

## A Hierarchical Model for Defining Priorities of Environmental and Non-Environmental Risk Factors of Childhood Diarrhea

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### Abstract

- Background** Acute diarrhea constitutes a major cause of morbidity and mortality, especially among the children.
- Objective** To identify and determine the contribution of each of the risk factors associated with diarrhea occurrence in children in the commercial capital of Yemen, city of Aden.
- Methods** This outpatient-based case-control and questionnaire study was conducted during the first half of 2010, on random population of a total 304 cases of diarrhea and 517 controls. The explanatory variables were grouped according to the conceptual model, and analyzed by using a hierarchical approach, to provide a more dynamic view of the transmission characteristics of childhood diarrhea. Non-conditional logistic regression was used, and odds ratio and population-attributable fractions were estimated.
- Results** Factors related to food handling made a smaller contribution to diarrhea occurrence, compare to much more contribution by environmental contamination (fecal-oral transmission), and contact with one has diarrhea/ high density of housing. However the most determinant for diarrhea occurrence was the contribution of the socioeconomic factors.
- Conclusion** The data indicates that factors from all hierarchical levels were implicated in spreading of diarrhea, with relative high role for environmental contamination, and contact / crowding in the transmission. This is compatible with a predominance of the parasitic over the viral, spread by these routes. Diarrhea control strategies must emphasize on policies that improving the socioeconomic circumstances, and reducing the environmental contamination for the prevention of diarrhea.
- Keywords** Diarrhea, risk factors, children, Yemen, hierarchical model

### Introduction

Although the majority of diarrhea in children is a result of infectious agents, the etiological profile and the annual incidence of diarrheal in different populations may vary with several risk factors. Determinants for diarrhea in children therefore is complex and the relative contribution of each, varies as a function of complex interactions between the etiological agents and the risk factors. These factors could be grouped as socioeconomic, environmental, and related to contacts<sup>(1-3)</sup>.

The factors can also be classified according to their place in a chain of causation, or a causal network as distal for socioeconomic conditions as that lead to lack of a refrigerator, or proximal as for consumption of food that was not kept in a refrigerator, and according to whether they are long lasting as due to sewage disposal, or transitory as due contact with someone with diarrhea, although the 'long lasting' factors may change, for example, as a result of improvements in the sewerage network. Such events of exposure are repeatable of a clustered data. Multilevel models or hierarchical network

<sup>(4)</sup> can be applied when events are repeatable to allow for correlation between the durations to events experienced by the same individual, or when individuals are clustered into higher-level units. Over the past twenty years multilevel modeling has become a standard approach in the analysis of clustered data. This study attempted to apply the hierarchical model in analyzing of the studied risk factors of diarrhea of children at Aden city.

### Methods

This was an outpatient-based case-control design study. Performed during the first half period of 2010, on random population includes the cases and controls of children less than ten years of age who were living in the commercial capital of Yemen, the city of Aden (in the southwest, at the tip of the Arabian Peninsula near the entrance to the Red Sea, with about half million population), and seen during their visit, suffering from diarrheal episode, at the outpatient-clinics at day working period to five governmental hospitals and health centers, and two private clinics, distributed among the governorate.

Cases were considered if the main reason for patients to attend the clinic was diarrhea, and when shows three or more of diarrheal episodes during the last 24 hours; not excluded if they had taken antibiotics prior to being seen in the clinic. Controls were children presenting at the same clinics for reasons other than diarrhea and included, healthy children presenting to the well baby clinic and immunization services; children attending for mild, non-chronic diseases; orthopedic procedures, pre- or post-operative assessments relating to small surgical procedures, or dermatological problems known not to be related with hygiene and sanitation. Cases, who reported any episode of diarrhea during the preceding 3 weeks, were considered as recurrent cases.

