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Acute Respiratory Infection and Routine Vaccination Impact on Occurrence of Diarrhea Amongst children Under-Five in Uganda

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ABSTRACT

BACKGROUND: Childhood diarrhea (CD) remains a major public health problem in Uganda and other countries in the region and acts as one of the leading contributors to child mortality. This study, guided by the socioecological model, investigates the association between CD with acute respiratory infection (ARI) and vaccination status of the child, factors whose impact on CD is lacking.

METHODS: The source of data was the Uganda Demographic and Health Survey (UDHS) 2011 dataset. Bivariate and multivariable logistic regression analysis was done to test for associations.

RESULTS: Children who had ARI were twice as likely to have CD as compared to children without ARI (AOR = 2.01; p<0.001) and children who had completed the routine vaccination schedule had some protection from CD (AOR = 0.771; p<0.001). Increasing age of the child as well as higher age and higher education level of the mother were found to be associated with less occurrence of diarrhea in the child.

CONCLUSION: Integrated management of ARI and diarrhea, completion of the routine immunization schedule and policy support for women in this region to attain higher education levels and engage in less early childbearing are encouraged to reduce on the occurrence of diarrhea in children. These factors provide a cost effective manner of reducing the health burden of diarrhea morbidity and mortality in the country.

KEYWORDS: Diarrhea in children or child or under-five, acute respiratory infection, pneumonia, vaccination or immunization and socio-ecological model.

INTRODUCTION AND BACKGROUND

Childhood diarrhea (CD) is one of the leading causes of morbidity and mortality in children under 5 years of age (1, 2) globally, and the majority of these cases are found in sub-Saharan Africa and South Asia (3). In 2015, 5.9 million children under the age of 5 years died with the majority from the African region (4). 10% of these deaths were attributed to CD (4). The highest incidence and deaths due to CD are in children less than

2 years of age (6, 7, 8, 9). Uganda is among the countries with a high burden of CD (10) and is ranked ninth among the 15 countries in the world with the highest burden of CD (11). The high burden of diarrhea in Uganda's children represents a significant burden not only on the health system, but also on the households that take care of the sick children, on growth, nutrition, development, and survival of the children. Single, sporadic episodes of diarrhea in healthy children are typically self-limiting, with no long-term consequences. However, several episodes per year in a child can result in nutritional deficits and long-term consequences such as growth faltering, impaired cognitive development, and poor school performance (12, 9). Without effective intervention, CD can result in rapid depletion of water and sodium regardless of the causative pathogenic agent, potentially resulting to death due to extreme dehydration (13). Children with diarrhea are at a higher risk of life-threatening dehydration than adults because water makes up a higher proportion of children's bodyweight and children have a higher metabolic rate, so they use more water in a day than older children and adults do (12). A child with diarrhea can lose body fluids as much as 3 times the circulating blood volume (12). Diarrhea in children can manifest as acute watery diarrhea, which is the most common type of diarrhea (14) and lasts less than 7 days. Less common types of CD are bloody diarrhea, referred to as dysentery, and persistent diarrhea, or diarrhea that lasts at least 14 days (15, 16). However, an acute episode can progress to persistent diarrhea (15). Although diarrhea in children in Uganda and other developing countries is a significant public health problem, it is preventable (17).

This study is grounded in the socioecological model (SEM) to illustrate how selected risk factors function in the different spheres of environmental and societal factors to impact the occurrence of CD.

RISK FACTORS FOR CHILDHOOD DIARRHEA

CD is caused by a wide array of pathogens, which include bacteria, viruses, and protozoa (18,19) The disease is attributed to factors such as poor sanitation practices and lack of adequate safe water (6, 20, 21, 22) which result in increased transmission of disease pathogens through consumption of contaminated food or water. Other risk factors that have been identified in literature include suboptimal breastfeeding practices (7, 23); living in a rural area (24); two or more siblings in the house (24); lack of, or incomplete vaccination of children (25); age of the child (7); low education level of the mother/caregiver (26, 21); early weaning, lack of awareness of good personal, and food hygiene practices (27). Factors where information is lacking is how an infection with ARI an equally common childhood disease and vaccination status of the child impact on the occurrence of CD.

