DERLEME / *REVIEW*

Cyclospora cayetanensis Infection

Cyclospora cayetanensis Enfeksiyonu

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ABSTRACT

Foodborne infections cause significant health problems worldwide. Among the causative agents of these infections, bacteria and viruses are more common, but there are also some protozoans. Among these protozoa, the infection caused by Cyclospora cayetanensis, which has been widely researched recently, is thought to be quite common in our country. Water and food contaminated with human feces are the main reservoirs of the agent. The agent is transmitted by fecal-oral route. Inattentions in eating habits, wrong practices, consumption of undercooked or raw foods, and contaminated drinking and utility water lead to infection. The infection affects the digestive system, and patients mainly suffer from diarrhea. C. cayetanensis symptoms are more severe in patients with HIV/AIDS. The infection is widespread in areas with poor hygiene and sanitation. Improving the hygiene conditions in these areas, washing vegetables and fruits well, filtering the water used for washing and drinking, and paying attention to general hygiene rules, especially hand hygiene, of the personnel working in the food production line significantly reduces the transmission and prevalence of infection.

Key words: *food hygiene; Cyclospora cayetanensis; food infection; protozoan*

ÖZET

Gıda kaynaklı enfeksiyonlar dünya çapında büyük sağlık sorunlarına neden olmaktadır. Bu enfeksiyonlara neden olan etkenler arasında bakteriler, virüsler daha çok sayıda olmakla birlikte bazı protozoonlar da bulunmaktadır. Bu protozoonlar içinde son zamanlarda çok araştırılan Cyclospora cayetanensis'in neden olduğu enfeksiyonun ülkemizde de oldukça yaygın olduğu düşünülmektedir. İnsan dışkısı ile kontamine olmuş su ve gıdalar etkenin başlıca rezervuarlarıdır. Etken fekal oral yolla bulaşır. Beslenme alışkanlıklarındaki dikkatsizlikler, yanlış uygulamalar, az pişmiş veya çiğ gıdaların tüketimi, kontamine içme ve kullanma suları enfeksiyonu ortaya çıkarmaktadır. Enfeksiyon sindirim sisteminde etkili olup, hastalarda daha çok ishal görülmektedir. C. cayetanensis semptomları HIV/AIDS'li hastalarda daha şiddetlidir. Enfeksiyon hijyen sanitasyonun yetersiz olduğu bölgelerde çok yaygındır. Koruma ve kontrolde ise bu bölgelerdeki hijyen koşullarının iyileştirilmesi, sebze ve meyvelerin iyi yıkanması, yıkama ve içmede kullanılan suların filtre edilmesi, gıda üretim hattında çalışan personelin başta el hijyeni olmak üzere genel hijyen kurallarına dikkat etmesi bulaşmayı ve enfeksiyon yaygınlığını büyük oranda azaltmaktadır.

Anahtar kelimeler: *gıda hijyeni; Cyclospora cayetanensis; gıda enfeksiyonu; protozoon*

Introduction

Foodborne infections constitute a significant health problem worldwide. WHO reports that one in three people is affected by yearly foodborne infections. Viruses, bacteria, and protozoa cause these infections and can infect foods at any stage, from farm to fork[1].

Among the factors that cause food infections are bacteria such as *Salmonella, Campylobacter, and Escherichia,* viruses such as *Norovirus, Hepatitis A virus, Rotavirus*, etc., and protozoans such as *Toxoplasma, Cryptosporidia* and *Cyclospora* are the most important[2].

Although many protozoan diseases have been known for a long time, new infective types are detected daily. *Toxoplasma, Babesia, Cryptosporidium, Eimeria, Theileria, Sarcocystis, Cyclospora* etc. They are essential protozoan species known to date regarding human and animal health[3]. Most of these protozoa are intracellular parasites and reproduce by sporulation[4].

Transmission of protozoa to humans occurs through contact with carrier animals or oral ingestion of infective cysts in the external environment. Water and soil play essential roles as intermediary sources in transmission[5].

