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REVIEW ARTICLE

Overview of Cryptosporidium spp.

Cryptosporidium spp.'ye Genel Bakış

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ABSTRACT

Cryptosporidium spp., the causative agent of Cryptosporidiosis, is an obligate intracellular and extracytoplasmic protozoan. Cryptosporidium spp. emerges as a public health problem transmitted by contaminated water and food due to its features such as the widespread occurrence of oocysts in nature, low infective doses, ability to pass through the filters of treatment plants, resistance to disinfectants, and ability to survive in water and soil for months at appropriate humidity and temperature. Transmission to humans usually occurs through the fecal-oral route by ingestion of oocysts. However, endogenous auto-infection can occur. Respiratory transmission has been reported. Cryptosporidium spp. infections may lead to serious life-threatening clinical conditions in children under two years of age and immunosuppressed patients. To prevent water and foodborne cryptosporidiosis outbreaks and protect public health, the causes of Cryptosporidium oocysts contaminating these resources should be determined, necessary precautions should be taken and combat methods should be determined. In this review, information on the life cycle, epidemiology, clinical findings, diagnosis, protection, and control of Cryptosporidium spp. is presented.

Keywords: Cryptosporidium, immunosuppressive, protozoan

ÖZ

Cryptosporidiosis etkeni olan Cryptosporidium spp., zorunlu intrasellüler ve ekstrasitoplazmik bir protozoondur. Cryptosporidium spp., ookistlerinin doğada yaygın olarak bulunması, enfektif dozlarının düşük olması, arıtma tesislerinin filtrelerinden geçebilmeleri, dezenfektanlara karşı dirençli olmaları, su ve toprakta uygun nem ve sıcaklıkta aylarca canlı kalabilmeleri şeklinde sıralanabilecek özellikleriyle kontamine su ve gıda ile bulaşan bir halk sağlığı problemi olarak karşımıza çıkmaktadır. İnsanlara bulaş genellikle ookistlerin fekal oral yolla alınmasıyla gerçekleşir. Ancak endojen oto-enfeksiyon da gelişebilmektedir. Respiratuvar bulaş bildirilmiştir. Cryptosporidium spp. enfeksiyonları iki yaş altı çocuklarda ve immünsupresif hastalarda hayatı tehdit eden ciddi klinik tablolara neden olabilmektedir. Su ve gıda kaynaklı cryptosporidiosis salgınlarının önlenmesi ve halk sağlığının korunması için Cryptosporidium ookistlerinin bu kaynakları kontamine etme nedenleri belirlenerek gerekli önlemlerin alınması ve mücadele yöntemlerinin belirlenmesi gerekmektedir. Bu derlemede Cryptosporidium spp.'nin yaşam döngüsü, epidemiyolojisi, klinik bulguları, tanısı, korunma ve kontrolü ile ilgili bilgilere yer verilmiştir.

Anahtar Kelimeler: Cryptosporidium, immünsupresif, protozoon,

Introduction

Cryptosporidium spp. is an opportunistic parasitic agent transmitted through oocysts in contaminated water and food. It can infect mainly the intestines and many organs, such as the lungs, pancreas, and gall bladder (1). Along with Giardia, it is the most common parasite in humans worldwide (2).

Cryptosporidium species were first described by Clarke in 1885 as spore clusters on the epithelium of a mouse stomach. In 1905, Ernest Edward Tyzzer demonstrated them in the gastric mucosa cells of mice and named them Cryptosporidium, which means hidden sporocysts in ancient Greek, because they do not have sporocysts in their oocysts, unlike other Coccidia species. The disease it causes has been called Cryptosporidiosis (3). Cryptosporidium spp., the agent of Cryptosporidiosis, is an obligate, intracellular, and extracytoplasmic protozoan (4).

Cryptosporidium species are included in the Apicomplexa group, Sporozoasida class, Coccidiasina subclass, Eucoccidiorida order, Eimeriorina suborder, and Crptosporidiidae family (5). There are approximately 22 species of Cryptosporidium spp., which are either zoonotic or anthroponotic. While the zoonotic species of the agent, Cryptosporidium parvum, infects both humans and animals, the anthroponotic species Cryptosporidium hominis is only a pathogen for humans (6). Additionally, C. canis, C. felix, C. meleagridis, and C. muris can also cause human infection (7).

