Research Journal of Pharmaceutical, Biological and Chemical Sciences

A comprehensive Evaluation of Transmission Methods for Cryptosporidium species with special emphasis to Cryptosporidium Parvum

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ABSTRACT

Cryptosporidiosis is an emerging protozoan disease of public health significance. Cryptosporidium parvum can cause gastrointestinal illness in a wide variety of mammals, like humans, cattle, sheep, goat, pig and horses throughout the world. The first case of human cryptosporidiosis was reported in 1976, and there are increasing numbers of documented infection with Cryptosporidium spp. since then. Now, it is considered a common enteric pathogen in humans and animals worldwide . Cryptosporidiosis can induce self-limiting diarrhoea in immunocompetent people or severe and prolonged diarrhoea in immunocompromised patients, such as those with AIDS, transplant recipients, those are receiving chemotherapy for cancer, and patients with immunosuppressive infectious disease. In developing countries, Cryptosporidium mostly infects children below five years of age and peaks in children below two years of age . The aim of current review was to illustrate the most important and common methods for the transmission of Cryptosporidium. Multiple transmission pathways are the cardinal problem in cosmopolitan nature of cryptosporidiosis ,thus extra attention and regimes required for termination of transmission pathways for complete eradication of the *Cryptosporidium* infection .
Keywords: Cryptosporidium parvum,   mode of transmission , zoonoses

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INTRODUCTION

Cryptosporidium species are increasingly recognized as important enteric pathogens (Cama et al., 2008;Sparks et al., 2015) . Cryptosporidiosis was initially recognized as a cause of diarrhea in compromised hosts. Shortly thereafter, zoonotic and waterborne transmission of the parasite was identified. Cryptosporidium is now considered one of the major causes of childhood diarrhea. In addition*, Cryptosporidium* has been documented as a key component of the vicious cycle of infection and malnutrition that are major contributors to childhood morbidity and mortality worldwide. The majority of human *Cryptosporidium* infections are attributed to two species: *C. hominis* and *C. parvum (Bennett et al., 2014;Cama et al. , 2008)* . However, at least 13 other species may infect humans(Chalmers and Katzer, 2013 ;Cama et al. , 2008) .Clinically, cryptosporidiosis causes watery diarrhea in healthy patients. In contrast to other causes, diarrhea caused by cryptosporidiosis tends to be more prolonged and can be chronic in compromised hosts, such as children with malnutrition .

Cryptosporidium parasites develop within the microvillus layer of intestinal epithelial cells, mainly found in the small intestines in immunocompetent hosts, but may be found throughout the GI tract and even the respiratory tract. Persistent infection is associated with villus atrophy, crypt hyperplasia, and variable increases in leucocytes in the lamina propria(Sparks et al. , 2015) . The symptoms of watery diarrhea and malabsorption are thought to be related to sodium malabsorption, electrogenic chloride secretion, and increased intestinal permeability, and severity of disease correlates with altered intestinal permeability(Sparks et al. , 2015) . The aim of current review was to illustrate the most important and common methods for the transmission of Cryptosporidium.

Risk Groups

Several groups have a risk of being exposed to Cryptosporidium oocysts contaminated materials and develop a clinical manifestations of intestinal and extra intestinal cryptosporidiosis such as: Children who attend childcare centers, including diaper-aged children(Painter et al., 2015); Childcare workers; Parents of infected children; People who take care of other people with cryptosporidiosis(Centers for disease control and prevention, 2017); International travelers; Backpackers, hikers, and campers who drink unfiltered, untreated water(Goh et al., 2004); People who drink from untreated shallow, unprotected wells; People, including swimmers, who swallow water from contaminated sources; People who handle infected cattle; contact with livestock (Roy et al., 2004);People exposed to human feces through sexual contact(Scallan et al., 2011;Centers for disease control and prevention, 2017) .
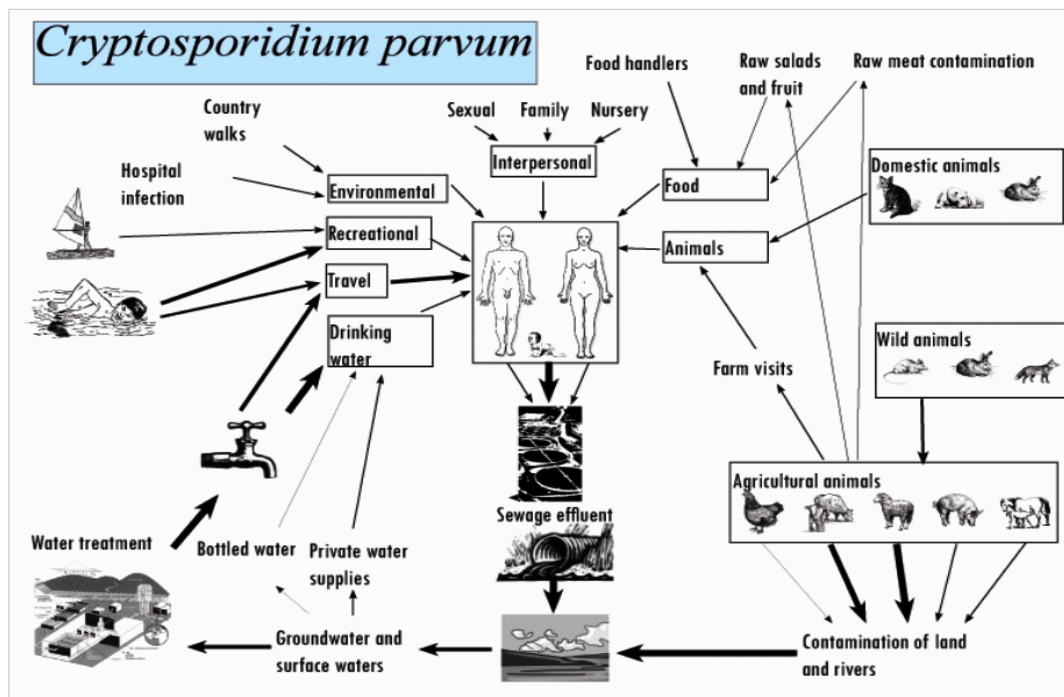