ARI & VACCINATIONS

ARI and CD together make up the top killers of children worldwide (9). Many times ARI and CD present as simultaneous comorbidities more than would be expected by chance alone (28, 29, 30) but this co-occurrence is not well understood (31, 29), and there is a paucity of studies that describe the relationship between the two diseases. In every 20 seconds, a young child under the age of 5 years succumbs to either of these two major but preventable diseases (10).

Pneumonia is a common and severe respiratory tract infection (33). Researchers often use the terms ARI, ALRI (acute lower respiratory infection) and pneumonia interchangeably (33). In the 2011 UDHS, ARI was used as a proxy measure for pneumonia (34). The potential severe consequence of pneumonia and diarrhea coinfection was demonstrated by a study done in Bangladesh (29) whereby both diseases were investigated to determine the risk factors for their concurrent presentation. Children presenting with both diseases had an over 80 times higher risk of death and a three times longer length of stay in hospital compared with those who had CD only. An understanding of the impact of ARI on development of CD is needed, considering the high burden of ARI as well as CD. Additionally, many of these children in Uganda do not get treatment for ARI (35, 36) thus potentially predisposing them to other infections such as CD.

Childhood routine vaccinations are a lifesaving public health initiative and have made a tremendous contribution in controlling infectious diseases in children (37). In the 2011 UDHS, data was collected on routine vaccinations received by children. A child was considered fully immunized if they had received all doses for each of the four childhood vaccines: polio, measles, BCG and DPT-HepB-Hib. Epidemiological evidence from studies show that childhood vaccinations confer non-specific benefits to children by changing morbidity and mortality of infections unrelated to their pathogen-specific purpose (38, 39, 23, 40,41,42) In Uganda, a study showed that BCG vaccination had non-specific effects (43). Children who had received BCG vaccination had substantially lower mortality rates than those who had not received the vaccination. However much remains to be learned regarding the mechanism by which routine childhood vaccines exert all-cause morbidity and mortality reduction (44) and specifically the protection against CD is missing. Scholars have noted that there were discrepancies in reduction in mortality due to CD from 2000 to 2011 in low and middle income countries (9). These discrepancies were attributed to differences in immunization rates and breastfeeding practices that were within the countries in these regions as there was not much improvement in treatment practices during this period. The information on whether vaccination has the potential to affect the occurrence of CD has been lacking.

METHODS

Quantitative methodology was used to assess the impact completion of childhood vaccinations and ARI have on the occurrence of CD in Uganda by use of a secondary dataset, the UDHS 2011 dataset. Data analysis was conducted using SPSS version 23.0. Permission to access the DHS data set was obtained. The target population was children in Uganda aged from birth to 5 years of age. UDHS collected data through 3 sets of questionnaires administered to sampled adults: household, men and women's questionnaire and the data is representative regionally and nationally (45). Data on children was captured by asking women, who were the mothers or immediate caregivers, information about their children who were born in the 5 years prior to the survey. More information about the data collection process for DHS is available on the DHS website (45).

CD was determined in the survey by asking the mother if the child had passed loose, watery stools three or more times in a day in the 2 weeks preceding the survey (34). WHO similarly describes diarrhea as the passage of loose, watery stools three or more times in the previous 24 hours (32).

Occurrence of ARI was determined by asking the mother if the child had a cough accompanied by short, rapid breathing in the 2 weeks preceding the survey (34). A variable of yes/no for ARI was computed. Vaccination status was determined through examination of the health card and through verbal report from the mother when the card was unavailable (34). Vaccination status was then computed as complete and partial or no vaccination if a child had received some but not all vaccinations or none of the vaccinations respectively.

The inclusion criteria were children under 5 years of age who were alive and had data on recent diarrheal illness. Preliminary analysis was conducted prior to running analysis to test for the assumptions of the statistical tests. Bivariate and multivariable logistic regression analysis was then conducted to predict the impact co-infection with ARI and the vaccination status of the child has on occurrence of CD. Odds ratio (OR), 95% confidence interval (CI), and p value (cut off = 0.05) were used to determine which variables were likely to predict the occurrence of CD. Potential confounders considered were age and sex of the child; age, education level and religion of the mother; number of children in the family; and location (urban or rural).

