WEB TABLE I EPIDEMIOLOGY OF CRYPTOSPORIDIUM IN ACUTE DIARRHEA FROM STUDIES WITH NON-DIARRHEAL CONTROLS

Author, year [Ref]	Place of study	Study population	Detection methods	Positivity rates	Associated risk	Clinical associates/ Remarks
Hospital-based studies						
Breurec, *et al.* 2015 [10]	Bangui, Central African republic	Age: < 5yr. Cases- 333 Controls 333	Microscopy followed by multiplex PCR	Cases- 42/333 (12.6) Controls- 9/333 (2.7) Attributable fraction= 10.5 (7.3–11.7)	Young age: Infants adjusted OR= 4.6 (1.8–11.7), toddlers OR= 2.9 (0.6–14.8) , Rainy season	
Nhampossa, *et al.* 2015 [11]	Rural Southern Mozambique	Age: <5 yr Cases- 784 Controls 1545	Immunoassays	a) 0-11 m- Case- 84/431 (20%), controls 86/861 (10%). b) 12-23 m- Case 44/233 (19%), control 46/502 (9%). c) 24-59 m- Case 11/120 (9%) controls 18/232 (8%)	Infancy: adjusted OR 15.26 (11.96–18.56),	Incidence rate was 2.10 (1.45–2.76) per 100 child years at risk
Tellivik, *et al.* 2015 [12]	Dar es Salaam, Tanzania	Age <2 yr Case- 701 Controls-588	Multiplex real-time PCR	Cases-16.3%, Controls-3.1% OR = 6.2; 95% CI: 3.7-10.4; P < 0.001;	Immunodeficiency- HIV positive 24.2, HIV negative 3.9%; OR = 7.9; 95% CI: 3.1–20.5: P < 0.001. Stunting- OR = 2.12; 95% CI: 1.2–3.8, P = 0.011;Rainy season: OR = 2.41; 95% CI: 1.5–3.8, P <0.001	*C.hominis* in 84.7% and C. parvum in 7.6%
Vadlamudi, *et al.* 2013 [13]	Birmingham, Alabama Retrospective 7 year cohort	Age: 3-17 year with inflammatory bowel disease- 7 positive cryptosporidium, 21 negative for infection	Stool rapid immunoassay test with immunocard STAT!®	7/170 (4.1%)	No differences in baseline characteristics	5/7 had severe dehydration 3/5 treated with NTZ recovered within 3 days
Wang, *et al.* 2013 [14]	China	Age- 1m-18yr Cases- 78 Controls- 499	Not mentioned	Cases-51.4% Controls- 2 %	Not evaluated	Positive had more co-infection than controls with Giardia, E.bieneusi and C. difficile

