WEB TABLE II EPIDEMIOLOGY OF CRYPTOSPORIDIUM IN ACUTE DIARRHEA FROM STUDIES WITHOUT NON-DIARRHEAL CONTROLS

Author, year	*Place of study*	*Study population*	*Detection methods*	*Positivity rates*	*Associated risk*	*Clinical associates/ Remarks*
Hospital-based studies						
Mengist, *et al.* 2015 [46]	Ababa, Ethiopia	Age: 1-18 yr. 180 HIV positive- 79 on HAART, 101 non-HAART	Modified Ziehl Neelsen staining	HAART- None Non-HAARt-4/101 (3.9%)	Low CD4 counts <350/mm3; adjusted OR, 95%CI: 13(10.5, 97.6), P<0.01] than in non-HAART group	No opportunistic parasite in those on HAART. *Entamoeba histolytica* was commonest; seen in 10%
Bera , *et al*. 2014 [47]	Delhi, India	Age: < 5 yr. 168 children with AD	Kinyoun method, followed by ELISA	Kinyoun method- 7/168 (4.1%), ELISA 48/168 (28.6%)	No association with breastfeeding, drinking water supply, contact with animals, malnutrition	Dehydration seen only in 4 patients.
Eraky, *et al.* 2014 [48]	Benha, Egypt	Age: 1-14 yr 430 samples	Microscopy followed by PCR	50/430 (11.6%)	Not mentioned	Increased detection of *C. parvum* (82%) than *C. hominis* (12%), mixed (6%)
Charles *, et al.* 2014 [49]	Haiti	Age: <15 yr 3602 children with AD	Luminexxtag GPP polymerase chain reaction in 210 samples for parasites	24/ 210 (11.4%)	No increased risk with seropositivity	HIV positive were at risk for invasive bacterial pathogens
Feng *, et al.* 2012 [50]	Shanghai, China	Age: 1 month–19 yr. 6284 Children	PCR and restriction fragment length Polymorphism analysis	102/6284 (1.6%)	Young age: <6m (8.4%, 95% CI 5.6–11.2) than older (1.9%, 95% CI 1.4–2.4)	
Haider *, et al.*, 2012 [51]	Karachi, Pakistan	Age: 0-19 yrs 339 stool Samples with abdominal pain, Vomiting, constipation, diarrhea and fever.	Kinyoun method	37/339 (10.9%)	More common in summers, no correlation with rainfall.	Cryptosporidium was mono-infection in 26/37. Diarrhea in 54%, abdominal pain in 48%, constipation in 38%, fever 30%, vomiting 28%
Elgun *, et al.*, 2011 [52]	Adana, Turkey	Age: <12 yr HIV positive children	Modified Ziehl–Neelsen staining, ELISA	5.2% by staining, 67.6% with ELISA		ELISA sensitivity-100%, specificity-80.1%

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Moyo , *et al.*, 2011 [53]	Dar es Salaam, Tanzania	Age:<5 years 280 with diarrhea (AD-84%, PD-9.6%, dysentery- 6%)	Immunocard STAT! Rapid Assay- (distinguishes Giardia from C. Parvum)	18.9% (51/280).		
Yu , *et al.* 2011 [54]	Hunan Province, China.	Age: <2yr 140 with AD	Auramine–phenol staining, modified acid-fast staining, and the polymerase chain reaction.	1.4%, (2/140)		PCR detected one additional case than rest two
Ajjampur , *et al.* 2010 [55]	Delhi, Trichy and Vellore, India	Age:<5 yr 2579 with AD	Microscopy, PCR-RFLP, and/or sequencing at the Small-subunit (SSU) rrna and Cpgp40/15 loci for species determination and subgenotyping, respectively	70/ 2,579 (2.7%)	Young Age: 75% children <2yr. Season: Hotter summers and dried winters in Delhi; negative correlation with humidity	*C.hominis* most type with subgenotypes- Ie, Ia, Ib, and Id
Idris , *et al.* 2010 [56]	Jakarta, Indonesia	Age: 6m- 18yr. 42 with HIV/ malignancy/ WHA <70%/ immuno-suppressive drug and PD or recurrent diarrhea	Modified Ziehl–Neelsen staining.	2/42 (4.7%)	Both were HIV positive (low CD4). Higher risk for any protozoal infection in toddler age <3 yr, WHA<70%, unhygienic water supply	Treatment: paromomycin syrup at 10 mg/kg three times a day for ten days.
Areeshi , *et al.*, 2008 [57]	Antananarivo, Madagascar.	Age: 1day-16 yr 215 with AD	Modified Ziehl–Neelsen Method and commercial enzyme immuno-assay (prospect). Confirmed samples were genotyped	12/215 (5.6%)	Young age: <2yr- 10/12 (83%) were in second year of life	*C. hominis* (Gp60 Type I) most frequent. Additional 4 children were false positive with EIA, later found negative with microscopy.
Natividad , *et al.* 2008 [58]	Philippines	Age: <18 yr 2160 stool samples	Merifluor Giardia-Cryptosporidium direct fluorescence kit	Solitary infection- 2.9%, Mixed infection with Giardia- 4.8%	Highest isolation 0-4 yr. No difference with gender. Higher risk in rainy season	
Pelayo , *et al.*, 2008 [59]	Havana, Cuba	Age: 2-8 yr Children with diarrhea(denominator NA)	Modified acid-fast staining, fluorescein-Labelled mixture of Giardia- and Cryptosporidium-specific monoclonal antibody and nuclear stain DAPI followed by PCR	30 children positive.	Higher risk if not BF in 2-5 yr group. Most infected children washed hands and fruits	Most common symptom- anorexia (68%), abdominal pain- 57%, Vomiting was rare (7%). All C. Hominis positive, none for C.parvum.

