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Clinical and social determinants of diarrhoeal disease in a rural HIV/AIDS clinic, South Africa: a case-control study

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Summary

Diarrhoeal diseases are a common cause of morbidity and are associated with mortality in HIV-infected populations. Little is known about the contribution of clinical and socio-environmental factors to the risk of diarrhoea in these populations in rural sub-Saharan Africa. We conducted a case-control study of people attending a rural HIV clinic with an episode of diarrhoea in Bushbuckridge, South Africa. Cases were defined as HIV-positive adults with symptoms of diarrhoea before or after initiation of antiretroviral therapy (ART). Controls without diarrhoea were randomly selected from clinic attendees. Structured questionnaires and case-file reviews were undertaken to describe clinical and socioenvironmental risk factors. We recruited 103 cases of diarrhoea from 121 patients meeting case definitions. Cases were more likely to be women ($P = 0.013$), aged over 45 years ($P = 0.002$), divorced or separated ($P = 0.006$), have limited formal education ($P = 0.003$), have inadequate access to sanitation facilities ($P = 0.045$), have water access limited to less than three days per week ($P = 0.032$) and not yet initiated on ART ($P < 0.001$). In multivariate analysis, diarrhoea remained associated with female gender (adjusted odds ratio [aOR]: 2.02, 95% CI 1.10–3.73), older age (aOR: 6.31, 95% CI 1.50–26.50), limited access to water (aOR: 2.66, 95% CI 1.32–5.35) and pre-ART status (aOR: 5.87, 95% CI 3.05–11.27). Clinical and socio-environmental factors are associated with occurrence of diarrhoeal disease among rural HIV patients in South Africa. Further intervention research is urgently needed, combining community- and clinic-based approaches, to improve access to water, sanitation and ART for rural areas with high HIV prevalence, along with structural interventions to address gender inequities.

Keywords

HIV/AIDS; antiretroviral therapy; diarrhoea; risk factors; environment; women; water; sanitation; rural; South Africa

INTRODUCTION

Many countries in southern Africa have demonstrated successes in rolling out antiretroviral therapy (ART) using public health approaches,¹ with over five million HIV-infected patients initiated onto treatment. Nevertheless, ART often remains inaccessible, and when made available may be often delivered at an advanced degree of immunosuppression, resulting in high pre- and post-ART initiation mortality rates due to opportunistic infections (OIs).²

Diarrhoea is a major cause of morbidity and mortality among people living with HIV (PLWH). Individuals initiating ART may be particularly susceptible to diarrhoeal diseases as a consequence of low CD4 counts, poor nutritional status and concomitant OIs.³ In some developing countries, diarrhoea can affect approximately 90% of people with acquired immunodeficiency syndrome (AIDS).³ Furthermore, despite having been treated with combination antiretroviral therapy, over 40% of HIV-positive individuals in developed countries will still have at least one diarrhoeal episode per year.⁴

Rural HIV-positive individuals are particularly susceptible to diarrhoea, with over 25% of deaths in a rural South African treatment programme attributable to diarrhoeal diseases.⁵ Compared with urban areas, a lower proportion of the population in rural South Africa has access to improved drinking-water sources such as piped water or covered wells (99% urban and 78% rural) and sanitation facilities such as a single-family ventilated pit latrine or flushing toilet (84% urban and 65% rural).⁶ Poor water supplies have been associated with mortality in HIV-infected community members;^{4,7,8} however, there has been little investigation of the risk factors for diarrhoeal episodes and death due to diarrhoea around the time of ART initiation.

This study describes the risk factors associated with diarrhoeal disease among people attending a rural South African ART clinic. Greater understanding of clinical and socioenvironmental risk factors could inform the development of interventions to reduce morbidity and mortality associated with diarrhoeal diseases among PLWH, targeted specifically at rural and remote areas with high HIV prevalence.

METHODS

Study design and setting

We conducted a case-control study to investigate risk factors associated with diarrhoea among patients presenting at the rural HIV clinic located within the Bushbuckridge sub-District, Mpumalanga Province, South Africa.

Bushbuckridge is a densely settled area in the north-east of South Africa, with approximately 523,000 inhabitants. Over 70% of households live on less than USD 1 per day, and rely mainly on migrant labour opportunities. The antenatal care HIV prevalence is estimated at 33.8%.⁹

The Rixile HIV clinic was started in 1999 and provided HIV counselling, testing and support groups. From 2003, it expanded to provide a comprehensive package of wellness care for HIV patients. From 2005, ART was offered free of charge. By October 2008, over 2000 patients (approximately two-thirds of whom are women) had initiated ART at the clinic, with treatment and care being offered by nurses and supervised by a physician.

