Risk and prognostic factors for diarrheal disease in Brazilian infants: a special case-control design application

Fatores de risco e prognósticos para diarréia entre crianças brasileiras: uma aplicação especial do delineamento de casos e controles

Sandra Costa Fuchs [1]
Cesar Gomes Victora [2]

[1] *Departamento de Medicina Social, Faculdade de Medicina, Universidade Federal do Rio Grande do Sul. Rua Ramiro Barcelos 2600, sala 415, Porto Alegre, RS 90035-003, Brasil. scfuchs@zaz.com.br*
[2] *Departamento de Medicina Social, Faculdade de Medicina, Universidade Federal de Pelotas. C. P. 464, Pelotas, RS 96001, Brasil.*

Abstract *The aim of this study was to examine the effect of demographic, socioeconomic, environmental, maternal reproductive, dietary, and nutritional variables on diarrhea risk and prognosis using a hierarchical framework. A case-control study of children aged 0-23 months in Greater Metropolitan Porto Alegre was conducted during the peak season for diarrhea in 1987-1988. Three groups were investigated, with 192 children each. The first group included hospitalized children with an episode of acute diarrhea complicated by moderate to severe dehydration. The second group included children with acute mild diarrhea without signs of dehydration who were identified in the same neighborhood as hospitalized cases. The third group consisted of controls without diarrhea. Mothers were interviewed by trained interviewers using a standardized questionnaire. Data analysis included a hierarchical approach to control for confounding, using conditional logistic regression. Comparison of the three groups aimed to identify risk factors for diarrhea complicated by dehydration, prognostic factors for dehydration, and risk factors for mild diarrhea. Low birth weight, stunting, and lack or breastfeeding acted simultaneously as risk and prognostic factors for diarrhea.*
Key words *Diarrhea; Child Health; Risk Factors; Case-Control Studies; Epidemiology*

Resumo *O objetivo deste estudo foi examinar o efeito de variáveis demográficas, sócio-econômicas, ambientais, reprodutivas maternas, dietéticas e nutricionais sobre o risco e o prognóstico de diarréia usando análise hierarquizada. Um estudo de caso-controle incluindo crianças entre 0-23 meses de idade, residentes na área metropolitana de Porto Alegre, foi realizado durante os meses de verão de 1987-88. Investigaram-se três grupos de 192 crianças, incluindo as hospitalizadas com um episódio agudo de diarréia e desidratação moderada a grave; as crianças com diarréia aguda leve e sem desidratação, identificadas na vizinhança dos casos, assim como crianças sem diarréia. Entrevistas padronizadas foram realizadas por entrevistadoras treinadas. Utilizou-se análise hierarquizada no controle de fatores de confusão. Calcularam-se razões de odds e intervalos de confiança de 95% através de regressão logística condicional. O emparelhamento de diferentes combinações de casos e controles permitiu invetigar fatores de risco para diarréia grave, fatores prognósticos e fatores de risco para diarréia leve. Baixo peso de nascimento, déficit altura-idade e ausência de aleitamento materno foram simultaneamente fatores de risco e prognóstico para diarréia.*
Palavras-chave *Diarréia; Saúde Infantil; Fatores de Risco; Estudos de Casos e Controles; Epidemiologia*

Introduction

Diarrheal diseases are still associated with a high mortality rate among children (Murray & Lopez, 1997), causing an estimated 1.5 million deaths in the year 2000 (Victora et al., 2000). Diarrhea is a worldwide problem, but the implications of diarrheal diseases are particularly evident in developing countries.

