long term effect of mental retardation and creating considerable demand for health service (1, 10). More than half of millions children die each year from diarrhea related dehydration in Ethiopia(4). It is one of the top leading causes of under-five morbidity and mortality in Ethiopia for decades. Diarrheal diseases have been persistently reported as the first causes of under-five visits to health facilities in the country(11, 12).

According to the Ethiopian Demographic and Health Survey 2005, the two week period prevalence of diarrhea among under five children was estimated to be 18%(13).

In developing countries behavioral, socio-economic and environmental factors influence child morbidity (5). A study conducted in Southern Ethiopia indicated that the occurrence of diarrhea is associated with, lack of latrine ownership, lack of home-based water treatment, lack of improved water source and consumption of left –over food(14). Access to medical care, improved hygiene, sanitation, safe drinking water, exclusive breastfeeding, and vaccines that prevent rotavirus are the critical component for diarrheal disease control (15).

Understanding childhood morbidity and identifying the causes of diarrhea is very crucial for the effective implementation of child health intervention programs for policy formulation and the general assessment of resource requirements and intervention prioritization.

There was lack of studies that evaluated the associations of socio-demographic characteristics, socio-economic, environmental and behavioral factors of childhood diarrhea in SNNPRS particularly in Halaba district. So, this study aimed to assess the magnitude and relationship of diarrhea among under- 5 children with the different demographic and socio-economic, environmental and behavioral factors.

Methods

Study design and setting

A community based cross sectional study was conducted from March to April 2017 in Halaba- special woreda, Southern, Ethiopia. Halaba-special woreda is located in the South west 315 km from Addis Ababa (the capital city of Ethiopia) and 89 km from Hawassa(capital city of SNNP regional state) in the Sothern direction.

Sample Size

Single population proportion formula was used to determine the sample size for the first objective using Open Epi version 7 and considering the following assumptions: 95% confidence level (1.96), Margin of error (0.05), expected prevalence of children with diarrhea from similar study conducted in Arbaminch district 19.6%(25), we had been consider 5% margin of error for P = 19.6%, design effect of 2 and adding 10% of the none respondent's. The final sample size was 530

Sampling Procedure

Multi-stage sampling procedures were used; first by selecting 16 kebeles (more than 20%) from the total seventy nine (79) kebeles using lottery method. From a total of 2582 households with under- 5 children in the selected kebeles were registered from family folders. Households were allocated to each Keble based on proportional to size, then systematic sampling (every kth households), (k was determined by, study population (2582 hh)/sample size (530) = 5), from households with under- five children was identify and register sequentially using family folders in the kebeles were include for the study. In case, where there were more than one under-five children in the same household, only one child was selected by lottery method to take information on child's health characteristics. Similarly in case, where there was more than one mothers/ care givers of under-five children in the same households, only one mothers/care givers was select by lottery methods.

Data Collection Tool And Procedure

Data was collected using WHO/ UNICEF and EDHS standard questionnaire(4). The questionnaire was written in English, translated into Amharic (local language), and then translated back into English to assure its consistency. The respondents were primarily mothers of eligible children-under five years of age, but in the absence of the mother, the next primary caregiver was interviewed. Pretest was done in 5% the respondents in another kebele of Halaba special district of Southern Ethiopia. The result of the pretest was used to correct some unclear ideas and statements. Five data collectors who were clinical nurses & two supervisors (Health Officers and BSC nurses) were trained for two days. House-to-house visit and interview of mothers/ care takers of under-five children was performed. The data collection was supervised by the supervisors and the principal investigator at the center. Their role was to daily check the consistency, clarity and completeness of the collected questionnaires. Incomplete and inconsistent data's were identified and necessary corrections were made during the data collection time.

Study Variable Outcome (Dependent) Variable

Two weeks prevalence of diarrhea

Explanatory (independent) Variable

Demographic & Socioeconomic status: income, place of residence, household size, maternal age, age of the child, maternal education, ethnicity, number of children, occupation, marital status, religion, etc.

Environmental & sanitation: type of water source, distance to the water source, amount of daily water consumption, availability of latrine, number of rooms, livestock in house, refuse disposal, etc.

Behavioral factors: method of water drawing and storage, feeding practices, action for diarrhea, duration of breast-feeding, time of introducing supplementary feeding, Vaccination status etc.