Study population and sampling procedures

Cases—Patients attending the HIV clinic provided the source population for this study, from which diarrhoeal cases and controls were recruited. Adult patients of 18 years or older who exhibited stable clinical status were recruited.

Cases were defined as confirmed HIV-infected individuals presenting to the HIV clinic (and attending for either pre-ART services or for ART follow-up care) with stools that were looser or more frequent than normal at the time of presentation. Cases were assessed by the nurse clinicians working in the HIV clinic, and all diarrhoeal cases were referred to a trained study coordinator using a referral form.

Controls—For each case recruited, three controls were randomly selected to participate in the study. Controls were patients attending the HIV clinic on the same days as the case and presenting without symptoms of diarrhoea. In order to select controls, a restricted random sampling method was undertaken on a daily basis using the HIV clinic attendance and appointment registers. The total number of visiting patients was used to stratify patients into four to six groups depending on their time of attendance on each clinic day. Simple random sampling was performed within each group using anonymous clinic attendance numbers assigned for the purposes of queuing. The blocks of patients were made up of about 20–30 patients depending on the day total. This sampling method for controls was chosen to allow for a representative sample that includes individuals consulting with clinicians in the HIV clinic at different times of the day. Controls were selected irrespective of their ART status.

Data collection

From July 2009 to February 2010, cases and controls completed a structured questionnaire administered by a trained interviewer in two local languages: Shangaan and Sepedi. Information collected included sociodemographic factors, water sources and utilization,¹⁰ and sanitation facilities and utilization. The interviewer also collected clinical data on the history of diarrhoea and associated symptoms, and on the self-management of diarrhoeal episodes. The interviewer reviewed clinic records for both cases and controls (separate consent was obtained) and data were collected on CD4 count, viral load, clinical staging, haemoglobin and anthropometric measures.

Data analysis

We compared the means of normally distributed data using the student's *t*-test and proportions of categorical data using χ^2 tests. We estimated the associations between prevalent diarrhoea and exposures using both univariate and multivariate logistic regression modelling. Variables identified *a priori* to be important predictors of diarrhoea and those significantly associated with diarrhoea on univariate analysis were included in the final logistic regression model using a backwards stepwise approach. Statistical analysis was conducted using STATA v11.1 (Stata Corp, College Station, TX, USA).

Ethical considerations

The study was granted ethical approval by the University of Witwatersrand (Johannesburg, South Africa) and Monash University (Melbourne, Australia). Permission to conduct the study was obtained from the provincial health research and ethics committee in Mpumalanga Province, South Africa and the hospital clinical manager where the study was conducted. Written informed consent was obtained from all participants.

RESULTS

Sociodemographic characteristics of cases and controls

During the study period, 121 patients presented with symptoms of diarrhoea meeting our case definition. Of these, 17 patients were not referred due to other clinical care priorities and one person refused to participate, leaving a total of 103/121 (85.1%) who agreed to participate in the study. About 317 controls were recruited and baseline characteristics of cases and controls are given in Table 1.

All participants in this study were of black African (Tsonga or Sepedi) ethnicity. The median age of cases was 39 years (interquartile range [IQR]: 32–47) and in controls 36 years (IQR: 31–42, $P = 0.004$). Participants who were controls were more likely to be women (211/317, 79.6%) than cases (82/103, 66.6%, $P = 0.013$), whereas cases (55/103, 53.4%) were more likely to have received only primary or no formal education compared with controls (117/317, 36.9%, $P = 0.003$). The proportions of individuals who were unemployed was high among both cases (80/103, 77.7%) and controls (236/317, 74.5%, $P = 0.803$).

Descriptive epidemiology of diarrhoeal disease

Patterns of diarrhoeal disease among cases—The mean number of stools experienced by cases within a period of 24 hours prior to their visit was four (median 3, IQR 2–4). Severe diarrhoea, defined as more than six stools in 24 hours, was reported by 10/103 (9.7%) cases. The majority of cases reported having stools that were watery 86/103 (83.5%) and yellowish 50/103 (48.5%) in consistency and colour, respectively. Diarrhoea was also described by most participants as recurrent (defined as two or more episodes in the preceding six months), with 100/103 (97.1%) reporting a mean of two episodes of diarrhoea (range 1–8) in six months. In 78/103 (75.7%) cases self-management was reported as the primary means of controlling their most recent diarrhoeal episode, with 55/103 (53.4%) resting and 23/103 (22.3%) increasing their fluid intake. Notably, only 1/103 (1.0%) individual reported using oral rehydration solutions during their most recent diarrhoeal episode.

