World Journal of Current Medical and Pharmaceutical Research
Content available at www.wjcmpr.com ISSN: 2582-0222

A GENERAL REVIEW ON *CRYPTOSPORIDIUM PARVUM*: PATHOGENESIS, DIAGNOSIS AND TREATMENT

Fatima Ibrahim Mohammad[1]*, Doaa Abd Alabas Muhammed Ridh[2], Osamah Faisal Kokaz[3]
[1,2] Department of Environment, College of Science, University of AL-Qadisiyah, AL-Diwaniyah, Qadisiyah, Iraq.
[3] Al-Muthanna University, Medicine College, Samawah, Iraq

Article History
Received on: 22-04-2023
Revised on: 08-05-2023
Accepted on: 02-06-2023
***Keywords*:**
Cryptosporidiosis, protozoan parasite, diarrhea, immunocompetent patients, immunocompromised patients.

Abstract

Cryptosporidium parvum is one causes of severe diarrheal disease worldwide and contributed to neonatal and early infect mortality. *C. parvum* is responsible for most zoonotic infections in human. *Cryptosporidium* is intra cellular protozoan parasite belong to phylum Apicomplexa. *Cryptosporidium* can spread to various organs and systems of the body especially pancreatic, hepatobiliary as well as extra- intestinal such as pulmonary system and leading to chronic disease and weakness.The infection can be acute and self-limiting illness in immunocomponent patients, whereas in immunocompromised cryptosporidiosis can become a chronic and life threaten disease.

***Corresponding Author**
Fatima Ibrahim Mohammad

DOI: https://doi.org/10.37022/wjcmpr.v5i3.264

Introduction

Cryptosporidium parvum is one causes of severe diarrheal disease worldwide and contributed to neonatal and early infant mortality. *C.parvum* causes cryptosporidiosis is a zoonotic intestinal disease that affects wildlife, neonatal cattle and humans (Masheminasab *etal.*,2022) causing acute gastroenteritis that characterized with diarrhea and abdominal pain.

The parasite causes lung infections that can also be fatal in the immunocompromised hosts, hence Cryptosporidiosis is considered one of riskiest opportunistic infections for them (Gerace *etal.*,2019).

Cryptosporidium was first detected by Tyzzer in 1907 (Tzipori and Widmer, 2008). *Cryptosporidium* was recognized as an opportunistic pathogenic parasite in 1976 where it was thought to be a nonpathogenic parasite (Meisel *etal.*,1976; Nime *etal.,*1976).

There are more than 30 species included in the genus Cryptosporidium, only 2 species commonly infect humans, namely *Cryptosporidium parvum* and *Cryptosporidium hominis* (Ryan *etal.*,2014; Thomson *etal.*,2017).

C.parvum is responsible for most zoonotic infections in humans (Ryan *etal.*,2014). *Cryptosporidium* is intracellular protozoan parasite belong to phylum Apicomplexa (Suarez *etal.,*2017).

This parasite can cause many symptoms such as diarrhea depending on the host and its immune status, the infection with *Cryptosporidium* can spread to various organs and system of the body especially pancreatic, hepatobiliary as well as extra-intestinal such as pulmonary system and leading to chronic disease and weakness (Leitch and He, 2012).

The infection can be a cute and self- limiting illness in immunocompetent patients, whereas in immunocompromised patients Cryptosporidiosis can become a chronic and life threaten disease (Kurniawan *etal*.,2013; Elwin *etal*.,2012).

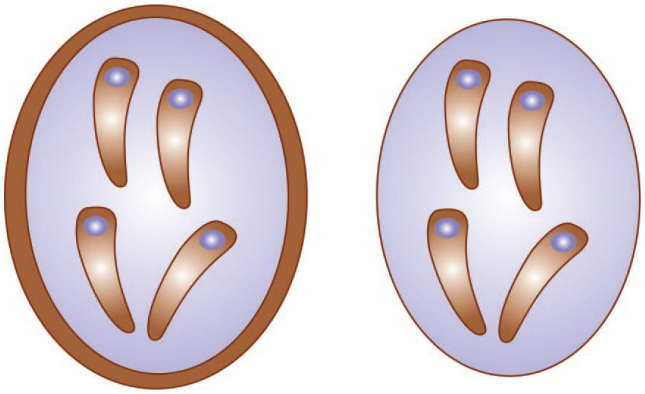
The infection of Cryptosporidiosis occurs mainly by digestion contaminated food and water with oocysts, oocysts that release sporozoite which invade the intestinal epithelium cells predominantly localized to the jejunum and ileum (Baldursson and Karanis, 2011; Chppell *etal*.,2006).