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Morse , *et al.*, 2007 [60]	Malawi.	Age: < 5 yr 848 stool samples over 22 months	Modified Ziehl–Neelsen(mzn), auramine phenol (AP), immunofluorescence (IF) followed by (PCR–RFLP) of oocyst-extracted DNA using 18S rrna and COWP gene loci.	5·9% (50/848)	Young Age- 85% were <2 yr. Higher rate in rainy season. No role of gender.	*C. hominis* in 48% and *C. parvum* in 18%. N18S rrna confirmed 100% cases.
Gatei , *et al.* 2006 [61]	Microbiological lab data, Kenya	Age: 0m- 5yr 4899 stool samples collected over 2 years	Modified Ziehl–Neelsen staining. Further Genotyping using nested PCR for 18S rrna	4%.	Young age: 13-24 months age (5.2%). PD- High OR (2.19; CI 1.463–3.29). Season- Driest seasons that follow slight rains. No role of gender	66.4% AD, 21% recurrent diarrhea, 9% PD. 51% had abdominal swelling and vomiting. 87% isolates were *C.hominis*
Hamedi , *et al.* 2005 [62]	Bandar Abbas Iran,	Age: 6m-7yr 245 with diarrhea	Modified Ziehl–Neelsen staining.	17/245 (7%) in AD. 6/14 (5.7%) in PD	Young age (<24m), underweight (P=0.01), those with siblings <10 yr age. Breastfeeding protective. No association with source of drinking water, parents' occupation,	Positive isolate- had longer duration of diarrhea (10 vs 3 days)
Dlamini , *et al.* 2005 [63]	Swaziland, Southern Africa	Age:<5 yr 48 with diarrhea	Anti-Cryptosporidium monoclonal antibody (TCS Water Sciences, UK) and stained with 4'6 diamidino-2-phenylindole (DAPI)	2/48 (4.2%)	NA	NA
Lee , *et al.* 2005 [64]	Chungju, Korea	Age: 0-10 yr 286 with diarrhea	Modified Acid-fast staining- positive considered as *C.parvum*	1/286 (0.3%)	NA	NA