Figure 1. Transmission pathways for *C. parvum. cited from (Nichols; et al., 2006)*

Routes of transmission

Direct contact transmission

Direct transmission of cryptosporidium oocysts is likely to be the most common form of transmission which occurs by the fecal-oral route from infected hosts, including animal-to-animal, animal-to-human (zoonotic), human-to-animal, and human-to human (anthroponotic) transmissions(Xiao and Feng, 2008;Thompson et al., 2016).

The nosocomial and day care centre based cryptosporidiosis are likely related to direct person-to-person spread where sanitation is difficult(Al-Warid et al., 2010).A higher prevalence of cryptosporidiosis was reported among Immunodeficient individuals ,HIV ,infected persons This risk is increased when individuals engage in high-risk sexual behavior(Hunter and Nichols, 2002). The high prevalence of Cryptosporidium spp. in AIDS patients is probably related to an increased risk of acquiring infection from infected contacts and prolonged excretion, which in turn increases the risk of subsequent transmission, However, the possibility of transmission related to other behaviors could not be ruled out(Thompson et al. , 2016).

Children who still wearing diapers and attend day care centers are at high risk for direct transmission of *Cryptosporidium* through intimate play or careless diaper changing practices(Azevedo, 2017). Infections acquired by children in the day care are transmitted to care-givers at the facility and to older children and adults who come in contact with the infected child at home(Da'as, 2010).

Cryptosporidium is shed in the fecal materials of infected humans and animals(Sánchez et al., 2017). *Cryptosporidium* infections acquired through several transmission routes such as by direct contact with contaminated materials , zoonotic transmission , foodborne transmission and waterborne transmission (Xiao, 2010).

The majority of human infections are caused by *C. hominis* and the cattle genotype of *C. parvum(Samra et al., 2016)*.Occasionally immunocompetent humans infected with Other *Cryptosporidium* species mainly *C. meleagridis, C. felis* and *C. canis (World Health Organization, 2009).* Species that have been reported only in immunocompromised individuals are *C. muris/andersoni* (evidence on species not conclusive) ;a cervine and pig genotype (Xiao et al., 2004;Ryan et al., 2014).

Zoonotic Transmission

Several outbreaks have been reported due to contact with infected calves (Gait et al., 2008).*Cryptosporidium* was reported in a wide range of wild animals which may serve as a reservoir for human infection (Oates et al., 2012;Abu Samra et al., 2013) .Since *C. parvum* was once considered to be the only species infecting humans, much attention has been given to zoonotic *C. parvum(Yang et al., 2017)* .*C. parvum* is divided in to *C. hominis* (once known as *C. parvum* genotype I) and *C. parvum* (once known as *C. parvum* genotype II)(Xiao, 2010).

Increased environmental contamination and trends in livestock production are factors that contributed to the emergence of cryptosporidiosis in animals (Sánchez et al. , 2017). In humans the zoonotic nature of infection, along with increased numbers of at-risk population have contributed to the rate intensification of the disease (Lal et al., 2016) .Unusual zoonotic species such as *C. meleagridis*, *C. canis* and *C. felis* have been described more frequently in humans from developing countries*(World Health Organization, 2009)*. However, in these countries, anthroponotic subtypes of *C. hominis* are the most common species responsible for human infections, while in industrialized countries *cryptosporidiosis* is mostly due to *C. parvum* (Xiao and Feng, 2008) . Because of the small infectious dose required (less than 10 oocysts, depending on isolates) ,*C. parvum* is a serious and frequent cause of waterborne diarrhea (Bouzid et al., 2013).