Although oral rehydration therapy has been available for approximately thirty years and its use has contributed to a major decline in the diarrheal mortality rate (Victora et al., 2000), diarrheal morbidity is still a major problem among under-fives, mostly in the first year of life. Pooled data published in 1992 from 22 longitudinal studies conducted in 12 countries showed that infants aged 6-11 months had a median incidence of five episodes of diarrhea per year (Bern et al., 1992). Several reports have identified socioeconomic, environmental, maternal, nutritional, and other characteristics as risk factors for diarrheal morbidity or mortality (Awasthi et al., 1996; Clemens et al., 1999; Mirza et al., 1997). Poverty, low parental schooling, poor sanitation, lack of water supply, crowding, early childbirth, short birth intervals, lack of breastfeeding, and malnutrition are factors associated with diarrhea (Awasthi et al., 1996; Brattacharya et al., 1995; Howie et al., 1990; Mirza et al., 1997; Raisler et al., 1999; Scariati et al., 1997).

Most studies have used cross-sectional or cohort designs as opposed to a case-control methodology. We found no case-control studies designed to simultaneously compare risk and prognostic factors for dehydrating diarrhea, using data from the same population. Identification of factors related simultaneously to the risk of acquiring diarrhea and its prognosis would be particularly relevant, potentially bolstering the effect of a particular intervention. We therefore examined the effects of socioeconomic, environmental, maternal reproductive, dietary, and nutritional variables on the risk and prognosis of diarrhea, using data from a 1987-1988 case-control study.

Participants and methods

Design

This was a case-control study including three groups: dehydrating diarrhea cases, mild diarrhea cases, and non-diarrhea controls.

Study definitions

Dehydrating diarrhea cases included children aged 0-23 months residing in Greater Metropolitan Porto Alegre, southern Brazil, enrolled from December 1987 to March 1988 from the city's two largest pediatric hospitals. Dehydrating diarrhea was defined as an episode of acute diarrhea (less than eight days duration) and presence of a persistent skinfold plus at least one of the following signs: sunken fontanel, dry mouth and tongue, sunken eyes, reduced urinary output, weak pulse, drowsiness, or irritability. Diagnosis of diarrhea was based on three or more loose or watery bowel movements within 24 hours for children older than 3 months or according to the mother's report of more frequent and poorly formed stools (as compared to normal) for younger children. All children meeting these criteria were enrolled from the largest pediatric hospital, and a systematic random sample of eligible children from the second hospital was included. Cases of mild diarrhea were defined as children with diarrhea in the seven days preceding the interview and without signs of dehydration. They were individually matched to the severe diarrhea cases by age (0-11, 12-23 months) and neighborhood. When a hospital case was identified, an interviewer visited this child's home to interview the mother. Starting at this site, the interviewer used a standard procedure to move around the neighborhood, visiting every house until a child with mild diarrhea was identified.

Non-diarrhea controls were children identified in the same neighborhood and from the same age bracket as dehydrating diarrhea cases, who had not presented diarrhea in the preceding seven days.

Figure 1 shows the framework for enrollment of cases and controls. Risk factors for dehydrating diarrhea were investigated by comparing cases of dehydrating diarrhea and non-diarrhea controls. Prognostic factors for dehydration were established by comparing cases of dehydrating and mild diarrhea. Finally, risk factors for mild diarrhea were ascertained by comparing cases of mild diarrhea with non-diarrhea controls.

Study variables and data collection

Standardized interviews with mothers or caretakers provided data on socioeconomic, maternal reproductive, demographic, nutritional, and health-care characteristics. The mother's skin color and key environmental characteris-

tics were assessed through observation by six trained interviewers. The variables presented in this paper included children's age (0-1, 2-3, 4-5, 6-8, 9-11, 12-17, or 18-23 months), family income (measured as "times the prevailing minimum wage"; ≤ 3.6 or > 3.6), father's presence in household and schooling (absent and illiterate or 1 or more years of schooling), mother's schooling (in years, ≤ 8 or > 8), type of housing (masonry construction versus shacks), water supply (indoor running water, outdoor running water on property, outdoor running water in neighborhood, public well, or river), flush toilet (yes or no), number of under-fives living in the house (1-2 or 3-6), home cleanliness (index based on observation of availability of soap for washing hands and towels for drying, food scraps in uncovered pans, pans kept covered on the stove, presence and number of flies in the kitchen or living room, feces or standing water in the yard, presence of pets), maternal age (≤ 20 years old versus > 20), twin birth (yes or no), birth order (1-2, 3, > 3), birth weight (reported by the mother or recorded on the birth certificate, categorized as < 2,500, 2,500-2,999, ≥ 3,000g), height-for-age, weight-for-height, and weight-for-age (all three in z-scores categorized as, ≤ 2, -1 to -1,9, > -1), previous hospitalization for any reason (yes or no), type of milk consumed (breast, breast + non-breast, non-breast), and current breastfeeding status (still breastfeeding, if breastmilk constituted any portion of the child's diet; stopped breastfeeding; never breastfed). Since breastfeeding may have been interrupted as a result of the diarrhea, children weaned during the episode were classified as still breastfed.