Recurrent diarrhea in the questionnaire which then excluded from estimation therefore include the cases of acute diarrhea occurs within a month period of last episode, persistent diarrhea

that was last longer than two weeks, and cases which diagnosed as a chronic cases. Control who reported any episode of diarrhea during the preceding 3 months, were rejected. Controls were frequently matched to cases only on the base of sex and age variables, but not on how they paid for the consultation, since no big difference concerning the cost of the consultation specially that of the medication between the stated and private clinics in Yemen generally.

The information collected was from a physician and laboratory examination and from the person responsible for the child, through answering a standard, pre-coded questionnaire. The questionnaire was designed to investigate the diarrhea and the potential roles of multiple risk factors of the diarrhea, and include seven sections; 1<sup>st</sup>, on personal data, includes; Patient's name, age, sex, address, and type of payment; 2<sup>nd</sup>, on socioeconomic characteristics, includes; Patient's mother age, learning level, race, and marital status, the presence or absence of father, employment situation of the guardian, type of accommodation (house, apartment or shack), family income, and number of household goods owned by the family, includes; stove, fridge, mobile, television, air-condition, washing-machine, car and PC; 3<sup>rd</sup>, on the environmental conditions, includes; characteristics of used water and toilet, regularity of water supply, and storage type of water, sewage disposal and frequent of garbage collection, presence of animals, feces, or garbage, and occurrence of flooding at or around the house; 4<sup>th</sup>, on food handling, includes; source of child's milk, presence or absence of a person who cook the food, food cook at separate kitchen, food stored in a refrigerator, and quality of consumed foods and liquids; 5<sup>th</sup>, on the contacts of the child, includes; contacts with someone has diarrhea, time spent by child outside of the home, crowding of the family/room, and number of children under five years old /room; 6<sup>th</sup>, on a child's health, includes; vaccinations, birth weight, day care attendance and mother's age at childbirth, and;

7<sup>th</sup>, on the diarrhea characteristics, diagnosis, and treatment. Include questions about the diarrhea type, episode, and starting date, symptoms, macroscopically and microscopically analysis of feces, and treatment. The total study children were 821, of whom 304 cases and 517 controls, distributed according to their ages into seven age groups; 0-5, 6-11, 12-23, 24-35, 36-47, 48-59, and 60 up to 120 months.

### Data Analysis

SPSS version 15.0 software, USA, was used for the univariate analysis for overall sample size, to explore the association between two variables, by calculating the odd ratio (OR) of Confidence Intervals (CI) 95% with the statistical significance at  $P < 0.05$ . The variables that presented  $P < 0.05$  in the univariate analyses were then included in the next stage, which was an intra-block multivariate analysis. Multivariate analysis was used to find out whether (or not) the factors, which were significantly identified in univariate analysis, remain independently associated with the risk of diarrhea. Univariate analysis and multivariate non-conditional logistic analysis were conducted, always keeping in the models the age and sex variables that being used in the frequency matching.

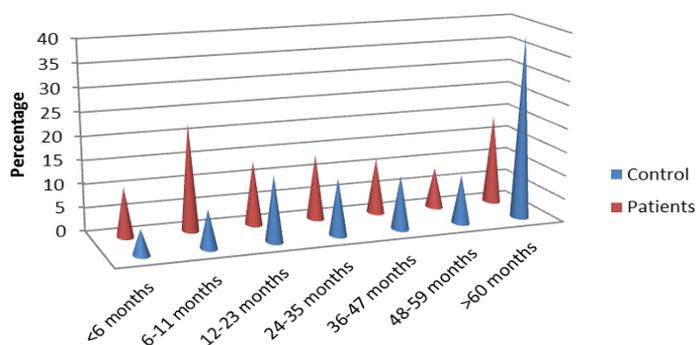
Finally, the set of variables with  $P < 0.05$  from the multivariate analysis in each block was input to hierarchical analysis. The model defined two hierarchical levels: level-1 (distal) includes the socioeconomic variables, and level-2 (proximal), includes the variables of the three block; environmental conditions, person to person contact, and food handling. Because we were interested in the effect of the distal level variables, our final estimate for the effect of distal variables is that before the introduction of proximal variables, whereas estimates of effect of the variables at the proximal level must be made after introducing the variables at distal level into the model, excluding variables with  $P > 0.05$ .