At least nine molecularly different types of *Cryptosporidium* have been found to infect humans(Magi et al., 2006). *C. hominis* and *C. parvum* are responsible for the majority of infections in humans(Ryan and Hijjawi, 2015). Excluding *C. parvum* pig genotype and *C.muris* , infection with these species have been reported in HIV positive individuals and among immunocompetent children and adults(Ghazy et al., 2015) .

One of the most important features of *Cryptosporidium* oocysts ,they are highly resistant to popular disinfectants ; beside the fact that they are discharged from infected humans and animals in large , and via effluent disposal, find their way to surface water(World Health Organization, 2009). Until recent years, an important concept was more acceptable that Only *C. parvum* which has been detected in most mammalian species was responsible for human infection(Gerardi and Zimmerman, 2016) .Recent reports have, described human disease with *C. meleagridis*, a turkey respiratory *Cryptosporidium* described in 1955 (Ryan et al., 2016). *C. meleagridis* has been detected in patients with cryptosporidiosis and in malnourished children with persistent diarrhea(Mmbaga and Houpt, 2017) .   Less clearly other researchers defined isolates of *C. felis* and *C. canis* have been reported in sporadic cases of human cryptosporidiosis (Tzipori and Ward, 2002;Certad et al., 2017).

In USA, due to the obvious separation between urban and rural populations   (>75%) human cryptosporidiosis are caused by *C. hominis* ,While bovine *C. parvum* is responsible for 61.5% of human cases (Roellig et al., 2017;Hunter et al., 2009) .In UK ,where communities are closely related to agricultural sources, 37.8% of human cryptosporidiosis was caused by *C. hominis (Tadesse, 2014) .* The human genotype is also notably predominant in Australia, Kenya, Guatemala and Peru, since it is responsible for 86 % of the human infections (Ghazy et al. , 2015) **.**

C.parvum is the most important zoonotic agent of cryptosporidiosis, with a large range and abundance of animal reservoirs, mainly in young farmed animals(Vasco et al., 2016) . As shown in figure (2.3), persons who come in direct contact with farm animals due to their occupation like veterinarians and veterinary students, or due to   recreational activities like people exposed to farm animals   and children visiting farms, may be at risk for infection (Cacciò and Putignani, 2014;Sánchez et al. , 2017;Utsi et al., 2016).   contact with farm animals directly was recognized as a important risk factor for sporadic cases of cryptosporidiosis in human (Yang et al. , 2017) .

Environmental contamination induced by calves play an important role in human infection ,due to the high prevalence of *C. parvum* infection and the high numbers of oocysts shed in faeces (more than 5 x 10^6 oocysts /gram)(Chalmers and Giles, 2010). Previously , it was supposed that all *C. parvum* infections to human were all of zoonotic in origin and calves have been embroiled as the major source of infectious oocysts, but further studies based on highly polymorphic markers have proven that certain subtypes of *C. parvum* are detected in humans but not in animals, and are likely to be transmitted via an anthroponotic cycle (King et al., 2017). For this reason, a considerable portion of human infection with *C. parvum* may not originate from livestock reservoirs (Grinberg et al., 2008). Nevertheless, calves are frequently infected with a *C. parvum* subtype that is commonly found in humans in the same geographic areas(Xiao, 2010;Feng et al., 2017) and epidemiologic studies have supported the occurrence of zoonotic transmission (Hunter et al., 2007;Ibrahim et al., 2016) .
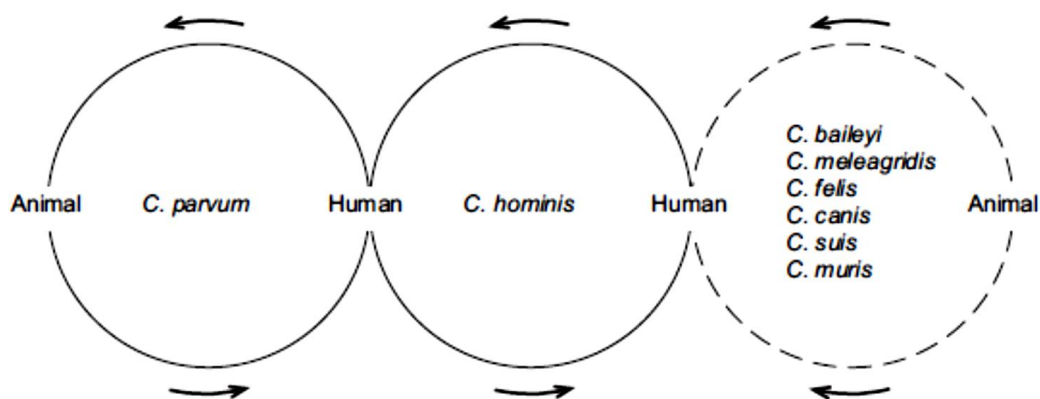