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Life Cycle

The life cycle of Cryptosporidium spp., characterized by six stages, the alternation of sexual and asexual fertilization, is completed in a single host. The only stage the parasite spends outside the host is the oocyst stage (8).

In the first stage of the life cycle (excystation), four infective sporozoites are released from the oocyst ingested by the host as a result of opening in the small intestine. These sporozoites enter the intestinal epithelial cells. The intestinal microvilli folds surround the parasite to form a membrane sac. In this way, the parasite shows an intracellular-extracytoplasmic settlement in the intestinal epithelial cells of the host (9). In the second stage of the life cycle (merogony), sporozoites first transform into trophozoites and then into type 1 meronts by asexual reproduction. 6-8 merozoites are formed from type 1 meronts. These merozoites enter new cells and begin sexual reproduction by reproducing asexually and transforming into either type 1 or type 2 meronts (4 merozoites). The third stage of the life cycle of Cryptosporidium spp. is gametogony. Merozoites formed from type 2 meronts transform into macro and microgametocytes, and then into either macro or microgametes. In the fourth stage of the life cycle (fertilization), microgametes fuse with macrogametes to form an oocyst (zygote). In the fifth stage, the oocyst wall is formed. While a two-layered oocyst wall is formed in approximately 80% of oocysts, a thin-walled structure is formed in 20%. The final stage of development, the sporogony stage, takes place inside the parasitic vacuole. After meiosis, four sporozoites are formed inside the thin-walled oocysts. These oocysts are ejected into the intestinal lumen and hatch there without leaving the host (5). This process is responsible for the recurrence of infection in the host, which is called autoinfection (4). Chronic cryptosporidiosis is observed in cases where the host cannot destroy this parasite. Thick-walled type 2 oocysts are sporulated and excreted with the host feces. Thus, the life cycle is completed in a single host (monoxen). Oocysts shed in the environment penetrate new hosts and begin a new life cycle (5).

Epidemiology

Cryptosporidium oocysts are widely found in nature due to their ubiquitous properties (10). In recent years, Cryptosporidium spp. has come to the forefront as a public health problem transmitted through contaminated water and food due to its characteristics, such as low infective doses of its oocysts, no necessity for a new host or maturation process, long incubation period, the ability of oocysts excreted in feces contaminating the environment for up to 60 days even if clinical symptoms are not seen, being able to pass through the filters of treatment plants with their 4-6 µm size, being able to be transported in air and water for long distances due to their small size, being resistant to disinfectants (e.g., chlorine), and being able to survive in water and soil for months at appropriate humidity and temperature (11-13). Therefore, waterborne outbreaks caused by Cryptosporidium spp. have been reported in history. This agent has been included in the category B pathogen list by the Centers for Disease Control and Prevention (CDC) (14).

Outbreaks caused by this parasite, particularly those from swimming pools, have been reported since the 1990s in many developed countries, including the United States (US), Canada, England, Scotland, and Japan. However, the most important of these occurred in Milwaukee, USA, in the spring of 1993, where 403,000 cases were reported (15). The Milwaukee outbreak is the largest waterborne outbreak on record, and during the outbreak, the presence of Cryptosporidium oocysts was shown in 90% of sewage samples, 75% in river water samples, and 28% in drinking water samples. Also in 1984, an outbreak of cryptosporidiosis occurred in two separate locations in a residential area with 5,900 people in Texas. It was determined that the drinking water for these two centers was supplied from the same artesian well, that the water was circulated without being filtered, while it was chlorinated just before being released to the network. After the outbreak, dye tests were used to definitively establish that sewage effluents were mixed with drinking water and that this mixing occurred at irregular intervals. However, the location where sewage effluents are mixed with drinking water could not be determined. In 1987, in an outbreak in West Georgia where an estimated 13,000 people were affected, it was determined that drinking water criteria met federal and state standards at the time, but when the stools of 489 people were examined, 61% were found to be positive for Cryptosporidium. Of the 322 people using alternative drinking water, 20% were found to be Cryptosporidium positive (3). When the national literature was examined, in a study conducted in the water resources of Mardin, the presence of Cryptosporidium spp. was determined to be 8.92% with the Kinyoun acid-fast staining method (16). In Iğdır

province, in the analysis of 69 spring water samples using native-Lugol, modified acid-fast staining, and nested polymerase chain reaction (nPCR) methods, Cryptosporidium spp. was found to be positive in 1 sample (1.4%) (17).

