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## Risk factors for shigellosis in Thailand

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Risk factors;  
Case-control study;  
Housefly;  
Fly species;  
Fly density

### Summary

**Objectives:** To assess the potential risk factors for shigellosis including housefly density.

**Methods:** A matched case-control study to investigate potential risk factors for shigellosis was conducted in a semi-urban area, Kaengkhohi District, Saraburi Province, central Thailand. *Shigella* cases were ascertained from a two-year population-based surveillance study detecting diarrhea and shigellosis in the area. The study evaluated a wide range of exposures, which were assessed by odds ratios (OR) adjusted for proxy markers of socioeconomic status: family income, and type of residence, using conditional logistic regression analysis.

**Results:** Hygiene behaviors such as regular hand washing ( $p < 0.05$ ), a clean environment surrounding the household ( $p < 0.001$ ), and the availability of water to flush the toilet ( $p = 0.08$ ) were associated with a reduced risk for shigellosis in the multivariate model. In contrast factors indicating a lower than average socioeconomic status, such as having to rent instead of owning one's housing ( $p < 0.001$ ) and a low family income ( $p < 0.01$ ) were associated with an increased risk for shigellosis. For children, breastfeeding showed a strong protective effect in reducing the risk of shigellosis ( $p < 0.01$ ). Prior to adjustment for environmental factors, fly density in the kitchen area was associated with an increased risk of shigellosis ( $p < 0.01$ ).

**Conclusions:** We found a correlation between socioeconomic status and the risk for shigellosis. To reduce shigellosis in this setting, we recommend interventions focused on three aspects: improved water supply and sanitation (especially latrines and garbage disposal) including fly control, health education on hand washing, and the promotion of breastfeeding.

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## Introduction

Diarrhea and dysentery are major causes of morbidity in many countries worldwide and affect those living in impoverished conditions most.<sup>1</sup> With the shift to urban living and improved socioeconomic status in Southeast Asia, the burden of diarrhea and shigellosis is expected to decline. However recent studies indicate that a considerable shigellosis burden remains in Thailand.<sup>2,3</sup> Few population-based studies on risk factors for shigellosis have been published, in particular in Thailand.<sup>4</sup> Most data have come from outbreak investigations, and such studies have shown associations between shigellosis and the consumption of unboiled water,<sup>5,6</sup> attending school,<sup>7</sup> contaminated food,<sup>7</sup> and household contacts.<sup>8</sup> There are few population-based studies on correlates of shigellosis risk even though the risk factors may differ between epidemic and endemic scenarios. Shigellosis has been shown to be associated with weaning practices, in particular among severely malnourished children.<sup>9–11</sup> Children cared for in day-care centers have been shown to have a higher risk for shigellosis than children who are cared for at home.<sup>12</sup>

Population-based surveillance for diarrhea and shigellosis was conducted in Kaengkhoi District, central Thailand between 2000 and 2002 to estimate the shigellosis burden in this part of Thailand.<sup>2</sup> During the first two years of surveillance, culture-confirmed shigellosis cases and healthy matched controls were enrolled in a case-control study. Data were collected on exposure to potential risk factors such as water supply and sanitation, hygiene behavior, and socioeconomic status. This paper reports potential risks adjusted for exposure to potential confounding factors.

## Methods

### Study population

The study area is located in Kaengkhoi District, Saraburi Province, Thailand, approximately 100 km northeast of Bangkok. The area includes a small city with some industry that is surrounded by rural villages that depend on agriculture for income. Data from the 2001 census maintained by government healthcare officers show a total population of 80 141 in the catchment area, including 5686 (7%) children under 60 months of age.

### Healthcare system

Healthcare utilization in Kaengkhoi District has recently been reviewed in detail.<sup>13</sup> In brief, the healthcare system has three tiers with the first contact being the community health center, usually a free-standing structure staffed by one or more nurses who provide basic health services, stabilize emergency patients for transport elsewhere, and perform uncomplicated deliveries. There are 20 community health centers in the study catchment area. Each health center provides care for a population of approximately 4000 individuals. Patients who cannot be adequately cared for at the community health center are transferred to the district hospital in Kaengkhoi, which is staffed by internists, pediatricians, and surgeons. Patients who require more specialist services or therapies not available in the district hospital are transferred to the provincial hospital near Kaengkhoi Dis-

trict. Some doctors working at government hospitals earn extra income by seeing patients at their private clinics in the evenings. A survey conducted in 2000 found 16 private clinics in the study area. Not all patients seek care at public or private clinics; some patients treat themselves with over-the-counter pharmaceuticals or traditional products. Residents are allocated to government health centers that can be the community health center or the outpatient department of a hospital. Current government policy encourages patients to attend their assigned primary healthcare provider by charging reduced user fees. All community health centers in the study area, the district hospital, and the provincial hospital participated in the surveillance study.

