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Rotavirus Diarrhoea in Apache Children: A Case-Control Study

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A case-control study of rotavirus diarrhoea in Apache children up to two years old was conducted at the White Mountain Apache reservation from 1 May through 15 December 1985 to identify risk factors for rotavirus diarrhoea. The mothers of fifty cases, forty-five hospital controls and twenty-five neighbourhood contols participated in this study. Exposure to other children with diarrhoea stood out as the single most important factor for acquiring rotavirus diarrhoea (Odds ratio = 14.0). Other significant risk factors were living in homes with septic tanks and in homes with 'poor environmental sanitation'. Minimizing contacts of children with diarrhoea therefore would be the most effective measure in preventing the spread of this disease in the community.

Following the discovery of rotaviruses by Bishop *et al*,[1] in 1974, they have emerged as the single most important aetiological agent of severe diarrhoea of children in both developed and developing countries.[2] Although the incidence of rotavirus diarrhoea is similar in both[2] there are likely to be different opportunities for exposure within individual countries.[2] In the US nearly all studies have been conducted in urban areas. Hospital data show that 35% of 1537 hospitalizations among children in Washington DC between January 1974 and July 1982 were for rotavirus gastroenteritis.[3] We are not aware of any studies that have identified specific risk factors for the acquisition of rotavirus diarrhoea in these urban settings. The rates for rotavirus diarrhoea are also high among Native Americans living on reservations who represent a neglected section of American society and suffer a disproportionate burden of infectious and chronic diseases.[4] Poverty, lack of adequate environmental sanitation and poor access to medical care have been the important contributing factors for this excess morbidity. Preliminary studies conducted at the White Mountain Apache reservation in South Western Arizona reported that rotaviruses were the most frequent aetiological agent identified in the stools of Apache children presenting with diarrhoea at the Whiteriver hospital. On average, 10% of stools tested positive for rotavirus antigen; during the peak seasons in summer and winter this figure ranged from 15% to 40%. Although the occurrence of rotavirus diarrhoea is endemic in this population, this reservation experienced an epidemic in a three-week period of October 1981. During the epidemic, 73% of 233 stool samples tested positive for rotavirus antigen; the highest rate of illness was in the age group three to five months.[5] To date only one study has investigated risk factors for acquiring rotavirus diarrhoea in this unique socio-cultural setting.[6] The major limitations of this study conducted on the San Carlos Apache reservation were the small sample size (16 cases and 12 controls identified over three months), and lack of detailed information on domestic and environmental sanitation factors, behavioural and dietary factors. Because epidemiological information on rotavirus infections on Native American reservations is limited and because diarrhoea is a major public health problem in these areas we undertook a case-control study on the White Mountain Apache reservation to identify risk factors for rotavirus diarrhoea that would provide an epidemiological basis for a control programme in this and other situations.

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BACKGROUND

Members of the White Mountain Apache residing on

the Fort Apache reservation in the White Mountain area of east-central Arizona are descendants of the Southern Athapascans. The reservation is a mountainous and timbered country in a zone of temperate climate. Most of the 9000 people live in small communities around Whiteriver, the largest city and centre of the tribal government. The Apache language is commonly spoken and traditional ceremonies and customs are practised. One-half of the population is under age 15 and about one-fifth under age five. Medical care for the entire community is provided by the 50-bed Indian Health Service hospital in Whiteriver and its outreach facilities.

METHODS

Study Population

The study population consisted of Apache children less than two years of age residing on the White Mountain reservation. The Whiteriver Indian hospital is the only hospital on the reservation and provides primary healthcare to members of the tribe at no cost. An excellent transportation system to and from the hospital is also available to patients at no cost. Patients with diarrhoea are seen at the outpatient clinic during regular clinic hours and at the emergency room during other times. There are no sources of private medical care on the reservation. Although the traditional medicine men of the tribe are consulted for illnesses, they do not prescribe native or other medications and function mainly as spiritual healers.

Case Definition and Selection

Cases were defined as children less than two years of age seen at the Whiteriver Indian Hospital with three or more loose or watery stools during the previous 24 hours which tested positive (2+) for rotavirus antigen by the ELISA assay[7] during the period 1 May through 15 December 1985. Patients with diarrhoea lasting for more than seven days were excluded from the study. Also excluded were patients seen at the hospital who usually resided outside the reservation. The nursing staff at the outpatient department and emergency room were instructed to obtain a rectal swab from every child less than two years of age who presented with diarrhoea.