Figure (2).Transmission cycles of human *Cryptosporidium* infections. Dotted cycle demonstrates rare transmission (Rimhanen-Finne, 2006)

A collection of evidences from epidemiologic investigations supported by molecular studies have elucidated the role of sheep in human cryptosporidiosis in the UK (Quílez et al., 2008), where five human outbreaks have been linked to contacts with lambs (Chalmers and Giles, 2010). In Italy ,A rare *C. parvum* subtype

was recovered from case of zoonotic transmission from infected lambs to a children(Cacciò et al., 2013).Goats can be infected with *C. parvum* and may also play a role in zoonotic cryptosporidiosis (Kaupke et al., 2017)

Regarding the acquiring cryptosporidiosis from pets, it is more critical, and immunocompromised individuals, the elderly and for children ; however, recent report suggests that pets are not a major risk factor for human cryptosporidiosis (de Lucio et al., 2017). Veterinarians are the best appropriate professionals to give correct information to individuals about the risk of cryptosporidium infection from their pets and what measures should be taken to minimize cryptosporidiosis in animals, especially to owners of high risk (i.e. immunocompromised)(Ghazy et al. , 2015).

The zoonotic potential of feline and canine cryptosporidiosis has considered as a major concern to both veterinarians and physicians, but the actual risk of transmission from pets to human appears to be minimal in developed countries (Thigeel, 2017). Immunocompromised individuals were the target of zoonotic transmission from pets, in which *C canis* and *C.felis* recovered from immunocompromised owners or pets handlers (Lucio-Forster et al., 2010;Friedmann and Son, 2009).

As results of close interactions between humans and companion animals, mostly cats, dogs and birds, this leads to sharing of living space and thus, sharing microorganisms that may cause disease (Bowman and Lucio-Forster, 2010;Chako et al., 2010). Cryptosporidiosis in dogs is generally asymptomatic and dogs less than 6 months of age are affected more often than the adults(Rimhanen-Finne et al., 2007).While in cats about 50% show diarrhea signs(Rimhanen-Finne et al. , 2007) . Zoonotic cryptosporidiosis from exposure to pets has not been documented in healthy adults but transmission of (bovine) *C.parvum* from companion (cats, dogs) to HIV infected persons has been reported (Certad et al. , 2017). Healthy children and adults infected with zoonotic cryptosporidium spp. *, C. felis, C. canis* and *C. meleagridis* (Figure 1) , (Desai et al., 2012;Xiao, 2010). There is only one report of possible transmission of *C. canis* between a dog and two siblings living in a household in Peru (Xiao, 2009) .

Rabbits are the natural host of *C. cuniculus* (Robinson and Chalmers, 2010), a species that is now known to infect humans(Chalmers and Katzer, 2013) . First identified as a human pathogen during a waterborne outbreak, *C. cuniculus* appears to be the third most commonly identified species in patients with diarrhea in the UK, after *C. parvum* and *C. hominis* (Chalmers, 2011) .The existence of identical *C. cuniculus* subtypes in humans and pets or wild rabbits suggest zoonotic potential(Zhang et al., 2012). Zoonotic transmission of *C. meleagridis*, an avian parasite that can infect humans, has been reported in Sweden (Silverlås et al., 2012) . Molecular characterization suggest laying hens or broiler chickens as the source of infectious oocysts(Laatamna et al., 2017). Fish, reptiles and amphibians appear not to pose a risk for human cryptosporidiosis(Palermo, 2016) .

Cryptosporidium species that infect mammals and other animals and the possibility of human infection illustrated in table (1).Common Transmission pathways for C. parvum illustrated in figure (2).

Table 1: *Cryptosporidium species* that infect mammals and other animals and the possibility of human infection (OIE, 2016)

Cryptosporidium species	Major host(s)	Usual site of infection	Infections reported in humans
C. andersoni	Cattle	Abomasum	Yes, but only rarely
C. baileyi	Poultry	Upper respiratory tract, Cloaca, ,kidney	No
C. bovis	Cattle	Small intestine	Yes, but only rarely
C. canis	Dog	Small intestine	Yes, occasionally
C. cichlidis	Tilapia	Stomach	No
C. cuniculus	Rabbit, humans	Small intestine	Yes, occasionally.
C. ducismarci	Tortoises	Intestine	No
C. erinacei	Hedgehog	Small intestine	Yes, but only rarely
C. fayeri	Marsupials	Intestine	Yes, but only rarely
C. felis	Cat	Small intestine	Yes, occasionally