Data management and analysis

The data was entered using Epi data software and analyzed using SPSS version 20. The data was checked before entering in to the software and cleaning before analysis. We were conducting Bivariate and Multivariate analysis to see the possible associated factors with diarrhea, with 95% Cl. Variables with p-value less than or equal to 0.25 during Bivariate analysis were enter into multivariate logistic regression models to control the effect of confounders. We reported the results as adjusted odds ratio (AOR) and 95% confidence intervals.

Ethical Consideration

Ethical approval was obtained from Institutional Review Board of Hawassa University, college of medicine and health science. Permission was also obtained from concerned body of Halaba special district health office. Consent was obtained from the mothers/caretakers of the children after clear explanation about the aim of the study. Confidentiality and privacy was maintained during data collection, analysis and reporting in which the information obtains from the respondents was not share with anyone other than the data collectors and principal investigators. Children with diarrhea during the data collection process were given ORS and health education relates to diarrhea by the data collectors and advised their family to taken them the nearby health institutions for better management.

Results

Demographic And Socio-economic Characteristics Of The Respondents

A total of 530 mothers/caretakers with under-five children were involved in the study with response rate of 100%. The mean family size living in the house was 7.23 (+ 2.24SD). The mean age of the respondents was 33.30 (+ 6.26SD) and of whom, majority of them 355 (67.0) were 19–36 years of age. Almost all of the respondents 519 (97.9%) were biological mothers, about 404 (76.2%) of the respondent were illiterates and 488 (92.1%) were married. Majority of the respondents 484 (91.3%) were house wife by occupation (Table 1).

Table 1 Socio-demographic and economic characteristics of the respondents in Halaba special district, Southern Ethiopia 2019

5-8 persons > 8 persons No of u-5 five children in the household(n = 530)	58 325	10.9
5-8 persons > 8 persons No of u-5 five children in the household(n = 530)		10.9
> 8 persons No of u-5 five children in the household(n = 530)	325	
No of u-5 five children in the household(n = 530)		61.3
	147	27.7
1 children		
	403	76
2 children	96	18.1
3or more children	31	5.9
Relationships of respondents (n = 530)		
mother	519	97.9
care taker	11	2.1
Age of mothers/care taker category (n = 530)		
18-26 years	11	2.1
27-36 years	355	67.0
37-45 ⁺ years	164	30.9
Marital status of respondent (n = 530)		
married	488	92.1
divorced	22	4.2
single	12	2.3
widowed	8	1.5
Occupation of the respondents (n = 530)		
housewife	484	91.3
merchant	24	4.5
farmer	13	2.5
other	9	1.7
Educational status of father (n = 488)		
Illiterate	366	69.1

Variable name	Frequency	Percentage (%)
Read& write	117	22.1
Elementary	5	0.9
monthly income		
< 500EBirr	361	68.1
500-1000EBirr	169	31.9
Availability of radio		
yes	201	37.9
no	329	62.1

Environmental characteristics of the households

About 438(82.6%) of the respondents had latrine. From the total latrines, 394(89.9%) of them were not improved type. Majority, 362 (82.6%) of the latrine were private. Among the total households who had latrines, feces was observed in 88(21.1%) on pit latrines hole. Most of the households 504 (95.1%) disposes their waste material improperly. About 471(88.9%) of the households used piped water as a source water. Only 321(60.56%) households had 20 liter or less per capita water consumption. Only thirty four 34 (6.4%) of the households treat their drinking water at home with bleach or chlorine (Table 2).

Table 2 Environmental characteristic of the households in Halaba special district, Southern Ethiopia 2019

Variable name	Frequency (n = 530)	Percentage (%)
Household floor type		
Mud	524	98.9
Cement	6	1.1
Types of roof material		
Thatched	461	87.0
corrugated iron sheet	69	13.0
Latrine availability		
yes	438	82.6
no	92	17.4
Type of latrine n = 438		
Improved	44	10.1
Unimproved	394	89.9
Latrine ownership n = 438		
private	362	82.6
shared with neighbor	76	17.4
Feces seen in outside the pit hole n = 438		
yes	88	20.1
no	350	79.9
Feces seen around the house compound		
No	129	24.3
yes	401	75.7
Hand wash facility		
Yes	395	75.5
No	135	24.5
Refuse disposal method		
Pit	26	4.9
Open field	504	95.1

Variable name	Frequency (n = 530)	Percentage (%)
Source of water		
Improved	471	88.9
Unimproved	59	11.1
Daily per capita water consumption		
Twenty liters and less	321	60.56
More than 20 liters	209	39.44
Time to water source		
<1 hour	166	31.3
>=1 hour	364	68.7
Home based water treatment		
yes	34	6.4
no	496	93.6

Behavioral Characteristics of The Respondents

Among the total respondents of 530 households, majority 494(93.2%) of children started supplementary food. About 411 (83.2%) of respondents were prepare adult foods (Enjera with wet or bread which is not diversified foods in each food items and 407 (76.8%) of the respondents feed their children using their hands or the child themselves. Only 155 (29.2%) of the respondents wash their hand using soap (Table 3).