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C. cayetanensis is one of the most researched parasites in recent years. Research has also shown that *C. cayetanensis* is a crucial foodborne protozoan that threatens public health worldwide[6]. *Cyclospora* infections are more prevalent in underdeveloped countries, particularly in Asia. The disease has been identified as the cause of 'Cyclosporiasis,' which has coccidian features in the gastrointestinal tract in humans. This disease, characterized by diarrhea, is also known as summer diarrhea or traveler's diarrhea in tropical regions [7].

History

Cyclospora protozoon was first discovered in the intestines of moles by Eimeria in 1870[8]. Its genus was defined as *Cyclospora* by the German scientist Schneider in 1881. Species of *Cyclospora* were first identified in insects, reptiles, and rodents rather than humans[9]. Until this parasite was named, it was called many different names, such as blue-green alga, Cryptosporidium-like, Cyanobacterium-like body or Coccidian-like body[10]. The first disease caused by *C. cayetanensis*, which is responsible for gastrointestinal disorders with these names, is thought to be the outbreak in Papua New Guinea in 1970[11]. After this protozoan was first isolated in Peru in 1994, its species name, *C. cayetanensis*, started to be used [9].

Morphology and life cycle of the parasite

C. cayetanensis taxonomically belongs to the subclass Coccidia of the Apicomplexa branch of the Eimeriidae family of the order Eucoccidiorida[10]. Oocyst, sporozoite, trophozoite, merozoite, microgametocyte, and macrogametocyte are the morphological shapes seen in the life cycle[11]**.** The oocysts of *C. cayetanensis* are 8–10 µm in diameter and spherical, and the cyst wall is colorless, double-layered, and thinner than 1 µm. The oocysts can sporulate in the external environment. A sporulated oocyst consists of two sporocysts, and each sporocyst consists of two sporozoites. Sporocysts are 4 × 6 µm in diameter and oval in shape. The sporozoites inside are banana-shaped, and their length varies between 1 × 9 µm[13]. *Cyclospora* sporozoites have a typical structure consisting of a polar ring, conoid, and rhopti. In the host, the protozoan reproduce sexually (gametogony) and asexually (merogony or schizogony)[14].

The life cycle of *C. cayetanensis* has not yet been fully described. Still, the sporulation process of the oocyst is well-known. The oocyst, formed in the parasite's intestinal cells, sporulates between 1–7 days at 22°C – 30°C outdoors after excretion in feces[16].

The season is another important factor affecting the oocyst's sporulation process and contamination. Environmental factors such as temperature and humidity are the most critical parameters of sporulation as they affect the viability of the oocyst[17]. Seasons worldwide vary depending on geographical location; for example, *C. cayetanensis* infection is more common between May and July in the USA and between April and June in Peru[18].

Human infection occurs through ingesting sporulated oocysts in contaminated food and water. Oocysts taken into the body become sporozoites due to the disintegration of the oocyst walls under the influence of bile, trypsin, and other factors in the gastrointestinal tract. These sporozoites settle in the epithelial cells of the small intestine (especially the jejunum) and form an intracellular life cycle there[9]. Symptoms appear in the host after incubating from 1 to 15 days (Figure 1).

Ways and sources of transmission of the parasite

Oocysts of *C. cayetanensis* are excreted in an unsporulated form from an infected body. These oocysts need sporulation in the external environment to gain infective properties[19]. Transmission is not possible through direct human-to-human contact; transmission occurs indirectly[20]. The disease occurs via the fecal-oral route, meaning people become infected by orally ingesting sporulated oocysts[16]. These oocysts may come from soil, fomites, or contaminated food and water[21]. Oocysts are durable in the external environment (in food and water) for a long time and do not lose their infective properties[6].

Indirect transmission of *C. cayetanensis* from person to person is relatively high. However, due to the sporulation process outside, environments are needed to create infection. It is caused by water, soil, food, and people contaminated with feces containing sporulated oocysts[22]. The main intermediary sources in the meeting are as follows.

Water

Water contaminated with feces is an important source of transmission of *C. cayetanensis* into the body[23]. There have been many reports of waterborne transmission of *C. cayetanensis*[24]. Oocysts are most commonly found in water used for agriculture[25]. Consuming untreated water and swimming in stagnant waters such as rivers and lakes are essential sources of infection[26].