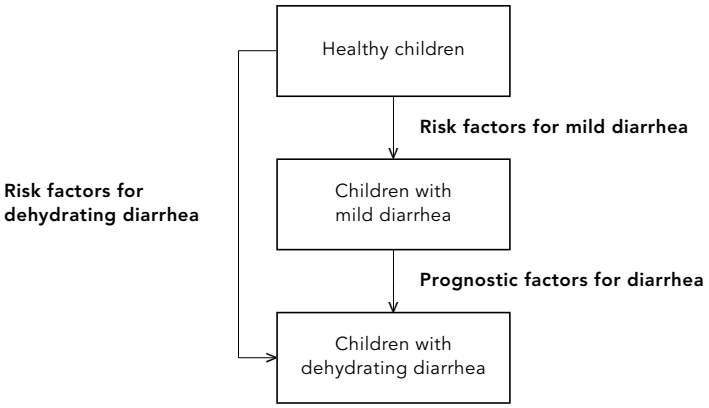
Sample size and strategies for data analysis

The sample size was calculated to detect an odds ratio of at least 1.5, with 80% power and 5% significance level (two-tailed) for a prevalence of exposure among controls ranging from 20% to 65%. Independent variables were grouped into different hierarchical levels of determination, ranging from distal determinants such socioeconomic characteristics, including environmental, maternal reproductive, and demographic factors, and leading to proximal determinants such as nutrition (anthropometry and diet). We included variables at each level based on the strength of association in the crude analyses (a p level < 0.1 was required).

One regression equation was fitted for each hierarchical level, also including variables from higher levels of determination (Victora et al., 1997). We conducted separate analyses for each case-control combination through conditional logistic regression using the Egret statistical package (Breslow & Day, 1980).

Figure 1

Framework for studying risk and prognostic factors for diarrheal diseases.



Results

All but eight children out of 200 identified with dehydrating diarrhea were studied. Seven children with mild diarrhea could not be interviewed and were replaced by their next-nearest eligible neighbor. All eligible children without diarrhea agreed to participate. Table 1 shows the distribution of target variables according to the diarrhea outcomes. Most of the characteristics of children with mild diarrhea showed an intermediate distribution between those from dehydrating diarrhea cases and non-diarrhea controls.

Table 2 shows that age was closely related to all diarrhea outcomes, but the groups at highest risk varied. Children in the first two months of life were protected from developing diarrhea, but once they acquired the disease, they were at about 23 times the risk of dehydration as compared to those in the 9-11 month age bracket. Infants aged two to three months had seven times the likelihood of developing dehydrating diarrhea as compared to those 9-11 months old. Due to matching, children aged 12-23 months had to be analyzed separately from those under 12 months. In the second year of life an increased risk of dehydrating diarrhea appeared in children aged 12 to 17 months. Our data analysis did not indicate any

Table 1

Distribution of variables for healthy children and according to diarrhea outcomes.

