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Case–control study to determine risk factors for diarrhea among children during a large outbreak in a country with a high prevalence of HIV infection☆

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SUMMARY

Objectives: Between January and March of 2006, over 35 000 diarrhea cases and 532 deaths were reported among children aged <5 years in Botswana. We conducted an investigation to characterize the outbreak, identify risk factors for diarrhea, and recommend control strategies.
Methods: We enrolled children <5 years of age presenting to the emergency department between March 2 and March 20, 2006. Cases had ≥3 loose stools per day and no antecedent diarrhea among household members. Controls had had no diarrhea since January 1, 2006. We conducted a multivariate logistic regression analysis controlling for socioeconomic status, age, and maternal HIV status.
Results: Forty-nine cases with median age of 12 months (range 0–45 months) and 61 controls with median age of 24 months (range 0–59 months) were enrolled; 33 (30%) were born to HIV-positive mothers. Case-parents were more likely to report storing household drinking water (adjusted odds ratios (AOR) 3.9, 95% confidence interval (CI) 1.2–15.7). Lack of hand washing after using the toilet or latrine (AOR 4.2, 95% CI 1.1–20.4) was more likely to be reported by case-parents. Case-children were less likely to be currently breastfeeding (AOR 30.3, 95% CI 2.0–1000.0). Five (10%) case-patients and no control-patients died. Multiple causal pathogens were identified.
Conclusions: During this diarrhea outbreak in a country with a national program to prevent mother-to-child transmission of HIV, ill children were less likely to be breastfed and more likely to have been exposed to environmental factors associated with fecal contamination. These findings underscore the importance of adequate access to safe water, sanitation, hygiene, and nutrition education among populations using breast milk substitutes.

1. Introduction

Each year, approximately 4 billion cases of diarrhea and 2.2 million diarrhea-related deaths occur worldwide, mostly among young children in developing countries.[1,2] Diarrheal diseases can be caused by numerous pathogens and transmitted through multiple vehicles. Persons living in developing countries with poor access to safe water, sanitation, or hygiene infrastructure have increased risk of exposure to viral, bacterial, and parasitic pathogens that can cause diarrheal diseases.

In Botswana, a politically stable, middle-income country, the relative burden of diarrhea morbidity and mortality has been lower than that in many other African countries.[3] The government has invested in health care, which is available free of charge at public clinics throughout the country. Piped water is also widely available. The HIV prevalence in Botswana is amongst the highest in the world, with an estimated prevalence of over 30% in pregnant women since 1995. Due to this high HIV prevalence in pregnant women, the government of Botswana implemented a national program for the prevention of mother-to-child transmission of HIV (PMTCT) in 1999.[4] The program provides free antiretroviral (ARV) treatment to HIV-positive pregnant women and ARV prophylaxis for their infants, and is the first PMTCT program in Africa to provide free infant formula for the first year of life for all infants born to HIV-infected mothers.[5]

Despite these efforts to safeguard public health, Botswana experienced a large diarrhea outbreak with high mortality among

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young children during the first quarter of 2006.[6] From November 2005 through March 2006, unusually heavy rains occurred; intermittent flooding was reported in some areas.[7] From January through March 2006, the Botswana Ministry of Health reported >35 000 diarrhea cases and 532 deaths among children <5 years of age.[8] This represented a 4-fold increase in diarrhea morbidity and a 25-fold increase in diarrhea mortality for this age group compared with the same quarter in 2005.

On February 26, 2006, at the request of the Botswana Ministry of Health, a multidisciplinary team from the United States Centers for Disease Control and Prevention (CDC) was deployed to assist with the investigation. At that time, due to limitations in national diarrheal surveillance and diagnostic capacity, the scope and nature of the outbreak were unclear. An initial aim of the investigation was to improve our understanding of the age and temporal distribution of the diarrhea cases, and to implement a mechanism for rapidly and reliably assessing the progression of the outbreak. We also aimed to identify diarrhea etiologies and risk factors for acquiring diarrhea, and to recommend appropriate strategies to prevent similar events from recurring.