Table 3
Behavioral characteristics of the respondents in Halaba special district, Southern Ethiopia 2019

	Frequency (n = 530)			
child start supplementary food				
Yes	494	6.8		
No	36	93.2		
Types of food the	child taken n = 494			
cow's milk	83	16.8		
adult food	411	83.2		
Material used to f	eed the child n = 494			
Hand	407	82.4		
cup with spoon	20	4		
Cup	23	4.7		
Bottle	44	8.9		
Hand washing methods				
Soap with water	155	29.2		
Ash with water	50	9.4		
Water only	325	61.3		

Demographic And Health Characteristics Of The Indexed Children

More than half of the children 280 (52.8%) were males and about 185 (34.9%) of the children were in the age category of 12-23 months. The mean age of under-five children were 22.75 ± 12.793 months. Of the total 474 eligible children for measles vaccine, about 430 (90.7%) were vaccinated, similarly from the total 530 children who were eligible for Rota vaccine, almost all 520 (98.1%) of them were vaccinated for Rota. About 113(21.3%) of children had experience diarrheal in the two weeks period preceding the data collection (Table 4).

Table 4 demographic and health characteristics of the index children in Halaba special district, Southern Ethiopia 2019

Variable name	Frequency (n = 530)	Percentage (%)			
Sex of the child					
Male	280	52.8			
Female	250	47.2			
Age category of the childre	en				
<=5months	38	7.2			
6-11 months	38	7.2			
12-23 months	185	34.9			
24-35months	124	23.4			
36-59 months	145	27.4			
Mean age of the children		22.75 ± 12.793 months			
Current breast feeding stat	tus n = 530				
exclusive breast feed	38	7.2			
partial breast feed	286	54.0			
not breast feeding	206	38.9			
Age at supplementary feeding n = 494					
< 6month	61	11.5			
At 6 months	433	81.7			
Rota vaccination n = 530					
yes	520	98.1			
No	10	1.9			

Factors Associated With Under - Five Diarrheal Disease

Prevalence of diarrheal disease over a period of two weeks preceding the study was 21.3%.

Water source for drinking [AOR: 4.476, 95% CI (1.962, 10.210)], time to water source [AOR: 2.252, 95% (1.139, 4.451)], feces seen outside the pit hole of latrines [AOR: 2.943, 95% (1.347, 6.429)], type of food [AOR: 6.985,95% (1.074, 45,433)] and bottle feeding [AOR: 8.269, 95% (1.086, 62.975)] were significantly associated variables on multivariate analyses (Table 5).

Table 5
Bivariate and Multi variant analysis of determinants of under - five diarrheal diseas in halaba special district, southern Ethiopia 2019.

Variable	Diarrheal di	sease (DD)	Odds Ratio (95% CI)	
	Yes (%)	No (%)	Bivariate (COR)	Multivariate (AOR)
Household family size				
2-4 persons	9 (1.7%)	49 (9.3%)	1	1
5-8 persons	53 (10%)	272 (51.3%)	1.061(0.492, 2.290)	0.479 (0.1561.476)
>8 persons	51 (9.6%)	96 (18.1%	2.892(1.316, 6.359)**	0.862 (0.211, 3.527)
Number of under-five children				
1 children	69(13%)	334(63%)	1	1
2 children	10(2%)	21(4%)	2.66(1.623,4.342)***	1.239 (0.611,2.513)
>=3 children	34(6%)	62(12%)	2.305(1.039,5.112)*	1.458 (0.47,4.526)
Educational status ofmothers/caretakers				
n = 530				
Illiterate	96 (18.1%)	309 (58.3%)	1	1
read write	15 (2.8%)	100 (18.9%)	0.483(0.268,0.87)*	0.575 (0.242, 1.363)
Elementary	2 (0.4%)	8 (1.5%)	0.805(0.168,3.854)	5.973 (0.956, 37.337)
Availability of radio in the household				
n 530				
Yes	30(5.7%)	171(32.3%)	0.520(0.328,0 .824)**	0.926 (0.493, 1.737)
No	83(15.7%)	246(46.4%)	1	1
Latrine availability n = 530				
Yes	65(12.3%)	373(70.8%)	0.160(0.098,0.260)***	0.481(0.005, 44.567)
No	48(9%)	44(8.3%)	1	1
Type of latrine n = 438				
Improved	7(1.6%)	38(8.6%)	1	1