RESULTS

Descriptive characteristics of children

Children meeting the inclusion criteria were 7,323. 3,668 (50.1%) were female and 3,655 (49.9%) were male. Age ranged from 0 to 59 months with a mean of 28.8 months and SD 17.3 months. The descriptive statistics are summarized in Table 1. 45.9% of households had two children under 5 years of age, 24% had one child under 5 years of age, 23.9% had three children under 5 years of age, 4.9% had four children under 5 years of age, and households with five or six children made up 2% of the sample.

Table1. Descriptive characteristics of children

Variable (Child)		Study sample (N = 7,323)	
		n	%
Age in months	0 -11	1,627	22
	Dec-23	1,464	20
	24-35	1,476	20
	36-47	1,407	19
	48-59	1,349	18
Sex	Females	3,668	50
	Males	3,655	50
Number of children in household	1	1,715	24
	2	3,289	46
	3	1,711	24
	4	353	4.9
	5	56	0.8
	6	34	0.5

Descriptive characteristics of women

14.5% had received no education, 63.4% had a primary-level education, 18.5% had secondary-level education, and 3.6% had a higher level education, which could be tertiary or university level. The majority of the sample was from rural households (85.9%), as compared to those from urban areas (14.1%). A higher proportion of the mothers belonged to the Catholic religion (41.3%), followed by Protestants (29.6%).

Table 2. Descriptive characteristics of women

Variable (Women)		Study sample (N = 7,323)	
		n	%
Age in years	15-19	413	5.6
	20-24	1,809	25
	25-29	2,177	30
	30-34	1,348	18
	35-39	1,001	14
	40-44	448	6.2
	45-49	127	1.7
Education level	No education	1,059	15
	Primary	4,642	63
	Secondary	1,355	19
	Higher	267	3.6
Residence	Urban	1,036	14
	Rural	6,287	86
Religion	Catholic	3,027	41
	Protestant	2,165	30
	Muslim	954	13
	Pentecostal	924	13
	SDA	139	1.9
	Other	114	1.6

Descriptive characteristics of CD, ARI and Vaccination status

1,766 (24.1%) children had a diarrhea episode in the in the 2 weeks preceding the survey with the highest proportion in the age group 0-11 months (43.0%). Occurrence of diarrhea decreased with increasing age. 15.2 % (1,113) had ARI in the 2 weeks preceding the survey with the highest occurrence in the age group (12-23 months). Vaccination status was determined only for children above 12 months of age to ensure that only children who should have completed the vaccination schedule were included. In the age group 12-23 months, 51.7% of the children were fully vaccinated, 44.5% were partially vaccinated, and 3.8% were not vaccinated (Table 5). Vaccination status for the subsequent age groups did not differ much from this age group.

Table 3. Descriptive characteristics of CD

	Diarrhea [N=7,323]				
Age group in months	No		Yes		Total
	n	%*	n	%*	N
0 -11	1,117	57	510	43	1,627
12-23	908	62	556	31	1,464
24-35	1,139	77	337	23	1,476
36-47	1,192	85	215	15	1,407
48-59	1,201	89	148	11	1,349
Total	5,557	76	1,766	24	7,323

Table 4. Descriptive characteristics of ARI

	ARI [N=7,317]				
Age group in months	No		Yes		Total
	n	%*	n	%*	N
0 -11	1,343	83	283	17	1,626
12-23	1,194	82	267	18	1,461
24-35	1,263	86	213	14	1,476
36-47	1,223	87	183	13	1,406
48-59	1,181	88	167	12	1,348
Total	6,204	85	1,113	15	7,317

Table 5. Percentage of children aged 12-23 months who were vaccinated

Vaccine	Percentage (%)
BCG	93.7
DPT-HepB-Hib1	92.3
DPT-HepB-Hib2	85.5
DPT-HepB-Hib3	72.3
P0lio 0	67.1
Polio 1	92.2
Polio 2	83.5
Polio 3	64
Measles	75.7
Fully vaccinated	51.7
Partially vaccinated	44.5
No vaccination	3.8
[a]Total number of children	1,464

Bivariate analysis

Demographic variables significant at bivariate level included age of the women (p<0.05); education level of the women (p<0.05); religion (p<0.05) and age of the children (p<0.05). Variables not significant at bivariate level were urban / rural residence (p=0.33); number of children in the household (p=0.904) and a child's gender (p=0.213).