C. fragile	Black spined toad	Stomach	No
C. galli	Chicken	Proventriculus	No
C. hominis	Humans	Small intestine	Yes, commonly
C. huwi	Guppy	Stomach	No
C. macropodum	Eastern grey kangaroo	Intestine	No
C. meleagridis	Birds, mammals	Intestine /respiratory tract	Yes
C. molnari	Sea bream	Intestine	No
C. muris	Rodents, ruminants	Stomach	Yes, but only rarely
C. rubeyi	Ground squirrels	Small intestine	No
C. nasorum	Fish	Stomach / intestine	No
C. parvum	Humans, pre-weaned mammalian livestock	Small intestine	Yes
C. proliferans	Rodents	Stomach	No
C. ryanae	Cattle	Small intestine	No
C. scrofarum	Pig	Small intestine	Yes, but only rarely
C. serpentis	Reptiles	Stomach	No
C. suis	Pig	Small intestine	Yes, but only rarely
C. tyzzeri	Mice	Small intestine	Yes, but only rarely
C. ubiquitum	Various mammals	Small intestine	Yes, occasionally
C. viatorum	Humans	Small intestine	Yes, occasionally
C. varanii	Reptiles	Intestine	No
C. wrairi	Guinea pig	Small intestine	No
C. xiaoi	Sheep, goat	Small intestine	No

Waterborne Cryptosporidiosis

Water contamination represents the main source of *Cryptosporidium* infections for humans (Fong, 2017). Contaminated drinking water and recreational water involved in multiple waterborne outbreaks of cryptosporidiosis(Cacciò and Chalmers, 2016). Livestock represent the main sources of *Cryptosporidium* contaminating isolates causing waterborne outbreaks of cryptosporidiosis (Olson et al., 2004;Thompson et al. , 2016).

The ubiquitous presence of contaminating Cryptosporidium spp. in the aquatic environment is related to the large number of hosts, very high number of oocysts shed by these hosts, and the oocysts stability (Smith et al., 2006;Cacciò and Widmer, 2013) . For this reason ,water represents an important medium for transmission of cryptosporidium spp. infection for the population, as well as cryptosporidiosis waterborne origin is a critical public health problem , mainly for populations at risk such as transplanted patients ,pregnant women, children, HIV-positive patients (Cacciò and Putignani, 2014). Waterborne transmission outbreaks of Cryptosporidium spp., Indeed represent (56.3 %) of entire reported outbreaks in last ten years (Cacciò and Putignani, 2014). Cryptosporidium spp. recovered from the entire water treatment system ,which indicates an unacceptable health risk, mainly for at risk immunocompromized individuals like ,pregnant women, children, HIV-positive and transplanted patients(Cacciò and Putignani, 2014) .Such evidence suggests that concentration must be placed on prevention of water contamination via human and animal wastes especially in licensed recreational waters(Dufour et al., 2012). *C. hominis and C. parvum linked* Outbreaks have reported in swimming pools, paddling or wading pools, water parks and fountains (Bruschi, 2017). Healthy swimming campaigns are required to increase awareness and practice of healthy behaviors while swimming, due to the fact that swimmers were the essential source of contamination with Cryptosporidium especially not swimming while ill with diarrhoea(Efstratiou et al., 2017). The healthy swimming campaigns have an im-

portant role in prevent cryptosporidiosis outbreaks liked to recreational water (Yoder et al., 2010) . The role of water in the transmission of Cryptosporidium in developing countries is less known (Baroudi et al., 2017). The potential for water born transmission in developing countries is promoted by the absence of monitoring system including sanitary and parasitological monitoring, and the burden of the Cryptosporidium infection is undoubtedly underestimated due to the shortage of convenient surveillance programs and the relative frailty of laboratory diagnosis (Chuah et al., 2016). Interruptions in water supplies that forced people to revert to drinking raw water caused a greater risk of Cryptosporidium infection, especially in young children(Amoueyan et al., 2017). Thus, poor reliability of drinking water supplies has an direct influence on the performance of health improvement targets (Piper et al., 2017).

Biological features of *Cryptosporidium* Which Facilitate Waterborne Transmission