For the distal variables, the population attributable fraction (PAF) was calculated in two ways: using the OR for the level alone, to reflect

the fraction attributed to the variable whether mediated by the proximal variable or not, and using the OR after including the proximal variables, to reflect the proportion of cases attributed to the effect of the variable, which is not mediated by the proximal variables included in the final model. The proportion of cases in each age group caused by each variable PAF was calculated, using the formula:  $[(\% \text{ of exposed cases}) \times (\text{OR}-1)/\text{OR}]$ . Age was tested as a possible interaction variable by means of the likelihood ratio test (Wald test). The analyses were carried out using the STATA statistical package, version 9.0 (STATA Corporation, 2003).

### Results

The total population of this investigation, that included and corroborated into the data analysis, was 814, of which 304 acute diarrheal cases and 517 controls. Irrespective of sex, the data in figure 1 shows the distribution of the control and the case children of the total population on the base of the age groups, were respectively, 28 (5.4%) and 32 (10.5%) less than 6 months; 42 (8.1%) and 69 (22.7%) between 6 and 11-; 72 (13.9%) and 41 (13.5%) between 12 and 23-; 62 (12.0%) and 42 (13.8%) between 24 and 35-; 59 (11.4%) and 36 (11.8%) between 36 and 47-; 53 (10.3%) and 26 (8.6%) between 48 and 59-; and 201 (38.9%) and 58 (19.1%) between 60 and 120- months old. In all of the cases, three or more evacuations were reported on at least 1 day (Figure1).



**Figure 1. Age group distribution of the total population into control subjects and those with acute diarrhea**

Risk Factors for Diarrhea, list of variables that were analyzed for their possible significant association with diarrhea in a univariate analysis, ( $P \leq 0.05$ ), are shown in table 1, for the socioeconomic variables, ranked as level 1. Table 1 shows that the factors of the children's mothers who were illiterate, < 18 years old, and of Somalia race, the housing type, and the family who had less than- enough income and 4 items analyzed, were significantly associated with diarrhea in the univariate analysis, ( $P \leq 0.05$ ). Both low educational attainment and living in a shack increased the likelihood that the child had diarrhea. Living in a shack had the strongest association (OR=3.11; 95%, CI=1.93-4.97). These factors remained significantly associated in the intra-block multivariate analysis. In the intra-block multivariate analysis,

inadequate housing type remained with the highest OR (3.05; 95%, CI=1.81–4.55). List of variables that were analyzed for their possible significant association with diarrhea in a univariate analysis, ( $P \leq 0.05$ ), are shown in table 2, for the exposure risk factors of environment, contacts, and food quality, ranked as level 2. The part A of table 2 revealed that most of the environmental exposure risk factors were associated with diarrhea in univariate analysis ( $P \leq 0.05$ ), with the exclusion of the variables relating to the type of toilet, and regularity of water supply. In the intra-block multivariate analysis, the following variables remained with  $P \leq 0.05$ ; presence of feces in the backyard, sewage disposal coverage system, and two garbage-related variables: frequency of garbage collection, and closeness to open sewage ditch/garbage dump.

**Table 1. OR for the univariate<sup>a</sup> and multivariate<sup>b</sup> associations between diarrhea and the level 1 variable in the block of socioeconomic factors**