### Study design

All shigellosis cases ascertained from the population-based surveillance study were eligible to be included in a matched case-control study. However, during the peak of the shigellosis season in June 2001, only 14 of the 50 shigellosis cases were recruited into the study (Figure 1). To be eligible to participate in the study, cases had to attend a study health facility with diarrhea (three or more loose stools, or at least one watery, bloody, or mucoid stool in the 24 hours prior to visiting the health facility) and *Shigella* had to be isolated from a rectal swab. For each case enrolled, two matched controls were randomly selected from the population list of the health center where the case resided (Figure 1). Controls were matched for sex and age with the cases: within three months for children under 2 years old; within six months for children under 5 years old; within twelve months for children under 16 years old; and within five years for adults aged 16 years and over. Individuals free from diarrhea or dysentery during the four weeks prior to recruitment were eligible to participate in the study as controls.<sup>14</sup> All study participants had to live in the study area for at least six months.

The same interviewer visited the households of cases and controls. A standardized questionnaire was administered to explore water supply, sanitation, behaviors related to hygiene, and other potential risk factors for diarrhea in the household of the respondent. Parents or guardians provided information on children. Water supply, sanitation, hygiene, and the presence of flies in the household were directly observed by the interviewer. Fly density was measured using a Scudder grill<sup>15</sup> in six different locations (toilet, kitchen, dish-washing area, rubbish area, animal pen, and other fly aggregating sites) in the house of the respondent. A fly net (17 inches diameter) was used to collect flies at the location with the highest fly aggregation. Flies were pinned and stored with the name and the address of the respondent. The species of flies were identified at the Department of Entomology, Faculty of Tropical Medicine, Mahidol University in Bangkok. Income estimates were based on the income of the respondent, and in the case of children was based on the income of their parents. The distance from the residence of the respondent to the healthcare facility was measured by motorcycle mileage.

### Laboratory methods

Healthcare providers collected rectal swabs from diarrhea cases, which were transported to Saraburi Provincial Hospital

by courier for *Shigella* isolation using standard bacterial culture method. *Shigella* isolates were confirmed by the reference laboratory (World Health Organization Salmonella and Shigella Center) at the Ministry of Public Health in Nonthaburi. The detailed laboratory methods have been described elsewhere.<sup>2</sup>

### Sample size

The number of cases and matched controls was selected to give 80% power to detect odds ratios (OR) of 2.0 or greater with 5% significance for risk factors with a prevalence of between 19% and 70% in the controls.

### Analysis methods

The matched case-control study was analyzed using conditional logistic regression. Stata/SE 8.0 (Stata Corporation, College Station, TX, USA) was used for the analysis. The odds ratios and 95% confidence intervals were estimated for the association between shigellosis and each risk factor, and the significance of the association was determined using likelihood ratio tests. Five variables potentially confounding any association with shigellosis were defined prior to analysis: the type of healthcare facility (community health center, private clinic, hospital), distance from home to health facility, type of residence, family income, and number of family members in the household. Two of these, type of residence and family income, demonstrated an independent association with shigellosis and were used to adjust all univariate associations. All variables with  $p < 0.1$  in the univariate analysis were included in a final multivariate model, but were dropped if the significance of the association after adjustment for other factors was  $p \geq 0.1$ . Associations with  $p < 0.05$  were regarded as significant.

### Ethics

All participants were provided with the written study information and further written consent was obtained from each participant (parent or guardian for children) before the household interview. The study received approval from the local government, Kaengkhoi District, Saraburi Province, Thailand; the Ministry of Public Health at Nonthaburi; the ethics review committee of the London School of Hygiene and Tropical Medicine, London, UK and the Secretariat Committee for Research Involving Human Subjects, World Health Organization, Geneva, Switzerland.

### Results

The assembly of the 403 participants in the study, 139 cases and 264 matched controls is shown in Figure 1. One hundred and twenty-five cases were matched to two controls and 14 cases were matched to one control. The matching ensured that cases and controls were similar in age (the median age was 5 years for both cases and controls), sex (57% of the cases and 58% of the controls were female), and residence. A similar proportion of cases and controls resided in each sub-district with a non-significant difference ( $p = 1.0$ , Chi-square test).

All five potential confounding factors (healthcare provider, distance to healthcare facility, type of residence, family income, and number of family members) showed an independent association with the risk of shigellosis ( $p < 0.1$ , Table 1). Individuals who rented their accommodation had a significantly higher risk of shigellosis (OR = 11.2, 95% CI 3.6–35.0) compared to those who owned their accommodation. People with a family income less than or equal to 5000 baht per month had more than two-fold increased risk for shigellosis ( $p < 0.01$ ) compared to those with no reported