Variable	/ariable Diarrheal disease (DD)		Odds Ratio (95% CI)	
	Yes (%)	No (%)	Bivariate (COR)	Multivariate (AOR)
Not improved	58(13.3%)	335(76.5%)	5.922(2.398,14.624)***	1.102 (0.323, 3.764)
Handwashing facility n = 530				
Yes	75(14%)	320(60.4%)	0.598(0.381,0.940)*	0.847(0.464, 1.544)
no	38(7.2%)	97(18.4%)	1	1
Feces seen on pit hole n = 438				
yes	30(6.8%)	59(13.5%)	1.002(1.001, 1.002)***	2.943 (1.347, 6.429)*
no	35(8.0%)	314(71.7%)	1	1
Feces around the compound				
n = 530				
Yes	62(11.7%)	67(12.6%)	6.351(4.035,9.994)***	1.549 (0.572, 4.193)
No	51(9.7%)	350(66%)	1	1
Source of water for drinking n = 530				
Improved	73(13.8%)	398(75%)	1	1
Not improved	19(3.6%)	40(7.5%)	11.478(6.297,20.923)***	4.476 (1.962, 10.210)***
Time to water source n = 530				
<1hour	17(3.2%)	149(28.1%)	1	1
>=1 hour	96(18.1%)	268(50.6%)	3.140(1.805,5.459)***	2.252 (1.139, 4.451)*
Type of food the child take n = 494				
Cow's milk	31(6.3%)	52 (10.5%)	1.399 (1.240, 2.663)*	6.985(1.074,45,433)*
Adult foods	79 (16%)	332 (67.2%)	1	1
Child feed method n = 494				
Hands	79 (16%)	328 (66.4%)	1	1

Variable	Diarrheal di	sease (DD)	Odds Ratio (95% CI)	
	Yes (%)	No (%)	Bivariate (COR)	Multivariate (AOR)
Cup with spoon	2 (0.4%)	18 (3.6%)	0.461 (0.105,2.029)	1.111(0.134, 9.196)
Cup	5 (1%)	18 (3.6%)	0.395 (0.091,1.722)	1.547(0.123, 19.485)
Bottle	17 (3.4%)	27 (5.5%)	6.594(3.426,12.690)***	8.269(1.086,62.975)***
Age of child(in month)				
<=5 months	4(0.8%)	34(6.3%)	1	1
6-11 months	22(4.2%)	16(3.0%)	11.687(3.451,39.582)***	4.086(0.169, 98.526)
12-23 months	40(7.5	145(27.4	2.345(0.786, 6.999)	1.011(0.037, 27.556)
24-35 months	18(3.4	106(20	1.443(0.457, 4.560)	0.627(0.022, 1.190)
36-59 months	29(5.5	116(21.9	2.125(0.698, 6.468)	1.166 (0.740, 1.836)
Current breast feeding status				
Exclusive breast feed	3(0.6%)	35(6.6%)	1	1
Partially breast feed	63(11.9%)	223(42.0%)	3.296(0.981,11.073)	0.346 (0.100, 3.311)
Not breast feed	47(8.9%)	159(30.0%)	3.449(1.015,11.718)*	2.247(0.664, 7.602)
Birth order of the child n = 530				
1-3th	19(3.6%)	118(22.3%)	1	1
4-6th	60(11.3%)	236(44.5%)	1.579(0.901,2.768)	1.386(0.580, 3.311)
7-9th	28(5.3%)	60(11.3%)	3.378(1.758,6.488)***	2.247(0.664, 7.602)
>=10th	3(0.6%)	6(1.1%)	3.105(0.715,13.381)	1.172(0.125, 11.017)

Discussions

The finding of this study shows that the two weeks period magnitude of diarrhea among under

Five years of age children was 113(21.3%). Households water Source; times to fetch water from the source and feces seen on pit hole of latrine were the only environmental factors which showed significant association with under-five diarrhea morbidity. Types of food that the children take and children feeding methods were behavioral factors that were significantly associated with under-five diarrheal diseases, after controlling other variables.