2. Methods

2.1. Setting

Francistown, located in the northeastern part of the country, appeared to be one of the most heavily affected areas; thus we focused our investigation on Nyangabgwe Hospital in Francistown. The 550-bed referral hospital has a catchment area that includes Francistown, Tutume Central, and North-East districts with a combined estimated population of 256 000 persons, of whom approximately 32 000 were children under the age of 5 years.

2.2. Diarrhea surveillance

On February 28, 2006, we initiated daily diarrheal surveillance in the Nyangabgwe Hospital emergency department. We retrospectively reviewed emergency department log books from November 15, 2005 through February 28, 2006, and reviewed them daily thereafter through March 27, 2006. A case of diarrhea was defined as an emergency department log book entry of diarrhea, acute diarrhea, gastroenteritis, acute enteritis, or dysentery. Patients with a log book entry of chronic diarrhea were excluded. Patient age, sex, and disposition after the emergency department visit were recorded.

2.3. Pediatric patient case–control investigation

We attempted to screen for eligibility all children aged <5 years presenting to the emergency department for medical care between 7:00 am and 5:00 pm from March 2 through March 20, 2006. A case was defined as ≥3 loose stools per day in a child who presented to the emergency department for medical care and was the first person in the household with diarrhea in 2006. The latter criterion was established to help elucidate environmental risk factors for diarrhea, rather than intra-household transmission. Patients presenting with diarrhea could have been referred from surrounding clinics or have come directly from the community. Those who met the case definition for diarrhea were enrolled as a case regardless of whether the current episode was a recurrent episode.

Controls were illnesses other than diarrhea in children who presented to the emergency department during the same period of enrolment as the cases but had non-diarrheal medical complaints and had no history of diarrhea since January 1, 2006. Common illnesses for which patients enrolled as controls sought medical attention included respiratory diseases, injuries, and malaria.

Following admission to the emergency department and after receiving initial medical treatments, patients were screened for eligibility and parents or guardians of eligible children were asked for informed consent to participate in the study. Caretakers of case- and control-patients were interviewed using a standardized questionnaire administered in the local language by a trained interviewer. Questionnaire topics included history of current illness, past medical history, food exposures, animal exposures, water sources, water storage and handling practices, and hygiene and sanitation behaviors. Mothers reported their own HIV status. We abstracted HIV status for enrolled children from medical charts. If an HIV test result was not available for a child and the mother reported her own HIV status as negative, we assumed the child was HIV-negative; otherwise, we classified the child as having an unknown HIV status.

After March 6, 2006, when measuring equipment became available, we measured heights and weights upon patient enrolment using a Seca model 210 portable child measuring mat (Seca GmbH & Co. KG, Hamburg, Germany) and a Tanita model BD-585 digital child scale (Tanita Corporation of America, Inc., Arlington Heights, IL, USA). We did not record weights and heights of children with height ≥100 cm or weight >20 kg or who refused to be measured. We defined acute malnutrition as weight-for-height *Z*-scores ≤-2 based on World Health Organization (WHO) guidelines (http://www.who.int/nutgrowthdb/about/introduction/en/index5.html). Because an unexpectedly high prevalence of malnutrition was found during the course of this investigation and we postulated that it may have contributed to the high mortality rate for diarrhea as reported by national surveillance, a post-hoc analysis of feeding practices was conducted among infants.

Cotton swabs were used to collect rectal stool specimens from cases and controls. When available, whole stool specimens were also collected. We conducted rotavirus testing on site using the Rotaclone ELISA kit (Meridian BioScience, Cincinnati, OH, USA). Due to limited availability of test kits, we completed rotavirus testing only on the first seven specimens collected from patients who provided whole stool. Swab specimens were transported in Cary–Blair medium on wet ice and plated on MacConkey agar within 24 h of collection. Growth from plates was collected on sterile cotton swabs, inoculated into fresh Cary–Blair medium, and stored at −70 °C until shipped in dry ice to the CDC laboratories in Atlanta, where they were tested for enteric pathogens. An initial shipment of specimens was delayed in transit and the cold chain could not be maintained; these specimens were not tested at CDC.

