Cryptosporidiosis: A Zoonotic Challenge in Waterborne Disease Management

Shameeran Salman Ismael[1,*] and Wasan Madhat Yousif Alnakshabandi[1]

[1]Department of Medical Laboratory Sciences, College of Health Sciences/University of Duhok, Duhok, Iraq
*Corresponding author: shameeran.Ismael@uod.ac

Abstract

Cryptosporidiosis is a zoonotic emerging disease caused by the protozoan parasite of *Cryptosporidium. It* is spread by food and drink and characterized by profuse watery diarrhea. Right now, there aren't effective medications or vaccinations on the market for the management and treatment of Cryptosporidiosis. We must learn more about the disease's transmission and spread, as well as how to break the cycle of transmission, to avoid cryptosporidiosis in both humans and animals. Understanding cryptosporidiosis, including its infectious stage, pathophysiology, life cycle, epidemiology, prior outbreaks, infection source, transmission, and high-risk groups, is the main goal of this chapter. The facts presented in this review will be useful in addressing upcoming human and animal *Cryptosporidium* infections and lowering the incidence of the disease.

Keywords: Emerging protozoan, Gastrointestinal infection, Cryptosporidiosis, Epidemiology, Outbreaks.

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Introduction

Cryptosporidiosis is the most common and prevalent waterborne parasitic and zoonotic disease caused by a coccidian protozoon parasite *Cryptosporidium* (Helmy et al., 2017). *Cryptosporidium* spp. is considered the major source of waterborne parasitic infection outbreaks globally (Gharpure et al., 2019). About fifty-eight million cases of diarrhea among children are identified per year, and these occurrences are linked to protozoal infections. In particular, the World Health Organization's "Neglected Disease Initiative" involved waterborne diseases like *Giardia* and *Cryptosporidium* (Savioli et al., 2008). In immunocompetent people, Cryptosporidium infections cause acute, self-limiting gastroenteritis, but in immunocompromised people, they can cause chronic, sometimes fatal diarrheal illness. Because of their developing immune systems, neonates are particularly vulnerable to infections, which can be contracted by ingesting small amounts of the parasite's oocysts (Dadonaite et al., 2019). *Cryptosporidium* is responsible for children's diarrhea in developing countries, and the disease is more potent in immunocompromised patients (Mosier & Oberst, 2000). The final host is infected with cryptosporidiosis by ingestion of sporulated oocysts with contaminated foods, vegetables, grass, or drinking of contaminated water, or through direct contact with infected animals or people (CDC, 2017). This chapter outlined cryptosporidiosis, the most important species that infect humans, its life cycle, and sources of infection, clinical manifestation, diagnosis, and disease prevention.

1.1. Causative Agent

Cryptosporidium species are intracellular coccidian parasites under the phylum Sporozoa (Apicomplexa) (Fayer et al., 2000, Hijjawi et al., 2002, Pal et al., 2016). The pathogenic human species responsible for disease and outbreaks are *C. parvum, C. cuniculus, C. hominis, and C. meleagridis, C. parvum* is considered the most common and pathogenic. Species that infect animals are *C. andersoni, C. baileyi, C. ducismarci, C. fragile, C. galli, C. meleagridis, C. parvum, C. ubiquitum, C. serpentis, C. varanii, and C. xiaoi* (Gaibova et al., 2017). It is commonly reported that the most significant species, *C. parvum* can infect both humans and animals (Pal et al., 2007, Mor et al., 2018). At this time, about 60 distinct genotypes of *Cryptosporidium* with varying molecular sequences have been identified. Subtypes of *Cryptosporidium* are identified by the number of repeats in each strand. In certain subtypes, the trinucleotide repeats are followed immediately by short, repetitive sequences (R). Eleven subtype families (IIa–IIk) with a minimum of 78 subtypes have been identified in *C. parvum* (Fayer, 2008, Ahmed & Karanis, 2020).

1.2. Transmission of Cryptosporidiosis

Cryptosporidium oocysts are released from stools, that's accidentally consumed and can spread directly from animal to animal, from animal to human, or from human to animal (Desai et al., 2012; Ismael et al., 2024). Among the indirect transmissions are cross-contamination of food items, food components, drinking water, and other clothes and footwear items used in livestock farms or wildlife parks that have come into contact with an infected person's or animal's excrement. It can live and infect the intestinal epithelium in humans and many vertebrate animals. Also, spreads from the stool into the surrounding environment through soil and water sources like rivers, ponds, sewage, slurry, and wastewater, as well as through many water containers, especially public water supplies that are not properly treated (Hubalek, 2003, Efstratiou et al., 2017, Tomazic et al., 2018). Cryptosporidiosis outbreaks have been documented in both industrialized and developing nations (Shirley et al., 2012, Ursini et al., 2020). These outbreaks are primarily caused by the virus's low infectious dose, diverse animal reservoirs, and resistance to chlorination (Bouzid et al., 2013, Adeyemo et al., 2019).