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Pereira , *et al.* 2002 [65]	Goiânia, capital of Goiás State in Brazil.	Age: 2wk-10 yr 445 Children with diarrhea	Direct immunofluorescent assay f/b immunomagnetic separation,	64/445 (14.4%) with DFA, 83/445(18.7%) with immunomagnetic separation	Risk- Infancy OR-0.5, 90%CI 0.36–0.68, P<0.0001, day care attendance (OR 2.1; 1.1-3.8), childhood contact with diarrhea (OR 1.9; 1.4-2.7), late rainfall (OR-3.7;1.7-8.3). No risk with gender (OR-2.2, CI=0.13-3.8). No relation with breast-feeding, diet and type of food hygiene, source and type of treatment of drinking water, presence of sewage, and animal exposure	
Torres , *et al.* 2001 [66]	Uruguay	Age: 1 to 20 m. 224with PD (135) or AD (89).	Modified Ziehl-Neelsen (Kinyoun) procedure	19/224 (8.4%) in diarrheal group.	NA	NA
Essers , *et al.* 2000 [67]	Bern, Switzerland	Age:5 weeks- 15 yr. 312 with AD	Use of auramine-carbolfuchsin And visualized by fluorescent microscopy on concentrated stool sample	15/312 (4.8%).	No etiology specific seasonality seen.	Children with cryptosporidial diarrhea were younger than those with bacterial infection
Burgner , *et al.* 1999 [68]	New South Wales, Australia	60 oncology patients with diarrhea (mean age 5.5 yr). 172 non-oncology patients with diarrhea (mean age 4 yr)	Modified Ziehl–Neelsen staining.	Nil in 149 samples of oncology patients vs 23/173 (13.3%) samples from non-oncology patients	NA	No seasonal variation seen. Only *C. Pavum* investigated for
Nath , *et al.* 1999 [69]	Banaras Hindu University, Varanasi	Age: 0-15 yr. Children with AD	M/E- counterstaining with methylene blue	99/1337(7.4%)	Detection higher in rainy season	Absence of fecal leucocytes and erythrocytes in all

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Enriquez , *et al.* 1997 [70]	Mexico city, Mexico	Age: <5yr 403 cases with AD	Modified Acid fast stain, Indirect IFA (OW50)	26/403 (6.4%)	Age below 1 yr. Weight for age deficit >25%-OR-2.9; Ci 1.1-7.5. Breastfeeding protective (9% vs 37%;P<0.01) No relation with gender, antibiotic use, dwelling characteristics, water supply	Majority cases had fever and vomiting No increased detection of seropositivity IFA detected 26; Staining only 20/26 (sensitivity 76.9%, specificity 98.9%)
Brannan , *et al.* 1996 [71]	Romania	Age: 12-52 m 60 HIV infected children and 32 malnourished (WAZ<65%) children	Immunofluorescent assay and trichrome-stained fecal smear. ELISA based IgA & IgG tested in positive subjects	11/60 (18%)in sero-positive vs nil among malnourished	Seropositivity and increasing severity of malnutrition	No increased detection of Giardia in positive cases
Gennari-Cordoso , *et al.* 1996 [72]	Uberlândia, State of Minas Gerais, Brazil	Age 0-12 yr 94 with AD	Safranin/Methylene Blue and the Kinyoun (modified) staining method	4.26%	Older age: 0-2yr=5.08%, 8-10yr =33.3%, Rainy season	Mixed infection in 20%
(b) Community–based studies						
Daniels, *et al*. 2015 [73]	Odisha, India	Age 6m-79 yr 85 stool samples	Immunomagnetic separation and direct immunofluorescence antibody tests	12%	Increased propensity for <2 yr (OR 0.8-17; p=0.09) No relation with gender, rural/ urban.	Geometric mean concentration of oocysts maximum in dog stool samples, followed by sheep, goat, cattle and buffalo. Cattle contributed to 61% of animal population and greatest environmental parasitic load. Water contamination higher in ponds than tube wells (95% CI: 2.9–10.1)
Helmy , *et al.* 2014 [74]	Ismailia province, Egypt	Age: <10 yr 165 stool samples with AD	Enzyme immunoassay (EIA), ICT, PCR	1.8%		Detection – 2.4% with EIA, 6.7% ICT, 49% PCR