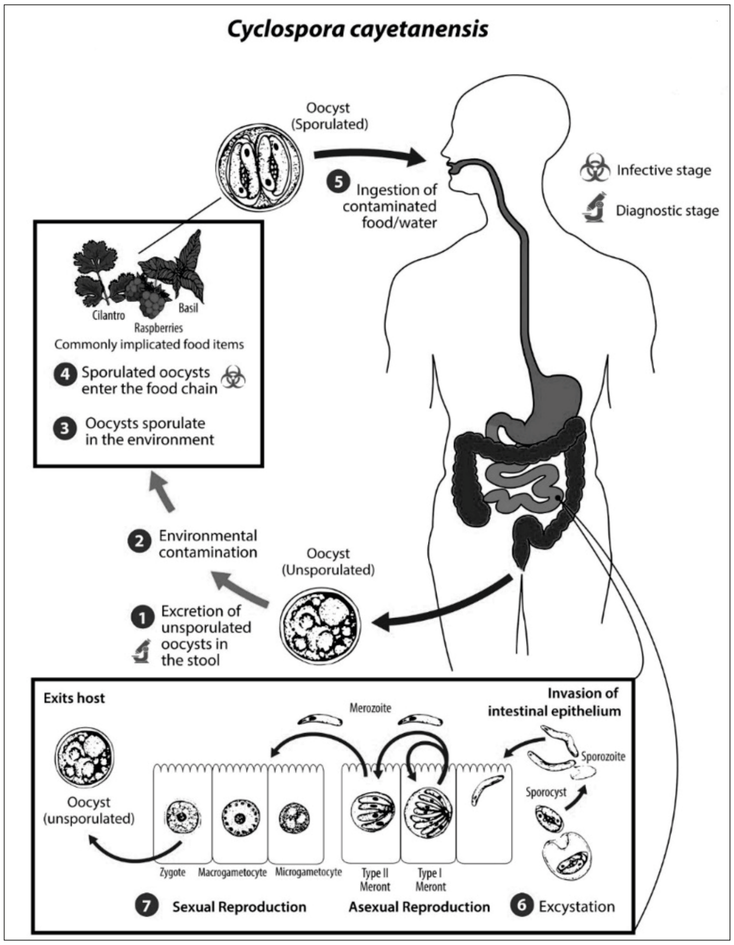

Figure 1. *Life discussion of C. cayetanensis*[66].

C. cayetanensis is a biological indicator to determine fecal contamination in Asian aquaculture waters. It shows whether the feces mixed with water are of human or animal origin[19].

Soil

Soil is one of the important sources of contamination and infection for *C. cayetanensis*[20]. Studies have shown that *contact with soil from C. cayetanensis* is a risk factor for infections in developing and developed countries[27]. The fact that vegetables and fruits are in contact with the soil during the growing process or irrigation paves the way for contamination[28]. In Venezuela, where most Cyclospora cases are associated with inadequate sanitation facilities, infections commonly occur due to soil contamination with feces. Consequently, there is an observed relationship between socioeconomic status and infection[29].

Person

C. cayetanensis is a species that has only been detected in humans so far. Although 17 different species of *Cyclospora* have been identified in many living things, none of them have the same characteristics as the *C. cayetanensis* species isolated from humans[22]. Therefore, *C. cayetanensis* was considered anthroponotic[30,31].

C. cayetanensis is prevalent in regions where agriculture is widespread, and handwashing is not a common practice[23]. People engaged in earthworks contaminate oocysts into foods during harvest time[32]. Once more, personnel working in the food production line are likely to transmit *C. cayetanensis* if they do not adhere to necessary personal hygiene rules [33].

Food

Carelessness or wrong practices in eating habits, such as consumption of undercooked or raw foods, increase parasitic infections[34]. Studies have reported that