Variables	Dehydrating diarrhea % (n = 192)	Mild diarrhea % (n = 192)	Healthy children % (n = 192)
Age (months)			
0-1	16	4	14
2-3	23	15	9
4-5	17	11	13
6-8	20	28	24
9-11	9	29	25
12-17	9	7	5
18-23	5	6	9
Gender			
Male	53	52	51
Female	47	48	49
Family income (times minimum wage)			
≥ 3,6	19	24	29
< 3,6	81	76	71
Father's presence and schooling (years)			
≥1	61	82	83
absent or 0	39	18	17
Maternal schooling (years)			
≥ 8	11	15	18
< 8	89	85	82
Mother's skin color			
White	53	68	66
Black	20	18	17
Mixed	27	14	16
Maternal work			
No	59	53	62
Yes	41	47	38
Type of housing			
Masonry	54	66	72
Shack	46	34	28
Water supply			
Indoor running water	52	58	68
Outdoor running water (on property)	31	28	20
Outdoor running (public)	11	10	9
Well or river	6	4	2
Use of refrigerator			
Yes	42	49	59
No	58	51	41
Number of under-fives in household			
1-2	77	86	89
3-6	23	14	11
Home cleanliness			
Yes	21	37	45
No	79	63	55

(to be continued on the next page)

gender-related differences in risk or prognostic factors for diarrhea.

Low socioeconomic status was one determinant of dehydrating diarrhea, although there was no significant association with mild diarrhea (Table 3). Low family income doubled the risk of dehydrating diarrhea, independently of the father's presence in the household or educational level or the mother's skin color. Paternal schooling was the main socioeconomic risk and prognostic factor for dehydrating diarrhea, while maternal education had no independent effect. Mixed skin color classification of mothers, although adjusted for other socioeconomic variables, was associated with a two-fold increase in the risk and in a poor prognosis for dehydration. Children of working mothers were less likely to have a poor prognosis than children of non-working mothers.

Table 4 shows that living in the same household with three to six other under-fives or lack of home cleanliness (in the kitchen, living room, and yard) increased the risk of dehydrating diarrhea, since both variables were associated with the risk of mild diarrhea as well as with a poor prognosis. Lack of a refrigerator was associated with a two-fold increase in the risk of developing mild diarrhea.

Children of mothers under 20 years of age had approximately four times the risk of dehydration, since this exposure was independently associated with risk and prognosis for dehydrating diarrhea (Table 5). Among the remaining maternal reproductive characteristics, higher birth order was associated with a poor prognosis, while twinship was associated with increased risk of dehydrating diarrhea.

Table 6 shows the strength of independent associations between nutritional status/feeding practices and diarrhea outcomes. Most nutritional variables were significantly associated with both the risk of dehydrating diarrhea and a poor prognosis, but not with risk of mild diarrhea. Low birth-weight children were at a significantly higher risk of developing dehydration as compared to normal-weight children. Poor nutritional status as measured by height-for-age resulted in a 4.5-fold increase in the risk of dehydrating diarrhea. Poor feeding practices accounted for both an increased risk and a worse prognosis. During the first two years of life, interrupting breastfeeding just prior to the onset of the episode resulted in a 6-fold increase in the risk of developing dehydrating diarrhea.

Discussion

Table 7 summarizes both risk and prognostic factors. Factors that increased the risk of dehydrating diarrhea were associated with a poor prognosis for a given episode of diarrhea rather than increasing the risk of mild diarrhea. Insofar as the study was able to ascertain, socioeconomic variables did not distinguish children at risk of developing mild diarrhea.

Children in low-income areas often have similar exposures, such as low parental education. The neighborhood-matched design did not allow the identification of these variables as risk factors for developing mild diarrhea. Although conditional logistic regression was performed and the analyses were based on discordant pairs, overmatching may still have affected the precision of odds ratios estimates (Rothman & Greenland, 1998).

Children were matched in two broad age categories to the dehydrating diarrhea cases. However, since there were residual differences and analyses were conducted within small intervals, age was both a risk and prognostic factor for dehydrating diarrhea. Children under two months were largely protected from mild diarrhea, but they were also at increased risk of dehydration, since the prognosis of diarrhea improved sharply with age. Furthermore, children aged two to three months were equally exposed to a high risk and poor prognosis for dehydrating diarrhea. These associations may be linked to feeding practices, particularly the interruption of breastfeeding.