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Sarkar, *et al*. 2013 [75]	Vellore, India. Prospective 2 yr	Age: 0-6m. 176: Protected (80)- family consuming bottled drinking water, Unprotected (80)- municipal drinking water supply	Stool microscopy, anti-Gp 15 antibody by ELISA and PCR 13/76 of asymptomatic children positive only by serology	186 episodes in 118 (67%) children.	No difference with type of drinking water. Risk with HAZ<-2 at 6 m age for diarrhea, not sp. Cryptosp. (OR-1.4, 1.03–1.91)	Diarrhea with cryptosporidium lasted longer (4d) & was more severe than non-cryptosp diarrhea.No associated with fever, vomiting 76 (64.4%) had only asymptomatic infection, 12 (10.2%) only diarrhea and 30 (25.4%) had both. *C. hominis* isolated in 80%
Wegayehu, *et al.* 2013 [76]	North Shewa Zone, Oromia Region, Ethiopia	aged 1-14 yr. 384 apparently healthy children	Modified Ziehl-Neelsen staining method	28/384 (7.3%)	Higher in those with close contact with cattle (8.5% vs 6.2; *P*=0.39). No difference with age or gender	
Mondal, *et al.* 2012 [77]	Mirpur, Dhaka, Bangladesh	Age 0-7 days 147 babies till 12m age	Real time PCR	18/420 (4.28%)	Children stunted at birth (r=0.25, *P*=0.057)	
Abu Samra , *et al.* 2012 [78]	Four sites in South Africa (part of rotavirus surveillance)	Age: 0-5 years Total 442 stool samples	Modified Ziehl–Neelsen staining. 80% subjected to molecular analysis (18S PCR and gp60 PCR)	12.2% (54/442);	Young age: 40/54 in infants	*C. hominis* more frequent (76%) than C. Parvum (20%)
Vahedi, *et al.* 2012 [79]	Mazandaran province, Iran	Age: child-adult. 475/962 with AD were <20 yr	Ziehl-Neelsen acid fast stain and Auramin Phenol fluorescence	0.1%	No difference with gender or age	
Vandenberg, *et al.* 2012 [80]	Brussels	Age: not specified 130 children	Microscopy, antigen tests, and real-time PCR	38/122 (31%)		29/38 (76%) symptomatic, 9/38 (24%) asymptomatic 27 symptomatic treated with Paromomycin for 2 weeks. 9 /27 also with nitazoxanide.
Sejdidni, *et al*. 2011 [81]	Albania	6m-16 yr. 321 healthy children	Formalin–ether concentration and Ziehl–Neelsen staining	0.3%	No relation with gender or age	
Siwila, *et al.* 2011 [82]	Kafue district, Zambia Prospective over 12 months	Age:36-72m 100 healthy children- 786 stool samples	Immunofluorescence microscopy	241/786 (30.7%). 86/100 had ≥1 positive episode	No relation with gender or season	Diarrhea frequent- 69/100. 63/69 were positive

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Adamu, *et al.* 2010 [83]	Nine regions of Ethiopia	Age 1-45 years 1034 diarrheal stool samples.	Modified Ziehl-Neelson staining. Gene analysis from positive samples for COWP, SSU-rrna and GP60 gene fragments	79/1034 (7.6%)	No relation with seropositivity. Direct physical contact with calves-35.4% (28/79)	*C. parvum* in 39/41, rest were *C. hominis*
Ajjampur, *et al.* 2010 [84]	Vellore, India. 2 year longitudinal follow up	Age: ≤2 yr. twenty subjects 1036 samples- 196 diarrheal and 840 surveillance samples	SSU RNA PCR based detection	35 episodes of cryptosporidiosis among 20 subjects.	Single vs multiple episodes- EBF as risk (P=0.001) No risk with gender, SES, maternal education, child's age, presence of animal in house	71% (25/35) had diarrhea, 28.6% (10/35) were asymptomatic. Relapses usually asymptomatic 31/35 episodes were due to *C. hominis*. Multiple episodes in 8/20 children (40%).
Mondal, *et al.* 2009 [85]	Mirpur, Urban slum, Dhaka, Bangladesh	Age: 2-5 years. 289 children	Modified Ziehl–Neelsen staining	Incidence episode /100 child year- 7.27 with WAZ >-2 and 12.19 with WAZ<-2	Low WAZ<-2 RR= 1.7 (1.1, 2.6); attributable proportion as 40%. No risk with age, stunting, drinking water source	
Cama, *et al.* 2008 [86]	Pampas de San Juan de Mirafl ores, Lima. 4-year longitudinal	Age: birth cohort. 368/533 children included	Modified Ziehl–Neelsen staining. Followed by genotyping with Gp 60	109/533(20.4%) children		Duration longer with *C. hominis* (10.3d) vs rest (5.8d)*. Diarrhea (in all) Rest-malaise, abdominal pain, vomiting with *C.parvum* only. None had fever or dysentery *C. hominis* in 70% f/b *C. Parvum* in 31%.
Chacín-Bonilla, *et al.* 2008 [87]	San Carlos island, Venezuela	Age: 1month-15 yr). 248 subjects *Also included adults till 86 yr*	Modified Ziehl-Neelsencarbolfuchsin staining	60/248 (24.2%).	Risk factors- extreme poverty, living in a hut or small residence, lack of sanitary latrine, contact with contaminated soil, overcrowding	
Kirkpatrick, *et al.* 2008 [88]	Dhaka, Bangladesh Prospective over 3 years	Age: 2-5 years. 226 Children-	Cryptosporidium antigen-detection kit (Techlab)	96/226 (42.4%)	No relation with age	Predisposition with HLA B*15 (OR 2.16; *P*=.04), DQB1*0301 allele (OR, 2.75; *P* =.005