Table 1. *C. cayetanensis epidemics in the world (2000–2015)63*

COUNTRIES	YEAR	NUMBER OF CASES	SOURCE OF INFECTION	ORIGIN OF INFECTION
ABD	2000–2015	2184	Peas, basil, coriander, lettuce, indeterminate	Guatemala, Mexico, Uncertain
Germany	2000	34	Salad, herbs	France, Italy, Germany
Australia	2010	266	Lettuce	Malaysia
United Kingdom	2015	79	Raspberry cake	Mexican
Indonesia	2001	14	Uncertain	Uncertain
Spain	2003	11	Raspberry juice	Guatemala
Sweden	2009	18	Pea	Guatemala
Canada	2001–2015	451	Thai basil, coriander, basil, garlic, indeterminate	ABD, Mexico, Uncertain
Colombia	2002	31	Salad, juice	Uncertain
Mexican	2001	97	watercress	Uncertain
Peruvian	2004–2005	164	Uncertain	Uncertain
Poland	2013	3	Drinking water	Indonesia
Türkiye	2005–2007	305	Drinking water, undetermined	Uncertain

outbreaks often occur following the consumption of freshwater oysters in Asia, revealing that 48% of these oysters harbor Cyclospora oocysts for up to 13 days [35]. Another transmission source is the consumption of fresh fruits and vegetables that are difficult to clean and contaminated with oocysts without washing[36]. These foods include raspberries, blackberries, greens, basil, coriander, and salad products[37]. Moreover, the incomplete removal of oocysts during food washing remains a significant source of infection [36].

Prevalence of C. cayetanensis cases in the world

Global research shows that cyclosporiasis occurs mainly in tropical and subtropical regions. The protozoan was first detected in endemic areas such as Haiti, Guatemala, Peru, and Nepal. It is more common in Central and South America and South East Asia, including India, Nepal, and Indonesia. The Middle Eastern countries, where our country is situated, are also among the regions where the disease is observed[38,39].

The first documented epidemic took place in Chicago in 1990, affecting 21 individuals. The outbreak was suspected to be linked to a broken water pump or food consumed at a party, yet the exact source could not be determined[40]. Two outbreaks were reported in 1995, affecting 32 people in New York and 38 in Florida. In the three years following these outbreaks, infections caused by *C. cayetanensis* were detected in an additional two thousand people[37].

The first case of *C. cayetanensis* in Türkiye was reported in 1998 in a patient with AIDS[41]. *C. cayetanensis* was detected in two people who returned from Türkiye to France in 2004 and five people in 2005[12]. Our country's first waterborne cyclosporiasis epidemic was reported in Izmir in 2007. *C. cayetanensis* was detected in two out of 554 individuals who visited the hospital with diarrhea[42]. In 2008, *C. cayetanensis* was detected in one of 138 children between the ages of 2 and 6 who were brought to the Maternity and Pediatrics Hospital in Kars with gastrointestinal complaints[43]. In 2012, *C. cayetanensis* was detected in 13 of 75 people with diarrhea in Diyarbakir[44]. According to these results, *C. cayetanensis* is our country's second most common protozoan. The global *C. cayetanensis* epidemics in recent years are presented in Table 1.

Symptoms

Symptoms appear 1 to 7 days after the *C. cayetanensis* oocyst is ingested and settles in the small intestine. These symptoms start as malaise[19,45]. In cyclosporiasis infection, defecation an average of 7 times daily is pathognomonic for the disease. It is characterized by symptoms of watery diarrhea, abdominal bloating, cramps, nausea, low-grade fever, fatigue, and weight loss. It is seen as severe, long-lasting, or chronic diarrhea in immunocompromised or immunocompromised patients (AIDS, children, the elderly)[46].

Symptoms last approximately 3 to 4 days; if treatment is not started during this period, the process may last up to several weeks[45]. Cyclosporiasis symptoms are more severe in HIV/AIDS patients. While an average of 3.5 kg of weight is lost during the disease, this weight loss increases to approximately 7 kg in HIV-positive patients[47]. While the average duration of diarrhea was 57.2 days in HIV-negative patients, it was observed to last 199 days in HIV-positive patients[48]. In places where the disease is endemic, symptoms are more asymptomatic[49]. Following a Cyclospora infection, Guillain-Barre syndrome,[50] and reactive arthritis syndrome (Reiter syndrome) may develop[51]. Cyclosporiasis, overall, has a low mortality rate[52]. However, if left untreated, infection can persist intermittently[22] (Table 1).