The effects of each socioeconomic risk factor were adjusted for those of all other such variables. Both very low household income and low paternal education were independent determinants of dehydrating diarrhea. Although most studies detected maternal schooling as a risk factor for childhood diarrhea (Hussain & Smith, 1999; Yoon et al., 1996), our study did not detect an association with mother's education. This may be explained by the inclusion of paternal schooling in the same model, attenuating the effect of the former (Desai & Alva, 1998) and suggesting that the effect of maternal education is not independent of socioeconomic level (Dargent-Molina et al., 1994). Maternal work had a paradoxical effect. Children of working mothers tended to be at increased risk of mild diarrhea (although statistically not quite significant) (Hussain & Smith, 1999) but at the same time had a better prognosis. Maternal work may keep women outside the home without simultaneously ensuring adequate child care (Lamontagne et al., 1998; Reed et al., 1996). However, once their children had developed diarrhea, working mothers reinforced their care and were thus able to prevent dehydration.

Although several environmental factors were significantly associated with diarrheal morbidity according to bivariate analysis, after adjusting for confounding only the lack of a refrigerator in the household remained as a risk factor for mild diarrhea (Hussain & Smith, 1999). Families living in this city seldom used open wells or rivers as their source of drinking and cooking water. Accordingly, the odds ratios were approximately equal to three but the confidence intervals were wide due to the low prevalence of exposure. Children of families who had outdoor running water had a two-fold risk of dehydrating diarrhea as compared to those with

Table 1 (continued from previous page)

Variables	Dehydrating diarrhea % (n = 192)	Mild diarrhea % (n = 192)	Healthy children % (n = 192)
Maternal age (years)			
≥ 20	76	80	88
< 20	24	20	12
Birth order			
1-2	41	52	54
3	22	20	13
> 3	37	28	33
Twin			
No	94	97	99
Yes	6	3	1
Birth weight (grams)			
> 3,000	54	67	73
2,999–2,500	22	22	18
< 2,500	24	11	9
Height-for-age (z score)			
> -1	30	59	64
-1 to -1.9	37	27	25
≤ -2	33	14	11
Weight-for-age (z score)			
> -1	46	63	73
-1 to -1.9	29	26	20
≤ -2	25	11	7
Type of milk consumed			
Breast	8	15	23
Breast + non-breast	17	23	23
Non-breast	75	62	54
Breastfeeding history			
Still breastfeeding	25	38	46
Stopped breastfeeding	70	59	50
Never breastfed	5	3	4

Table 2

Association between demographic variables and diarrhea outcomes.

Variables	Dehydrating diarrhea Crude odds ratio (95% CI)	Prognosis of diarrhea Crude odds ratio (95% CI)	Mild diarrhea Crude odds ratio (95% CI)
Age (months)			
0-1	2.6 (1.3-5.5)	23.1 (6.9-77.8)	0.2 (0.1-0.6)
2-3	7.1 (3.0-16.5)	7.1 (2.9-17.4)	1.2 (0.6-2.5)
4-5	3.5 (1.6-7.5)	6.8 (2.7-17.3)	0.9 (0.4-1.7)
6-8	2.4 (1.2-4.8)	3.2 (1.4-7.4)	0.9 (0.5-1.5)
9-11	1.0	1.0	1.0
p level*	< 0.001	< 0.001	0.05
12-17	3.7 (1.0-13.1)	0.8 (0.3-2.5)	0.9 (0.6-1.3)
18-23	1.0	1.0	1.0
p level*	0.03	0.80	0.60
Gender			
Male	1.0	1.0	1.0
Female	0.9 (0.6-1.4)	0.9 (0.6-1.5)	0.9 (0.6-1.3)
p level*	0.70	0.90	0.60

* p level assessed by likelihood ratio test.

Table 3

Association between socioeconomic variables and diarrhea outcomes.