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Abreu-Acosta, *et al.* 2007 [89]	Santa Cruz de Tenerife, Canary islands, Spain	Stool surveillance for 0-60 year. Only 9 patients had age record as <12 yr	Modified Ziehl-Neelsen stain and PCR	Cases: 4/9 (44.4%)	Isolation higher in immunocompromised (18.2%) than immunocompetent (4.6%); P<0.05. No relation of age or gender.	Only 9 subjects had recorded age <12 yr
Carvalho-Almeida, *et al.* 2006 [90]	São Paulo City, Brazil	Age: 4-72 m. 64 children- Stool samples after 10-35 days of occurrence of index case	Kinyoun Method, a modified Ziehl-Neelsen technique	13/64 (20.3%).	Young Age<1yr-53.8% (7/13). No association with drinking water source or contact with pets	Symptoms in those tested positive-diarrhea, low fever, vomiting.
Bentley, *et al.* 2004 [91]	Highlands of Central Guatemala,	Age: 2-13 yr with diarrhea or abdominal pain	Kinyoun's modified acid-fast stain2	14% with diarrhea and abdominal pain, 21% with diarrhea& 29% with abdominal pain	Infection not affected by age	
Laubach, *et al.* 2004 [92]	Lake Atitlan, Guatemala	Age: 2-13 yr. 100 children with AD and abdominal pain	Kinyoun's modified Acid-fast stain	32%	No risk with seasonality. Males aged 2-5 yr lower prevalence.	Postulated-Higher prevalence due to contact with lake
Valentiner-Branth, *et al.* 2003 [93]	Bandim II and Belem of Bissau, the capital of Guinea-Bissau.	Age: 0-3 weeks. 200 children- Prospective till 2 yr.	Modified Ziehl-Neelsen technique	Incidence- 0.33%.	Higher in boys (OR, 5.35; 95% CI, 2.15 to 13.3, P=0.01). No relation with breastfeeding	Pathogenecity of *C. parvum* high (OR, 4.53; 95% CI, 2.75 to 7.46)
Miller, *et al.* 2003 [94]	Trujillo, Venezuela	Age: 4m-5 yr. 45 children	Kinyoun acid-fast stain	33/45 (73%)		Possible that their investigation coincided with an outbreak in this community
Mederios , *et al.* 2001 [95]	RibeirãoPreto, Brazil	Age: <10 yr. 1836 children with AD, Prospective 4 yr study	Modified Kinyoun method	34/1836 (1.8%)	Young age <2yr-88.2%	
Perch, *et al.* 2001 [96]	Guinea-Bissau, West Africa	Age: <5yr. 2681 children over 7 yr period	Modified Ziehl–Neelsen technique.	351/2681 (13.1%).	Young age: 6-11m. No relation with gender (RR-1.02 (0.84–1.25). risk in rainy season	Abstract only

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MØlbak, *et al.* 1997 [97]	Bandim II, Guinea-Bissau, West Africa.	Age: <5yr. 1064 children from 301 households. 3y prospective diarrhea surveillance.	Modified Ziehl–Neelsen staining.	236/1064 (22%)	Young age <1yr-108/236. No association with baseline weight, height.	Those with infection had subsequent poor weight gain
Checkley, *et al.* 1995 [44]	Lima, Peru.	Aged 0-3 months. 207 children. Prospective cohort over 2 years.	Light microscopy followed by both acid-fast and monoclonal Antibody fluorescent-labeled stains	94/207 (45%).	Age: 18-23 months old (RR-5.71; 1.43-22.81); HAZ<-2SD higher OR 1.52 (0.82-2.82). No relation to weight	Symptomatic cryptosporidiosis had less weight gain- 0-5months= 427gm (34-888), 6-12 months=208 gm (134-549)

HAART- Highly active antiretroviral therapy, RFLP- restriction fragment length polymorphism, PCR- Polymerase chain reaction, ICT- Immunochromatographic test. : IFA- ImmunofluorescenceAssay, HAZ- Height for Age Z score, WAZ- weight for age Z score, AD- Acute diarrhea, ND- Non-Diarrhea, PD- Persistent diarrhea.