Cryptosporidium has Several features that facilitate waterborne transmission ,primarily large numbers of oocysts excreted by infected hosts in which up to 10^{10} *Cryptosporidium* oocysts excreted during symptomatic infection(Ng-Hublin et al., 2014). Lack of, or reduced, host specificity increases the potential for environmental spread and contamination ,this reflected by up to 10^7 oocysts per gram of feces in infected calves *C. parvum* infections reported from a variety of mammals, including human beings, domestic livestock, pets and feral animals (Lim et al., 2008;Vermeulen et al., 2017). Robust nature of oocysts enhances their survival for long periods of time in favorable environments before ingestion by potential hosts , Oocyst survival is enhanced in moist cold environments (such as those found in temperate regions),e.g., a small proportion of viable oocysts can survive for 12 month suspended in water(Sissay and Mehari, 2013) . Environmental robustness of oocysts enables them to survive some water treatment processes ,in which waterborne outbreaks indicate that oocysts can survive physical treatment and disinfection(Zhou et al., 2014). Oocysts are insensitive to disinfectants commonly used in water treatment. Small size of oocysts(4.5–6 μm) aid their penetration through sand filters(Ryan et al., 2017) . Low infectious dose means that few viable oocysts need to be ingested for infection to establish in susceptible hosts , Small numbers of *C. parvum* oocysts can cause infection in humans(Messner and Berger, 2016). Infectious dose is dependent upon oocyst isolate [ID50 = 9–1042 oocysts]; 10 oocysts can cause infection in juvenile nonhuman primates; 5 oocysts can cause infection in gnotobiotic lambs(Dufour and Bartram, 2012) . Excretion of oocysts into water courses facilitates spread to, and entrapment in, freshwater and marine shellfish, Viable oocysts can accumulate within shellfish(Smith and Nichols, 2007). Up to 5×10^3 *C. parvum* oocysts have been reported per shellfish. *C. parvum*, *C. hominis*, and *C. meleagridis* oocysts have been detected in various shellfish(Simjee, 2007;Smith and Nichols, 2007) . Excretion of oocysts in feces facilitates spread to water by water-roosting refuse feeders, Viable oocysts excreted by transport hosts such as seagulls and waterfowl(Bruschi, 2017).

Airborne transmission

Cryptosporidium oocysts characterized by their small size (4.5–6 μm) rendering them light enough to be carried out via wind facilitating airborne transmission and infection takes place via inhalation of infected droplets contaminated by oocysts (King et al., 2015). Zoonotic transmission was reported after inhalation of droplets containing cryptosporidium oocysts from experimentally infected calf (Mascaró et al., 1994;Sponseller et al., 2014). Respiratory cryptosporidiosis of zoonotic origin was reported in immunocompetent veterinarian who administered oral fluids to a calf with confirmed cryptosporidial diarrhea subsequently developed intestinal cryptosporidiosis with respiratory manifestations after sniffing the contents of the stomach tube while it was positioned in the animal (Sponseller et al. , 2014;Hoлyng et al., 1987)

Respiratory cryptosporidiosis has been reported for the first time in Turkey flocks with cough, nasal and ocular discharge, poor weight gain, and absence of gastrointestinal signs (Sponseller et al. , 2014;Hoerr et al., 1978) . Respiratory tract cryptosporidiosis has been confirmed for chickens ,partridges , peacocks , pheasants and quail (Sponseller et al. , 2014) . The scarceness of other etiologic agents detected in respiratory tract beside the loss of gastrointestinal manifestations and pathological findings have encouraged to prove cryptosporidium as a primary agent of avian respiratory disease that is capable of transmission via droplets and fomites(Sponseller et al. , 2014) .

Naturally occurring respiratory cryptosporidiosis was reported sporadically in calf with cryptosporidial diarrhea(Sponseller et al. , 2014;Mascaró et al. , 1994) ; several sheep from an abattoir (Fleta et al., 1995;Sponseller et al. , 2014) and in rhesus macaques, experimentally infected with simian immunodeficiency

virus , subsequently developed disseminated cryptosporidiosis of the respiratory and gastrointestinal tracts and the bile and pancreatic ducts(Sponseller et al. , 2014;Blanchard et al., 1987) .

Respiratory cryptosporidiosis was reported for the first time among children with immunodeficiency , in tracheal autopsy of children with congenital hypogammaglobulinemia and intestinal cryptosporidiosis(Sponseller et al. , 2014;Boothe et al., 1980) , autopsy in the bronchial trees of children with severe combined immunodeficiency(Kocoshis et al., 1984), endotracheal and fecal samples obtained from a newborn diagnosed with an immunoglobulin deficiency (O'Halloran et al., 1987). Cryptosporidium oocysts were recovered from aspirate of sputum and maxillary sinus from an adolescent with congenital hypogam-maglobulinemia and chronic intestinal cryptosporidiosis(Sponseller et al. , 2014). In immunocompromised humans ,the extra intestinal cryptosporidiosis was reported and Cryptosporidium was recovered from the biliary tract , lungs, and pancreas (Leitch and He, 2012).   Recent evidence indicates that respiratory cryptosporidiosis may occur commonly in immunocompetent children with cryptosporidial diarrhea and unexplained cough(Kumar et al., 2016) .