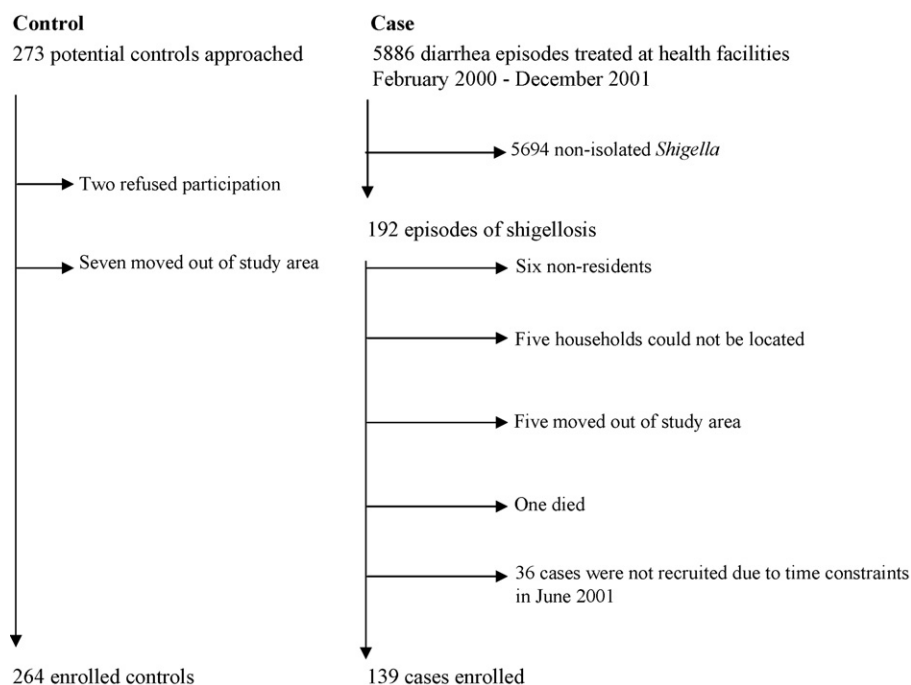


Figure 1 Consort chart for case/control recruitment.

**Table 1** Association between risk of shigellosis and socioeconomic and demographic variables in Kaengkhoi, Thailand

Factors	Levels	Cases <i>N</i> = 139 <i>n</i> (%)	Controls <i>N</i> = 264 <i>n</i> (%)	Univariate analysis OR (95% CI)	<i>p</i> Value <sup>a</sup>	Adjusted analysis <sup>c</sup> OR (95% CI)	<i>p</i> Value <sup>a</sup>	
Usual health facilities visited by family members ( <i>N</i> = 253)	Health Center	43 (50)	82 (49)	1.0	<i>p</i> < 0.001	NA		
	Private clinics/ outside KK <sup>b</sup>	4 (5)	42 (25)	0.2 (0.1–0.7)				
	KK <sup>b</sup> hospital	39 (45)	43 (26)	2.1 (0.9–4.7)				
Distance from home to health facilities ( <i>N</i> = 253)	<5.6 km	58 (67)	103 (62)	1.0	<i>p</i> > 0.01	NA		
	5.6–10 km	21 (24)	31 (19)	1.3 (0.7–2.6)				
	>10 km	7 (8)	33 (20)	0.4 (0.1–0.9)				
Type of residence ( <i>N</i> = 398)	Owned	35 (25)	96 (37)	1.0	<i>p</i> < 0.001	NA		
	Rented	24 (17)	11 (4)	11.2 (3.6–35.0)				
	Relatives' house	65 (47)	136 (52)	1.3 (0.8–2.3)				
	Public or work accommodation	14 (10)	17 (7)	2.5 (1.0–6.1)				
Family income ( <i>N</i> = 394)	No income	21 (15)	58 (23)	1.0	<i>p</i> < 0.01	NA		
	≤5000 baht	70 (51)	84 (33)	2.3 (1.2–4.3)				
	>5000 baht	46 (34)	115 (45)	1.0 (0.5–2.0)				
Family members ( <i>N</i> = 402)	Up to 3 members	35 (25)	48 (18)	1.0	<i>p</i> > 0.01	NA		
	4	39 (28)	85 (32)	0.7 (0.4–1.2)				
	5	27 (19)	58 (22)	0.7 (0.4–1.3)				
	6	11 (8)	39 (15)	0.4 (0.2–1.0)				
	7–11	27 (19)	33 (13)	1.2 (0.6–2.5)				
Trend over groups <sup>d</sup>				1.0 (0.9–1.1)	<i>p</i> > 0.1			
Drinking bottled water ( <i>N</i> = 402)	No	93 (67)	202 (77)	1.0	<i>p</i> < 0.01	1.0	<i>p</i> > 0.01	
	Yes	46 (33)	61 (23)	2.6 (1.4–5.1)				2.4 (1.1–5.2)
Having an amount of water in the latrine (for flushing) ( <i>N</i> = 381)	No	7 (5)	2 (1)	1.0	<i>p</i> < 0.01	1.0	<i>p</i> > 0.01	
	Yes	126 (95)	246 (99)	0.2 (0.03–0.7)				0.2 (0.03–0.9)
Having toilet paper in the latrine ( <i>N</i> = 381)	No	130 (98)	230 (93)	1.0	<i>p</i> > 0.01	1.0	<i>p</i> > 0.01	
	Yes	3 (2)	18 (7)	0.3 (0.1–1.1)				0.2 (0.05–1.1)
Defecating in the household area instead of using latrine ( <i>N</i> = 367)	No	82 (64)	174 (73)	1.0	<i>p</i> > 0.01	1.0	<i>p</i> > 0.01	
	Yes	46 (36)	65 (27)	2.3 (1.1–4.7)				2.0 (1.0–4.4)
Frequency of hand washing per day ( <i>N</i> = 387)	Up to 3	94 (70)	145 (58)	1.0	<i>p</i> < 0.01	1.0	<i>p</i> > 0.01	
	>3 times	41 (30)	107 (42)	0.5 (0.3–0.8)				0.5 (0.3–0.9)
Washing hands before meals ( <i>N</i> = 390)	Never	47 (35)	46 (18)	1.0	<i>p</i> < 0.01	1.0	<i>p</i> > 0.001	
	Sometimes	51 (38)	127 (50)	0.4 (0.2–0.7)				0.5 (0.3–0.8)
	Regularly	37 (27)	82 (32)	0.4 (0.2–0.8)				0.4 (0.2–0.9)