Table 6. Bivariate analysis of demographic variables and CD

Variable	Diarrhea (N = 7,323)				
	No *(N = 5,557)* ***n (%)***	**Yes** *(N = 1,766)* ***n (%)***	**COR**	***p*-value**	**95% CI**
Maternal age in years					
15-19 (ref)	267 (64.6)	146 (35.4)	1	-	
20-24	1,276 (70.5)	533 (29.5)	0.76	0.018	0.60-0.95
25-29	1,697 (78.0)	478 (22.0)	0.51	<0.001	0.41-0.64
30-34	1,075 (79.7)	273 (20.3)	0.46	<0.001	0.36-0.59
35-39	782 (78.0)	220 (22.0)	0.51	<0.001	0.39-0.66
40-44	362 (80.6)	87 (19.4)	0.43	<0.001	0.32-0.59
45-49	98 (77.2)	29 (22.8)	0.53	0.008	0.33-0.84
Residence					
Urban (ref)	798 (77.10)	237 (22.9)	1	-	
Rural	4,759 (75.7)	1,528 (24.3)	1.08	0.33	0.92-1.26
Education					
None (ref)	827 (78.1)	232 (21.9)	1	-	
Primary	3,434 (74.0)	1,208(26.0)	1.25	0.005	1.07-1.47

Secondary	1,063 (78.5)	292 (21.5)	0.98	0.831	0.80-1.19
Higher	233 (87.3)	34 (12.7)	0.52	0.001	0.35-0.76
Religion					
Catholic (ref)	2,342 (77.4)	684 (22.6)	1	-	
Protestant	1,637 (75.6)	528 (24.4)	1.1	0.132	0.97-1.25
Muslim	690 (72.3)	264 (27.7)	1.31	0.001	1.10-1.54
Pentecostal	681 (73.7)	243 (26.3)	1.22	0.021	1.03-1.44
SDA	118 (84.9)	21 (15.1)	0.6	0.038	0.37-0.97
Other	88 (77.2)	26 (22.8)	0.98	0.958	0.63-1.54
Age of child (months)					
6-11 (ref)	472 (57.0)	359 (43.0)	1	-	
Dec-23	908 (62.0)	556 (38.0)	0.81	0.019	0.63-0.96
24-35	1,139 (77.2)	337 (22.8)	0.39	<0.001	0.32-0.47
36-47	1,192 (84.7)	215 (15.3)	0.24	<0.001	0.19-0.29
48-59	1,201 (89.0)	148 (11.1)	0.16	<0.001	0.13-0.20
No. of children					
≥ 3 (ref)	1,635 (75.9)	519 (24.1)	1	-	
≤ 2	3,791 (75.8)	1,247(24.2)	1.01	0.904	0.89-1.13
Sex of child					
Male (ref)	2,751 (75.3)	904 (24.7)	1	-	
Females	2,806 (76.5)	862 (23.5)	0.93	0.213	0.83-1.04

Multivariable analysis

Two multivariable regression models using binary logistic regression were created by fixing each of the main independent variables (ARI and Vaccination status) at a time while controlling for other variables. The covariates that were statistically significant at bivariate analysis level and those that possessed a p-value of ≤ 0.2 were included in the multivariable regression models. Number of children in the family, the sex of the child and residence variables did not meet this criterion and were left out of the multivariable regression models. The main assumptions for using binary logistic regression were met prior to running the models. Children who had ARI were twice as likely to have diarrhea as compared to children who did not have ARI (AOR= 2.01, p<0.001). The control variables of age of the mother, education level, religion contributed significantly to this model (p<0.001 for all variables).