Variables	Dehydrating diarrhea Adjusted odds ratio[1] (95% CI)	Prognosis of diarrhea Adjusted odds ratio[2] (95% CI)	Mild diarrhea Adjusted odds ratio[3] (95% CI)
Family income (times minimum wage)			
≥ 3.6	1.0	1.0	1.0
< 3.6	1.8 (1.0-3.1)	1.2 (0.6-2.1)	1.4 (0.9-2.2)
p level*	0.04	0.60	0.15
Father's presence and schooling (years)			
≥ 1	1.0	1.0	1.0
absent or 0	2.7 (1.6-4.8)	2.7 (1.6-4.6)	0.9 (0.5-1.7)
p level*	< 0.001	< 0.001	0.90
Maternal schooling (years)			
≥ 8	1.0	1.0	1.0
< 8	1.5 (0.8-2.7)	1.4 (0.7-2.8)	1.5 (0.8-2.6)
p level*	0.20	0.30	0.20
Mother's skin color			
White	1.0	1.0	1.0
Black	1.7 (0.9-3.1)	1.4 (0.8-2.5)	0.9 (0.5-1.6)
Mixed	2.2 (1.2-4.1)	2.3 (1.2-4.2)	1.1 (0.7-1.9)
p level*	0.02	0.03	0.90
Maternal work			
No	1.0	1.0	1.0
Yes	1.1 (0.7-1.7)	0.6 (0.3-0.9)	1.4 (0.9-2.1)
p level*	0.80	0.02	0.09

* p level assessed by likelihood ratio test.
Odds ratios were adjusted for:
[1] father's schooling and presence, mother's skin color, family income;
[2] father's schooling and presence, mother's skin color, maternal work;
[3] maternal work.

Table 4

Association between environmental variables and diarrhea outcomes.

Variables	Dehydrating diarrhea Adjusted odds ratio[1] (95% CI)	Prognosis of diarrhea Adjusted odds ratio[2] (95% CI)	Mild diarrhea Adjusted odds ratio[3] (95% CI)
Type of housing			
Masonry	1.0	1.0	1.0
Shack	2.3 (1.1-5.0)	1.1 (0.6-1.9)	1.0 (0.6-1.7)
p level*	0.03	0.80	1.00
Water supply			
Indoor running water	1.0	1.0	1.0
Outdoor running water (on property)	2.1 (1.1-4.3)	0.9 (0.5-1.6)	1.5 (0.9-2.7)
Outdoor running (public)	1.0 (0.4-2.6)	1.0 (0.4-2.5)	0.8 (0.3-2.1)
Well or river	3.0 (0.7-12.5)	1.8 (0.5-6.0)	3.3 (0.9-12.9)
p level*	0.08	0.70	0.09
Use of refrigerator			
Yes	1.0	1.0	1.0
No	1.1 (0.6-2.2)	0.7 (0.4-1.2)	1.8 (1.2-2.9)
p level*	0.70	0.16	0.009
Number of under-fives in household			
1-2	1.0	1.0	1.0
3-6	2.4 (1.0-5.6)	1.9 (1.0-3.6)	1.5 (0.8-2.9)
p level*	0.03	0.05	0.20
Home cleanliness			
Yes	1.0	1.0	1.0
No	2.9 (1.5-5.6)	2.0 (1.2-3.4)	0.9 (0.6-1.4)
p level*	< 0.001	0.007	0.60

* p level assessed by likelihood ratio test.
Odds ratios were adjusted for variables described in Table 2 plus:
[1] number of under-fives, type of housing, water supply, home cleanliness;
[2] number of under-fives, home cleanliness;
[3] use of refrigerator, water supply.

Table 5

Association between maternal reproductive variables and diarrhea outcomes.