Level 1: Socioeconomic Factor		No. of Patients	No. of Controls	OR <sup>a</sup>	95%CI	OR <sup>b</sup>	95%CI
<b>Mother's Race</b>	Arabic	272	475	2.32	2.09-2.61	2.28	2.04-2.54
	Asian	06	12				
	Somalia	26	30				
<b>Mother's education</b>	Not educated	290	295	2.56	2.37-2.70	2.39	2.2-2.63
	1ry education	10	186				
	High education	04	56				
<b>Mother's Age</b>	≥18	16	12	2.28	2.12-2.4	2.09	1.89-2.51
	<18	288	505				
<b>Marital Status</b>	Married	296	494				
	Single	08	22				
	Others	0	01				
<b>Biological Father</b>	Present	286	488				
	Not	18	29				
<b>Family Income</b>	Excellent	10	18	2.45	2.13-2.81	2.08	2.01-2.29
	Fair	148	293				
	Poor	110	206				
<b>Total Goods Owned</b>	> 4 items	149	297	2.49	2.09-2.93	2.3	2.0-2.63
	Up to 4 items	155	220				
<b>Housing</b>	House	204	372	3.11	1.93-4.97	3.05	1.81-4.55
	Apartment	80	119				
	Shack	20	26				
<b>Mother Work</b>	Not working	270	451				
	At home	01	03				
	Outside home	33	63				

<sup>a</sup> Adjusted for sex, and age. <sup>b</sup> Odds ratio from the intra-block multiple regression.

Among the contact factors, crowding at room/home and contact with a person with diarrhea, were significantly associated ( $P < 0.05$ ) in the univariate and the multivariate analysis (Table 2B). Although a three of the exposures related to food handling variables, includes; the type of water offered to the child; the child

having eaten outside the home, and the children having had formula milk or readymade porridge containing milk powder, were associated with diarrhea in the univariate, only later two variables were associated with diarrhea in the intra-block multivariate analysis (Table 2C).

**Table 2a. OR for the univariate<sup>a</sup> and multivariate<sup>b</sup> associations between diarrhea and the level 2 variables in the blocks of environmental, contact, and food handling factors**

Level 2a. Environmental Factors		No. of patients	No. of Controls	OR <sup>a</sup>	95%CL	OR <sup>b</sup>	95%CL
Open Sewage Ditch/Garbage Nearby	Yes	135	215	2.48	2.07-2.92	2.04	1.73-2.58
	No	169	302				
Feces in the Backyard	Yes	260	441	2.88	2.24-2.75	2.49	2.09-3.01
	No	44	76				
Sewage Disposal Cover System	Sewage network	227	349	1.91	1.04-1.98	1.19	1.01-1.49
	Open/other	77	168				
Frequency Of Garbage Collection	Daily/every 2 <sup>nd</sup> day	200	275	2.80	2.27-3.41	2.51	2.09-2.99
	Others	104	242				
Toilet Characteristics	With water flush	145	220	2.82	2.50-3.46	2.39	2.07-2.82
	Others	159	297				
Presence of Animals at Home	Yes	116	221	2.82	2.50-3.46	2.39	2.07-2.82
	No	188	296				
Water Supply	Piped	275	445	2.82	2.50-3.46	2.39	2.07-2.82
	others	29	72				
Regularity of Water Supply	At least daily	148	195	2.82	2.50-3.46	2.39	2.07-2.82
	<once a day	156	322				
Storage Vessels	With lid	178	266	2.82	2.50-3.46	2.39	2.07-2.82
	without	126	252				
Flooding in the Household	Never	132	247	2.45	2.05-2.88	1.99	1.63-2.33
	sometimes	172	270				

Level 2b. Contact Factors		No. of patients	No. of Controls	OR <sup>a</sup>	95%CL	OR <sup>b</sup>	95%CL
Child in contact with one has diarrhea	Yes	49	56	2.90	2.53-3.54	2.90	2.98-2.87
	No	255	460				
Crowding (people/room)	Up to 2 persons	182	298	1.93	1.55-2.46	1.94	1.77-2.28
	2 or more child	122	129				
No. of children under 5 years old/house	Up to one child	192	339	1.38	1.19-1.59	1.13	1.00-1.37
	2 or more child	112	178				
Child spend > 1 day outside house	Yes	40	43	1.38	1.19-1.59	1.13	1.00-1.37
	No	264	474				