Life cycle

Cryptosporidium parvum complete its life cycle, both sexual and a sexual phases in a single host infection is initiated by ingestion of food and water contaminated with feces containing oocysts, the oocysts contains four sporozoites which are released in the intestine (Paniker, 2013).

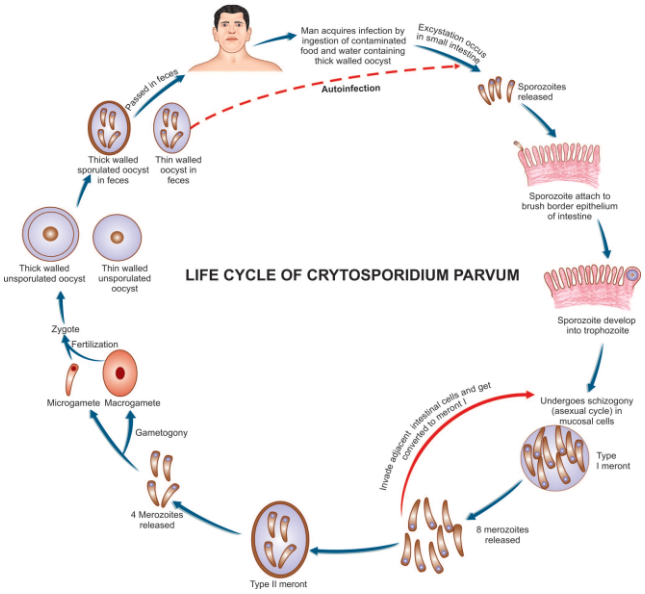
Then, the parasite undergoes a sexual or schizogony reproduction leading to the production of eight merozoites within a type 1 meront, within the parasite phorous vacuole (Bouzid *etal*.,2013). The merozoites can propagate the infection to other sites of the intestine within invade the neighboring epithelial cells, the merozoites can undergo a sexual stage characterized by production of thin walled oocysts that auto infect the host and multiplication of merozoites (type 1 meront) and sexual stage characterized by formation of type 1 meront, which after recognition in microgametocytes and macrogametocytes to form the zygote (Tzipori and Ward,2002).

The zygote will form four sporozoites within thin or thick walled oocysts through a process called sporogony. The thick walled are prodected by resistant wall oocyst release through feces into the environment, ready to infect new individual (Bouzid *etal*.,2013; Jenkins *etal*.,2010) as figure (1):



A B

Figure (1): Oocysts of *Cryptosporidium parvum.* A. Thickwalledoocyst B. Thinwalledoocyst



Figure(2): life cycle of *Cryptosporidium parvum*

Pathogenesis

Cryptosporidium infection usually produces about of watery diarrhea in immunocompetent persons, although the infection in some persons may not lead to the symptoms (Khalil *etal*.,2018; Shoultz *etal*.,2016 and Adler *etal*.,2017).

The infection with cryptosporidiosis can be occur due to direct contact with infected animals particularly calves or drink contaminated water (Bouzid *etal.,*2018) *Cryptosporidium* infections are common in individuals no have weakened immune system such as human immunodeficiency (HIV) transplant patients and cancer (Bouzid *etal*., 2013; Wang *etal*.,2018; Florescu and Sandkovsky *etal*.,2016).

Crypatosporidiosis caused in over 50,000 deaths every year (Shirley *etal*.,2012; Wang *etal*.,2018).

Cryptosporidium is one of the most important protozoan pathogen that cause water borne outbreaks world (Bouzid *etal*.,2013; Adler *etal*.,2017 and Rehn *etal*.,2015).