Sanitation and hygiene in cases and controls—Non-ventilated pit latrines were the predominant toilet type used by both cases 81/101 (80.2%) and controls 263/314 (83.8%, $P = 0.045$), with piped toilet facilities accessible to only 4/101 (3.9%) cases and 25/314 (8.0%) controls. There was a higher proportion of individuals without access to sanitation facilities (and who reported open defaecation) among cases (16/101, 15.8%) compared with controls (26/314, 8.3%, $P = 0.05$). In addition (and where data were available), 22/87 (25.3%) cases and 69/291 controls (23.7%, $P = 0.763$) reported sharing sanitation facilities with other households. An average of two households shared sanitation facilities in both cases (range 2–3) and controls (range 2–5).

Water utilization in cases and controls—Water was obtained mainly from publicly shared piped sources for both cases (60/103 [58.2%]) and controls (165/317 [52.1%]) ($P = 0.570$). Inadequate sources, such as unprotected wells and rivers were the primary source of water for 10/103 (9.7%) cases and 40/317 (12.6%) controls ($P = 0.566$). Water was purified in 23/103 (22.3%) cases and 89/317 (28.1%) controls ($P = 0.432$). Water supply was available throughout seven days of the week for 56/103 (54.4%) cases and 195/317 (61.5%) controls ($P = 0.032$). For 33/317 (10%) controls and a higher proportion of cases 21/103 (20.4%), water supply was available only three days in a week or less ($P = 0.042$). Women and girls (<15 years old) in households were largely responsible for collection of water from supply sources compared with men in both cases and controls, as shown in Figure 1.

Risk factors associated with diarrhoeal disease

In univariate analysis, sociodemographic factors associated with prevalent diarrhoeal disease were female gender (odds ratio [OR]: 1.96, 95% CI 1.15–3.34), older age (>45 years) (OR: 4.71, 95% CI 1.51–14.69), having only primary or no formal education (OR: 1.95, 95% CI 1.25–3.01) and being divorced or separated (OR: 2.47, 95% CI 1.39–4.37) (see Table 1). Absence of sanitation facilities was associated with diarrhoea (OR: 3.84, 95% CI 1.13–13.10). Limited water availability, three days or less per week, was associated with a two-fold increase in the odds of diarrhoea (OR: 2.22, 95% CI 1.19–4.13) compared with full-week access to water. Usage of surface water was not associated with diarrhoea (OR 0.90, CI 0.40–2.05), but most people (56%) who used surface water also employed water purification measures, as opposed to those who did not use surface water ($P < 0.001$).

Individuals who were not taking ART had four-fold increased odds of diarrhoeal disease (OR: 4.60, 95% CI 2.56–8.25) compared with individuals on ART. There was no association between WHO clinical stage and diarrhoea ($P_{\text{trend}}=0.595$) and although weight of less than 55 kg was associated with diarrhoea (OR: 2.05, 95% CI 1.10–3.83), there was no strong association observed across weight strata ($P_{\text{trend}}=0.056$). Neither advanced immunosuppression ($\text{CD4} < 50 \text{ cells}/\mu\text{L}$) at first clinical attendance (OR: 0.70, 95% CI 0.33–1.50 – not shown in table) nor at most recent CD4 count measurement (OR: 1.67, 95% CI 0.49–5.65) was associated with prevalent diarrhoea.

In multivariate analysis, adjusting for educational status, and gender, individuals older than 45 years had a six-fold increased odds of diarrhoea compared with individuals in the 18–25 year age group (OR: 6.31, 95% CI 1.50–26.50). In addition, women had twice the odds of presenting with diarrhoeal disease (OR: 2.02, 95% CI 1.10–3.73) compared with men. Individuals whose water access was limited to three days or less in a week had three-fold increased odds for occurrence of diarrhoea compared with individuals with full-week access (OR: 2.66, 95% CI 1.32–5.35). Non-utilization of ART was strongly associated with diarrhoea, with six-fold increased odds of diarrhoea compared with individuals taking ART (OR: 5.87, 95% CI 3.05–11.27).