Variables	Dehydrating diarrhea Adjusted odds ratio[1] (95% CI)	Prognosis of diarrhea Adjusted odds ratio[2] (95% CI)	Mild diarrhea Adjusted odds ratio[3] (95% CI)
Maternal age (years)			
≥ 20	1.0	1.0	1.0
< 20	3.8 (1.6-8.9)	2.4 (1.2-4.6)	1.6 (0.9-3.0)
p level*	< 0.001	0.01	0.10
Birth order			
1-2	1.0	1.0	1.0
3	2.1 (0.9-4.8)	1.8 (0.9-3.3)	1.7 (0.9-3.1)
> 3	1.2 (0.5-2.4)	2.3 (1.2-4.5)	0.8 (0.5-1.4)
p level*	0.20	0.03	0.08
Twin			
No	1.0	1.0	1.0
Yes	11.6 (0.9-143)	1.4 (0.4-5.3)	2.0 (0.4-9.2)
p level*	0.03	0.60	0.40

* p level assessed by likelihood ratio test.
Odds ratios were adjusted for variables described in Table 3 plus:
[1] twin, maternal age;
[2] maternal age, birth order;
[3] birth order.

Table 6

Association between nutritional variables and diarrhea outcomes.

Variables	Dehydrating diarrhea Adjusted odds ratio[1] (95% CI)	Prognosis of diarrhea Adjusted odds ratio[2] (95% CI)	Mild diarrhea Adjusted odds ratio[3] (95% CI)
Birth weight (grams)[4]			
> 3,000	1.0	1.0	1.0
2,999–2,500	2.4 (1.2-4.9)	1.3 (0.7-2.3)	1.0 (0.6-1.7)
< 2,500	3.6 (1.5-8.8)	3.2 (1.6-6.3)	0.9 (0.5-1.8)
p level*	0.002	0.002	0.90
Height-for-age (z score)			
> -1	1.0	1.0	1.0
-1 to -1.9	1.4 (0.6-3.4)	2.5 (1.2-5.1)	0.9 (0.5-1.5)
≤ -2	4.5 (1.3-15.5)	4.2 (1.8-9.9)	1.5 (0.8-3.0)
p level*	0.04	< 0.001	0.30
Weight-for-age (z score)			
> -1	1.0	1.0	1.0
-1 to -1.9	1.5 (0.5-4.2)	1.7 (0.9-3.1)	1.3 (0.7-2.3)
≤ -2	1.9 (0.2-16.9)	2.2 (0.9-5.0)	1.5 (0.7-3.4)
p level*	0.70	0.09	0.50
Type of milk consumed			
Breast	1.0	1.0	1.0
Breast + non-breast	1.5 (0.4-5.1)	0.8 (0.3-2.5)	1.2 (0.6-2.3)
Non-breast	6.0 (1.9-14.6)	2.3 (0.9-5.9)	1.2 (0.7-2.2)
p level*	< 0.001	0.03	0.80
Breastfeeding history			
Still breastfeeding	1.0	1.0	1.0
Stopped breastfeeding	6.4 (2.3-17.3)	2.5 (1.2-5.0)	1.1 (0.7-1.7)
Never breastfed	0.7 (0.1-3.7)	3.8 (0.5-31.0)	0.5 (0.2-1.8)
p level*	< 0.001	0.02	0.50

* p level assessed by likelihood ratio test.
Odds ratios were adjusted for variables described in Table 4 plus:
[1] birth weight, age of the children, weight-for-age, type of milk, previous hospitalization;
[2] birth weight, age of the children, height-for-age, type of milk;
[3] age of the children, weight-for-age, type of milk;
[4] not adjusted for age of the children.

indoor running water. Families tended to use the same sink for washing hands, diapers, clothes, and kitchen utensils. In addition, the number of under-fives in the home and home cleanliness were associated with the severity but not with the incidence of diarrhea (Gorter et al., 1998; Vasquez et al., 1999). One might expect environmental factors to be primarily associated with incidence and rather than severity of diarrhea. However, children in sub-standard environments may have been subjected to greater microbial loads and therefore presented more severe disease (al-Mazrou et al., 1995).

Children of teenage mothers were at greater risk of dehydration, suggesting that these mothers were less prepared to deal with the disease (al-Mazrou et al., 1995). High birth order was associated with increased severity of diarrhea, and twins were at greater risk of dehydrating diarrhea, independently of maternal age.