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Amatya, *et al.* 2011 [15]	Nepal	Age: <15 yr Cases-863 Controls-100	Modified Ziehl Neelsen method	Cases-4.1% Controls- 0%	Age- 6-10 yr	
Opintan, *et al.* 2010 [6]	Accra, Ghana. Cross sectional <5 years	Age: 0-60 m Cases- 170 (145 AD and 13 PD), Controls-104	Single locus Quantitative qPCR on fecal DNA	Cases- 14/170 (8.2%), Controls- 1/104 (0.9%), OR = 9.244 [95% CI 1.197–71.4], *P* = 0.011)	Malnutrition WAZ<-1 OR-9.244 (1.197–71.371); P=0.011	NA NA
Haque, *et al.* 2009 [16]	Dhaka hospital Bangladesh	Age: ≤14 yr cases-1088 ; Controls-1623	Antigen detection kits, real-time PCR assay,	Cases- 94/2039 (4.6%);controls- 41/1623 (2.5%)	Young age <12m age (57/1088 cases vs 14/485 controls; p=0.037).	Cases less likely to have abdominal pain, than control subjects (15% *vs.* 37%; *P*<.001) *C.hominis* most frequent (61%), followed by *C.parvum*,
Abu-Alrub, *et al.* 2007 [17]	West bank, Palestine Prospective, hospital based	Age: 1m-15 yr 760 cases, 62 ND controls	Modified acid fast staining	Cases- 11.6% Controls- 3.2%	Young age: Incidence 14.4% <5 yr, 7.7% 5 to 10 yr, 5.9% 11 to 15 yr. Rural area or refugee camps than urban area	NA
Mirzaei M, 2007 [18]	City of Shiraz, Fars Province, Iran	Children <15 yr-Cases-51; controls-38	Ziehl-Neelsen acid-fast staining.	Cases- 18/51 (35.3%) Controls (2.6%)	NA	
Mukhopadhyaya, *et al.* 2007 [19]	Western Nepal. Prospective (6 years).	Age: Below 5 years AD-155, PD-204, ND control-100	Modified acid fast staining	AD- nil, PD- 2/204 (0.1%), controls- nil	Lack of breastfeeding for PD. No relation with water source/ sanitary practices	
Sanchez-Vega, *et al.* 2006 [20]	Mexico	Age < 1 year Cases-100 Controls-100	Modified Kinyoun acid-fast technique, and observed by light microscopy at 100×, 400×,1,000×.	Cases- 18% Controls-0%	Incidence higher in males 77.78%. Sanitation and hygiene was adequate	All cases had fever and abdominal distension, none had vomiting and dehydration
Olesen, *et al.* 2005 [21]	Stool collection centre, Denmark. Prospective	Age: 0-5 years. Cases-424 Controls-870	Ziehl-Neelsen acid fast staining	Cases- 1.7% (6/351), Controls-0%	NA	NA

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Roy, *et al.* 2004 [22]	Foodborne Diseases Active Surveillance Network (foodnet) across seven states in US	Age <6m->65 yr. *Cases (positive crytosporidiosis) - 282 ND controls-490	Acid-fast staining, direct fluorescent antibody staining, or commercial ELISA	NA	Risk- international travel OR- 7.7 (2.7 to 22.0), contact with cattle (OR = 3.5; 95% CI = 1.8 to 6.8), contact with persons >2 to 11 years of age with diarrhea (OR = 3.0; 95% CI = 1.5 to 6.2), and freshwater swimming (OR = 1.9; 95% CI = 1.049 to 3.5). Eating raw vegetables was protective (OR = 0.5; 95% CI = 0.3 to 0.7).	
Adjei, *et al.* 2004 [23]	Accra, Ghana	Age <5yr 277 with AD and 77 ND controls	The modified Ziehl Neelson staining procedure	Cases-- 27.8% Controls- 15.6%	Age- 12-24m. Weight for age deficit >25%. No role of gender, water supply, history of antibiotic therapy or contact with animal	Most common symptom- fever (71-75%), nausea (47% cases)
Khan, *et al.* 2004 [24]	Dhaka, Bangladesh	Age: <5 yr *Cases- 46 positive for cryptosporidium, 46 controls with negative growth	Modified Acid-fast staining	Prevalence- 47/1672 (2.8%) in stool samples.	No risk with age, gender, breastfeeding, malnutrition (WAZ, HAZ or WHZ), pulse rate, history of contact with animals, water supply	Watery diarrhea (96%) and vomiting (57%) were most common features. Only 11% dehydrated and 13% had fever. PD occurrence was higher in Cases than controls
Al Braiken, *et al.* 2003 [25]	Jeddah, Saudi Arabia	Age: <5yr Cases-63 Controls-190	Modified Acid-fast staining	Cases-32%, controls-4.7%; P<0.001	No risk with age or gender.	
Nunez, *et al.* 2003 [26]	Havana City, Cuba	Age: Pediatric age Cases-113 Controls- 288	Modified Ziehl-Neelsen techniques	Cases- 13/113 (11.5%) nil in controls	No difference with age or gender.	Those with cryptosporidial diarrhea had longer diarrhea duration & higher risk for PD than those with isolated cyclopspora (*p*<0.01)