DISCUSSION

The key findings from this case-control study of diarrhoeal disease were the strong associations observed among participants who had not yet initiated ART, those with poor sanitation facilities and water supply, older people and women. We hypothesize that a complex interplay between HIV-related clinical factors, socioenvironmental determinants and gender contribute to the risk and impact of diarrhoeal disease in rural HIV patients.

First, we found a strong protective effect of ART against diarrhoeal disease, as previously shown elsewhere.¹¹ Although in recent years there have been impressive increases in the number of people living with HIV who have initiated ART, United Nations Programme on HIV/AIDS (UNAIDS) estimates that coverage for those who are in immediate need of treatment (defined as a CD4 count of less than 350 cells/ μL) in Southern Africa may be as low as 37%.¹² Additionally, there is a growing body of evidence to suggest that considerable barriers exist between HIV diagnosis and initiation of ART, leading to long delays with prolonged periods of immunosuppression.¹³ Reducing delays in initiation for those who are ART eligible would have a substantial impact on mitigating the burden of morbidity and mortality associated with diarrhoeal diseases, in addition to dramatically impacting HIV prevalence and incidence.¹⁴

Second, this study showed increased risk of diarrhoea associated with unreliable and inconsistent access to water and poor access to sanitation facilities. Water access is

considered a basic necessity to the South African population;¹⁵ however, in this study, 15% of participants were able to access water for three days or less in a week. Adequate quantities of clean water are also needed to manage diarrhoeal episodes, and up to 80 additional litres may be required per person daily.¹⁶ A further 12% of patients used surface water for drinking purposes. Household-based water quality interventions have been shown effective to decrease diarrhoeal episodes among PLWH.^{17,18} Surface water use was not associated with diarrhoea in this study, possibly due to a positive association with household-level water quality interventions. This suggests the need for additional interventions for obtaining adequate quantities of water in addition to water quality interventions for the prevention of diarrhoea. More information on water quality, quantity and intrahousehold utilization patterns is required.

In addition, 11% of patients reported a complete lack of sanitation facilities, while the majority used pit latrines. Sharing of sanitation facilities was also a noticeable practice in the study population, and this behaviour may increase the risk of transmitting infective diarrhoeal agents.⁸ Presence of a latrine in the household has been associated with fewer episodes of diarrhoea among PLWH.¹⁷ Limited access to water and sanitation facilities is not confined to rural areas such as the population studied here. Indeed, a rapid-growing urban informal settlement with high prevalence of HIV¹⁹ is also likely to have poor levels of municipal and private service provision. For example, in Cape Town the estimated coverage of any sanitation facility is 15%, using a standard of one toilet per five families.²⁰

Third, this study showed that women were more at risk of diarrhoea than men. A number of possible structural (socioeconomic and cultural) determinants may act to place women at increased risk of diarrhoea. In this community women are largely responsible for the care of children, the elderly, and ill household members, including those with diarrhoea, which may expose women to increased risk of infection, particularly in the context of limited water for hand washing. We observed a gendered pattern of water collection, predominantly a responsibility of women and girls. Further research may be necessary to explore these gendered patterns in association with risk and vulnerability to diarrhoeal disease. We suggest that the observed gender differences may be a marker of deeper structural factors (such as increased domestic workload and disempowerment), which contribute to women's increased risk of disease in general and susceptibility to diarrhoea specifically when HIV-positive. Previous studies have suggested that HIV-negative women may be at increased risk of severe bacterial disease,²¹ and our study adds evidence of increased diarrhoeal risk among the HIV-positive population.

In recent years there has been increased attention given to the social determinants of health.^{22,23} These data support the growing body of evidence that the inequitable distribution of power, money and resources, especially between men and women, are major contributors to disease burden. Structural interventions that uplift the position of women and girls in society, particularly in rural and remote areas could be an appropriate means of reducing the burden of diarrhoeal disease among HIV-positive women.²⁴ Improving formal education of women may also increase women's chances of survival in the context of HIV and other debilitating conditions.²⁵

The study had a number of limitations. Recall and social desirability biases may have influenced patients' responses, particularly with regard to water and sanitation facilities. Furthermore, the study design did not allow for assessment of hygiene practices, an important contribution to water-borne diarrhoeal disease transmission in immune-competent²⁶ and PLWH;¹⁷ hand washing may be as effective as water provision.²⁶ We asked about water and sanitation in the home, so we do not know about access and utilization outside the home. Additionally, while we were able to access baseline CD4 count

results and most recent results, we did not take samples for measurement at the time of the diarrhoeal episode. Therefore, it is possible that an association between diarrhoea and concurrent degree of immunosuppression may have been missed. Additionally, we did not have access to HIV viral load measurements, which may have been important predictors of diarrhoea. Although we used standard case definitions for diarrhoea, participants may have under- or overreported frequency of episodes.

