

Supplemental Material

Supplemental Table 1: Primer sequences for DEC pathotype assays

DEC	Target gene(s)	Name	Sequence (5' to 3')	Reference
EAEC	<i>aaiC</i>	EAEC215F ¹	ATTGTCCTCAGGCATTTCAC	Boisen <i>et al.</i> , 2008
		EAEC215R ¹	ACGACACCCCTGATAAACA	
EAEC	<i>aatA</i>	EAEC650F ¹	CTGGCGAAAGACTGTATCAT	Schmidt <i>et al.</i> , 1995
		EAEC650R ¹	CAATGTATAGAAATCCGCTGTT	
EIEC	<i>ipaH</i>	EIEC423F ³	CTGGTAGGTATGGTGAGG	Luscher and Altwegg, 1994
		EIEC423R ³	GGAGGCCAACAATTATTTCC	
EPEC/ EHEC	<i>eae</i>	EPEC881F ¹	CCCGAATTCGGCACAAGCATAAGC	Luscher and Altwegg, 1994
		EPEC881R ¹	CCCGGATCCGTCTCGCCAGTATTCG	
EPEC	<i>bfpA</i>	EPEC300F ¹	GGAAGTCAAATTCATGGGGG	Taniuchi <i>et al.</i> , 2012
		EPEC300R ¹	GGAATCAGACGCAGACTGGT	
ETEC	<i>LT</i>	ETEC508F ²	CACACGGAGCTCCTCAGTC	Taniuchi <i>et al.</i> , 2012
		ETEC508R ²	CCCCCAGCCTAGCTTAGTTT	
	STp	STp_VX67356F ²	TCTTTCCCTCTTTTAGTCAG	Rodas, <i>et al.</i> , 2009
		STp_VX67356R ²	ACAGGCAGGATTACAACAAAG	
	STh	STh_ST64111F ²	TTCACCTTTCCCTCAGGATG	
		STh_ST64111R ²	CTATTCATGCTTTCAGGACCA	

*Table modified from Taniuchi, 2012. ^{1,2, and 3} indicate the multiplex set.

The multiplex PCR reactions contain 12.5µL of 2X KAPA Taq Ready Mix with Dye, 3µL of DNA template, 4 µL of primer master mix, and 5.5µL of sterile deionized water to a final volume of 25µL. The thermal cycling profile is as follows: 94°C for 3 min; followed by 26 cycles of 94°C for 1 min, 55°C for 1.5 min, and 72°C for 1.5 min, with a final extension at 72°C for 10 min.

Supplemental Table 2: Details of antibiotics used for antimicrobial susceptibility test on all bacterial isolates

Pathogens	No. of Isolates		Antibiotics						
	Case	Control	AMP	AZM	CIP	CRO	ERY	NAL	SXT
<i>Aeromonas</i> spp.	180	148	✓	✓	✓	✓	-	✓	✓
<i>Arcobacter</i> spp.	11	13	-	✓	✓	-	✓	✓	-
<i>Campylobacter</i> spp.	29	21	-	✓	✓	-	✓	✓	-
Diarrheagenic <i>E. coli</i>	160	154	✓	✓	✓	✓	-	✓	✓
<i>Plesiomonas shigelloides</i>	107	71	✓	✓	✓	✓	-	✓	✓
<i>Salmonella</i> spp.	93	104	✓	✓	✓	✓	-	✓	✓
<i>Shigella</i> spp.	24	1	✓	✓	✓	✓	-	✓	✓
<i>Vibrio parahaemolyticus</i>	2	0	✓	✓	✓	✓	-	✓	✓
<i>Yersinia enterocolitica</i>	1	0	✓	✓	✓	✓	-	✓	✓

Antibiotics: ampicillin (AMP), azithromycin (AZM), ciprofloxacin (CIP), ceftriaxone (CRO), erythromycin (ERY), nalidixic acid (NAL), and trimethoprim/sulfamethoxazole (SXT).