1.3 Life cycle of Cryptosporidiosis

Humans are infected by consuming sporulated oocysts. After ingestion of sporulated oocysts, in the small intestine, the excystation occurs and the four sporozoites are released and invade the rims of the intestinal epithelial cells (Tzipori & Ward, 2002, Tzipori & Ward, 2008). Asexual reproduction began and two times schizogony occurs (Chalmers et al., 2011), the result of the first schizogony is eight merozoites are released and invade a healthy epithelial cell and the second schizogony takes place and form four merozoites (Bouzid et al., 2013). Then merozoites are released and invade another intestinal cell and sexual reproduction begins followed by the forming of male and female gametes, zygote, ookinete, and oocyst, two types of oocysts are produced thin-walled and thick-walled oocysts, the thin-walled type is responsible for the autoinfection and the thick-walled is a pass with stool and considered the source for infection as seen in Figure 1 (Jenkins et al., 2010, Khan et al., 2019).

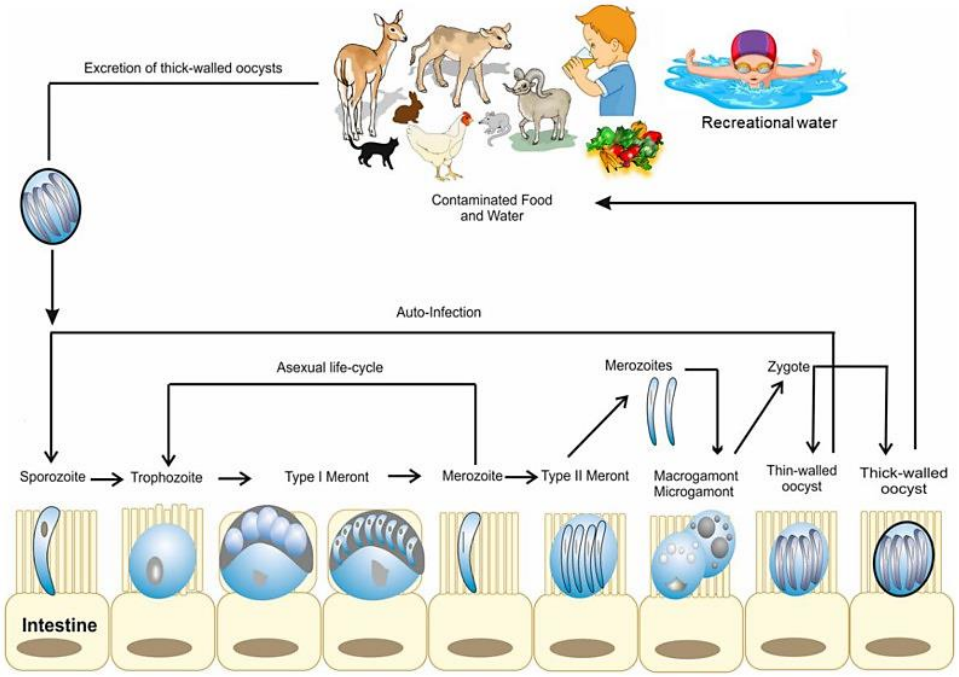

Fig. 1: Cryptosporidiosis life cycle (Etzold et al., 2014)

2.4. Prevalence of Cryptosporidiosis

An estimated 30 to 50 percent of deaths in young people worldwide are attributed to *Cryptosporidium* infections, which are also the second leading cause of diarrhea and pediatric mortality after rotavirus (Striepen, 2013). There have been 325 documented cases of parasitic protozoan disease up to 2007, with *C. parvum* accounting for 50.8% of these cases, with 93% of these cases occurring in North American and European nations. Of these, 30 percent of outbreaks were reported to have originated in Europe, with the UK responsible for 24 percent of all outbreaks worldwide (Karanis et al., 2007) Australia was the continent where Cryptosporidium outbreaks were most common, followed by North America and Europe (Baldursson & Karanis, 2011). North America accounted for 36% of the total number of publications, then followed by the European Union (31%), Asia (19%), South and Central America (7%), Oceania (5%), and Africa (3%), according to a recent study that demonstrated the scientific motivation provided to the surveillance of parasitic protozoan illness to fifty-three nations (1970 to 2016) (Efstratiou et al., 2017).