Level 2c. Food handling Factors		No. of patients	No. of Controls	OR <sup>a</sup>	95%CL	OR <sup>b</sup>	95%CL
Child on milk	Breastfed	131	175	2.42	2.00-2.89	1.82	1.58-2.26
	Can`s milk/other	173	342				
Type of water offered to the child	Filtered/boiled	128	195				
	/minerals others	176	322				
Child consumed food not stored in a refrigerator	Yes	208	367				
	No	96	150				
Child consumed food outside home	Yes	87	181	2.46	2.07-2.90	2.40	2.20-3.63
	No	217	336				
Child consumed food from floor	Yes	52	57	1.97	1.50-2.38	1.93	1.76-2.13
	No	252	460				
Absence of person routinely prepares food	Yes						
	No						
Separate kitchen	Yes	273	470				
	No	31	47				

<sup>a</sup> Adjusted for sex, and age. <sup>b</sup> Odds ratio from the intra-block multiple regression

Table 3 shows the results from the final multivariate hierarchical analysis. The estimated values for socioeconomic variables are those who shown significant association in the final intra-block model, and for the proximal levels in the model including the distal level. The effects of house type, illiterate mother, owning of up to four items, sewage disposal system, were greater in groups from 3 to 10 years old the effect of presence nearby of sewage ditch/garbage was greatest in children between 2 and 5 years old. The variables that increased the risk of diarrhea by >50% were: shack-type housing (OR=3.01), contact with people with diarrhea (OR=2.9), and sewage disposal system

(OR=2.8). The variables with the strongest effect were not those responsible for the largest number of cases. The PAF for socioeconomic variables was 43%, and the large proportional contribution towards this was from low educating level for the mother (16%) and ownership of less than four household items (14%), and shack-type housing (10%). The block of variables relating to person-to-person contact presented a total PAF of 28%, predominantly made up of contact with people with diarrhea in the previous 10 days, and overcrowding, with PAFs of 16% and 9%, respectively, while that related to environmental conditions and food handling were 17% and 12% respectively.

**Table 3. OR & PAF derived from hierarchical multiple regression <sup>a</sup> on the risk factors for diarrhea.**

Level 1		OR	CI 95%	PAF(%) <sup>b</sup>
Socioeconomic Factors	Mother with no education	2.31	2.02-2.64	16
	Family of low income	2.34	2.15-2.56	14
	Shack-type housing	3.01	1.69-4.57	10
Level 2		OR	CI 95%	PAF(%) <sup>b</sup>
Environmental contamination	Present nearby of swage ditch/garbage Dump	2.43	2.07-2.90	09
	Open sewage disposal system/Others	2.80	2.08-3.64	08
Food preparation	Child ate food outside of the home	2.28	2.08-2.51	0.9
	Child not on breastfeed	2.65	2.42-2.89	0.8
Contact/crowding	Contact with one has diarrhea	2.90	2.28-3.39	16
	Three or more people per room/home	2.31	2.02-2.70	09

<sup>a</sup> Adjusted for sex, and age. <sup>b</sup> Population attributable fraction.

## Discussion

This case-control study, examined risk factors for diarrhea among children less than 10 years old in the city of Aden/Yemen. The present analysis addresses diarrhea as a public health issue, without presenting here the data from analysis of; child's health section, current treatment approaches; the complex interactions between the different etiological agents and the several diarrheal risk factors, as well as the part of data concerning the univariate analysis of exposure to diarrhea under the influence of the studied variables, since it has been carried out before<sup>(5)</sup>.

The presentation of this study that almost all of the risk exposure factors which associated with diarrhea in univariate analysis, were remained associated with diarrhea in the multivariate analysis ( $P < 0.05$ ), and that the multivariate hierarchical model of benefit in presenting the obtained new resultant values which mediating the effects, on the diarrhea burden, of the socioeconomic variables following to the interrelation in this model between the socioeconomic variables of level 1, with the different risk factors of level 2 (environmental contamination, food handling, and person-to-person contact), may interpret the implication of various infectious agents (parasitic, bacterial or viral) into the etiology of diarrhea, since each of these pathological agents have different transmission mechanisms and depend on complex social and environmental factors, particularly in large cities.