Selection of Controls

Hospital controls were selected at the Whiteriver Hospital from outpatient and inpatient records of children who visited the hospital within two weeks of the date of diagnosis of the case. Controls were matched for sex and age within two months. Since diarrhoea is a primary care type illness, controls were chosen from a variety of other non-diarrhoeal illnesses that were also categorized as primary care type. Controls who also had diarrhoea during this two-week period were excluded. For each case a list of all potential controls meeting the definition was compiled. The first five potential controls, ordered by age closest to that of the case within each age and sex stratum, comprised the sampling frame. Two attempts were made to contact the mother of the first control on this list. One of these attempts was made at noon to interview working mothers who came home for lunch to attend their children. If a control could not be contacted after two attempts, the next control was selected from the list. A case was dropped from the analysis involving hospital controls if none of the five controls in its age- and sex-matched stratum were available for interview.

Neighbourhoods were defined as areas served by the same water-supply system. A roster of children less than two years of age distributed by neighbourhoods was compiled from records available at the Johns Hopkins project. Records maintained at the community health division of the Whiteriver hospital and the tribal housing authority were reviewed to complete this list. Within each neighbourhood, subjects were stratified by age and sex. The first five children within each age, sex and neighbourhood strata who most closely matched to the age of the case comprised the sampling frame for neighbourhood controls. The method of selecting a control from this sampling frame was similar to that used for hospital controls.

Data Collection

The medical records of the cases and controls were abstracted by one of the authors (SM) to obtain identifying information and past illness experiences. A study questionnaire was designed to collect data on known and potential risk factors for acquiring rotavirus diarrhoea. The questionnaire was divided into five sections: socio-demographic information, residence history, exposure history, dietary information and sanitation. It was administered to the mothers of cases and controls at their homes and the home visit was made within ten days of the date of diagnosis. The purpose of the study, risks and benefits were explained and oral consent obtained. If the mother was not at home, the adult member in the house who was responsible for the child's care was interviewed. The questions were read to the respondent and terms not understood were explained. The interview took about fifteen to twenty minutes.

An environmental survey of the yard surrounding the house was then conducted. This was done by walking around the house and surveying the yard for five

minutes. The number of animals in the yard was counted and the presence of animal stools was noted. The extent of littering by wet and dry garbage was categorized as 'much' if more than half the yard was littered and 'some' if half the yard was littered. The number of dirty diapers around the yard was also counted. The condition of the garbage bins was observed and these were classified as unprotected if they were not raised above ground or if they lacked secure lids. The presence or absence of screen doors and standing water in the yard was also recorded. A scoring system (Table 1) was developed based on these factors and homes were ranked according to a summary index. Since there are no previous data on the relative importance of each of these factors with respect to risks for causing diarrhoea we assumed that they might all be equally important from a sanitation point of view. We therefore decided to assign them equal weights and analyse them separately as well as by the summary score. Homes with a score of four or more were categorized as 'poor sanitation' and those with a score of one to four as 'fair sanitation'.

The results of the sampling and testing of water for organics, inorganics and faecal contamination kept at the Division of Environmental Health in the Whiteriver Hospital were reviewed for the years 1983–1985 to determine the frequency and seasonality of contamination of any water system on the reservation.

TABLE 1 *Scoring system for environmental sanitation Summary index*

Factor	Response	Score
Animals in the yard	Yes	1
	No	0
Animal stool in the yard	Yes	1
	No	0
Unprotected garbage bins	Yes	1
	No	0
Dry trash on the ground	Much	1
	Some	0.5
	None	0
Wet garbage on the ground	Much	1
	Some	0.5
	None	0
Dirty diapers on the ground	> 3	1
	1–3	0.5
	0	0
Standing water in the yard	Yes	1
	No	0
Small wooden house	Yes	1
	No	0
Lack of screen doors	Yes	1
	No	0

Maximum possible score = 9
Minimum possible score = 0
Maximum score observed in survey = 5.5
Minimum score observed in survey = 1
Poor sanitation = 4 or greater
Fair sanitation = Less than 4

Laboratory Methods

Rectal swabs were obtained from cases, stored in phosphate buffer medium and sent to the Johns Hopkins Enteric Laboratory as soon as possible, usually within the same day of collection. The ELISA assay was used to detect rotavirus antigen.[7]