Low birth weight, lack of breastfeeding, and malnutrition have been associated with disease burden and increased mortality (D'Souza, 1997; Hussain & Smith, 1999). Particularly for diarrheal diseases, most studies have analyzed risk and prognostic factors without proper control for potential confounding variables (Dargent-Molina et al., 1994; Teka et al., 1996).

Adjustment for confounding variables is necessary because higher socioeconomic status is known to be associated both with lower rates of diarrhea and breastfeeding practices during infancy. Even children selected from the same neighborhood had different exposure levels, as shown in this study for severity of the diarrheal episode. Lack of breastfeeding had a greater effect on risk of dehydration than on prognosis of diarrhea, but unlike other studies it was not associated with mild diarrhea. Since mixed-fed and weaned infants consume greater amounts of supplemental liquids, the protective effect of breastmilk was shown by comparing total breastfed with non-breastfed children (Raisler et al., 1999). Due to the small number

Table 7

Summary of p values for findings on risk and prognostic factors for diarrhea outcomes.

Variables	Dehydrating diarrhea	Prognosis of diarrhea	Mild diarrhea
Age (first year of life)	< 0.001	< 0.001	0.05
Age (second year of life)	0.03	0.80	0.60
Gender	0.70	0.90	0.60
Family income	0.04	0.60	0.15
Father's presence and schooling	< 0.001	< 0.001	0.90
Maternal schooling	0.20	0.30	0.20
Mother's skin color	0.02	0.03	0.90
Maternal work	0.80	0.02	0.09
Type of housing	0.03	0.80	1.00
Water supply	0.08	0.70	0.09
Use of refrigerator	0.70	0.16	0.009
Number of under-fives in household	0.03	0.05	0.20
Home cleanliness	< 0.001	0.007	0.60
Maternal age	< 0.001	0.01	0.10
Birth order	0.20	0.03	0.08
Twin	0.030	0.60	0.40
Birth weight	0.002	0.002	0.90
Height-for-age	0.04	< 0.001	0.30
Weight-for-age	0.70	0.09	0.50
Type of milk consumed	< 0.001	0.03	0.80
Breastfeeding history	< 0.001	0.02	0.50

of children in some categories, confidence intervals were wide and included unity (prognostic factor).

This study discussed the application of a case-control design to address an issue usually examined by cohort studies. In a cohort study a group of healthy children needs to be identified and followed up for a certain period of time to detect diarrheal episodes. Although most children have self-limiting diarrhea, a few progress to dehydration. At this point it would be theoretically possible to assess the three outcomes: risk factors for mild diarrhea, prognosis of the diarrheal episode, and risk factors for dehydrating diarrhea. However, since a diarrheal episode mandates the use of oral rehydration therapy, such an approach would be ethically unfeasible. Second, dehydration complicates less than 5% of all diarrheal episodes, and a large number of children would have to be followed up in order to obtain a sufficient sample. A case-control design overcame both the potential ethical issue (since children were selected after the outcome occurred) and logistic problems related to the sample size.

Some additional methodological issues need to be highlighted. Ideally, cases and controls would come from the same population in order to make valid comparisons about exposure conditions. To assure the validity of this case-control study, community controls were selected from the same neighborhood as the cases treated in the reference hospitals. These controls were expected to have been identified as cases if they had developed dehydrating diarrhea.

However, individual matching led to potential similarities regarding exposure. For example, matching controls to cases according to age was particularly relevant to allow the identification of breastfeeding status and other age-dependent exposures. Although this approach is advantageous, overmatching could be a potential problem since case and controls were likely to share the same environmental conditions, therefore leading some exposures to not be identified as risk or prognostic factors.

Finally, this study discussed a unique application of a case-control design to assess risk and prognostic factors simultaneously; an approach that would usually require a cohort study. Besides, the introduction of explanatory variables in the analysis according to a conceptual framework of determination demonstrated that in the same setting, different variables might act as risk, prognostic, and/or confounding factors, depending on the outcomes.

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