Supplemental Table 3: Distribution of subject enrollment across the enrolling hospitals

Study site	No. of subjects			Grand Total
	Cases	Controls	Follow up cases	
Anlong Veng Referral Hospital	254	196	146	596
Battambang Referral Hospital	41	42	9	92
Military Reginal 5 Hospital	198	184	145	527
Oudormeanchey Hospital	298	286	274	858
SvayPor Health Center	127	83	101	311
Grand Total	918	791	675	2384

Supplemental Table 4: Details of infection types in cases

Infection types	Cases (N=918)	
	n	%
Bacteria (sole)	198	22%
Bacteria and Parasite	29	3%
Bacteria more than 1 species	102	11%
Parasite (sole)	23	3%
Parasites more than 1 species	1	0%
Virus (sole)	110	12%
Virus and Bacteria	51	6%
Virus and Parasite	11	1%
Virus more than 1 species	5	1%
Virus and Bacteria and Parasite	3	0%
Grand Total	533	58%

Supplemental Table 5: Details of enteropathogen subtypes

Organism	Subtype	% of organism	CASE		CONTROL	
			N	%	N	%
<i>Aeromonas</i>	<i>Aeromonas caviae</i>	41.2%	81	8.8%	54	6.8%
	<i>Aeromonas hydrophila</i>	23.5%	38	4.1%	39	4.9%
	<i>Aeromonas veronii</i> biovar <i>sobria</i>	35.4%	61	6.6%	55	7.0%
<i>Arcobacter</i>	<i>Arcobacter butzleri</i>	66.7%	11	1.2%	5	0.6%
	<i>Arcobacter cryaerophilus</i>	8.3%	0	0.0%	2	0.3%
	<i>Arcobacter</i> spp.	25.0%	0	0.0%	6	0.8%
<i>Campylobacter</i>	<i>Campylobacter coli</i>	32.0%	11	1.2%	5	0.6%
	<i>Campylobacter hyointestinalis</i>	8.0%	0	0.0%	4	0.5%
	<i>Campylobacter jejuni</i> subsp. <i>doylei</i>	2.0%	1	0.1%	0	0.0%
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i>	52.0%	17	1.9%	9	1.1%
Diarrheagenic <i>E. coli</i>	<i>Campylobacter</i> spp.	6.0%	0	0.0%	3	0.4%
	EAEC-aaiC	23.6%	38	4.1%	36	4.6%
	EAEC-aaiC, aatA	20.1%	27	2.9%	36	4.6%
	EAEC-aatA	22.3%	35	3.8%	35	4.4%
	EIEC-ipaH	1.3%	3	0.3%	1	0.1%
	EPEC-eae	21.7%	35	3.8%	33	4.2%
	EPEC-eae, bfpA	0.0%	0	0.0%	0	0.0%
	ETEC-lt	3.8%	6	0.7%	6	0.8%
	ETEC-lt, st-Ia	1.9%	4	0.4%	2	0.3%
	ETEC-lt, st-Ib	0.3%	1	0.1%	0	0.0%
	ETEC-st-Ia	1.9%	4	0.4%	2	0.3%
	ETEC-st-Ib	1.9%	6	0.7%	0	0.0%
	STEC-stxII (LF)	1.0%	1	0.1%	2	0.3%
	STEC-stxII, eae (LF)	0.3%	0	0.0%	1	0.1%
<i>Plesiomonas</i>	<i>Plesiomonas shigelloides</i>	100.0%	107	11.7%	71	9.0%
<i>Salmonella</i>	<i>Salmonella</i> group B	23.4%	26	2.8%	20	2.5%
	<i>Salmonella</i> group C	39.1%	34	3.7%	43	5.4%
	<i>Salmonella</i> group D	5.1%	4	0.4%	6	0.8%
	<i>Salmonella</i> group E	18.3%	18	2.0%	18	2.3%
	<i>Salmonella</i> group F	0.0%	0	0.0%	0	0.0%
	<i>Salmonella</i> group G	5.6%	4	0.4%	7	0.9%
	<i>Salmonella</i> group H	1.0%	1	0.1%	1	0.1%
	<i>Salmonella</i> group I	3.0%	4	0.4%	2	0.3%
	<i>Salmonella</i> group K	0.5%	0	0.0%	1	0.1%
	<i>Salmonella</i> group N	0.0%	0	0.0%	0	0.0%
	<i>Salmonella</i> group O	3.0%	1	0.1%	5	0.6%
	<i>Salmonella</i> spp.	1.0%	1	0.1%	1	0.1%