Trend over groups <sup>d</sup>				0.7 (0.5–0.9)	$p < 0.01$	0.6 (0.5–0.9)	$p > 0.001$
Using baskets as rubbish bin in the kitchen ( $N = 401$ )	No	122 (88)	245 (94)	1.0	$p > 0.01$	1.0	$p > 0.01$
	Yes	17 (12)	17 (6)	2.1 (1.0–4.4)		2.1 (0.9–5.0)	
Disposal of rubbish (without bin) near the kitchen ( $N = 379$ )	No	79 (60)	170 (69)	1.0	$p > 0.01$	1.0	$p > 0.01$
	Yes	54 (40)	76 (31)	1.7 (1.0–2.7)		1.7 (1.0–2.8)	
Cleanliness in front of the household area ( $N = 378$ )	No rubbish	12 (9)	43 (17)	1.0	$p < 0.001$	1.0	$p < 0.001$
	Little rubbish	10 (8)	50 (20)	0.6 (0.2–1.7)		0.4 (0.1–1.3)	
	Some rubbish	45 (34)	64 (26)	2.9 (1.3–6.6)		2.3 (1.0–5.6)	
	A lot of rubbish	64 (49)	90 (36)	2.9 (1.4–6.4)		2.0 (0.9–4.5)	
Trends over groups <sup>d</sup>				1.5 (1.2–2.0)	$p < 0.001$	1.4 (1.1–1.8)	$p < 0.01$
Animal observed in the household area ( $N = 396$ )	No	50 (37)	112 (43)	1.0	$p > 0.1$	NA	
	Yes	87 (63)	147 (57)	1.4 (0.9–2.1)			
Animal feces observed in the household area (among households with animals in the household) ( $N = 186$ )	No	39 (53)	71 (63)	1.0	$p > 0.01$	1.0	$p > 0.01$
	Yes	34 (47)	42 (37)	2.3 (1.1–5.1)		2.9 (1.2–7.3)	
Cleanliness of the fridge ( $N = 279$ )	Fair to very clean	41 (40)	93 (53)	1.0	$p > 0.01$	1.0	$p > 0.01$
	Dirty to very dirty	61 (60)	84 (47)	1.7 (1.0–2.9)		1.7 (1.0–3.0)	
Cooking on the table at least 60 cm height ( $N = 395$ )	No	107 (78)	169 (66)	1.0	$p < 0.01$	1.0	$p > 0.1$
	Yes	30 (22)	89 (34)	0.5 (0.3–0.8)		0.8 (0.4–1.4)	
Cooking on the floor ( $N = 400$ )	No	20 (15)	65 (25)	1.0	$p > 0.001$	1.0	$p > 0.1$
	Yes	118 (85)	197 (75)	2.0 (1.1–3.5)		1.5 (0.8–2.8)	
Visiting school ( $N = 393$ )	No	74 (54)	106 (41)	1.0	$p < 0.01$	1.0	$p > 0.01$
	Yes	62 (46)	151 (59)	0.4 (0.3–0.8)		0.5 (0.3–0.9)	
Having visitor(s) from outside village ( $N = 390$ )	No	109 (81)	178 (70)	1.0	$p > 0.001$	1.0	$p > 0.01$
	Yes	26 (19)	77 (30)	0.5 (0.3–0.9)		0.6 (0.3–1.1)	
Breastfeeding ( $N = 205$ )	No	69 (97)	123 (92)	1.0	$p > 0.01$	1.0	$p > 0.01$
	Yes	2 (3)	11 (8)	0.3 (0.07–1.4)		0.3 (0.06–1.4)	
Frequency of milk feeding per day ( $N = 204$ )	≤1 times	28 (40)	42 (32)	1.0	$p > 0.01$	1.0	$p > 0.01$
	2–5	40 (56)	72 (54)	0.7 (0.4–1.4)		1.0 (0.4–2.1)	
	>5	3 (4)	19 (14)	0.1 (0.01–0.8)		0.1 (0.01–0.9)	
Trends over groups <sup>d</sup>				0.5 (0.3–1.0)	$p > 0.01$	0.6 (0.3–1.1)	$p > 0.01$
Fly density in the kitchen area ( $N = 403$ )	None	98 (71)	212 (80)	1.0	$p > 0.01$	1.0	$p < 0.01$
	≥1 flies	41 (29)	52 (20)	1.8 (1.1–3.0)		2.3 (1.3–4.1)	

Table 1 (Continued)