Access to clean and adequate water and food is currently a problem in underdeveloped countries. It is estimated that the inability of non-industrialized countries to keep up with population growth and the inability to meet the increasing demand for clean and safe drinking water due to migration to urban areas will continue to affect the spread of diseases (18). Therefore, the prevalence of Cryptosporidium spp. infection is higher in developing countries (10). Cryptosporidiosis is reported to occur at an incidence of 1-9% in people with a healthy immune system in developed countries and at an incidence of 7-20% in developing countries (19).

Epidemiological studies reveal that the geographical distribution of Cryptosporidium spp. varies around the world. Studies have reported that C. parvum and C. hominis are responsible for 90% of cryptosporidiosis cases (5). While C. hominis is common in North and South America, Australia, China, Japan, and Africa, C. parvum is more common in Europe and New Zealand, especially in the UK (20).

Cryptosporidium spp. infections can cause serious life-threatening clinical conditions in children under two years of age (19). This age group may pose a risk for prolonged Cryptosporidium spp. infection even if immunodeficiency tests are normal because there may be defects in the natural immune system and lymphocyte functions (21). When international data are examined in the literature, the Cryptosporidium positivity rate in children presenting with diarrhea varies between 10 and 25% (22). In studies conducted in our country, in Van and Izmir, among children presenting with acute diarrhea, the presence of Cryptosporidium spp. oocysts in stool samples were reported at a frequency of 2.2% and 13.5% (19). In another study, it was observed that the prevalence of Cryptosporidium spp. was higher in children, especially in prolonged diarrhea (23).

Cryptosporidium spp. can cause severe infection, especially in immunocompromised individuals, due to its intracellular location and its ability to cause autoinfection (6). The rate of Cryptosporidium infection in HIV-positive patients is 14% in developed countries and 24% in developing countries. In studies conducted on immunocompromised individuals in Türkiye, the prevalence of Cryptosporidium spp. has been reported to be between 0-35.5% (5).

The parasite is transmitted through infected food and drinks, contaminated water (swimming pools, hot springs, jacuzzis, lakes, rivers, and streams) with human or animal feces, and uncooked consumption of contaminated food (19). In recent years, transmission through unpasteurized fruit juices has been frequently mentioned (7). People are usually infected by ingesting oocysts via the fecal-oral route (6). However, endogenous autoinfection can also occur. The transmission route of oocysts can be summarized as human to human, animal to human, and environment to human. This parasite can pass from the waste of infected animals to drinking water sources during periods of heavy rainfall (7). Respiratory transmission has also been reported (24).

Family members, daycare centers, pre-school, and similar institutions constitute an important source of direct transmission from person to person. It has been reported that the infection rate is high in some occupational groups (veterinarians, livestock breeders, and farm workers), those traveling to endemic areas, and those in close contact with infected people (25). Farm animals are an important source of transmission. Cattle, sheep, goats, and pigs play a role as reservoirs in the transmission of the disease agent (26). Contamination of the product with manure during production, irrigation water, agricultural workers, food processors, kitchen workers, washing water, kitchen counters, and tools and equipment constitute a potential source of cryptosporidiosis outbreaks. In a study conducted on food industry workers in the Van region, the rate of the asymptomatic carrier was determined as 1.27% (27). Vegetables, fruits, and salads consumed raw without a heating process, unpasteurized milk and apple juice, dairy products, meat, offal, and various seafood (mussels, oysters) are foods that carry a risk in cases of cryptosporidiosis (5,28). In India, the rate of Cryptosporidium spp. was determined as 6% in fresh vegetables (coriander, lettuce, tomatoes, cucumbers, cabbage, red pepper, mint, carrots, and radishes) purchased from different sales points (29).