2.4. Sample size and statistical analysis

Possible risk factors identified during hypothesis generation included environmental and sanitation exposures, such as stored household drinking water, compromised latrines, animal dung, sewage and flood waters, as well as feeding behaviors, such as breastfeeding or replacement feeding. Exposure rates for these factors were unknown among the general population, and we based our sample size calculations on estimated rates of water storage. Assuming an exposure rate for storage of household drinking water of 50% among controls and 75% among cases, and a control to case ratio of 1:2 based upon emergency department visit trends at the time of the investigation, we estimated that a sample size of 52 controls and 107 cases was required to detect a statistical difference with 80% power and 95% certainty.

We analyzed data using SAS version 9.1 (SAS Institute, Cary, NC, USA). Frequencies were generated for categorical data, and means, medians, and ranges for continuous variables. We used reported ownership of a refrigerator as a proxy for high socioeconomic status (SES). To identify independent risk factors for diarrhea, we selected variables associated with diarrhea at a 0.2 significance level in the bivariate analysis. These variables were then individually tested in

multivariate logistic regression models controlling for age, SES, and maternal HIV status; variables that retained at least a 0.05 significance level were considered statistically significant associations. Testing was done to identify interactions between infant feeding variables and the sanitation variables. We calculated 95% confidence intervals (95% CI) using exact methods for adjusted odds ratios (AOR). Weight-for-height *Z*-scores were calculated using Epi Info 2002 (CDC, Atlanta, GA, USA). Sensitivity analyses were performed to assess the potential effects of unknown or missing responses to maternal HIV status. In one sensitivity model all mothers of case-children with an unknown or missing HIV status were classified as being HIV-positive and all mothers of control-children with an unknown or missing HIV status were classified as HIV-negative. These classifications were reversed in a second sensitivity model.

2.5. Human subjects

Caregivers of patients who met the case–control case definition were asked to provide written, voluntary informed consent to participate in the study. The study was exempted from formal ethics approval by CDC's institutional review board because the investigation was deemed to be public health practice with intent to rapidly respond to a disease outbreak. The protocol was reviewed and approved by the Botswana Ministry as a public health emergency response to a disease outbreak.

3. Results

3.1. Diarrhea surveillance

Between November 15, 2005 and March 27, 2006, 1204 emergency department visits met the surveillance case definition for diarrhea. Among these visits, 746 (62%) were for children <5 years of age and 395 (33%) were for adults ≥18 years of age; 614 (51%) were visits by females. Seven hundred and twenty-five (60%) patients presenting with diarrhea to the emergency department were admitted to the hospital; 511 (71%) were children <5 years of age. The number of cases began to increase during the second half of December, peaked in February, and returned to baseline in late March. The rise in cases appeared to increase as the amount of rainfall recorded increased (Figure 1).

3.2. Pediatric patient case–control investigation

Among 124 patients <5 years of age who were approached to participate in the study, caregivers of three (2%) patients refused, and 11 (9%) children who were recruited were later excluded from the analysis for failure to meet the case or control definitions. Overall, we enrolled 49 cases and 61 controls. The median age among cases was 12 months (range 0–45 months) and among controls was 24 months (range 0–59 months) (Wilcoxon rank-sum, $p = 0.002$). Twenty-six (53%) of 49 case-children and 22 (36%) of 61 control-children were aged ≤12 months (Chi-square, $p = 0.07$). Twenty-two (45%) of 49 case-children and 31 (53%) of 59 control-children were female (Chi-square, $p = 0.04$). Fourteen (29%) of 48 case-children and 24 (44%) of 55 control-children lived in households with a refrigerator (Chi-square, $p = 0.02$).