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Tumwine, *et al.* 2003 [27]	Uganda	Age: 0-60m Cases (AD/ PD)- 1779 Controls-667	modified acid fast staining and PCR-RFLP for *C.parvum* only.	Cases- 444 (25.0%) Controls- 57 (8.5%); (r2=80.2, *P* = 0.0001)	Higher if low maternal education. Risk if , wasting (OR 1.59,1.27–1.99), underweight (OR 1.42 1,1.14–1.78), stunting (OR 1.31 1.04–1.64) No difference with gender, or if breastfed
Kirkpatrick, *et al.* 2002 [28]	Port-au-Prince, Haiti. Prospective	Age: <18 months in 3 groups. 17 with cryptosporidial diarrhea, 17 with non-cryptosporidial diarrhea, 15 as healthy controls	Ziehl-Nielsen modified acid-fast Stain and Gram stain,	Cases- 28/60 (46%)	Lack of breast feeding, low HAZ (p=0.03) low WAZ (p=0.01), vitamin A deficiency (p=0.04). No association with low WHZ
Bern, *et al.* 2000 [29]	Guatemela Stool surveillance	Age: 3 months-19 years Cases- 697 Controls- 2709	Modified AFB staining, ultraviolet epifluorescence. Direct IFA with *Cryptosporidium*-specific OW50 monoclonal antibody.	Cases- 7.1% Controls- 5.3% (p-NS)	Young age <2yr; p=0.03). Seasonality-rainy season.
Albert, *et al.* 1999 [30]	Dhaka, Bangladesh	Age <5 yr Cases- 814 with age matched ND controls.	Modified acid fast staining	Cases- 11(1.4%) Controls-3(0.4%) ; p=0.03	Anthropometry comparable between two groups
Cegielski, *et al.* 1999 [31]	Tanzania.	Age: 15-60 months Cases- 55 with AD, 59 with chronic diarrhea, 20 controls	Kinyoun and auramine-rhodamine stains and direct fluorescent monoclonal antibodies	Cases:AD- 7/55 (13%), Chronic diarrhea 5/59 (8%) Controls- Nil	Young age (p0.4 Malnutrition Seropositivity- No relation Environmental hygiene- no relation
Iqbal, *et al.* 1999 [32]	Rawalpindi, Pakistan	Aged <5yr Cases-475 Controls-150	For *C.parvum* only-modified Ziehl-Neelsen stain	Cases- 10.3%; controls-3.3%	Young age: 19–24 months of age (21.8% cases and 10% controls). No association with gender, Sociodemographic Information, drinking water supply, and contact with domestic animals

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Katsumata, *et al.* 1998 [33]	Surbaya, Indonesia- hospital and community based	Age: 0 to ≤60 mo *Hospital based-* Cases- 917 AD Controls-1043 *Community-* Cases- 257 AD Control- 4111	Phase-contrast Microscopy at 6003 magnification followed by Kinyoun staining	*Hospital based-* cases- 2.8% Controls- 1.4% *Community:* Cases-8.2% Controls- 0.7%	Young Age <2 years (OR-0.95, 0.89-0.99), Rainy season (OR-10.65, 1.38-82.17), contact with cats (7.05, 3.61-13.76), overcrowding (OR-1.46,1.19-1.79). No relation with gender, drinking water supply, bathing in public bath	NA
Chacin Bonilla, *et al.* 1997 [34]	Maracaibo, Zulia State, Venezuela.	Age:0-60 mo Cases- 310 Controls-150	Modified Ziehl-Neelsen stain	Cases-11.2% Controls- 6%	No age differences or difference in malnutrition prevalence. No effect of breastfeeding	Duration of AD 5-16 days. Dehydration seen in 91.2% positive cases. Mostly stools were watery
(b) Community-based studies						
Mills, *et al.* 2015 [35]	Multicentric- 8 sites - Dhaka, Bangladesh; Fortaleza, Brazil; Vellore,India; Bhaktapur, Nepal; Loreto, Peru; Naushero Feroze, Pakistan; Venda, South Africa; and Haydom, Tanzania	Age: 17 day till 24 months Prospective 2145 children: 7318 diarrhoeal and 24 310 non-diarrhoeal stools	Enzyme immunoaassay	Attributable fraction - 2.0 (1.3-2.6) in <12 months; highest; and 3.8% (2.8-4.7)in 12-24 months	Maximum isolation of cryptosporidium coincided with peak diarrheal season at each site	
Bodhidatta , *et al.* 2010 [36]	Western Thailand. Prospective	Age-3m-5 year old Cases-236, Controls-236	ELISA based kits	Cases- 4/207 (2%) Controls-12/227 (5%); p-NS	NA	NA