Factors	Levels	Cases N = 139 n (%)	Controls N = 264 n (%)	Univariate analysis OR (95% CI)	p Value <sup>a</sup>	Adjusted analysis <sup>c</sup> OR (95% CI)	p Value <sup>a</sup>
Total fly density in the household (N = 403)	None	34 (25)	81 (31)	1.0	p > 0.01	1.0	p > 0.1
	1–5 flies	23 (17)	59 (22)	1.0 (0.5–2.0)		1.1 (0.5–2.3)	
	6–15	27 (19)	50 (19)	1.5 (0.7–2.8)		1.4 (0.7–3.0)	
	16–35	29 (21)	40 (15)	2.0 (1.0–3.8)		1.8 (0.9–3.7)	
	≥36	26 (19)	34 (13)	2.5 (1.1–5.3)		2.5 (1.1–5.7)	
Trend over groups <sup>d</sup>				1.3 (1.1–1.5)	p < 0.01	1.2 (1.0–1.5)	p > 0.01

<sup>a</sup> Likelihood ratio test.

<sup>b</sup> Kaengkhoh.

<sup>c</sup> Adjusted for type of residence and family income.

<sup>d</sup> Analysis of trend across the categories.

income. Even though all were significant in the univariate analysis, after adjustment for other factors only two variables – type of residence and family income – remained significant and were included in all multivariate models.

After adjustment for type of residence and family income, the following associations were significant at  $p < 0.1$  in univariate analyses:

### Water use, latrine use, and hand washing habits

Drinking bottled water increased the risk for shigellosis (OR = 2.4, 95% CI 1.1–5.2,  $p = 0.02$ , Table 1). The presence of water for flushing or toilet paper in the latrine had a protective effect against shigellosis ( $p < 0.05$ ). People not using latrines and having to defecate in the environment around the household showed a two-fold increased risk for shigellosis compared to latrine users ( $p = 0.06$ ). Regular hand washing (three times a day or more) reduced the risk for shigellosis significantly (OR = 0.5, 95% CI 0.3–0.9,  $p = 0.02$ ). Similarly washing hands regularly before meals reduced the risk for shigellosis significantly (OR = 0.4, 95% CI 0.2–0.9,  $p = 0.01$ ). Hand washing after meals (OR = 0.4, 95% CI 0.2–1.0,  $p = 0.02$ ), before cooking (OR = 0.2, 95% CI 0.04–0.8,  $p = 0.05$ ), and after defecation (OR = 0.4, 95% CI 0.2–0.8,  $p = 0.04$ ) appeared protective against shigellosis.

### Household cleanliness and cooking facilities

Using an open, unhygienic basket as a rubbish bin in the kitchen increased the risk for shigellosis (OR = 2.1, 95% CI 0.9–5.0,  $p = 0.08$ , Table 1). Rubbish disposal (with no rubbish bin) close to the kitchen increased the risk for shigellosis (OR = 1.7, 95% CI 1.0–2.8,  $p = 0.06$ ). The presence of animals in the household had no significant effect on the risk of shigellosis but the presence of animal excreta in the household increased the risk for shigellosis nearly three-fold (OR = 2.9, 95% CI 1.2–7.3,  $p = 0.02$ ) after the adjustment for socioeconomic status. The correlation of other household variables such as the cleanliness of the refrigerator and cooking facilities are shown in Table 1.

### Other associations with shigellosis

Adults and children visiting school appeared to be protected against shigellosis (OR = 0.5, 95% CI 0.3–0.9,  $p = 0.03$ , Table 1). Having visitors from outside the village was also associated with protection against shigellosis (OR = 0.6, 95% CI 0.3–1.1,  $p = 0.07$ ). Children who drank milk more than five times a day were highly protected against shigellosis compared to children who only drank milk once a day or less (OR = 0.1, 95% CI 0.01–0.9,  $p = 0.02$ ). Fly density in the household correlated with the risk of shigellosis. However, only fly density in the kitchen area was independently significant (OR = 2.3, 95% CI 1.3–4.1,  $p < 0.01$ ). Houseflies (*Musca domestica*) were found in 53% of the study households.

### The final model

The final model included household cleanliness, water for flushing the latrine, hand washing (before meal), visiting



**Table 2** Final model of the association between risk of shigellosis and other independent variables in Kaengkhroi District, Thailand