Cryptosporidium is live in the intestine of infected humans and animals in the form of oocysts, which released in the feces (Bouzid *etal*.,2013) after infection, Cryptosporidium alters the infection of the intestinal barrier, increasing its absorption, secretion of fluid, permeability, electrolytes, the severity, persistence and thereby and effect of the infection depend on the immunocompromised status (Kumar etal.,2018; petry *etal*.,2010).

The oocyst are very resistant to chlorine, chlorine dioxide and chloramines which are commonly used in water system disinfection and remain vital in the environment for a long time (Shirvastava *etal*.,2017). human can infected with *Cryptosporidium* by touching anything in contact with contaminated feces but the most common mode of transmission occur by ingestion of oocysts in contaminated water, food or air by inhalation of aerosolized droplets through secretions or by coughing (Petry *etal*.,2010; Sponseller *etal*.,2014).

Immunocompromised patients are more susceptible to infection than individuals with a healthy immune system. In the patients with HIV/ AIDS the disease is difficult to treat and can even result in death where the parasite often causes a

chronic prolonged form of a disease (Wang *etal*.,2018). In this patients this disease characterized by malabsorption and fever and can cause inflammatory disease of the biliary tree leading to sclerosing cholangitis, biliary tract obstruction, papillary stenosis and pancreatitis (Wang *etal*.,2018; Wang *etal*.,2018). For this reason, cryptosporidiosis in patients with acquired immune deficiency syndrome is considered one of the riskiest opportunistic infections (Wang *etal*.,2018).

Diagnosis

1-Stool examination: is usually made by identifying the presence oocysts of four to six µm in diameter in the feces of the infected individuals (Khurana and Chaudary,2018; Ahmed and Karanis, 2018).

The feces sample must be concentrated using the formation ether sedimentation befor to microscopic examination for detection of oocysts in feces while the oocysts of *Crtptosopridium* in un concentrated fecal smears can be observed by phenol auramine or acid fast (modified Ziehl-Neelson method) staining where the oocysts stain red and bright yellow, respectively (Khurana and Chaudhary,2018; Omoruyi *etal*.,2014).

2-Serodiagnosis: for detection of *Cryptosporidium* antigens there are good sensitivity and specificity techniques such as the enzyme linked immunosorbent assay (ELISA) and immune chromatographic test (Agnamey *etal.*,2011; Hawash,2014).

In previous studies have shown that antigen/ antibody based detection techniques are in effective in the burden of cryptosporidium in the patients in blew the minimum threshold (Hawash,2014).

3-Molecular diagnosis: Polymerase Chain Reaction (PCR) is also used to detect viable cysts (Paniker,2013). PCR now accepted in most laboratories for the detection of *Cryptosporidium* in the feces as the gold standard (Friesen *etal*.,2018; Autier *etal*.,2018).

Treatment

Nitazomamide or Parmomycin can be partially effective in few patients with AIDS, although no chemotherapeutic agent effective against cryptosporidium has been identified. Antiretroviral therapy can be improvement in immune status and lead to progress of cryptosporidiosis. There are other treatment methods include supportive therapy with electrolytes, fluids and nutrient replacement (Paniker, 2013).

Conclusion

Cryptosporidium parvum can cause lung infections that can be fatal in the immunocompromised patients hence cryptosporidiosis is considered one of riskiest opportunistic infections. There are more than 30 species included in the genus cryptosporidium, only two species commonly infect humans, are C. parvvmand C.hominis. Nitazomamide and parmomycin are effective in few patients with AIDS as well as antiretroviral therapy can be improvement in immune status.

Funding

No Funding

Conflict of Interest

All authors are declared that no Conflict of Interest.