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Samie , *et al.* 2009 [37]	Vhembe district, South Africa Cross sectional	Age 5-15 years. Case- 39 Controls- 256	The modified Ziehl Neelson staining procedure	Cases- 17.9% Controls- 14.4% ; P=0.56	NA	NA
Wongstitwilairoong , *et al.* 2007 [38]	Sangkhlaburi, Thailand. Prospective	Age:3m- 5year 236 cases of diarrhea and 236 ND controls	DMSO-MAFB staining and prospect *Giardia/Cryptosporidium* Microplate Assay, an enzyme immunoassay	Detection- 0.8% cases vs 2.5% controls	No gender differences	Only 4 detected by smear and additional 12 by EIA assay
Robertson , *et al.* 2002 [39]	Melbourne and Adelaide, Australia.	Aged 0-18 years *Cases (positive crytosporidiosis) -335 Control (healthy)- 1331	Detection confirmed by accredited Pathology laboratory	NA	Swimming in public pool OR- 2.7 (1.9-3.8), contact with <6 yr old with diarrhea OR-7.4 (4.0- 13.8), drinking unboiled water OR-3.1 (1.5-6.5), calf contact OR- 5.1 (1.5-17.3)	NA
Peuch , *et al.* 2001 [40]	New South Wales, Australia. Telephonic interview	Age: < 15 years. Cases- 100 Controls-200	NA	NA	Risk if swimming in untreated water 4.8 (1.1-20.3) or public pool 2.7 (1.4-5.1). Protective- bottled water 0.4 (0.2-0.9) No difference with gender, childcare contact, contact with pets.	Abdominal cramps frequent in cases.
Newman , *et al.* 1999 [41]	Fortaleza, Northeastern Brazil Prospective 4 year cohort	Age: Birth till 4 years. Total 1054 stool samples from 189 children	Modified Acid-fast and auramine stains	Cases: AD- 8.4%, PD- 16.5%, Control- 4%	Low B.wt, overcrowding. Malnutrition, age or gender- No increased risk	Vomiting, mild fever common. Dehydration rare 15 cases of recurrent cryptosporidium infection.
Nath , *et al.* 1999 [42]	Sunderpur, Varanasi	Age: < 5yr Cases- 607 Controls- 529	Safranine-methylene blue stain.	Cases- 23/607 (3.8%), Controls- 9/529 (1.7%)	Age: 49-60m and 13-24m. No gender risk.	Majority (63.3%) were mucoid stools. None positive for RBC or WBC
Agnew , *et al.* 1998 [43]	Fortaleza, Brazil.	Age: 3-27 months. Total 154: 43 Cases: positive cryptosporidium,	Modified acid-fast and auramine stains	Cases: 43/154 (27.9%) Controls: NA	Young age <1 yr (p<0.05). Lower HAZ (p<0.01)	Mean duration of cryptosporidial diarrhea 12.3± 2.0 days. Significant lower

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Checkley , *et al.* 1995 [44]	Lima, Peru. Prospective cohort over 2 years.	207 children aged 0-3 months	Light microscopy followed by both acid-fast and monoclonal Antibody fluorescent-labeled stains	Detection rate 45% (94/207): 63% in asymptomatic infection.	Higher risk of asymptomatic infection in 0-5 months old	Weight gain in symptomatic infection - 338 gm less; asymptomatic infection-154gm less than those without diarrhea and not infected.

IFA- Immunofluorescence Assay, qPCR- real time polymerase chain reaction, PCR-RFLP−Polymerase chain reaction- restriction fragment length polymorphism, ELISA- enzyme-linked immunosorbent assay, HAZ- Height for Age Z score, WAZ- weight for age Z score, AD- Acute diarrhea, ND- Non-diarrhea, PD- Persistent diarrhea.