Diagnosis

Because *C. cayetanensis* is intracellular, diagnosing cases in routine analysis[53] is complex. In cases where cyclosporiasis is suspected, it is diagnosed only by microscopic examination and molecular diagnosis of stool samples performed by experts[54]. Microscopy examines the size and shape of *C. cayetanensis* in the feces and the presence of unsporulated oocysts. *C. cayetanensis* oocysts and *cryptosporidium* spp. since the oocysts are close in size, they are likely to be confused. For a definitive diagnosis, waiting for the oocysts to sporulate[39] is necessary. The samples taken are incubated at 23–30°C for 7 to 15 days, and oocysts are examined after sporulation has occurred[9].

The sampling step is vital in diagnosis. Due to the low number of oocysts in the feces, the multiplicative method must be employed[40]. Formol ethyl acetate or Shether's sugar flotation method is used for the bulking method[55]. The sample is preserved in 2.5% potassium dichromate for PCR analysis and 10% formalin for microscopic diagnosis and staining. Samples can be frozen for long periods for diagnosis[54,56].

Samples taken from the stool are stained with acid-resistant dyes (Modified Ziehl-Neelsen (hot method) or Kinyoun (cold method)) and examined with a light microscope[57]. *Cyclospora* oocysts are seen under the microscope as 8–10 µm in size and spherical, resembling a morula in the middle. In its differential diagnosis, *C. cayetanensis* is examined with a fluorescence microscope using its autofluorescence feature. Here, *C. cayetanensis* oocysts are seen as light blue at 330–380 nm in size or green at 450–490 nm in size[58].

The identification of *C. cayetanensis* in food is made by microscopic examination of swabs taken into the food[59]. If multiplication is necessary, formalin-ether precipitation or sucrose flotation techniques increase the amount of oocysts. It is easily detected under the microscope by observing its spherical structures of 8–10 µm in size[60]. Environmental Protection Agency (EPA) techniques 1622 and 1623.1, employed in the USA to detect cryptosporidium oocysts in waters, are also used for *Cyclospora* oocysts[39].

Treatment

The use of Trimethoprim-Sulfametaxazole (TMP-SMX) is recommended in the treatment of cyclosporiasis. Studies found that a 5–25 mg/kg dose stopped oocyst excretion in children after three days of treatment[61].

Prevention and Control

To ensure the protection and control of *C. cayetanensis*, the parasite's life cycle, the disease's epidemiology, hygiene conditions, and the climate of the environment where the agent is found must be taken into account. The factor is generally associated with regions with poor hygiene and economic conditions. Suppose the general hygienic conditions in these regions are improved. In that case, the burden of water and food contaminated with feces can be reduced[39]. Good agricultural practices should be implemented to prevent cyclosporiasis. The aim here is to reduce the role of protozoa in transmission. The purification and use of water in agricultural practices reduce the occurrence of the disease[46]. Water should be filtered to be protected from contaminated water, and irrigation should be carried out by providing filtration[62]. It is important to pass shellfish from where they are grown to clean waters before catching/collecting them and to subject them to heat treatment to reduce microbial contamination[63]. If hygienically questionable water is used to clean fresh vegetables and fruits, the water used should be boiled or filtered[64]. Another cleaning method before consuming fresh vegetables and fruits is to disinfect them. Vegetables and fruits immersed in Sodium dichloroisocyanurate solution for disinfection have been reported to reduce the number of parasites, including *C. cayetanensis*[65]. It is treated with magnesium oxide nanoparticles to prevent sporulation of *C. cayetanensis* oocysts in water to be used in agricultural areas. This prevents sporulation and ensures that the water is safe. The hygienic status of people working in agricultural areas, which is an important factor in contamination, should be checked. If the farmer has any symptoms of gastroenteritis, he should not be allowed to come into contact with food. Preventing access to contaminated water during personal hygiene, practicing thorough handwashing, and ensuring proper sewage disposal are vital measures to prevent *C. cayetanensis* infection. Compliance with general hygiene rules has an essential place in preventing the disease. There is no vaccine yet for *C. cayetanensis*[64].

Conclusion

C. cayetanensis is a protozoan that infects humans through food. What makes this protozoan significant is its presence in the foods we consume daily and in water, which is a crucial element in our lives. Infection occurs via the fecal-oral route. These oocysts ingested through food cause chronic diarrhea in humans. It causes long-lasting health problems for public health. Prevention is to wash vegetables and fruits and remove soil residue. However, the water should be boiled or filtered while washing with appropriate filtration systems due to the possibility of water contamination. Drinking water must be used after it has been purified. It is recommended that the person affected by the infection receive the necessary training and comply with personal hygiene rules.