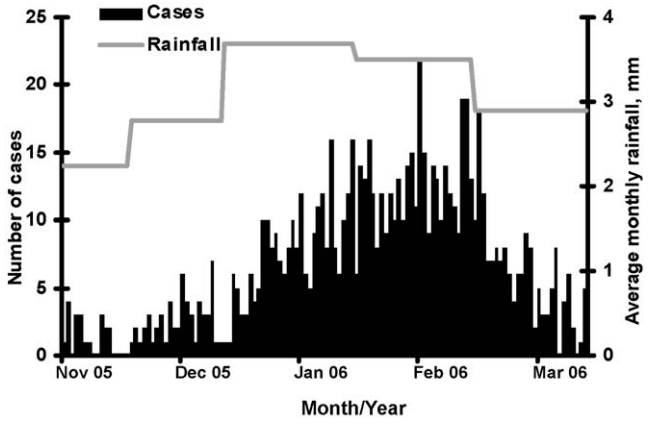

Figure 1. Number of children <5 years of age presenting with diarrhea to the emergency department of a large referral hospital and average rainfall during that period, Botswana, November 15, 2005–March 27, 2006 ($N = 746$).

Among the 49 case-children, most experienced poor feeding (74%), fever (68%), and vomiting (67%) during their illness. Bloody diarrhea was reported by 10 (20%), and long-lasting diarrhea, defined as diarrhea lasting ≥14 days, was reported by 12 (25%) of these patients. Twenty-one (57%) of 37 case-children's mothers and 12 (25%) of 49 control-children's mothers were HIV-positive (Chi-square, $p = 0.002$); two (4%) of 49 case-children and two (3%) of 61 control-children were HIV-positive (Fisher exact, $p = 1.0$) (Table 1). Weights and heights were available for 71 (65%) children. Among those, acute malnutrition was present in 12 (48%) of 25 case-children and two (9%) of 22 control-children (Chi-square, $p = 0.004$). Six (43%) of the 14 malnourished children were infants <12 months of age. Thirty-one (63%) of 49 case-children and 23 (38%) of 61 control-children were hospitalized (Chi-square, $p = 0.009$). Among the hospitalized patients, five (16%) of the 31 case-children and none of the control-children died during the hospital admission (Chi-square, $p = 0.02$).

In bivariate analysis, feeding variables including drinking ultra heat-treated milk, raw milk, fresh milk, powdered milk or juice; or eating porridge, eggs, meat, or fruits were not associated with diarrhea at a 0.2 significance level and were therefore excluded from the multiple logistic regression models. Variables related to exposure to various animals and their excrement or living in a rural residence were also excluded. After controlling for child's age and SES, case-children were twice as likely as control-children to have an HIV-positive mother. Furthermore, case-children were 30 times less likely than control-children to have breastfed during the 7 days prior to developing their current illness. After controlling for child's age, SES, and maternal HIV status, caretakers from homes of case-children were more likely than caretakers from homes of control-children to have reported: drinking water stored in open buckets or other vessels within the home; and not washing their own hands after using the toilet or latrine. Neither current formula feeding nor child HIV infection was a risk factor for diarrhea, though 53 (48%) children had an unknown HIV status. Twelve (25%) mothers of case-children and 12 (20%) mothers of control-children had an unknown HIV status. Sensitivity analysis models did not produce differing results. No significant interactions were identified between infant feeding practices, sanitation practices, age, and SES.

Among cases, seven and nine whole stool specimens were tested for viral and parasitic pathogens, respectively; none were positive for rotavirus and two (22%) yielded *Cryptosporidium spp*. Thirty-five (71%) rectal swabs from 49 case-patients and 39 (64%) from 61 control patients were received by the CDC laboratories; 28 (80%) rectal swabs from case-patients and 24 (62%) from control-patients were viable and tested for bacterial pathogens. Among specimens from case-patients, eight (29%) of 28 specimens yielded *Escherichia coli*, of which five (18%) were enterotoxigenic and two (7%) were enteropathogenic; two (7%) yielded *Shigella* and one (4%) yielded *Salmonella*. One of the specimens tested yielded more than one pathogen. Among specimens from control-patients, one (4%) of 24 specimens yielded an enteropathogenic *E. coli* and the remaining did not yield any pathogens.