Clinical Findings

The incubation period of infections caused by Cryptosporidium varies from 5 to 28 days (3). Cryptosporidiosis causes abdominal pain, nausea,

vomiting, diarrhea, weight loss, and anorexia in humans (30). Diarrhea can be acute or chronic, transient, intermittent or continuous, in severe diarrhea, fluid loss can be up to 25 L/day (21).

Infection usually limits itself in immunocompetent individuals and resolves within a few weeks (30). In immunocompromised individuals, the course of infection can be short-term and rapidly resolving diarrhea or chronic diarrhea resulting in life-threatening cholera-like diarrhea, malabsorption, and malnutrition. Symptoms are particularly severe in patients with acquired immunodeficiency syndrome (AIDS), viral diseases such as measles, leukemia, gammaglobulinemia, insulin-dependent diabetes, renal failure, solid organ transplantation, and cancer treatment. In these patients, diarrhea may last longer than two months, and oocyst excretion with feces, severe dehydration, weight loss, and malnutrition may be observed throughout the infection (2,31). Although the main location of Cryptosporidium spp. is the intestines, extraintestinal involvement (bile ducts, pancreas, stomach, respiratory system, kidney) may also be seen in immunocompromised patients. When systematic screening is performed, it has been reported that Cryptosporidium spp. colonization is up to 70%, especially in patients with hyperimmunoglobulin M syndrome, among primary immunodeficiencies, and this leads to serious problems ranging from sclerosing cholangitis to hepatitis and end-stage liver disease (21). It has been reported that biliary system involvement may be seen in 10-30% of patients diagnosed with AIDS from secondary immune deficiencies, that is, it may occur as acalculous cholecystitis, sclerosing cholangitis, and pancreatitis (19). Pulmonary cryptosporidiosis is characterized by cough (10). Intestinal symptoms and fever are frequently observed and may be fatal (7).

Diagnosis

In the diagnosis of Cryptosporidium infections, stool, sputum, or bile samples are evaluated with microscopic, molecular, serological, histopathological, and culture methods (11,32,33).

However, it is difficult to evaluate Cryptosporidium oocysts in direct microscopic examinations due to their small size. Microscopic examination after acid-fast staining is accepted as the minimum method for diagnosis (34). However, it has been reported that the sensitivity of microscopic methods is low, the workload is high and is prone to personnel mistakes (35).

In recent years, with the widespread use of molecular methods, it has been reported that the detection rate of Cryptosporidium spp. in foods has increased, and the sensitivity and specificity of the method are high. (36). Additionally, thanks to genomic studies, detailed information about the biology of the parasite has been obtained. These studies have also helped to understand the antimicrobial resistance mechanism of the parasite (37). Although polymerase chain reaction (PCR) is a fast and highly sensitive method, there are many limiting factors for the method. First of all, an appropriate extraction method should be used for DNA isolation. Bile salts, bilirubin, complex polysaccharides, and other components in stool are structures that can exhibit inhibitory properties in the PCR technique. Therefore, to use the PCR technique routinely in stool-based studies, the risk of contamination should be eliminated and oocysts should be meticulously isolated from the sample. Also, the selection of appropriate primers in terms of the reliability of the test is very important for the sensitivity of the study (5).

In the Enzyme-Linked ImmunoSorbent Assay (ELISA) method, one of the serological diagnostic methods, the stool sample is emulsified with the sample dilution fluid. The diluted stool sample and the conjugate with the monoclonal antibody specific to the parasite antigen are put in the wells of the microplates. These wells contain polyclonal antibodies that will bind to the Cryptosporidium oocyst antigen. If oocysts are present in the stool sample, the polyclonal antibodies in the microplates and oocyst-specific monoclonal antibodies in the conjugate bind. Nonspecific combinations are removed by washing. When the substrate is added, color formation occurs due to the enzyme-antibody-antigen complex (38). The sensitivity of ELISA methods is higher than microscopic methods. However, cross-reaction with other microorganisms limits the use of the method (39).