Data Analysis

Non-participants (eligible cases and controls who could not be traced or who refused) and participants were compared by demographic characteristics and water supply systems. The frequency distributions of risk factors for cases, hospital controls and neighbourhood controls were calculated and compared, using the Chi-square test for independent samples and McNemar's test for paired samples. When the expected frequency in any cell was less than five, Fisher's exact test was applied. Student's *t*-test was used to compare the means for selected variables. The odds ratio (OR) was used as a measure of the strength of the association. A matched and unmatched analysis were done to derive ORs for risk factors. Confidence limits were calculated by Woolf's method.[8] These analyses were done for hospital and neighbourhood controls separately. Confounding and interaction were examined by stratification. The conditional logistic regression model was used to simultaneously adjust for the confounding effects of certain social and demographic variables. These variables are mother's educational status, mother's employment status and mother's age. Risk factors were entered into the model one at a time leaving one in, along with the above social and demographic factors which were entered together. Adjusted ORs were derived by taking the exponent of the regression coefficient; standard errors of the coefficient were used to calculate the 95% confidence limit.

RESULTS

During the study period from 1 May to 15 December 1985 the number of stools tested by the Johns Hopkins Laboratory are listed by month and aetiology in Table 2. Peaks were observed in May and November.

Of the 78 eligible cases of rotavirus diarrhoea 50 were traced and interviewed. Of the 50 cases 36% were six months or less of age and 72% were female. Twenty-seven mothers of the eligible cases were not available at their homes despite two attempts on two days. There was only one refusal. There were no significant differences between 27 non-participant cases and the 50 participant cases with respect to age, sex and water supply system.

TABLE 2 *Percentage distribution of stools from Apache children by pathogen and month—Johns Hopkins laboratory 1 May–15 December 1985*

Month	No. stools tested	%*Shigella*	% Rotavirus	% *Campylobacter*	% Other
May	119	3.3	11.8	0.8	-
June	155	3.2	3.8	8 4	-
July	156	3.2	7.7	3.8	-
August	207	6.7	7.2	3.9	0.9
September	145	1.4	5 5	-	1 4
October	147	3.4	4.1	2.7	0.7
November	141	0 7	11.3	2 1	0.7
1–15 December	51	9.8	1.9	-	0.7
Total	1121	3.7	6.9	3.1	0 6

Hospital controls could be identified for only 45 of the 50 cases. Seventeen (39.5%) of the 45 cases and controls were six months or less of age at the time of interview. Of the hospital controls 82% were diagnosed as acute otitis media. Native Americans are known to have the highest incidence of acute otitis media in the world.[4] It is therefore expected that this illness would be heavily represented in the control group. Because of the small population size of the reservation and the need to match neighbourhood controls by sex, age within two months, and water supply we could obtain neighbourhood controls for only 24 of the 50 cases.

Risk Factors

Cases compared to hospital controls. The risk factors that were significantly associated with rotavirus diarrhoea in our study are listed in Table 3. They were a history of exposure to another child with diarrhoea, living in homes with septic tanks, or with frequent toilet facility breakdowns, and homes categorized as 'poor sanitation' based on the summary index. Exposure to another case of diarrhoea was defined as physical contact with another child with diarrhoea or sharing toys, clothes or other belongings of the contact child during the seven days prior to onset of diarrhoea. A home was categorized as having frequent breakdowns of toilets if there were more than three toilet breakdowns during the preceding six months. Table 4 shows the associations observed for the factors surveyed in the environmental sanitation survey. All the risk factors were observed in a higher proportion of case homes than control homes.

Elevated ORs were also observed for several other factors but they were not statistically significant at the 5% level. These were exposure to other children in diapers, use of a babysitter, use of a daycare centre and use of a pacifier (dummy) seven days prior to onset of illness and the presence of a pit privy at home.

Elevated ORs that were not statistically significant were also detected for 'not currently breastfeeding' and 'never breastfed' responses (Table 5). The mean duration of breastfeeding was 88 days (+ 20.6 SE) for controls and 79 days (+ 17.5 SE) for cases. The mothers of seven cases and twelve controls reported breastfeeding at the time of diagnosis. All of them were also receiving formula at that time. Since breastfeeding was on demand and varied from day to day we could not arrive at any feasible method of quantifying the relative intake of breastmilk and formula. We also could not assess the importance of feeding mode, ie breastfeeding versus bottle feeding because those who were breastfed also received formula by bottle. There were no differences between the two groups with respect to reported intake of fruit juices, formula and pasteurized milk. To determine if untreated water from the tap could be a vehicle for transmission of rotavirus, we compared the proportion of cases and controls

TABLE 3 *Cases and hospital controls—risk factors significantly association with rotavirus diarrhoea in Apache children*

Factor	Cases/Controls No. = 45 + −/− +	Odds ratio	Adjusted odds ratio	95% CL
Exposure to other children with diarrhoea	14/1	14 0	61.9	2 9–1337.9
Septic tank at home	11/4	2.8	1.7	0.57–4.9
*Frequent toilet breakdowns	8/1	8.0	2.9	0.5–16.4
**Poor environmental sanitation	17/5	3.4	3.0	1.03–8.9

*Frequent toilet breakdowns were defined as the occurrence of more than three breakdowns in the preceding six months.