In a sub-group analysis of feeding practices among all infants, irrespective of case status, 13 (52%) of 25 infants aged <12 months

Table 1
Risk factors for diarrhea among children <5 years of age presenting to the emergency department of a large referral hospital; case–control investigation, Botswana, 2006

Variable	Case (*N* = 49)	Control (*N* = 61)	Odds ratio (95% confidence interval)	
	n/*N* (%)	*n*/*N* (%)	Crude	Adjusted
HIV status				
Child HIV-positive	2/49 (4%)	2/61 (3%)	1.3 (0.2–9.2)	2.1 (0.2–26.0)[c]
Mother HIV-positive[b]	21/37 (57%)	12/49 (25%)	4.0 (1.6–10.2)	2.2 (1.0–5.0)[c]
Environmental exposures[d]				
Overflowing latrines	9/49 (18%)	3/61 (5%)	4.3 (1.1–17.1)	6.3 (0.7–317.6)[a]
Parents report not washing own hands after toileting	16/49 (33%)	10/61 (16%)	2.5 (1.0–6.1)	**4.2 (1.1–20.4)**[a]
Store drinking water	47/49 (96%)	41/61 (67%)	11.5 (2.5–52.0)	**3.9 (1.2–15.7)**[a]
Difficult access to latrine	11/49 (22%)	8/61 (13%)	1.9 (0.7–5.2)	3.0 (0.7–14.0)[a]
Standing water near the home	25/49 (51%)	20/61 (33%)	2.1 (1.0–4.6)	2.5 (0.9–7.5)[a]
Rural residence	35/49 (71%)	37/61 (61%)	1.6 (0.7–3.6)	0.9 (0.1–6.2)[a]
Feeding-related factors				
Not currently breastfeeding	24/26 (92)	15/22 (68)	5.6 (1.0–30.6)	**30.3 (2.0–1000.0)**[c,e]
Current formula feeding	10/26 (39)	7/22 (32)	1.3 (0.4–4.4)	5.3 (0.9–62.7)[c,e]

[a] Controlled for age in months, socioeconomic status, and maternal HIV status.
[b] Among mothers with known HIV status.
[c] Controlled for age in months and socioeconomic status, but not for maternal HIV status.
[d] During the 7 days before developing current illness.
[e] Among infants <12 months of age.

born to mothers whose HIV status was negative were currently breastfeeding; none of the HIV-positive mothers were currently breastfeeding (Figure 2). Overall, approximately 40% of infants were receiving neither breast milk nor formula, but instead received a variety of substitutes including pasteurized and unpasteurized cow's milk, ultra heat-treated milk, or no milk.

4. Discussion

We report a large diarrhea outbreak among children in a middle-income African country with a high prevalence of HIV infection and a national PMTCT program that provides infant formula for children of all HIV-infected mothers. During this outbreak, children with diarrhea were significantly less likely than children without diarrhea to be breastfed before developing diarrhea. This association was remarkably strong and is consistent with other research showing the clear benefits of breastfeeding in reducing non-HIV-related morbidity in children, particularly diarrheal disease.[9]

This diarrhea outbreak highlights the difficult decisions surrounding infant feeding for children of HIV-positive mothers in resource-limited settings. Each year, approximately 700 000 infants acquire HIV infection from their mothers.[10] Without intervention, rates of mother-to-child HIV transmission range from 5% to 10% during pregnancy, 15% to 20% during delivery, and 5% to 20% while breastfeeding.[11–14] In most developed countries, ARV therapy, elective cesarean-section delivery, and avoidance of breastfeeding have decreased mother-to-child HIV transmission rates to less than 2%.[12,15] PMTCT programs that incorporate some of these practices are rapidly expanding in many developing countries; however, limited data are available to guide policies for feeding infants born to HIV-positive mothers in developing countries.[16–21] The WHO guidelines state that when breast milk replacement is acceptable, feasible, affordable, sustainable, and safe, all breastfeeding by HIV-positive mothers should be avoided.[22] If these conditions cannot be met, then exclusive breastfeeding is recommended for children of HIV-positive mothers, with weaning time dependent on the severity of the mother's disease.[21]