The direct fluorescent antibody (DFA) method is another serological diagnostic method, which detects the surface antigens of the parasite. This method is more sensitive (99%) and specific (100%) compared to microscopic examinations and is accepted as the reference method. With DFA, the stool sample in which the agent is sought is put on a slide and fixated, and fluorescein isothiocyanate (FITC)-labeled monoclonal antibodies are used. Oocysts are detected by examination using a fluorescence microscope (40).

Histopathological methods were used in the diagnosis

of Cryptosporidium spp. before the 1980s. In intestinal biopsies, eosin and hematoxylin stains were used to search for small and round parasite oocysts in microvilli, but species differentiation could not be made. It is not preferred today because it is an invasive method, requires rapid evaluation of biopsies, is not economical, and requires a long time to process (41).

With culture methods, in colon cancer cells and iliocecal adenocarcinoma cells, it is possible to detect infective oocysts of Cryptosporidium spp. resistant to the effects of inhibitors in water samples. It has also been reported that cell culture methods detect the concentration of Cryptosporidium spp. oocysts. In addition to these positive sides, there are also negative sides, such as the need for various materials for culture and the need for 1-3 days to observe oocyst morphology (42).

Treatment

An effective treatment approach against Cryptosporidium has not yet been established because its basic biology is not fully understood. For this reason, the infection can become chronic and reach life-threatening levels (43-45).

Lack of knowledge about biochemical and metabolic pathways underlies treatment limitations. Studies show that Cryptosporidium does not have functional mitochondria and lacks the active Krebs cycle, but notes that it encodes all glycolytic enzymes. Since the parasite primarily uses anaerobic oxidation of glucose in energy metabolism, enzymes and other products involved in the glycolytic pathway may be potential targets for anticryptosporidial drugs. Other studies conducted with apicomplexan parasites have shown that antiparasitic treatment can be achieved by inhibiting glycolysis (43,45).

ATPases are a family of proteins that actively transport ions and aminophospholipids across the membrane. Studies indicate that Cryptosporidium requires a P-ATPase family to maintain homeostasis during its passage through intracellular and extracellular environments. Additionally, a new P-ATPase (CpATPase3) of this agent has been characterized. It is thought that these pathways can be used for drug development (46).

Some research suggests that essential oils may be effective against C. parvum. It is known that essential oil molecules such as carvacrol, linalool, thymol, and eugenol have antimicrobial effects, but no detailed study has been conducted on their antiprotozoal activities (47).

In the immunocompetent patient group, water and electrolyte replacement therapy is usually sufficient (22). An effective chemotherapeutic agent is needed because it causes life-threatening clinical symptoms in the immunocompromised patient group (44). Paromomycin, rifampicin, rifabutin, HIV protease inhibitors, macrolides, and nitazoxanide are the agents used for treatment in these patients (22,48). Halofuginone and toltrazuril are among the agents whose therapeutic properties are evaluated (49).

A study found that heparin sulfate is effective against this agent. It has been noticed that the effect of Cryptosporidium is inhibited when the C.parvum elongation factor 1a protein (CpEF1a), which is responsible for the spread of this parasite, interacts with heparin. For this reason, it is thought that heparin sulfate may be a promising agent in the treatment of Cryptosporidium (50).

Protection and Control

Consumption of water determined not to comply with drinking water standards leads to serious health problems regarding public health (13). Therefore, Cryptosporidium, which is considered a potential bioterrorism agent resistant to standard water disinfectants, must be purified from water (7). Chlorination alone is not effective in eliminating Cryptosporidium oocysts. Removal of oocysts from drinking water by coagulation, sedimentation, filtration, and disinfection methods are the primary procedures that should be performed in cases of waterborne cryptosporidiosis. Correct application of these traditional processing techniques ensures a success rate of 99% or more. Following the critical times when oocysts can pass through the filtration barrier, a backwash process that ensures the filtration of waste should be applied. The addition of a coagulant or the frequency of the backwash process minimizes the passage of oocysts (6,51,52).

Besides, water inspections should be carried out by relevant institutions, water should be analyzed at regular intervals, and contamination of natural resources or canal systems with agricultural, domestic, and industrial waste should be prevented. Especially in provincial and district centers, it may be appropriate to provide water from the network system to fountains that cannot be supplied with quality source water (13).