References

1. Internet access www.who.int/topics/foodborne_ diseases /en //; 2023(accessed 29.04.2023).
2. İrfan E. Yeni ve yeniden önem kazanan gıda kaynaklı bakteriyel zoonozların epidemiyolojisi: Veteriner Hekimler Derneği Dergisi. 2016;87(2):63–76.
3. Arisue N, Hashimoto T. Phylogeny and evolution of apicoplasts and apicomplexan parasites: Parasitology International. 2015;64(3):254–9.
4. Adl SM, Leander BS, Simpson AG, Archibald JM, Anderson OR, Bass D, et al. Diversity, nomenclature, and taxonomy of protists: Systems Biology and the Future of Medicine. 2007;56(4):684–9.
5. Frazier WC, Westhoff DC. Food Microbiology. Indian: McGraw Tepesi;1993.
6. Mead PS, Slutsker L, Dietz V, McCaig LF, Bresee JS, Shapiro C, Griffin PM, Tauxe RV. Foodrelated illness and death in the United States. Emerging Infectious Diseases. 1999;5:607–25.
7. Steinhart CE, Doyle ME, Cochrane BA. Food Safety. Department of Food Microbiology and Toxicology University of Wisconsin, Madison, 10th edition. 1996;561–4.
8. Soave R, Johnson WD. Cyclospora: conquest of an emerging pathogen. The Lancet. 1995;345(8951):667–8.
9. Ortega YR, Gilman RH, Sterling CR. A new coccidian parasite (Apicomplexa: Eimeriidae) from humans. Journal of Parasitology. 1994;80(4):625–9.
10. Abou el Naga, IF. Studies on a newly emerging protozoal pathogen: Cyclospora cayetanensis. J. Egypt. Soc. Parasitol. 29, 575–586, 1999.
11. Ashfort RW. Occurrence of a undescriptive coccidian in man in Papua New Guinea: Annals of Tropical Medicine and Parasitology. 1979;73:497–500.
12. Ortega YR ve Sanchez R. Update on *C. cayetanensis*, a Foodborne and waterborne parasite. Clinical Microbiology Reviews. 2010;23(1):218–34.
13. Ortega YR, Sterling CR, Gilman RH, Cama VA, Díaz F. Cyclospora species: A new protozoan pathogen of humans. The New England Journal of Medicine. 1993;328:1308–12.
14. Ortega YR, Nagle R, Gilman RH, Watanabe J, Miyagui J, Quispe H, Kanagusuku P, Roxas C, Sterling CR. Pathologic and clinical findings in patients with cyclosporiasis and a description of intracellular parasite life-cycle stages. The Journal of Infectious Diseases. 1997;176:1584–9.
15. Connor BA, Reidy J, Soave R. Cyclosporiasis: Clinical and histopathologic correlates: Clinical Infectious Diseases. 1999;28, 1216–22.
16. Ortega YR, Sterling CH, Gilman RH. Cyclospora cayetanensis. Advances in Parasitology. 1998;40:399–418.
17. Shlim DR, Cohen MT, Eaton M, Rajah R, Long EG, Ungar BLP. An alga- like organism associated with an outbreak of prolonged diarrhea among foreigners in Nepal: American Journal of Tropical Medicine and Hygiene. 1995;1092–7.
18. Soave R, Herwaldt BL, Relman DA. Cyclospora. Infectious Disease Clinics of North America. 1998;12:1–12.
19. Fletcher SM, Stark D, Harkness J. Enteric protozoa in the developed world: a public health perspective. Clinical Microbiology Reviews. 2012;25(3):420–49.
20. Chacín-Bonilla L. Transmission of *C. cayetanensis* infection: A review focusing on soil-borne cyclosporiasis. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2008;102:215–6.
21. Hall RL, Jones JL, Hurd S, Smith G, Mahon BE, Herwalt BL. Population-based active surveillance for Cyclospora. Clinical Infectious Diseases. 2012;54:7.
22. Mansfield LS, Gajadhar AA. *C. cayetanensis*, a food and waterborne coccidian parasite. Veterinary Parasitology. 2004;126:7390.
23. Tandukar S, Ansari S, Adhikari N, Shrestha A, Gautam J, Sharma B, Rajbhandari D, Gautam S, Nepal HP, Sherchand JB. Intestinal parasitosis in school children of Lalitpur district of Nepal. BMC Research Notes 6. 2013;449.
24. Hale D, Aldeen W, Carroll K. Diarrhea associated with Cyanobacteria-like bodies in an immunocompetent host. An unusual epidemiological source. Indian Journal of Critical Care Medicine. 1994;27:144–5.
25. Tram NT, Hoang LM, Cam PD, Chung PT, Fyfe MW, Isaac-Renton JL, Ong CS. Cyclospora spp. in herbs and water samples collected from markets and farms in Hanoi, Vietnam. Tropical Medicine and International Health. 2008;13:1415–20.
26. Bern C, Hernandez B, Lopez MB, Arrowood MJ, Mejía MA, Merida AM, et al. Epidemiologic studies of C. cayetanensis in Guatemala: Emerging Infectious Diseases. 1999;5:766–74.
27. Mundaca CC, Torres-Slimming PA, Araujo-Castillo RV, Morán M, Bacon DJ, Ortega Y, Gilman RH, Blazes DL. Use of PCR to improve diagnostic yield in an outbreak of cyclosporiasis in Lima, Peru. Trans. R. Soc. Trop. Med. Hyg. 102, 712–717, 2008.
28. Monaghan JM, Hutchison ML. Distribution and decline of human pathogenic bacteria in soil after application in irrigation water and the potential for soil-splash-mediated dispersal onto fresh produce. Journal of Applied Microbiology. 2012;112(5):1007–19.
29. Chacín-Bonilla L, Barrios F, Sanchez Y. Epidemiology of *C. cayetanensis* infection in San Carlos Island, Venezuela: Strong association between socio-economic status and infection: Transactions of the Royal Society of Tropical Medicine and Hygiene. 2007;101:1018–24.