**Homes with poor environmental sanitation were defined as those who had a sanitation index score of four or more based on the environmental survey.

TABLE 4 *Cases and hospital controls—matched analysis environmental sanitation risk factors.*

Factor	Cases + Controls − No = 45	Cases − Controls + No. = 45	Odds ratio	95% CL
Animal in yard	6	5	1.2	0.36– 3.9
Animal stool in yard	2	2	1.0	0.14– 7.1
Unprotected garbage bins	13	4	3.3	1 1 –10.1
Dry trash in yard				
Much	7	1	7.0	0 86–56.9
Some	10	5	2.0	0.68– 5.8
None	28	39	1 0	
Wet garbage in yard				
Much	10	1	10.0	1.2 –78.1
Some	9	6	1.5	0.46– 3.7
None	26	38	1.0	
Dirty diapers in yard				
> 3	6	1	6.0	0.72–49.8
1–3	3	2	1.5	0.25– 8.9
0	36	42	1.0	
Standing water in yard	8	2	4 0	0 84–18.8
Wooden shack	5	4	1 25	0.33– 4.6
No screen doors	3	1	3.0	0 31–28 8
Summary Index 4+ Poor	17	5	3 4	1 30– 9.2

whose mothers reported that they used untreated water from the tap to mix the formula, and found no difference.

We then explored any potential interaction between age, sex and current breastfeeding histories. For ages six months and below, a history of not currently breastfeeding was associated with an OR of 6.7 compared to 1.2 for those aged above six months and 1.97 for all ages combined. The Woolf's test for heterogeneity was not significant at the 5% level.

No association was found for attendance at a native ceremony, or other large gatherings where food was served, exposure to other children using a pacifier (dummy), source of water supply and animal ownership during the seven days prior to onset of diarrhoea.

Three socio-demographic factors were identified as possible confounding factors. These were mother's age, mother's educational status and mother's employment status. Adjusted ORs were derived for all risk factors using the conditional logistic regression procedure. After adjustment the associations observed for septic tank at home and frequent toilet breakdowns lost their statistical significance (ie the confidence limits on the OR included one) (Table 3).

Cases compared to neighbourhood controls. Neighbourhood controls were selected in order to match on water supply system. Since the transmission of rotaviruses may be waterborne, we planned to examine associations with risk factors after controlling for the confounding effects of water supply source. However comparisons of cases and hospital controls showed that water supply system was not a risk factor. For nearly all other risk factors, the direction of the associations were similar among hospital and neighbourhood controls. Table 6 presents the ORs comparing cases and neighbourhood controls for the significant risk factors that were observed with hospital controls. A significant association was observed for exposure to another case of diarrhoea.

We then examined associations after combining the two control groups. However we observed that this increase in sample size did not detect any significant association other than those observed with hospital controls alone.

TABLE 5 *Cases and hospital controls—matched analysis dietary factors in Apache children with rotavirus diarrhoea*

Factor	Cases + Controls − No. = 45	Cases − Controls + No = 45	Odds ratio	95% CL
Never breastfed versus ever breastfed	12	9	1.3	0.50–3.1
Not currently breastfeeding versus currently breastfeeding	10	5	2.0	0.70–5.9
Fruit juice versus no fruit juice	12	13	0.92	0.41–2.0
Water from tap versus sterile water from store	10	11	0.90	0.38–2.1
Formula versus pasteurized milk	3	3	1.0	0.20–4.9

TABLE 6 *Cases and neighbourhood controls—risk factors significantly associated with rotavirus diarrhoea in Apache children*

Factor	Cases/Controls No. = 24 +−/−+	Odds ratio	95% CL
Exposure to other children with diarrhoea	5/0		1.22–∞
Septic tank at home	3/0		0 58–∞
*Frequent toilet breakdowns	3/0		0 58–∞
**Poor environmental Sanitation	7/3	2.3	0.59–8.9

*Frequent toilet breakdowns were defined as the occurrence of more than three breakdowns in the preceding six months.
**Homes with poor environmental sanitation were defined as those who had a sanitation index score of four or more based on the environmental survey.