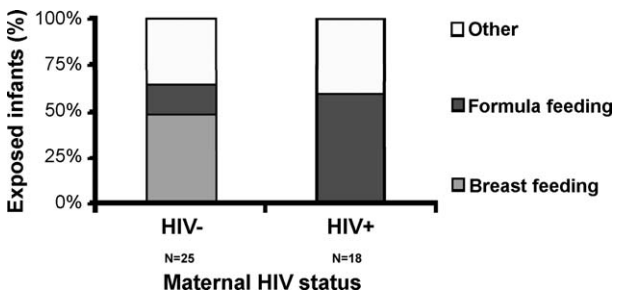

Figure 2. Proportions of infants <12 months of age in combined case and control populations exposed to breastfeeding, formula feeding, or other feeding fluids during the 2 weeks prior to interview, by maternal HIV status; case–control investigation, Botswana, March 2006.

Although providing replacement feeding to infants of HIV-positive mothers eliminates the risk of HIV transmission through breast milk, replacement feeding may expose the infant to pathogens that cause diarrhea.[23–25] Infant formula should be prepared under hygienic conditions, with vigilant hand washing before handling formula; sterilized cups, bottles and nipples; and safe water to mix the formula.[26] Prepared infant formula, if not used immediately, should be kept refrigerated and discarded within 24 h to limit microbiological growth. If any of these steps are compromised, the infant formula or feeding bottles can become contaminated,[27,28] resulting in diarrhea in the infant.[29,30] It is unlikely that optimal conditions for preparation and storage of infant formula exist on a national scale in most developing countries. Programs that promote the use of infant formula should address these concerns and thoroughly educate program participants about safe formula preparation and handling.

In this investigation, roughly half of infants born to HIV-negative mothers were being breastfed, and almost 20% of these mothers were feeding their infants formula. The high rates of formula use among mothers with negative or unknown HIV status may reflect a spill-over effect from the promotion of replacement feeding targeted at HIV-positive mothers, an outcome hypothesized to develop by cultural diffusion theory.[31] Where formula promotion policies exist, additional programming may be required to reinforce breastfeeding and safe formula preparation and handling among community members who are not the policy target audience, but who may be influenced by the policies nonetheless. Moreover, 40% of infants, regardless of maternal HIV status, were fed neither breast milk nor formula. It is unclear why this large proportion of infants received suboptimal nutrition. Childhood malnutrition remains a major problem in many countries, and the mutually amplifying effects of diarrhea and malnutrition pose a major threat to young children in the

developing world.[32–35] The pattern of inappropriate infant feeding we observed, if representative of the larger population of infants and older children, may partially explain the high rates of malnutrition and mortality observed during this outbreak.[6]

We also found that children who developed diarrhea were more likely to have lived in households that stored drinking water. Wide-mouth buckets, which are easily contaminated by hands or utensils, were the most commonly reported storage vessel for household drinking water. In another survey of pediatric diarrhea patients hospitalized during this outbreak, over half of pediatric stool specimens tested for multiple pathogens yielded more than one pathogen.[36] Similarly, laboratory testing of case-patients in this investigation showed patients were infected with a variety of enteric pathogens. Together, these findings suggest that the heavy rains may have induced sewage overflow from inadequately maintained latrines, causing widespread contamination of water distribution systems, stored household water, and living areas with multiple enteric pathogens. Children who were not breast-feeding, and were therefore at higher risk of exposure to contaminated water and feeding utensils, were more likely to develop diarrhea and visit the emergency department.