According to an epidemiological study from three African and three Asian sites, *Cryptosporidium* spp. was the second most common parasite that caused severe diarrhea and substantial morbidity in children aged 12 to 23 months (Kotloff et al., 2013). It is predicted that more than 2.9 million children under the age of 24 months in sub-Saharan Africa contract Cryptosporidium each year (Squire & Ryan, 2017). Sixteen water-borne protozoa outbreaks were documented in Latin American nations between 1979 and 2015; the most prevalent protozoa in these outbreaks were Cryptosporidium spp. (Rosado-García et al., 2017). Another study was done by Khan et al. (2019), which found that the primary source of infection in children was *C. parvum*. The findings showed that people who had diarrhea had a higher chance of contracting *Cryptosporidium* and that several environmental factors might potentially be important in the parasite's transmission.

The prevalence of cryptosporidiosis in Iraq differed from city to city and from year to year. The prevalence of infection in Iraq from 2002 to 2020. In 2002, the prevalence of infection among adults was 100% in Basrah City (Mahdi & Ali, 2002), was high in Diwaniya City at 35.74% (Mahdi and Ali, 2004), in Mosul City (Mukhtar and Sherefat, 2005), in Kut City, Iraq, a high prevalence was reported among children less than twelve years old at 33.99% (Rahi *et al.,* 2013), in Kirkuk City was low at 6.7% (Salman *et al.,* 2016), in Erbil City among pediatrics was 10.77% (Kanabe & Darogha, 2017). In Duhok City, a low prevalence rate was reported by Hussein & Meerkhan (2019), and a high prevalence rate was reported in both Baghdad City (Whaeeb *et al.,* 2020) and in Duhok City (Al-Saeed and Abdo, 2020), which were 44.5% and 67.0%, respectively; finally, in Duhok City, it was as high as usual in 2024, at 17.1% (Ismael *et al.,* 2024). Lack of knowledge and regular testing to identify this parasite may be the cause of the high prevalence of Cryptosporidiosis. Also, since many people are affected and there are related socioeconomic consequences, the effects of waterborne epidemics are rather substantial, and the oocysts are extremely resistant to both biological and chemical threats (Khan et al., 2019).

The economic and health consequences of cryptosporidiosis outbreaks linked to polluted water sources can be severe. An estimated 96.2 million Dollars was spent on the massive waterborne outbreak in Wisconsin, which impacted 403,000 people (Corso et al., 2003). According to estimates, a waterborne cryptosporidiosis outbreak in Sweden, where the attack rate was 45% of the country's 60, 000 inhabitants, resulted in 50,000 sick leave days (Ridderstedt et al., 2018). Public water supplies are frequently condemned, water boil notices are posted, and bottled water is provided when Cryptosporidium oocysts are found in them. Over 120,432 persons were impacted by a boil water order that was in effect for 158 days during a recent waterborne outbreak in Ireland, which cost over 19 million EUR (Chyzheuskaya et al., 2017).

2.5. Clinical Manifestations and Risked Population

In both immunocompetent and immunodeficient individuals, *Cryptosporidium* has been identified as a cause of gastrointestinal disorders (Rossle & Latif, 2013). Cryptosporidiosis is characterized by severe diarrhea that can sometimes be fatal. Watery diarrhea and dehydration are the most severe symptoms in immunocompromised individuals, but symptoms in immunocompetent individuals typically resolve on their own. Additionally, AIDS may be lethal for immunocompromised patients (Pal, 2007, Chukwuma, 2019).

Risk populations are poor nations, immunocompromised patients, and children. Due to a lack of resources and knowledge about illness prevention and control, the disease is more common in developing nations than in developed ones. Although cryptosporidiosis is rare in immunocompetent individuals, it causes 10% to 15% of cases of severe diarrhea in underdeveloped nations, especially in undernourished children under five. Outbreaks of cryptosporidiosis have been linked to tainted drinking water or swimming pools in several countries (Lebbad et al., 2021). People who are immunocompromised due to infection with HIV are more likely to develop Cryptosporidiosis, and most of the time, having the parasite is linked to diarrheal illness (Pozio and Morales, 2005). Malignant neoplasms, organ transplants, and primary immunodeficiency disorders increased the possibility of infection in these individuals; one and multiple species of *Cryptosporidium* were found in these patients (Hunter and Nichols, 2002).