30. Zerpa R, Uchima N, Huicho L. Cyclospora cayetanensis associated with watery diarrhea in Peruvian patients. American Journal of Tropical Medicine and Hygiene. 1995;98(5):325–9.
31. Garcia-Lopez HL, Rodriguez-Tovar LE, Medina-De la Garza CE. Identification of Cyclospora in poultry: Emerging Infectious Diseases. 1996;2(4):356–7.
32. Kniel KE, Lindsay DS, Sumner SS, Hackney CR, Pierson MD, Dubey JP. Examination of attachment and survival of T. gondii oocysts on raspberries and blueberries. Journal of Parasitology. 2002;88(4):790–3.
33. Buisson YJ, Marie JL, Davoust B. These infectious diseases imported with food: Bulletin de la Société de Pathologie Exotique. 2008;101:343–7.
34. Orlandi PA, Chu DM, Bier JW, Jackson GJ. Parasites in the food supply. Food Technology. 2002;56:72.
35. Graczyk TK, Ortega YR, Conn DB. Recovery of waterborne oocysts of *C. cayetanensis* by Asian freshwater clams (Corbicula fluminea) . American Journal of Tropical Medicine and Hygiene. 1998;59:928–32.
36. Sterling CR, Ortega YR. Cyclospora: an enigma worth unraveling. Emerging Infectious Diseases. 1999 5(1):48–53.
37. Herwaldt BL. Cyclospora cayetanensis: Review, focusing on the outbreaks of cyclosporiosis in the 1990. Clinical Infectious Diseases. 2000;31:1040–57.
38. Cama VA ve Ortega YR. Cyclospora cayetanensis. In Foodborne Parasites, 2nd ed.;Ortega, Y. R., Sterling, C. R., Eds.;Springer: Berlin/Heidelberg, Germany, pp. 41–56, 2018.
39. Shields JM, Olson BH. PCR-restriction fragment length polymorphism method for detection of *C. cayetanensis* in environmental waters without microscopic confirmation: Applied and Environmental Microbiology. 2003;69:4662–9.
40. Özcel MA. Tıbbi Parazit Hastalıklar. İzmir: Meta Basım;2007.
41. Koç AN, Aygen B, Şahin I, Kayabaşı Ü. Cyclospora sp. associated with diarrhea in a patient with AIDS in Turkey. Turkish Journal of Medical Sciences. 1998;28:577–8.
42. Aksoy Ü, ve Tuncay S. Diyareli hastalarda intestinal koksidiaların araştırılması: Mikrobiyoloji Bülteni. 2007;41:127–31.
43. Arslan MÖ, Sarı B, Kulu B, Mor N. Kars doğum ve çocuk bakımevi hastanesine gastrointestinal yakınmalarla başvuran çocuklarda bağırsak parazitlerinin yaygınlığı: Türkiye Parazitoloji Dergisi. 2008;32(3):253–6.
44. Çiçek M, Palancı Y, Ceylan A, Tuncer Ö, Muhsin K. Evaluation of demographic, clinic and treatment features of patients and a cross-sectional survey of cyclosporiasis in patients with diarrhea in Southeastern Turkey: African Journal Microbiology Research. 2012;6(12):2949–55.