Factors	Levels	Cases n (%)	Controls n (%)	Adjusted analysis OR (95% CI)	p-Value <sup>a</sup>
Type of residence (N = 398)	Owned	35 (26)	96 (37)	1.0	p < 0.001
	Rented	24 (17)	11 (4)	20.3 (3.5–117.6)	
	Relatives' house	65 (47)	136 (52)	1.2 (0.6–2.4)	
	Public/work accommodation	14 (10)	17 (7)	2.1 (0.5–9.2)	
Family income (N = 394)	No income	21 (15)	58 (22)	1.0	p < 0.01
	≤5000 baht	70 (51)	84 (33)	3.7 (1.5–8.7)	
	>5000 baht	46 (34)	115 (45)	1.8 (0.8–4.3)	
Cleanliness in front of the household area (N = 378)	No rubbish	12 (9)	43 (17)	1.0	p < 0.001
	Little rubbish	10 (8)	50 (20)	0.3 (0.1–1.0)	
	Some rubbish	45 (34)	64 (26)	2.4 (0.9–6.5)	
	A lot of rubbish	64 (49)	90 (37)	2.0 (0.8–5.1)	
Trends over groups <sup>b</sup>				1.5 (1.1–1.9)	p < 0.01
Having an amount of water in the latrine (for flushing) (N = 381)	No	7 (5)	2 (1)	1.0	p > 0.01
	Yes	126 (95)	246 (99)	0.2 (0.03–1.4)	
Washing hands before meals (N = 390)	Never	47 (35)	46 (18)	1.0	p > 0.01
	Sometimes	51 (38)	127 (50)	0.4 (0.2–0.7)	
	Regularly	37 (27)	82 (32)	0.5 (0.2–1.1)	
Trend over groups <sup>b</sup>				0.6 (0.4–1.0)	p > 0.01
Visiting school (N = 393)	No	74 (54)	106 (41)	1.0	p > 0.01
	Yes	62 (46)	151 (59)	0.5 (0.2–1.0)	
Having visitor(s) from outside the village (N = 390)	No	109 (81)	178 (70)	1.0	p > 0.01
	Yes	26 (19)	77 (30)	0.5 (0.2–1.1)	
Breastfeeding (N = 205)	No	69 (97)	123 (92)	1.0	p < 0.01 <sup>c</sup>
	Yes	2 (3)	11 (8)	0.05 (0.01–0.6)	

<sup>a</sup> Likelihood ratio test p-value adjusted for type of residence, family income, cleanliness in front of the household, having water in the latrine, washing hands before meals, visiting school, and having visitors from outside the village.

<sup>b</sup> Analysis of trend across the categories.

<sup>c</sup> For breastfeeding, analysis restricted to children under 5 years of age: likelihood ratio test p-value adjusted for type of residence, family income, and household cleanliness.

school, having visitors from outside, and breastfeeding (Table 2). The socioeconomic factors included in the final model were type of residence and family income. Some rubbish or a lot of rubbish in front of the household showed a two-fold increased risk of shigellosis ( $p < 0.001$ ). An amount of water (for flushing) in the latrine showed an 80% protective effect (OR = 0.2, 95% CI 0.03–1.4,  $p = 0.08$ ). Regular hand washing before meals was associated with 50% protection against shigellosis (OR = 0.5, 95% CI 0.2–1.1,  $p < 0.05$ ), similar to visiting schools (OR = 0.5, 95% CI 0.2–1.0,  $p < 0.05$ ) and having visitors (OR = 0.5, 95% CI 0.2–1.1,  $p = 0.08$ ). Breastfeeding was associated with the strongest protective effect reducing the risk of shigellosis by 95% (OR = 0.05, 95% CI 0.01–0.6,  $p < 0.01$ ). Fly density was not independently significant in the final model.

## Discussion

This is the first population-based case-control study on risk factors for shigellosis across all ages. However, the high incidence of shigellosis among children resulted in children being the dominant age group in our sample. We found

several factors independently associated with an increased risk for shigellosis: renting accommodation instead of owning the accommodation, a low family income, dirty environment surrounding the household, and inadequate sanitation and hygiene. Our study found that visiting school and having visitors from outside reduced the risk of shigellosis, whereas other studies, usually conducted during shigellosis outbreaks, have shown that social gatherings and school contacts increase the risk of shigellosis.<sup>7,16,17</sup> Our study coincided with a campaign for hand washing and tooth brushing after lunch among the schools in the study area, which may have reduced shigellosis transmission. Hand washing alone or hand washing accompanied with tooth brushing may interrupt *Shigella* transmission. If so, this school-based intervention could be a powerful strategy for control and prevention of shigellosis including diarrheal diseases.<sup>8,16,18</sup>

Breastfeeding was found to have the strongest independent protective effect of the factors under investigation, reducing the risk of shigellosis by 95%. However, the estimate of this effect was relatively imprecise with wide 95% confidence interval, due to the low number of cases and controls of breastfeeding age in the study. Earlier studies found that

breastfeeding reduced the risk for shigellosis by 50–60%, which is consistent with our estimate.<sup>10,11,19</sup> Moreover, it has been shown in a case-control study in Bangladesh that breastfeeding may reduce the severity of shigellosis (defined by rectal temperature above 102 °F (39 °C), severe neurologic manifestation, or severe dehydration) by 50% (OR = 0.49,  $p = 0.01$ ) among children aged under three years.<sup>9</sup>

We found hand washing before meals, after meals, before cooking, and after defecation was associated with a reduced risk for shigellosis. Our findings are consistent with others that found an inverse association between hand washing and shigellosis.<sup>20,21</sup> In our study hand washing, especially hand washing before meals, was associated with a decreased risk for shigellosis.

The presence of water for flushing the latrine was found to reduce the risk of shigellosis as was observed in a diarrhea study in Malaysia.<sup>22</sup> Perhaps this finding suggests that water quantity as well as water quality are essential to protect health.<sup>23,24</sup> Our finding that household cleanliness, here defined as rubbish in front of the household, was associated with an increased risk of shigellosis is novel. It is possible that this association is a residual effect of socioeconomic status not removed by adjustment for type of accommodation and income. Alternatively, stagnant latrines without water for flushing and rubbish in front of the household may be independent environmental exposures.