Data on faecal contamination of water samples from all the different water systems were available for the years 1983–1985. None of the samples tested positive for faecal contamination. The levels of inorganics, organics and radiochemicals were also within the standards set by the Environmental Protection Agency.

DISCUSSION

Since this is a hospital-based case-control study our study sample comprised only cases of severe rotavirus diarrhoea that were brought to the hospital for treatment. It therefore excluded mild cases whose mothers felt did not warrant medical attention. Also our control population was not tested for rotavirus antigen. Thus a certain proportion of them may have been asymptomatically infected at the time of the study. We determined the rate of asymptomatic infection in this population from data collected for a prospective cohort study of children followed from birth to age three years that was conducted to determine the age- and sex-specific incidence of aetiological-specific diarrhoeas on the reservation. A total of 860 stool samples from children who were asymptomatic were tested for rotavirus antigen and of these only 12 tested positive giving a very low rate of asymptomatic infection equal to 0.01%. Comparisons of ORs from hospital and neighbourhood controls did not show discrepant results. This consistency also reduces the likelihood that selection factors explain our findings.

Exposure History

The strong association we observed for exposure to another child with diarrhoea, has also been reported in other studies in the US[12] and the developing world.[10] Except for one case, all the contacts came from households other than the household of the index case or control.

In contrast to the study by Engelberg *et al*,[6] our study does not demonstrate an association with animal ownership. For cases and controls who reported owning animals we also asked about animal contact behaviour ie children playing with pets, animals roaming about in the house, and pets sleeping in the kitchen. No differences were observed between cases and controls. Attendance at a sunrise ceremony during the seven days prior to onset of diarrhoea also did not emerge as a risk factor. This is the most frequent ceremony on the reservation and celebrates a girl's onset of menarche. It is held every weekend and starting at sunrise involves the chanting of sacred songs, dancing and feasting. In our study only two cases and three hospital controls reported attendance at the ceremony during the seven days prior to onset of illness. None of them consumed any uncooked or semi-cooked food items at that time. It is likely that very small children are not taken to these ceremonies.

Dietary Factors

Our data on the role of breastfeeding are inconclusive because of sample size constraints and the absence of children in exclusive feeding groups. Comparison of our findings with other studies in the US is limited by the fact that risk ratios in those studies were derived for no breastfeeding versus exclusive breastfeeding while in our study none of the cases and controls were exclusively breastfed. Risks were therefore calculated for a breastmilk and formula group versus a formula group. Since breastfeeding was on demand we also could not quantify the intake of breastmilk. In contrast to our finding of a weak association with absence of breastfeeding, the prospective study conducted in the US by Duffy *et al*,[11] showed no difference in the infection rates of rotavirus infection in exclusively breastfed infants as compared to exclusively formula fed infants. Our data do not suggest that solid foods eaten at regular meal times are a vehicle for the transmission for rotaviruses. These foods are either commercially available baby foods given to young children or regular adult diet for older children. The baby foods when purchased are packed and bottled hygienically, therefore have a low risk of environmental contamination compared to weaning foods prepared at home.

Environmental Factors

Nearly all homes on the reservation are served by indoor plumbing. The two case homes and three hospital-control homes that had no tap inside the house had a tap outside the home that provided a continuous supply of water. Case and control homes therefore did not differ by water availability. Several positive associations were however detected for sewage disposal

facilities. The use of septic tanks for excreta disposal emerged as a risk factor (OR = 2.8 (1.9–9.9)). In consultation with environmental health engineers we learned that residents on the reservation could not afford to maintain the septic tanks regularly. As a consequence the tanks filled with sludge and overflowed, contaminating the area around the house. The finding that frequent breakdowns of toilets is a risk factor is consistent with the importance of adequate maintenance of sanitation facilities. Frequently cited problems by residents were clogging of the commodes with trash and malfunctioning of the flush system. This led to overflow of the commode and faecal contamination of floor of the bathroom and surrounding areas. In relation to our finding that an unprotected garbage bin was a risk factor we observed that bins that were placed at ground level without secure lids on them attracted a variety of stray animals who rummaged through them for food. Children were also seen playing in garbage spilled over from such unprotected bins.

We conclude that the most important measure to reduce the incidence of rotavirus diarrhoea on the reservation is the minimizing of contacts of children with diarrhoea. The elimination of septic tanks, safe garbage storage and disposal methods and the adoption of handwashing practices during childcare and feeding are additional steps that could prevent the spread of rotavirus diarrhoea in this community.

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