 The presence of various cryptosporidial forms lining the bronchial epithelium of lung sections suggests that the protozoan may be capable of propagating within the human respiratory tract in much the same way that it parasitizes the gastrointestinal epithelium(Mukerjee et al., 2015) . Likewise, demonstration of intramacrophagic oocysts and extracellular invasive forms (sporozoites or merozoites) in respiratory secretions implies an active life cycle within the respiratory tract, where transmission of oocysts may be facilitated by coughing or expectoration(Sifuentes and Di Giovanni, 2007;O'hara et al., 2011).

 Findings from animal models, human case reports, and a few epidemiological studies suggest that Cryptosporidium may be transmitted via respiratory secretions, in addition to the more recognized fecal-oral route(Florescu and Sandkovsky, 2016). It is postulated that transmission of Cryptosporidium oocysts may occur by inhalation of aerosolized droplets or by contact with fomites contaminated by coughing(Sponseller et al. , 2014). Delineating the role of the respiratory tract in disease transmission may provide necessary evidence to establish further guidelines for prevention of cryptosporidiosis (Sponseller et al. , 2014).

Food borne transmission

 Cryptosporidium is listed as a rare notifiable protozoan causing food borne illness in most countries, and therefore are often overlooked during monitoring (Dodd et al., 2017). The general lack of information on foodborne cryptosporidiosis is compounded by routine methods that are insufficient to detect low numbers of oocysts in suspected food and water samples; inadequate epidemiological data collection; and loss of outbreak samples because of consumption, destruction, or inaccurate recall (Budu-Amoako et al., 2011).

 The true nature of foodborne cryptosporidiosis has not been adequately quantified (Squire and Ryan, 2017).The contamination of foods with Cryptosporidium might occur by a number of means and at various points along the farm-to-fork continuum (Robertson, 2016). Some possible sources of contamination include direct contamination by infected farm workers or food handlers and indirect contamination by oocyst contaminated water used in irrigation, washing, or processing foods(Dixon, 2015). livestock considered potentially important source of contamination of foods is (Dixon, 2009).Livestock can have a high prevalence of infection with Cryptosporidium ,and infected animals can shed a high number of oocysts (Santín, 2013). During peak shedding, infected animals, mainly young animals, can excrete ,10^7 Cryptosporidium oocysts per gram of feces for a number of days (Budu-Amoako et al. , 2011). Therefore, produce in the field could become contaminated when livestock defecate near crops, when crops are irrigated or washed with water accessed by livestock or contaminated through agricultural runoff, or when manure is intentionally applied to arable land(Boyer et al., 2009) . In addition to produce, products of animal origin such as milk and meats could also be subject to contamination with oocysts from livestock. (Budu-Amoako et al. , 2011) .

 There are several sources and routs of food contamination with cryptosporidium oocysts. Use of oocyst contaminated feces (night soil),farmyard manure and slurry as fertilizer for crop cultivation(Simjee, 2007;Putignani and Menichella, 2010) .Contamination of crops by pasturing infected livestock near crop ,defecated of infected feral hosts onto crop(Simjee, 2007;Barbosa-Canovas et al., 2009).Direct contamination of foods following contact with oocyst contaminated feces transmitted by coprophagous transport hosts (bird and insects)(Putignani and Menichella, 2010). Using of contaminated wastewater for irrigation ,as well as

aerozolization of contaminated water used for insecticide and fungicide sprays and mists (Simjee, 2007;Sampson et al., 2017).Aerosols from slurry spraying and muck spreading also play a critical role for food borne cryptosporidiosis(Putignani and Menichella, 2010) .Washing " salad ",vegetable ,or those consumed raw, in contaminated water (Putignani and Menichella, 2010).Poor personal hygiene food handler (Smith and Nichols, 2010).Use of contaminated water for making ice and frozen chilled foods(Putignani and Menichella, 2010).Use of contaminated water for making products which receive minimal heat or preservative treatment(Putignani and Menichella, 2010;Simjee, 2007) . Ingestion of viable oocysts from raw or under-cooked shellfish which accumulate human infectious oocysts from their contaminated aquatic environment(Smith et al. , 2006;Smith and Nichols, 2010).

Other source of transmission

Soil

Faecal contamination of soil and surface water can ultimately lead to contamination of fresh foods, sources of water(Al-Habsi et al., 2017) . livestock faeces containing oocysts were applied to soil blocks which were then intermittently irrigated. Oocysts moved within the soil for up to 70 days, the oocysts persistence in soil depends on soil types, in clay soil is more than silt soil , while it did not found in sandy soil (Gong et al., 2017;Al-Warid et al. , 2010).

Migratory Birds

Billions of birds travel across national and international borders of different area around the world .These birds play a significant role in the ecology and circulation of pathogenic organisms. They carry patho-gens that can be transmitted at 'stopovers' and that can be dangerous for domestic animals and humans (Georgopoulou and Tsiouris, 2008) Although the migration of the birds is a spectacular and natural phenome-non, it also creates unavoidable dangers for public health(Bengis et al., 2004).