CONCLUSION

In this rural HIV clinic population, we found that diarrhoeal episodes were associated with delays in ART initiation, sociodemographic and environmental factors such as gender and age and poor access to water and sanitation. We hypothesize that the interplay of these factors is dependent on social determinants of disease such as gender power relations and access to water, sanitation and health services. Reducing the burden of diarrhoeal disease will require a multifaceted approach encompassing improved early access to ART, gender sensitive approaches to acceleration of water and sanitation availability and interventions to redress gender inequities.

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Figure 1.
The adult and child female burden of collecting water from supply sources for cases and controls

Table 1

Univariate and multivariate associations with prevalent diarrhoea in antiretroviral therapy clinic attendees

Variable	No (%) of controls (<i>n</i> = 317)	No (%) of cases (<i>n</i> = 103)	Univariate analysis			Multivariate analysis		
			OR	95% CI	<i>P</i> value	OR	95% CI	<i>P</i> value*
Gender								
Male	106 (33.4)	21 (20.4)	1		0.013	1		0.020
Female	221 (66.6)	82 (79.6)	1.96	1.15–3.34		2.02	1.10–3.73	
Age (years)								
18–25	28 (8.8)	4 (3.9)	1		0.002	1		
26–35	130 (41.0)	33 (32.0)	1.78	0.58–5.42		2.90	0.75–11.20	0.037
36–45	110 (34.7)	33 (32.0)	2.10	0.69–6.42		3.77	0.95–14.91	
46	49 (15.5)	33 (32.0)	4.71	1.51–14.69		6.31	1.50–26.50	
Level of education obtained								
Any secondary/tertiary education	200 (63.1)	48 (46.6)	1		0.003	1		0.290
Any primary/no education	117 (36.9)	55 (53.4)	1.96	1.25–3.07		1.38	0.77–2.74	
Marital status								
Married	116 (36.6)	25 (24.3)	1		0.006	1		0.088
Never married	122 (38.5)	36 (34.9)	1.34	0.77–2.42		0.70	0.36–1.38	
Divorced or separated	79 (24.9)	42 (40.8)	2.47	1.39–4.37		1.45	0.77–2.74	
Water access								
Water available 7 days/week	195 (61.5)	56 (54.4)	1		0.042	1		0.013
Water available 4–6 days/week	89 (28.1)	26 (25.2)	1.02	0.60–1.73		0.86	0.48–1.56	
Water available 0–3 days/week	33 (10.4)	21 (20.4)	2.22	1.19–4.13		2.66	1.32–5.35	
Water supply								
Piped water to own/neighbour’s house	98 (30.9)	27 (26.2)	1		0.566			
Public tap/borehole	165 (52.1)	60 (58.2)	1.32	0.79–2.22				
Unprotected well/surface water	40 (12.6)	10 (9.7)	0.91	0.40–2.05				
Buy water from shop/truck	14 (4.4)	6 (5.8)	1.56	0.55–4.43				
Sanitation								
Plumbed toilet/septic tank/composting toilet/ VIP	25 (7.8)	4 (3.9)	1		0.050	1		
Pit latrine	263 (83.0)	81 (79.4)	1.92	0.65–5.69		1.72	0.53–5.59	0.010
No facilities available	26 (8.2)	16 (15.7)	3.85	1.13–13.10		2.82	0.73–10.92	
Taking ART								
Yes	291 (91.8)	73 (70.9)	1		<0.001	1		<0.001
No	26 (8.2)	30 (29.1)	4.60	2.56–8.25		5.87	3.05–11.27	
Most recent CD4 count (cells/μL)								
>200	142 (71.4)	34 (64.2)	1		0.571			
51–200	47 (23.6)	15 (28.3)	1.33	0.67–2.66				
50	10 (5.0)	4 (7.6)	1.67	0.49–5.65				

* Likelihood ratio

OR, odds ratio; VIP, ventilated improved pit latrine; ART, antiretroviral therapy