Availability of safe water, reliable sewage disposal facilities, and good hand washing practices are essential in efforts to reduce diarrhea morbidity in developing countries, and are important for safe formula feeding or when exclusive breastfeeding with early weaning are practiced.[37–39] When water sources are not adequately treated or when prolonged household storage of drinking water is necessary, point-of-use water treatment with diluted bleach, flocculent-disinfectant combinations, boiling, solar disinfection and filters have been shown to be effective in reducing drinking water contamination and the incidence of diarrhea in children.[40–45]

During this outbreak, we also found that children of parents who did not report washing their own hands after using the toilet or latrine were more likely to develop diarrhea than children of parents who did report washing their own hands. It is well known that hand washing interventions plus provision of soap can reduce the incidence of diarrhea by up to 53% in developing world settings.[43,46,47]

The findings presented in this investigation are subject to several limitations. The study population enrolled was hospital-based and the findings may not be representative of the general population of Botswana. However, the hospital where the investigation took place is the second largest referral hospital in the country and provided healthcare services to residents in one of the regions of Botswana most heavily affected during this outbreak. Also, since the investigation began after the peak of the outbreak, there was a substantial reduction in number of cases presenting to the emergency department after the investigation started, resulting in the termination of the study prior to enrolling the estimated sample size. This investigation did not differentiate the various breastfeeding practices defined by the WHO: exclusive breastfeeding, predominant breastfeeding, mixed feeding, or replacement feeding; therefore, we were able only to estimate the protective benefits of any current breastfeeding during this study. Some caretakers may have failed to recall exposures or episodes of diarrhea that occurred up to 3 months before the investigation, leading to possible misclassifications of exposure and case status, respectively. Because our investigation was not designed to assess risk factors for malnutrition or mortality, we are limited to describing these conditions among children with diarrhea in our study. Missing data is another source of potential bias, though our sensitivity analysis showed that missing data for maternal HIV status did not alter the findings of this investigation. Another limitation is that we obtained anthropometric measurements upon enrolment, when rehydration therapy might not have been completed. Thus results likely overestimate the prevalence of malnutrition in this population. Due to limited resources, we were unable to obtain weight measurements upon hospital discharge. Nonetheless, we observed a significant burden of severe malnutrition, including many cases of kwashiorkor, among these children. The overall sample size was small, limiting our power to detect more associations between feeding methods and disease. Finally, we were also unable to collect many whole stool specimens for parasitic or viral testing, and 25% of rectal swab specimens had no bacterial growth because either the sample quality was compromised during transport or because of previous antibiotic use.

While this outbreak began waning before our investigation was completed, we attempted to minimize morbidity and mortality by sharing interim and final results with public health officials in the ministries of health and water services, conducting in-depth educational activities on pediatric nutrition among primary health care workers, and providing seminars on management of pediatric diarrhea among hospitalized patients for clinical staff. The impacts of these activities are unknown.

Although the PMTCT program in Botswana has successfully and dramatically decreased mother-to-child transmission of HIV infection among infants born to HIV-positive mothers, the exceedingly high diarrhea morbidity and mortality reported during this outbreak emphasized the complexities of infant feeding decisions for HIV-infected women in settings with poor access to safe water, sanitation, and hygiene infrastructure.[25] The WHO recommends careful discussion with HIV-positive mothers about risks and benefits of each feeding method in the context of individual circumstances.[22] As PMTCT programs expand worldwide, countries planning to implement replacement feeding or early weaning programs for HIV-positive mothers should ensure access to a continuous and adequate supply of formula, safe water, and sufficient sanitation infrastructure to clean and store feeding bottles, and provide counseling on good hand washing practices, formula handling, and infant nutrition.[22] Additionally, provisions should be made to counsel HIV-negative mothers to breastfeed. Regardless of HIV status, breastfeeding is a critical barrier to diarrheal diseases. To help prevent diarrheal morbidity and mortality, access to safe water, appropriate hygiene promotion, and sanitation infrastructure are imperative for all mothers choosing to feed their children infant formula.

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