Informed Consent

Not Applicable

Ethical Statement

Not Applicable

Author Contribution

All authors contributed equally

References

1. Adler S , Widerstrom M, Lindh J, Lilja M. Symptoms and risk factors of Cryptosporidium hominis infection in children: data from a large waterborne outbreak in Sweden. *Parasitol Res*. 2017;116(10):2613–18.
2. Agnamey P , Sarfati C, Pinel C, Rabodoniriina M, Kapel N, D utoit E, et al. Evaluation of four commercial rapid immunochromatographic assays for detection of Cryptosporidium antigens in stool samples: a blind multicenter trial. *J Clin Microbiol*. 2011;49(4):1605–7.
3. Ahmed SA , Karanis P. Comparison of current methods used to detect Cryptosporidium oocysts in stools. *Int J Hyg Environ Health*. 2018;221(5):743–63.
4. Autier B , Belaz S, Razakandrainibe R, Gangneux JP, Robert -Gangneux F. Comparison of three commercial multiplex PCR assays for the diagnosis of intestinal protozoa. *Parasite*. 2018;25:48.
5. Baldursson, S. and Karanis, P.(2011). Waterborne transmission of protozoan parasites: review of worldwide outbreaks – an update 2004–2010. Water Res. 45 (20),6603–6614.
6. Bouzid M , Hunter PR, Chalmers RM, Tyler KM. Cryptospor idium pathogenicity and virulence. *Clin Microbiol Rev*. 2013;26(1):115–34.
7. Bouzid M , Kintz E, Hunter PR. Risk factors for Cryptosporidium infection in low and middle income countries: A systematic review and meta-analysis. *PLoS Neglected Trop Dis*. 2018;12(6):e0006553.
8. Chappell, C.L.; Okhuysen, P.C.; Langer-Curry, R.; Widmer, G.; Akiyoshi, D.E. and Tanriverdi, S**.** (2006). *Cryptosporidium hominis*: experimental challenge of healthy adults.Am. J. Trop. Med. Hyg. 75, 851–857.
9. Elwin, K.; Hadfield, S.J.; Robinson, G. and Chalmers, R.M.(2012).The epidemiology of sporadic human infections with unusual cryptosporidia detected during routine typing in England and Wales, 2000- 2008. Epidemiol Infect; 140: 673-683.
10. Florescu DF , Sandkovsky U. Cryptosporidium infection in solid organ transplantation. *World J Transplant*. 2016;6(3):460–71.
11. Friesen J , Fuhrmann J, Kietzmann H, Tannich E, Muller M, I gnatius R. Evaluation of the Roche LightMix Gastro parasites multiplex PCR assay detecting Giardia duodenalis, Entamoeba histolytica, cryptosporidia, Dientamoeba fragilis, and Blastocystis hominis. *Clin Microbiol Infect*. 2018;24(12):1333–7.
12. Gerace, E., Presti, V. D. M. L., & Biondo, C. (2019). Cryptosporidium infection: epidemiology, pathogenesis,

and differential diagnosis. *European Journal of Microbiology and Immunology*, *9*(4), 119-123.