1.6. Diagnosis

There are several techniques used for diagnosis as mentioned in Table 1. Cryptosporidiosis can be directly detected in fecal samples using a variety of techniques, such as microscopy identification of the oocysts, which counts the number of oocysts in the stools using sedimentation or flotation methods (Under a microscope, the detection of oocysts limit has been recorded to be as low as 50,000 to 500,000 oocysts per gram of stool). The most common methods for directly detecting *Cryptosporidium* oocysts are either unstaining microscopy or the modified Ziehl-Neelsen stain, in which the oocysts are colored purple on a blue backdrop (Chartier et al., 2013). Monoclonal antibodies that react with the oocyst wall antigen are also frequently utilized in immunofluorescent antibody-based (IFA) staining procedures. Compared to other conventional staining techniques, these are less expensive and have a high sensitivity (Garcia et al., 1983, Cacciò & Widmer, 2013).

The most effective techniques for screening a large number of samples, especially in epidemiological surveys, are thought to be serological approaches. Enzyme-linked immunoelectron transfer blots and enzyme-linked immunosorbent assays (ELISA) are among the serological testing. In comparison to immunofluorescence approaches, enzyme immunoassay techniques are more sensitive, quicker, simpler, and less expensive (Fayer & Xiao, 2007). It is also possible to utilize rapid immunochromatographic tests (Helmy et al., 2014, El-Missiry *et al.*, 2019), which use monoclonal antibodies to detect the proteins in the oocyst cell wall (Papini & Cardini, 2006).

Table 1: Different techniques are used for the diagnosis of Cryptosporidiosis:

Diagnostic Technique	Description	References
Microscopy	Utilizes modified Ziehl-Neelsen staining to identify oocysts in stool samples.	Omoruyi et al., 2014
Immunochromatography	Rapid test detecting Cryptosporidium antigens in fecal samples.	Khurana & Chaudhary, 2018
Enzyme-Linked Immunosorbent Assay (ELISA)	Detects antigens in stool samples, offering higher sensitivity than microscopy.	Barwari & Ismael, 2011; Abdou et al., 2022
Polymerase Chain Reaction (PCR)	Molecular method detecting Cryptosporidium DNA in various samples, including stool and biopsy.	Costa et al., 2021, Haji & Ismael, 2023
Loop-Mediated Isothermal Amplification (LAMP)	Simple and specific molecular technique for detecting Cryptosporidium DNA in environmental samples.	Karakavuk et al., 2014
Histological Examination	Involves using stains like haematoxylin and eosin on biopsy samples to identify oocysts.	Khurana & Chaudhary, 2018
Electron Microscopy	Direct visualization of oocysts; historically used but less common due to high costs and complexity.	Khurana & Chaudhary, 2018

1.7. Prevention of Cryptosporidiosis

The primary preventive measures include drinking water that has been treated, eating cooked meals when visiting places with contaminated food supplies, disinfecting swimming pools, preventing patients with diarrhea from swimming, washing hands after using restrooms or changing children's diapers, and using protection techniques for safe sex as shown in Figure 2. (Manyazewal et al., 2018, Firouzivand et al., 2021). Given the difficulty of treating cryptosporidiosis, lowering the oocyst count may help to lessen the infection's severity and enable young animals and children to build immunity through appropriate colostrum feeding. More care must be taken with personal hygiene when handling animals and children who have diarrhea (Innes et al., 2020). Immunocompromised individuals and young children are not recommended to handle animals that are diarrheal (Pal, 2007).