Although most parasitic infections can be treated, several control programs should be implemented to reduce infection rates. People should be informed and hygiene conditions should be provided. In case of an outbreak, cooperation should be established between different centers, health authorities and academicians should act together, cases and their contacts should be quickly identified, necessary precautions should be taken and the outbreak should be brought under control in a short time (15).

Conclusion

To prevent water and foodborne cryptosporidiosis outbreaks and protect public health, the causes of Cryptosporidium oocysts contaminating these resources should be determined, necessary precautions should be taken and combat methods should be determined.

Author's Contribution:

DB conducted the literature review and wrote the article.

References

1. Laksemi DA, Suwanti LT, Mufasirin M, Suastika K, Sudarmaja M. Opportunistic Parasitic Infections in Patients with Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome: A Review. Vet World 2019; 13(4): 716-25.

2. Leder K, Weller PF. Epidemiology, clinical manifestations, and diagnosis of cryptosporidiosis. Available from:URL:https://www.uptodate.com/contents/epidemiology-clinical-manifestations-and-diagnosis-ofcryptosporidiosis.

3. Yalçın S, Doğan NY. Determination of Cryptosporidium spp. by Molecular Methods in Different Water Resources of Erzincan Province. Erzincan University Journal of Science and Technology 2019; 12(1): 1-13.

4. Wang P, Li S, Zou Y, Du ZC, Song DP, Wang P, et al. The Infection and Molecular Characterization of Cryptosporidium spp. in Diarrheic Pigs in Southern China. Microb Pathog 2022; 165: 105459.

5. Şahin S, Ağaoğlu S, Alemdar S. Cryptosporidium ve Cryptosporidiosis. Türkiye Klinikleri; 2018; 35-41.

6. Ulusan Bağcı Ö, Caner A. miRNA Expression Profile in Ileocecal Adenocarcinoma Cells Infected with Cryptosporidium. Mikrobiyol Bul 2022; 56(3): 449-465.

7. Aksoy Ü. Bioterorism, Prasites as Potential Bioterrorism Agents and Biosecurity studies. Mikrobiyol Bul 2006; 40: 129-139.

8. Fayer R. General biology. In: Fayer R, Xiao L. eds. Cryptosporidium and Cryptosporidiosis. Boca Raton: CRC Press; 2008; 1-42.

9. Chalmers RM, Davies AP. Clinical cryptosporidiosis. Exp Parasitol 2010; 124(1): 138- 46.

10. Caccio SM, Putignani L. Epidemiology of Human Cryptosporidiosis. In: Caccio S, Widmer G, eds. Cryptosporidium: parasite and disease. Vienna: Springer; 2014; 43-79.

11. Ryan U, Hijjawi N, Xiao L. Foodborne cryptosporidiosis. Int J Parasitol 2018; 48(1): 1-12.

12. Vanathy K, Parija SC, Mandal J, Hamide A, Krishnamurthy S. Cryptosporidiosis: A mini-review. Trop Parasitol 2017; 7(2): 72-80.

13. Atasever M, et al. Investigating the Quality of Public Fountain Water in Gümüşhane Province and the Presence of Cryptosporidium spp. Using the PCR Method. Turkish Journal of Agriculture-Food Science and Technology 2024; 12(9): 1530-1538.

14. Tin D, Sabeti P, Ciottonea GR. Bioterrorism: An Analysis of Biological Agents Used in Terrorist Events. Am J Emerg Med 2022; 54: 117-121

15. Ruh E, Özkan AT. Outbreaks Due to Parasites: Examples from the World and Türkiye. Mikrobiyol Bul 2023, 57(2): 317-329.

16. Çuhadar V, Şengül M, Mete E. Investigation of Cryptosporidium parvum in Water Resources in Mardin Province. Turk Mikrobiyol Cemiy Derg 2023; 53(3): 156–162.

17. Akkaş Ö, Gürbüz E, Aydemir S, Şahin M, Ekici A. Investigation of Giardia spp., Cryptosporidium spp. and Cyclospora cayetanensis in Samples Collected from Different Spring Waters Iğdır, Türkiye. Turkiye Parazitol Derg 2023;47(2):71-7.