The study confirms that inadequate water supply and sanitation are principal risk factors for shigellosis. Contaminated water supply has been documented as a cause of shigellosis outbreaks worldwide.<sup>6,25–27</sup> Surprisingly our findings show drinking bottled water increases the risk for shigellosis. Explanations include contamination of the bottled water or that those households having only access to poor quality water make use of bottled water.<sup>28,29</sup>

Earlier studies isolated enteric pathogens including *Shigella* species from houseflies, *Musca domestica*,<sup>30,31</sup> the predominant species in 53% of the study households. Ours is the first study to show a correlation between fly density in the household and a risk for shigellosis. The strongest correlation was observed in the kitchen area strongly suggesting contamination of foods through contact with flies.<sup>32</sup> Although fly density was not significant in the final risk factor model, the trend with increased numbers of flies in the univariate analysis was strongly suggestive of an increased risk of shigellosis. Other environmental factors such as rubbish in front of the household and latrines without water for flushing may contribute to the presence of flies and were a confounder for the effect of flies in this analysis.

This case-control study utilized the district-wide active surveillance of diarrhea patients to identify cases of shigellosis,<sup>2</sup> most of whom were recruited into our study. Some cases with less severe shigellosis and cases attending health-care providers not participating in our surveillance may have been missed. To minimize bias, controls were matched on age, sex, and residence, which are known to be associated with shigellosis.<sup>19,33</sup> Proxy variables for socioeconomic status were used to adjust associations in the analysis. The majority of shigellosis cases were children, but risk factors were assessed across all age groups. Risk factors for shigellosis may differ between adults and children, but our study did not have sufficient power to consider age groups separately. The statistical power of the study was not sufficient to evaluate

rare exposures. This lack of power resulted in relatively imprecise estimates, indicated by wide confidence intervals for some exposures. A further limitation of our study was the un-blinded status of the investigator visiting the households and conducting interviews to the case/control status of the participant. This knowledge could have introduced bias in the data collection, although the agreement of our findings with earlier studies suggests otherwise.

Our study findings suggest a clear message for three areas in which interventions to prevent shigellosis should be concentrated. Firstly, there should be a provision of safe water, sanitation, and fly control in all households. Water in the latrine and garbage disposal should be improved. The avoidance of dumping or burning rubbish around the household and the control of flies in the household should be essential steps in the future prevention of shigellosis. Secondly, the promotion of hygiene, especially hand washing, suggests that effective health messages may be provided through schools. Thirdly, breastfeeding should be promoted to all mothers with young children.

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## References

1. Kotloff KL, Winickoff JP, Ivanoff B, Clemens JD, Swerdlow DL, Sansonetti PJ, et al. Global burden of *Shigella* infections: implications for vaccine development and implementation of control strategies. *Bull World Health Organ* 1999;77:651–66.
2. Chompook P, Samosornsuk S, Von Seidlein L, Jitsanguansuk S, Sirima N, Sudjai S, et al. Estimating the burden of shigellosis in Thailand: 36-month population-based surveillance study. *Bull World Health Organ* 2005;83:739–46.
3. Lee H, Kotloff K, Chukaseram P, Samosornsuk S, Chompook P, Deen JL, et al. Shigellosis remains an important problem in children less than 5 years of age in Thailand. *Epidemiol Infect* 2005;133:469–74.
4. Echeverria P, Taylor D, Leksomboon U, Bhaibulaya M, Blacklow NR, Tamura K, et al. Case-control study of endemic diarrheal disease in Thai children. *J Infect Dis* 1989;159:543–8.
5. Taylor DN, Bodhidatta L, Brown JE, Echeverria P, Kunanusont C, Naigowit P, et al. Introduction and spread of multi-resistant *Shigella dysenteriae* I in Thailand. *Am J Trop Med Hyg* 1989;40:77–85.
6. Swaddiwudhipong W, Karintraratana S, Kavinum S. A common-source outbreak of shigellosis involving a piped public water