The distribution of diarrhea according to the pathogenic agents in Aden as one of the cities of the developing countries is not resembled to what occurs in the context of the developed countries<sup>(5)</sup>. In the developed countries, the viral etiological agents predominate over the bacterial or parasitic agents; a context where the importance of direct contact between people has been consistently demonstrated. This emphasizes the importance of direct contact between children for the transmission of pathogenic agents in these environments and accords with the growing importance of viral

agents, beside also other agents spreading by interpersonal routes including *Shigella*, *Giardia* and *Cryptosporidium*, in the pathogenesis of diarrhea<sup>(6,7)</sup>.

The presenting by Rashid and Abbas<sup>(5)</sup> in children of Aden city, of higher frequency of diarrheal cases due to the parasitic etiology than that of the viral cause, may interpreted in view of our finding that the variables of a relatively high PAF such as contact with one has diarrhea and three or more people per room (28%), presence nearby of sewage ditch/garbage dump and sewerage disposal system (17%), and child ate food outside of the home (9%), which collectively increased the risk of diarrhea by >50%, may therefore considered a strong possible transmission route of diarrhea of parasitic etiology.

Contact with human excreta can be primary, when defecating, or secondary due to contact with released sewage in children's playing sites and passages, and sanitation is the most powerful tools in controlling primary or secondary contact with sewage. However, availability of a sewerage system does not always necessarily mean a low incidence in acute diarrheal diseases<sup>(6)</sup>. Undoubtedly, individual sanitation and the supervision role of the parents are the most powerful tools in controlling primary or secondary contact with sewage. What corroborate this explanation, is the finding of significant ( $P < 0.05$ ) association with diarrhea of children of age groups 2-5 years old who where were closeness to open sewage ditch/garbage dump<sup>(5)</sup>, and also the notion that Giardiasis is common in other societies like Salvador, where 13.7% of young children were found to be infected, and that gastrointestinal pathogens (e.g. bacteria or parasite) are predominantly transmitted by food or water, whereas person-to-person transmission is a major route for the transmission of viral diarrhea among children<sup>(6-8)</sup>.

Regarding food, we found an association between diarrhea and the child having eaten outside of the home, and also an association with child's not on breastfeed. These may be

related to the quality of the care taken in preparing the food offered to the child. There is evidence that food prepared at home carried a lower risk of diarrhea, while the introduction of new foods to young children increases the risk of diarrhea<sup>(3,9)</sup>. Of the exposures traditionally associated with diarrhea, such as deficient water supply and inadequate sewage disposal<sup>(10)</sup>, only the later appear in the final model. This is in a partial agreement with other study<sup>(7)</sup>, which showed that both were not appear in the final model. Irregularity in water supply (may reduce the frequency of good hygiene practices like washing hands and objects...etc, or could even lead to direct contamination of the water) showed no association with diarrhea<sup>(11)</sup>. Appearance of inadequate sewage disposal in the final model of our study is in a good agreement with the longitudinal study carried out in Salvador<sup>(12)</sup>, suggesting that access to a sewerage system may have a strong influence on the incidence of diarrhea.

Since the risk factors with high ORs in our data were very limited, the PAF therefore may be more useful for defining priorities for interventions that would have a greater impact in reducing the disease burden. Our results show that socioeconomic factors include shack type-housing, low schooling of mother, and ownership of less than four items (level 1) were responsible for a large proportion of the diarrhea burden, with PAF of 49% that reduced to 43% after controlling for the exposures studied (level 2). This is in consistent with the finding of other studies<sup>(7)</sup>.

In conclusion, diarrhea is a complex multifactorial process related to the precarious living conditions, and to transitory factors occurred shortly before the episode. The risk factors identified here do not include water (traditional risk factors for diarrhea) but sanitation, probably reflecting the needs for investment in establishing of sanitation network to begin in Aden city as soon as possible. Improvement of environmental sanitation and domestic hygiene and raising the socioeconomic

status including the education of the population will contribute to the elimination of the underlying causes of acute diarrhea.

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