18. Macpherson CN, Gottstein B, Geerts S. Parasitic food-borne and water-borne zoonoses. Rev Sci Tech 2000; 19(1): 240-58.

19. Şen ZS, et al. A Rare Complication of Acute Diarrhea Caused by Cryptosporidium: Possible Hepatobiliary System Involvement in a Child without Immunodeficiency. Mikrobiyol Bul 2019; 53(4): 464-471.

20. Shrivastava AK, Kumar S, Smith WA, Sahu PS. Revisiting the global problem of cryptosporidiosis and recommendations. Trop Parasitol 2017;7(1):8-17.

21. Rodrigues F, Davies EG, Harrison P, McLauchlin J, Karani J, Portmann B, et al. Liver disease in children with primary immunodeficiencies. J Pediatr 2004; 145(3): 333-9.

22. Miman Ö, Saygı G. Temel Tibbi Parazitoloji. Istanbul: Istanbul Bookstore. 2018:241-248.

23. Dabas A, Shah D, Bhatnagar S, Lodha R. Epidemiology of Cryptosporidium in pediatric diarrheal illnesses. Indian Pediatrics 2017; 54(4): 299-309.

24. Bensen R, Fuentebella J, Fridge JL, Bass DM. Enteric parasites, pp: 463-77. In: Wyllie R, Hyams JS, Kay M (eds), Pediatric Gastroenterology and Liver Disease. 2016, 5th ed. Philadelphia: Elsevier Inc.

25. Usluca S, Aksoy Ü. A Waterborn Parasite: Cryptosporidium. Dokuz Eylül Üniv Tıp Fakültesi Derg 2006; 20(1): 65-74.

26. Çiçek M, Körkoca H, Gül A. Investigation of Cryptosporidium spp. in Workers of the Van Municipality Slaughterhouse and in Slaughtered Animals. Türkiye Parazitol Derg 2008; 32(1):8-11.

27. Körkoca H, Göz Y, Ataş AD, Kurtoğlu MG, Ekici K, Berktaş M. Prevalence of Cryptosporidium spp. in asymptomatic food workers. Türkiye Parazitol Derg 2013; 37(4): 241-4.

28. Ryan U, Fayer R, Xiao L. Cryptosporidium species in humans and animals: current understanding and research needs. Parasitology 2014; 141(13): 1667-85.

29. Utaaker KS, Kumar A, Joshi H, Chaudhary S, Robertson LJ. Checking the details in retail: occurrence of Cryptosporidium and Giardia on vegetables sold across different counters in Chandigarh, India. Int J Food Microbiol 2017; 263:1-8.

30. Aydemir S, et al. Investigation of the Effect of Pasteurization on the Viability of Cryptosporidium parvum in Cow's Milk by Propidium Monoazide qPCR. Mikrobiyol Bul 2023; 57(4): 660-666.

31. Cryptosporidium, pp: 312-5. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. Red Book: 2015 Report of the Committee on Infectious Diseases. 2015, 30th ed. Elk Grove Village, IL: American Academy of Pediatrics.

32. Karabey M, Can H, Öner TÖ, et al. Cryptosporidium spp. during chemotherapy: a cross-sectional study of 94 patients with malignant solid tumor. Ann Saudı Med 2021; 41(5); 293-298.

33. Robertson LJ. Cryptosporidium as a Foodborne Pathogen. 1st ed. New York: Springer; 2014; 1-10.

34. Usluca S, Babur C, Kilic S. Current Status in Intestinal Parasitic Infections: A Reference Laboratory Results. KLIMIK Derg 2020; 33(3): 307-314.

35. McHardy IH, Wu M, Shimizu-Cohen R, Couturier MR, Humphries RM. Detection of intestinal protozoa in the clinical laboratory. J Clin Microbiol 2014;52(3): 712-20.

36. Checkley W, White AJ JR, Jaganath D, Arrowood MJ, Chalmers RM, Chen XM. et al. A review of the global burden, novel diagnostics, therapeutics, and vaccine targets for Cryptosporidium. Lancet Infect Dis 2015;15(1):85- 94.