- supply in northern Thai communities. *J Trop Med Hyg* 1995; **98**:145–50.
7. Hoge CW, Bodhidatta L, Tungtaem C, Echeverria P. Emergence of nalidixic acid resistant *Shigella dysenteriae* type 1 in Thailand: an outbreak associated with consumption of a coconut milk dessert. *Int J Epidemiol* 1995; **24**:1228–32.
  8. Gaudio PA, Sethabutr O, Echeverria P, Hoge CW. Utility of a polymerase chain reaction diagnostic system in a study of the epidemiology of shigellosis among dysentery patients, family contacts, and well controls living in a shigellosis-endemic area. *J Infect Dis* 1997; **176**:1013–8.
  9. Clemens JD, Stanton B, Stoll B, Shahid NS, Banu H, Chowdhury AK. Breast feeding as a determinant of severity in shigellosis. Evidence for protection throughout the first three years of life in Bangladeshi children. *Am J Epidemiol* 1986; **123**:710–20.
  10. Ahmed F, Clemens JD, Rao MR, Sack DA, Khan MR, Haque E. Community-based evaluation of the effect of breast-feeding on the risk of microbiologically confirmed or clinically presumptive shigellosis in Bangladeshi children. *Pediatrics* 1992; **90**:406–11.
  11. Ahmed F, Clemens JD, Rao MR, Khan MR, Haque E. Initiation of food supplements and stopping of breast-feeding as determinants of weaning shigellosis. *Bull World Health Organ* 1993; **71**:571–8.
  12. Sempertegui F, Estrella B, Egas J, Carrion P, Yerovi L, Diaz S, et al. Risk of diarrheal disease in Ecuadorian day-care centers. *Pediatr Infect Dis J* 1995; **14**:606–12.
  13. Samosornsuk S, Jitsanguansuk S, Sirima N, Sudjai S, Tapchaisri P, Chompook P, et al. Preferences for treatment of diarrhoea and dysentery in Kaengkhohi district, Saraburi province, Thailand. *J Health Popul Nutr* 2004; **22**:113–8.
  14. Ramasoota P, Sutthienkul O, Supanvanich S, Sittichokesakulchai V. Factors related to becoming a carrier among *Shigella flexneri* patients in Prae provincial hospital. *Journal of Epidemiology (in Thai)* 1993; **1**:37–43.
  15. Raybould JN. Further studies on techniques for sampling the density of African house fly populations. II. A field comparison of the Scudder grill and the sticky-flytrap method for sampling the outdoor density of African house flies. *J Econ Entomol* 1966; **59**:644–8.
  16. Mohle-Boetani JC, Stapleton M, Finger R, Bean NH, Poundstone J, Blake PA, et al. Communitywide shigellosis: control of an outbreak and risk factors in child day-care centers. *Am J Public Health* 1995; **85**:812–6.
  17. Weissman JB, Gangorosa EJ, Schmerler A, Marier RL, Lewis JN. Shigellosis in day-care centres. *Lancet* 1975; **1**:88–90.
  18. Newman CP. Surveillance and control of *Shigella sonnei* infection. *Commun Dis Rep CDR Rev* 1993; **3**:R63–8.
  19. Ahmed F, Clemens JD, Rao MR, Ansaruzzaman M, Haque E. Epidemiology of shigellosis among children exposed to cases of *Shigella* dysentery: a multivariate assessment. *Am J Trop Med Hyg* 1997; **56**:258–64.
  20. Birmingham ME, Lee LA, Ntakibirora M, Bizimana F, Deming MS. A household survey of dysentery in Burundi: implications for the current pandemic in sub-Saharan Africa. *Bull World Health Organ* 1997; **75**:45–53.
  21. Khan MU. Interruption of shigellosis by hand washing. *Trans R Soc Trop Med Hyg* 1982; **76**:164–8.
  22. Knight SM, Toodayan W, Caique WC, Kyi W, Barnes A, Desmarchelier P. Risk factors for the transmission of diarrhoea in children: a case-control study in rural Malaysia. *Int J Epidemiol* 1992; **21**:812–8.
  23. Lewin S, Stephens C, Cairncross S. Reviewing the health impacts of improvements in water supply. *Urban Health Newsl* 1997:34–47.
  24. Cairncross S. More water: better health. *People Planet* 1997; **6**:10–1.
  25. Egoz N, Shmilovitz M, Kretzer B, Lucian M, Porat V, Raz R. An outbreak of *Shigella sonnei* infection due to contamination of a municipal water supply in northern Israel. *J Infect* 1991; **22**:87–93.
  26. Rosenberg ML, Weissman JB, Gangarosa EJ, Reller LB, Beasley RP. Shigellosis in the United States: ten-year review of nationwide surveillance, 1964–1973. *Am J Epidemiol* 1976; **104**:543–51.
  27. Pal S, Sengupta P, Sen D, Bhattacharya S, Deb B. Epidemic shigellosis due to *Shigella dysenteriae* type 1 in South Asia. *Indian J Med Res* 1989; **89**:57–64.
  28. Jensen PK, Ensink JH, Jayasinghe G, van der Hoek W, Cairncross S, Dalsgaard A. Domestic transmission routes of pathogens: the problem of in-house contamination of drinking water during storage in developing countries. *Trop Med Int Health* 2002; **7**:604–9.
  29. Kaltenthaler EC, Drasar BS. The study of hygiene behaviour in Botswana: a combination of qualitative and quantitative methods. *Trop Med Int Health* 1996; **1**:690–8.
  30. Levine OS, Levine MM. Houseflies (*Musca domestica*) as mechanical vectors of shigellosis. *Rev Infect Dis* 1991; **13**:688–96.
  31. Echeverria P, Harrison B, Tirapat C, McFarland A. Flies as a source of enteric pathogens in a rural village in Thailand. *Appl Environ Microbiol* 1983; **46**:32–6.
  32. Mensah P, Yeboah-Manu D, Owusu-Darko K, Ablordey A. Street foods in Accra, Ghana: how safe are they? *Bull World Health Organ* 2002; **80**:546–54.
  33. Boyce JM, Hughes JM, Alim AR, Khan M, Aziz KM, Wells JG, et al. Patterns of *Shigella* infection in families in rural Bangladesh. *Am J Trop Med Hyg* 1982; **31**:1015–20.