Table 5: Logistic Regression Results for ARI and CD

	COR	*p*-value	C.I.	AOR	*p*-value	C.I.
ARI	2.2	<0.001	1.91-2.50	2	<0.001	1.74 - 2.32

Variables adjusted in the model are age of the child and age, education level, and religion of the mother.

Full vaccination of children offered some protection to CD. These children were 0.77 times less likely to have an episode of diarrhea as compared to children not vaccinated or partially vaccinated.

Table 6: Logistic Regression Results for Vaccination Status in Children Aged Above 12 Months and CD

Vaccine status	COR	*p*-value	C.I.	AOR	*p*-value	C.I.
No and partial (ref)	1			1		
Full vaccination	0.7	<0.001	0.66-0.84	0.8	<0.001	0.68 - 0.88

Note. Variables adjusted in the model are age, education level, and religion of the mother.

DISCUSSION

Age of the child was significantly associated with CD. Occurrence of CD was highest in the age group 0-11 months and decreased with increasing age of the child. Some studies have shown similar findings with the highest incidence and deaths due to diarrhea occurring in children less than 2 years of age (6, 7). In the second half of an infant's life, though the child's immunological capability increases with age; the child is transitioned from exclusive breastfeeding to solid foods, which may lead to exposure to contaminated weaning foods leading to diarrhea. Other variables that had an association with diarrhea included maternal education level, maternal age and religion.

Low education level of the mother or caregiver was a risk factor for CD. Children of women who had achieved the highest education level had the most protection from diarrhea when compared to children of women with no education. This finding was similarly seen in other studies (26, 21,46). Higher education level of the mother could act as protective against diarrhea by increasing the likelihood of better health outcomes through increased knowledge of disease prevention and better usage of health care services. In this study sample, the education level of women was quite low, whereby the majority of the mothers had attained only primary-level education (63.4%). Most of the women were in the age group 20-29 years, an age when they should have completed secondary education.

Maternal age is another risk factor for CD. Children of older women were less likely to have diarrhea as compared to children of younger women. Previous research has shown similar findings (47), whereby younger mothers reported diarrhea more frequently in their children than older women did. Religion had mixed findings with higher odds of having diarrhea among Muslim and Pentecostal children while among children of SDA women, the likelihood of CD was lower. Other religions had no significant findings. All groups were compared to Catholics who were the dominant religion. The residence of the child had no association with the occurrence of diarrhea in this study.

Children from rural areas did not show a significant difference from children in urban areas in regards to CD. However, given that the majority of the children were from rural areas, with only 15% being from urban areas, the data on residence did not provide a good comparison. Some studies have shown an association of childhood diarrhea and residence (48, 24) whereby children from rural areas were more likely to report occurrence of diarrhea as compared to children from urban areas. This association was not observed in this study. The number of children within the households in this study ranged from one to six, and the highest percentage of respondents reported two children in the household (45.9%). Households that had few children (two or fewer children) did not show a significant difference in occurrence of CD when compared to households that had three or more children. This is in contrast with other findings (21), which showed that in households with two or fewer children, the risk of diarrhea decreased significantly compared to households with more than three children. Similarly, in a another study carried out in Cameroon (49) there was a higher occurrence of diarrhea in children who were from households that had more than two siblings.

Children who had ARI had a higher likelihood of having diarrhea and even with control of other variables that may influence the occurrence of diarrhea, it was seen that the likelihood of having diarrhea increased when a child already had ARI. The significant findings of the association between ARI and diarrhea have important implications. Children who have ARI are likely to have diarrhea, and this finding calls for extra vigilance for these children so that they are closely monitored to avoid them subsequently having diarrhea. This could have great repercussions for the child because comorbidity of the two diseases in the child is likely to result in more dire consequences (29). The results also suggest that an integrated approach to the prevention and management of the two diseases would be beneficial. This finding builds on evidence provided by a study carried out in Bangladesh (29) that investigated risk factors for concurrent presentation of these diseases in resource-constrained communities. It was seen that children presenting with diarrhea and pneumonia had an over 80 times higher risk of death and a three times longer length of stay in hospital compared with those who had diarrhea only. From this study we cannot conclude the order of occurrence but irrespective of which disease precede the other, control of one infection is likely to reduce the occurrence of the other disease, and thus a coordinated solution to both diseases should be considered. In interpreting these results, it is noted that variables other than age of the child and age, religion, and education level of the mother that may confound or mediate this association but were not available in the data set were not investigated. Data on these variables might permit a more nuanced understanding of this association. Nevertheless, the results demonstrate findings indicating potentially important practical applications. A child appearing at the health system with ARI is an opportunity to prevent a future case of CD.