Supplemental Table 5: Details of enteropathogen subtypes (Continued)

Organism	Subtype	% of organism	CASE		CONTROL	
			N	%	N	%
<i>Shigella</i>	<i>Shigella boydii</i> 2	8.0%	2	0.2%	0	0.0%
	<i>Shigella flexneri</i> 1a	8.0%	2	0.2%	0	0.0%
	<i>Shigella flexneri</i> 2a	28.0%	7	0.8%	0	0.0%
	<i>Shigella flexneri</i> 4a variant	24.0%	5	0.5%	1	0.1%
	<i>Shigella sonnei</i>	32.0%	8	0.9%	0	0.0%
<i>Vibrio</i>	<i>Vibrio parahaemolyticus</i>	100.0%	2	0.2%	0	0.0%
<i>Yersinia</i>	<i>Yersinia enterocolitica</i>	100.0%	1	0.1%	0	0.0%
Norovirus	NoV-GI	14.6%	5	0.5%	2	0.3%
	Nov-GII	85.4%	32	3.5%	9	1.1%
Sapovirus	Sapo-124	78.3%	25	2.7%	11	1.4%
	Sapo-5	21.7%	5	0.5%	5	0.6%

Supplemental Table 6.1: Details of antimicrobial resistance profiles for enteric bacterial pathogens

Pathogens	AMP				AZM				CIP				CRO				NAL				SXT			
	CASE	%	CONTROL	%	CASE	%	CONTROL	%	CASE	%	CONTROL	%	CASE	%	CONTROL	%	CASE	%	CONTROL	%	CASE	%	CONTROL	%
<i>Aeromonas</i>	180	100%	148	100%	21	12%	14	9%	20	11%	11	7%	31	17%	24	16%	99	55%	87	59%	48	27%	31	21%
<i>Diarrheagenic E. coli</i>	128	80%	110	71%	75	47%	62	40%	40	25%	22	14%	60	38%	39	25%	99	62%	78	51%	93	58%	66	43%
<i>Plesiomonas</i>	52	49%	38	54%	1	1%	0	0%	17	16%	12	17%	4	4%	0	0%	22	21%	14	20%	12	11%	7	10%
<i>Salmonella</i>	42	45%	48	46%	3	3%	5	5%	5	5%	10	10%	11	12%	9	9%	18	19%	26	25%	19	20%	32	31%
<i>Shigella</i>	15	63%	1	100%	0	0%	0	0%	15	63%	1	100%	1	4%	0	0%	17	71%	0	0%	20	83%	1	100%
<i>Vibrio</i>	2	100%	NI	NI	0	0%	NI	NI	0	0%	NI	NI	0	0%	NI	NI	0	0%	NI	NI	0	0%	NI	NI
<i>Yersinia enterocolitica</i>	1	100%	NI	NI	0	0%	NI	NI	0	0%	NI	NI	0	0%	NI	NI	0	0%	NI	NI	0	0%	NI	NI

Antimicrobial resistance profiles are shown as a percentage for selected enteric bacterial pathogens from cases and controls for the antibiotics ampicillin (AMP), azithromycin (AZM), ciprofloxacin (CIP), ceftriaxone (CRO), nalidixic acid (NAL), and trimethoprim/sulfamethoxazole (SXT). NI - no isolate.

Supplemental Table 6.2: Details of antimicrobial resistance profiles for enteric bacterial pathogens (*Arcobacter* and *Campylobacter*)

Pathogens	AZM				CIP				ERY				NAL			
	CASE	%	CONTROL	%	CASE	%	CONTROL	%	CASE	%	CONTROL	%	CASE	%	CONTROL	%
<i>Arcobacter</i>	11	100%	13	100%	1	9%	8	62%	4	36%	5	38%	2	18%	8	62%
<i>Campylobacter</i>	4	14%	9	43%	26	90%	17	81%	1	3%	3	14%	27	93%	18	86%

Antimicrobial resistance profiles are shown as a percentage for selected enteric bacterial pathogens from cases and controls for the antibiotics azithromycin (AZM), ciprofloxacin (CIP), erythromycin (ERY), and nalidixic acid (NAL).