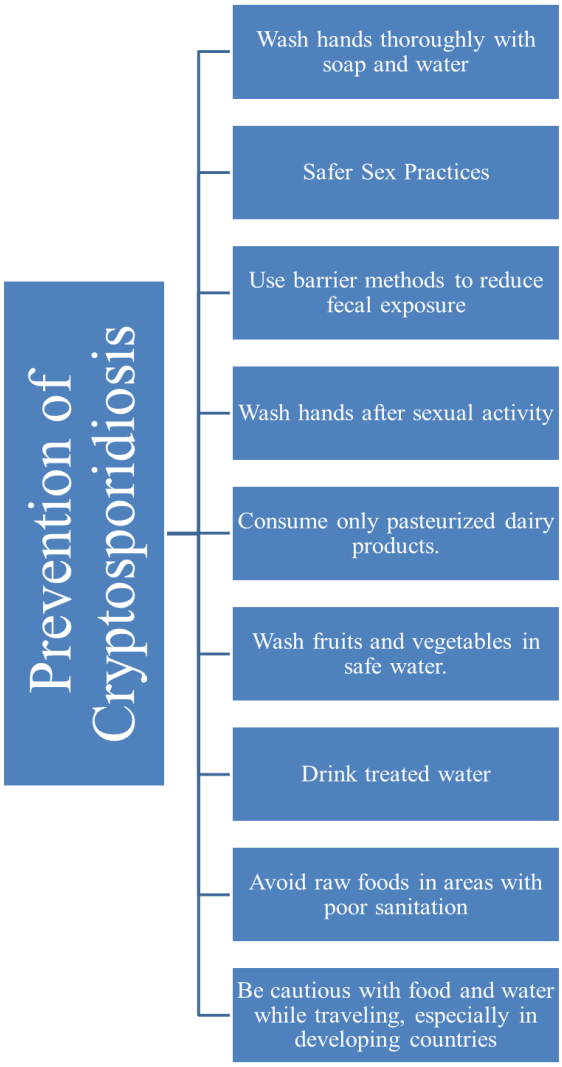

Fig. 2: Illustrated the prevention of Cryptosporidiosis

1.8. Treatment

According to Lima et al. (2011), the optimal treatment for cryptosporidiosis includes adequate hydration and electrolyte maintenance, anti-motility medicines, anti-parasitic medications, nutritional support, and immunosuppressive reversal. Nitazoxanide, on the other hand, may reduce the risk of death in malnourished infants and presumably reduce the severity of diarrhea (Amadi et al., 2002). Its effectiveness has also been verified among adults according to Rossignol et al. (2006). Also, it is important to treat infected domestic animals, due to zoonotic species (Innes et al., 2020).

Effective therapies for cryptosporidiosis were not found during the initial evaluation of the substances that were accessible. Several medications that were formerly thought to be useful have not worked in clinical studies (Cabada & White, 2010). Nitazoxanide is the only medication approved for the treatment of *Cryptosporidium*. In the 1980s, nitazoxanide was created by joining a thiazole ring. Nitazoxanide is a broad-spectrum anti-parasitic that has been used in controlled trials for giardiasis and cryptosporidiosis, as well as a deworming agent (Rossignol et al., 2001, Bailey & Erramouspe, 2004). Other medications such as bovine anti-cryptosporidium immunoglobulin, spiramycin, and azithromycin have also been shown to have some effect in case series (Cabada & White, 2010). Children with cryptosporidiosis appeared to respond more effectively to azithromycin than to two anthelminthic medications (Allam & Shehab, 2002). Additionally, it is frequently utilized in combination with paromomycin/nitazoxanide in weakened hosts, as some individuals have reduced parasite clearance and stool frequency (Legrand et al., 2011). In HIV/AIDS patients, paromomycin, which some anti-*Cryptosporidium* efficacy in immunocompetent individuals, is likewise ineffective. Restoring immunological conditions by a combination of antiretroviral therapy is necessary for symptom resolution. For patients with cryptosporidiosis, combination antiretroviral and antiparasitic therapy appears to be beneficial, particularly when used with a protease inhibitor-based treatment that appears to have some extra anti-parasitic action (Cabada & White, 2010).

Nanoparticles (NPs) have been generating a lot of attention lately in the fields of drug delivery and therapy (De Jong & Borm, 2008). The invention of nanoparticles into intelligent coating systems for therapeutic substances enables controlled release medication delivery to the intended locations. Furthermore, this targeted delivery increases patient compliance with lower dose frequency and lessens therapeutic side effects (Rizvi & Saleh, 2018). The FDA of the United States has approved chitosan nanoparticles a naturally occurring cationic polysaccharide that is mucoadhesive and biocompatible, for use in medication delivery (Sorlier et al., 2001, Moawad et al., 2021). *In vitro,* it was established that chitosan nanoparticles conjugated with polyvinyl alcohol inhibit the attachment of *Cryptosporidium* sporozoites to enterocytes in cases of cryptosporidiosis (Luzardo Álvarez et al., 2012, Ahmed et al. 2019).

Conclusion

Cryptosporidium infections are prevalent in both people and animals. The two categories most at risk for infection are immunocompromised people and children under twelve years. The majority of *Cryptosporidium*-related foodborne outbreaks are zoonotic. Regular surveillance systems and the implementation of the One Health approach are necessary to stop disease outbreaks. In order to stop and/or lessen future epidemics globally, food safety and water cleanliness are essential. Considering the sources of infection (people and animals), the transmission pathways, the environmental survival of oocysts, and the risk factors can help prevent and control *Cryptosporidium* infections. There are currently no effective medications or vaccinations to cure or prevent infection in people or animals.

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