In this study the magnitude of under-five diarrhea was almost similar with the studies conducted in Benishngul-Gumuz (22.1%), in Shebedino district Southen, Ethiopia (19.6%), Ghana (19.2%) and Kersa district, Eastern Ethiopia (22.5%, (17, 18, 29, 30). This study was relatively low compared to a study done in Arba-Minch (31%) (1), Debrebirehan referral hospital (31.7%) (12) and Enderta woreda Northern, Ethiopia (35.6%) (31), but this is relatively high compared to a studies conducted in Debre Berhan Town (12.2%) (18) and Wolitta Soddo Town Southern, Ethiopia (11%) (3). This discrepancy in magnitude with the high and low magnitude of the above study could be, due to the population difference, their difference in socio demographic, basic environmental and behavioral characteristics of the respondents.

In this study children from households who were used unimproved water source were increased the risk of diarrheal morbidity compared to children from households who use improved water source. Which is consistent with a cross-sectional studies done in Kenya (32) and a community based unmatched case-control study conducted in Derashe district, Southern Ethiopia(33). This is can be explained by unimproved water source tends more prone to contaminated by pathogenic microorganisms than improved water source and thus increased under-five diarrhea morbidity. But not consistent with cross-sectional studies done in Wolitta Soddo Town, Southern, Ethiopia(3).

Children from households who spent one or greater than one hour to water source were 2 times more probable to have diarrhea than those children from households who spent less than 1 hour to water source. Our findings was consistent with other studies reported that spent more time to fetched water was showed strong association with under-five childhood diarrheal morbidity (34). One way of contamination water is during transportation, it could be due to the fact that, the time to the water source is too long, which results uncover of the container while they rest everywhere.

The odds of having diarrhea in children who lived in households where there were feces seen on the outside pit hole of the hole of latrines were 2.9 times more at risk to have diarrheal morbidity than the odds of children who lived in households where there were no feces seen outside the pit of latrines. our study finding agreed with a cross sectional study conducted in Debre_ Berhan Town (22) and Gummer woreda (35). It is true that, presence of feces on the pit latrine would be prone children to be contaminated with feces while they defecated as well as other vehicles. This is also an important implication that the mere presence of latrine facility does not have a grant for prevention of excreta-related disease, but it is the proper utilization that had a vital importance.

Children of mothers/care takers who feed cow's milk in addition to breast milk to the children were about 7 times more probable to develop under five diarrheal diseases compared to children of mothers/care takers who feed adult food to the children. It is consistence with study conducted in USA(36).

Feeding children using the bottle was independently risk factors for the occurrence of under-five diarrheal diseases. Our finding was in line with a Community-based cross-sectional study done in Kenya (32) and other community based cross-sectional study conducted in Gummer district, Gurage Zone, Southern Ethiopia (35). This is due to the possibilities that contamination of the feeding bottle, due to poor handling of the mothers/care takers. It is also the fact that bottles are not simple to clean the left over foods, as result microorganisms got the chance to multiply inside the bottle finally children become diarrheal disease.

The strength of this study is that- it was community based and that it particularly addressed acute childhood diarrheal morbidity in rural community with 100% response rate. However, there were some limitations in this study. There could be recall or social desirability bias. Also, the study design was cross sectional and it couldn't show the causal effect.

Conclusions

In conclusion, the magnitude of diarrhea among under -five children was relatively high. Improper use of latrines, source of water of for drinking, times to water source, types of food and methods of feeding were the factors associated with acute childhood diarrheal. The authors of the study recommend availing improved water sources for the community. The community is also advised to use latrine appropriately and use appropriate food and method of feeding to reduce the risk of diarrheal. Food hygiene and general sanitation is highly recommended.

Acronyms And Abbreviations

CHIS: Community health information system, EDHS: Ethiopian Demographic Health Survey, HC: health centers, HH: House Hold, HWTS: Home water treatment system, MDG: Millennium Development Goal, SNNPRS: South Nation Nationality People Regional State, UNICEF: United, Nation International Children's fund, WHO: World Health Organization

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from Institutional Review Board of Hawassa University, college of medicine and health science. Consent was obtained from the mothers/caretakers of the children after clear explanation about the aim of the study.

Consent for publication

Not applicable

Availability of data and materials

Data will be available upon reasonable request from the corresponding author

Competing interests

The authors have declared that no competing of interests exists.

Funding

No funding was obtained for this study.

Authors' contributions

EM designed the study, participated in the data collection, performed analysis and interpretation of data and drafted the paper and revised the manuscript. AN and BF assisted with the design, took part in drafting the article or revising it critically for important intellectual content; gave final approval of the version to be published; and agree to be accountable for all aspects of the work.

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