In recent decades, migratory birds and wildlife have been incriminated in and associated with emergent and resurgent diseases .They are implicated in the transmission of zoonoses and other microbial pathogens by three main mechanisms, namely: migratory birds act as biological carriers, migratory birds act as mechanical carriers and carriers of infected ectoparasites (Jourdain et al., 2007).

Cryptosporidium spp oocysts could be distributed by birds over wide areas (Georgopoulou and Tsiouris, 2008). Subsequently, it was shown that Canada geese (*Branta canadensis*) might serve as accidental carriers of cryptosporidia infectious to humans and probably plays a minor role in the animal-to-human transmission cy-cle of the *Cryptosporidium* spp. including the two common species *C. hominis* and *C. parvum* have also been identified in birds (Ryan, 2010) .

Genus *Cryptosporidium* has a large diversity of avian hosts and low specificity for avian species(Nakamura et al., 2009). Recent articles indicated that a total of 10 novel avian genotypes have been identified in birds (Ryan, 2010).

The mode of transmission can either be direct or indirect. Direct transmission is caused by the migratory bird itself via intimate contact, contact by inhalation of discharged respiratory droplets from coughing or sneezing or by infectious faeces. Indirect transmission occurs via an arthropod, such as a flea, mite, mosquito, sand fly or tick, or an inanimate vehicle like water, food, soil, etc. In addition, the airborne spread by droplet nuclei, dust etc. is considered to be an indirect mode of transmission(Hubalek 2004) .The mode of transporta-tion of pathogens by migratory birds depends on the route of transmission(Georgopoulou and Tsiouris, 2008).

The effective transmission of pathogens by migratory birds can be influenced by seasonality during mi-gration and immune status of migratory birds, the immense stress caused by migration on birds leads to di-minishes their resistance to infections, increases the shedding rate of infectious agents (Bengis et al., 2004;Georgopoulou and Tsiouris, 2008) .

Mollusca

Numerous studies have shown that various freshwater and marine mollusks can ingest and carry *Cryptosporidium* oocysts (Downey and Graczyk, 2007;Lucy et al., 2008) .

Flies and insects

C. parvum oocysts can be transported by filth flies*(Musca domestica)* not only from cattle sources but from any unhygienic source contaminated with *C. parvum*, i.e., toilets, abattoirs, trash, carcasses, landfill and sewage (Szostakowska et al., 2004) . Also, synanthropic flies are reported as major epidemiologic factors responsible for the mechanical spread of Cryptosporidium oocysts(Conn et al., 2007)

Cockroaches

Oocysts of C. parvum were found in the intestinal tracts of cockroaches (*Periplaneta americana*), they resist and stay infective , suggesting that cockroaches had a role in disseminating the parasite (Al-Warid et al. , 2010) (Alam et al., 2013)reported that oocyst of Cryptosporidium were recovered from (9.09%)   of cockroaches fecal materials .

Beetles

Oocysts also were recovered from the external surfaces of different beetles species. Dung beetles can potentially disseminate Cryptosporidium oocysts(Xiao, 2009) . Dung beetles of the genera *Onthophagus, Ataenius*, and *Aphodius* which collected from facilities and pastures housing domestic sheep, dairy cattle, beef cattle, and horses as well as fields frequented by Canada geese and white-tailed deer have capability of disseminating oocysts in the environment (Al-Warid et al. , 2010;AL-Gelany 2003) .

Testing of infectivity of *C parvum* oocysts ingested by dung beetles, *Anoplotrupes stercorosum*, *Aphodius rufus,* and *Onthophagus fracticornis*, demonstrated that the oocysts passed unaltered through the mouthparts and gastrointestinal tracts of these beetles (Graczyk et al., 2005). Thus, coprophagic beetles can be involved in the epidemiology of cryptosporidiosis by transmission of infective oocysts of Cryptosporidium.

Crabs

Atlantic blue crabs can also serve as potential vectors of *Cryptosporidium* in an experimental setting (Graczyk et al., 2007) . under experimental condition, *Cryptosporidium* oocysts were detected in the eluting fluid from crabs after they were exposed to 2×10^4 *C. parvum* oocysts in water (Xiao, 2009). Overall, 74.8% of the inoculated oocysts were recovered from crab, hand wash water, and tank water.   A single crab was carried approximately 7.6×10^2 oocysts on its external surfaces, and approximately 10.4% of oocysts carried by the crabs ended up on the hands of a person who was handling these crabs during the experiment(Xiao, 2009).

CONCLUSION

Multiple transmission pathways are the cardinal problem in cosmopolitan nature of cryptosporidiosis ,thus extra attention required for termination of such pathways for complete eradication of the Cryptosporidium infection   .

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