Among children aged 12 to 23 months, 51.7% were fully vaccinated, while 3.8% had received no vaccinations and 44.5% were partially vaccinated. Findings indicated that children who were fully vaccinated had some protection from diarrhea as compared to the group that was not or was partially vaccinated. Previous studies (23, 44) have elucidated that childhood vaccines confer non-specific benefits that contribute to reduction in all-cause morbidity and mortality in children and this study has added to the evidence base that there is some protection to CD when children are fully vaccinated. Additionally, a child who has been taken for immunization has a higher chance of also receiving vaccines against diarrhea for instance the rotavirus and pneumococcal vaccine, where they are available. The study revealed other important findings. The vaccination coverage was 51.7% in this group of children. This means that Uganda falls way below the target set by WHO to achieve at least 90% vaccination coverage nationally in all countries and 80% coverage in every district by the year 2020 (50). Uganda falls short of WHO recommendations. Another study in Uganda revealed similar vaccination coverage at 51% for children aged 12-23 months (51). Additionally, the proportion of children who had been partially vaccinated was quite high (44.5%). This implies that as vaccines were received at health care facilities, caregivers were at some point exposed to the health system, but for various reasons, the children were not taken to the health facility to complete the immunization schedule. Additionally, the coverage for BCG vaccine, which is the first vaccine administered at birth or at first contact with a health care provider, was very high (93.7%), indicating a high level of healthcare services access followed by a gradual decline in vaccination coverage, such that only 75.7% received the measles vaccination given at 9 months. The reasons for immunization dropout could be explored further to help improve the immunization completion rate.

The role of maternal age and education play relative to protecting children from CD is further shown as the strength of the associations in the multivariable logistic models weakened when these factors were added to the models giving further evidence that higher age and higher education level in the mother play a role in protecting a child from diarrheal disease.

Findings from this study reconfirm the significance of the SEM in explaining how socioeconomic and environmental factors influence the occurrence of disease. The socioecological framework has shown that these factors operate at different levels of the socially organized environment. They operate from the individual level in factors such as the child's age, caretaker's age, and caretaker's education level, to the family and community environment that would take the child to the health center. The influence of the higher systems such as the macro systems level, which involves the health care system that is involved in prevention and control of other diseases such as ARI and provision of vaccines, is seen. The role of the public policy systems that would discourage early childbearing and support higher educational attainment for women is seen to play a role as well.

STUDY LIMITATIONS

All analyses were limited to the variables and data captured by the UDHS; therefore, other factors that may have an influence on the occurrence of diarrhea were not captured in this analysis. Another limitation was that the information provided by the mothers on diarrhea and ARI required recall of past events accounts which were not validated by medical personnel or health records. Likewise, mothers who did not have vaccination cards for their children could have provided inaccurate information on their children's vaccinations.

CONCLUSION

The increased risk of CD seen when a child has ARI should lead to greater emphasis on an integrated approach to the prevention and management of the two diseases and early treatment of either disease to prevent occurrence of the other. Completion of the routine vaccination schedule confers some protection to the occurrence of CD. Care givers should be encouraged and supported for their children to be fully vaccinated as this not only offers protection against vaccine preventable diseases but there is an added non-specific benefit of protection against CD. Presence of ARI, vaccination and education level of the mothers are all modifiable risk factors that have an impact on diarrhea in children and should be considered in prevention programs targeting diarrhea in children.

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