13. Hasheminasab, S. S., Conejeros, I., D. Velásquez, Z., Borggrefe, T., Gärtner, U., Kamena, F., ... & Hermosilla, C. (2022). ATP Purinergic Receptor P2X1-Dependent Suicidal NETosis Induced by Cryptosporidium parvum under Physioxia Conditions. *Biology*, *11*(3), 442.
14. Hawash Y . Evaluation of an immunoassay-based algorithm for screening and identification of giardia and cryptosporidium antigens in human faecal specimens from saudi arabia. *J Parasitol Res*. 2014;2014:213745.
15. Jenkins MB , Eaglesham BS, Anthony LC, Kachlany SC, Bow man DD, Ghiorse WC. Significance of wall structure, macromolecular composition, and surface polymers to the survival and transport of Cryptosporidium parvum oocysts. *Appl Environ Microbiol*. 2010;76(6):1926–34.
16. Khalil IA , Troeger C, Rao PC, Blacker BF, Brown A, Brewer TG, et al. Morbidity, mortality, and long-term consequences associated with diarrhoea from Cryptosporidium infection in children younger than 5 years: a meta-analyses study. *Lancet Glob Health*. 2018;6(7):e758-68.
17. Khurana S , Chaudhary P. Laboratory diagnosis of cryptosporidiosis. *Trop Parasitol*. 2018;8(1):2–7.
18. Kumar A , Chatterjee I, Anbazhagan AN, Jayawardena D, Pr iyamvada S, Alrefai WA, et al. Cryptosporidium parvum disrupts intestinal epithelial barrier function via altering expression of key tight junction and adherens junction proteins. *Cell Microbiol*. 2018;20(6):e12830.
19. Kurniawan, A.; Dwintasari ,S.W.; Connelly, L.; Nichols, R.A.; Yunihastuti, E.; Karyadi, T. and Djauzi,S.(2013). *Cryptosporidium* species from human immunodeficiency-infected patients with chronic diarrhea in Jakarta, Indonesia. Ann Epidemiol; 23: 720-723.
20. Leitch ,G.J. and He,Q.(2012). Cryptosporidiosis-an overview. J Biomed Res; 25: 1-16.
21. Meisel JL , Perera DR, Meligro C, Rubin CE. Overwhelming watery diarrhea associated with a cryptosporidium in an immunosuppressed patient. *Gastroenterology*. 1976;70(6):1156–60.
22. Nime FA , Burek JD, Page DL, Holscher MA, Yardley JH. Acu te enterocolitis in a human being infected with the protozoan Cryptosporidium. *Gastroenterology*. 1976;70(4):592–8.
23. Omoruyi BE , Nwodo UU, Udem CS, Okonkwo FO. Compara tive diagnostic techniques for cryptosporidium infection. *Molecules*. 2014;19(2):2674–83.
24. Paniker,CK jayaram.(2013).paniker's textbook of medical parasitology .seventh edition. Indian Council of Medical Reserch, New Delhi, India. Page 276.
25. Petry F , Jakobi V, Tessema TS. Host immune response to Cryptosporidium parvum infection. *Exp Parasitol*. 2010;126(3):304–9.
26. Rehn M , Wallensten A, Widerstrom M, Lilja M, Grunewald M, Stenmark S, et al. Post-infection symptoms following two large waterborne outbreaks of Cryptosporidium hominis in Northern Sweden, 2010-2011. *BMC Public Health*. 2015;15:529.
27. Ryan U , Fayer R, Xiao L. Cryptosporidium species in humans and animals: current understanding and research needs. *Parasitology*. 2014;141(13):1667–85.
28. Shirley DA , Moonah SN, Kotloff KL. Burden of disease from cryptosporidiosis. *Curr Opin Infect Dis*, 2012;25(5):555–63.
29. Shoultz DA , Hostos EL, Choy RK. Addressing Cryptosporidium Infection among Young Children in Low-Income Settings: The Crucial Role of New and Existing Drugs for Reducing Morbidity and Mortality. *PLoS Neglected Trop Dis*. 2016;10(1):e0004242.
30. Shrivastava AK , Kumar S, Smith WA, Sahu PS. Revisiting the global problem of cryptosporidiosis and recommendations. *Trop Parasitol*. 2017;7(1):8–17.
31. Sponseller JK , Griffiths JK, Tzipori S. The evolution of respiratory Cryptosporidiosis: evidence for transmission by inhalation. *Clin Microbiol Rev*. 2014;27(3):575–86.
32. Suarez CE , Bishop RP, Alzan HF, Poole WA, Cooke BM. Adv ances in the application of genetic manipulation methods to apicomplexan parasites. *Int J Parasitol*. 2017;47(12):701–10.
33. Thomson S , Hamilton CA, Hope JC, Katzer F, Mabbott NA, Morrison LJ, et al. Bovine cryptosporidiosis: impact, host-parasite interaction and control strategies. *Vet Res*. 2017;48(1):42.
34. Tzipori S , Ward H. Cryptosporidiosis: biology, pathogenesis and disease. *Microbes Infect*. 2002;4(10):1047–58.
35. Tzipori S , Widmer G. A hundred-year retrospective on cryptosporidiosis. *Trends Parasitol*. 2008;24(4):184–9.
36. Wang RJ , Li JQ, Chen YC, Zhang LX, Xiao LH. Widespread occurrence of Cryptosporidium infections in patients with HIV/AIDS: Epidemiology, clinical feature, diagnosis, and therapy. *Acta Trop* 2018, 187:257–63.
37. Wang ZD , Liu Q, Liu HH, Li S, Zhang L, Zhao YK, et al. Prevalence of Cryptosporidium, microsporidia and Isospora infection in HIV-infected people: a global systematic review and meta-analysis. *Parasites Vectors*. 2018;11(1):28.