37. Donato B. Tuft Veterinary School scientists decode Cryptosporidium genome. 2004; http:/www./vet. tufts.edu/

38. Control and Prevention Diagnostic Procedures for Stool Specimens. 2004. Available from: URL https://www.cdc.gov/dpdx/diagnosticprocedures/index.html

39. Roellig DM, Yoder JS, Madison-Antenucci S, Robinson TJ, Van TT, Collier SA. et al. Community laboratory testing for Cryptosporidium: multicenter study retesting public health surveillance stool samples positive for Cryptosporidium by rapid cartridge assay with direct fluorescent antibody testing. PLoS One 2017; 12(1): e0169915

40. Yavuz U, Özkan AT. Antigen Detection Methods in Diagnosis of Amebiasis, Giardiasis, and Cryptosporidiosis. Türkiye Parazitol Derg 2009; 33 (2): 140-150.

41. Fayer R. Ungar BL. Cryptosporidium spp. and cryptosporidiosis. Microbiol Rev 1986; 50(4): 458-483

42. Barrett TJ. Molecular subtyping for epidemiology: issues in the comparability of patterns and interpretation of data In D. H. Persing et al. (ed.), Molecular microbiology, diagnostic, principles, and practice. ASM Press, Washington, DC. 2004: 259-268.

43. Üner A, Tanrıverdi S, Caner A, Değirmenci A. Cryptosporidium'larda moleküler biyolojik yapı ve çalışmalar. Özcel A, Tanyüksel M, Eren H (eds). Moleküler Parazitoloji Books. 2009; 22: 631-47.

44. Köreng B. Entamoeba histolytica/Entamoeba dispar, Giardia lamblia ve Cryptosporidium spp. tanısında mikroskobi, TRIAGE ve ELISA yöntemlerinin karşılaştırılması. Yüksek Lisans Tezi, Çukurova Üniversitesi, Sağlık Bilimleri Enstitüsü, Parazitoloji Anabilim Dalı, 2011.

45. Cook WJ, Senkovich O, Hernandez A, Speed H, Chattopadhyay D. Biochemical and structural characterization of Cryptosporidium parvum Lactate dehydrogenase. Int J Biol Macromol 2015; 74: 608-619.

46. LaGier MJ, Keithly JS, Zhu G. Characterisation of a novel transporter from Cryptosporidium parvum. Int J Parasitol 2002; 32(7): 877–87.

47. Dominguez-Uscanga A, Aycart DF, Li K, Witola WH, Andrade Laborde JE. The anti-protozoal activity of thymol and a thymol ester against Cryptosporidium parvum in cell culture. Int J Parasitol Drugs Drug Resist 2021; 15: 126–33.

48. Xiao L, Fayer R, Ryan U, Upton SJ. Cryptosporidium taxonomy: recent advances and implications for public health. Clin Microbiol Rev 2004; 17(1): 72-97.

49. Büget E, Büyükbaba-Boral Ö, Kırkoyun-Uysal H, Nazlıcan Ö, Öğüt T, Şengür G. Türkiye'de bir AIDS hastasında ilk mikrosporidiyaz ve solunum sistemini tutan ilk kriptosporidiyaz olgusu. Türk Mikrobiyol Cem Derg 2000; 30(3-4): 166-70.

50. Inomata A, Murakoshi F, Ishiwa A, Takano R, Takemae H, Sugi T, et al,. Heparin interacts with elongation factor 1a of Cryptosporidium parvum and inhibits invasion. Sci Rep 2015; 5: 11599.

51. Xiao L, Cama VA. Cryptosporidium and Cryptosporidiosis. In: Ortega YR, ed. Foodborne Parasites. Food Microbiology and Food Safety. Newyork, USA: Springer; 2006; 57-86.

52. Sudradjat A, Sandhyana Angga M, Barlian K, Nastiti A. Assessing Log Reduction Values of Conventional Water Treatment Plants with Microbially Highly Polluted Raw Water Sources. J Eng Technol Sci 2022; 54(1): 220101.