45. Goodgame RW. Understanding intestinal spore forming protozoa: Cryptosporidia, Microsporidia, Isosopora and Cyclospora. Annals of Internal Medicine. 1996;124:429–41.
46. Ortega YR, Mann A, Torres MP, Cama V. Efficacy of gaseous chlorine dioxide as a sanitizer against C. parvum, *C. cayetanensis*, and E. intestinalis on produce. Journal of Food Protection. 2008;71:2410–2414.
47. Shlim DR, Cohen MT, Eaton M, Rajah R, Long EG, Ungar BLP. An alga-like organism associated with an outbreak of prolonged diarrhea among foreigners in Nepal. American Journal of Tropical Medicine and Hygiene. 1991;45:383–9.
48. Schubach TM, Neves ES, Leite AC, Araújo AQC, Moura H. *C. cayetanensis* in an asymptomatic patient infected with HIV and HTLV-1. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1997;91:175.
49. Behera B, Mirdha BR, Makharia GK, Bhatnagar S, Sattagupta S, Samantaray JC. Parasites in patients with malabsorption syndrome: a clinical study in children and adults. Digestive Diseases and Sciences. 2008;53:672–9.
50. Richardson RF, Remler BF, Katirji B, Murad MH. Guillain-Barré syndrome after Cyclospora infection. Muscle and Nerve. 1998;21:669–671.
51. Connor BA, Johnson E, Soave R. Reiter syndrome following protracted symptoms of Cyclospora infection: Emerging Infectious Diseases. 2001;7:453–4.
52. Burrell C, Reddy S, Haywood G, Cunningham R. Cardiac arrest associated with febrile illness due to U. K. acquired *C. cayetanensis*: The Journal of Infectious Diseases. 2007;54:13–15.
53. Curry A, Smith HV. Emerging pathogens: Isospora, Cyclospora and Microsporidia: Parasitology. 1998;117:143–59.
54. Eberhard ML, Pieniazek NJ, Arrowood MJ. Laboratory diagnosis of cylospora infections: Archives of Pathology and Laboratory Medicine. 1997;121:792–7.
55. Visvesvara GS, Moura H, Kovacs-Nace E, Wallace S, Eberhard ML. Uniform staining of Cyclospora oocysts in fecal smears by a modified safranin technique with microwave heating. Journal of Clinical Microbiology. 1997;35:730–3.
56. Cann KJ, Chalmers RM, Nichols G, O'Brien SJ. Cyclospora infections in England and Wales:1993 to 1998. Commun Dis Public Health. 2000;3:46–49.
57. Korkmaz M, Ok ZÜ. Parazitolojide Laboratuvar. İzmir: Meta Basım;2011.
58. Garcia LS. ve Bruckner DA. Diagnostic Medical Parasitology 3. ed. Washington. DC. USA. ASM PressWashington DC, 1997.
59. Becker SL, Vogt J, Knopp S, Panning M, Warhurst DC, Polman K, et al. Persistent digestive disorders in the tropics: Causative Infectious Pathogens and Reference Diagnostic Tests. BMC Infectious Diseases. 2013;13:37.
60. Li J, Wang R, Chen Y, Xiao L, Zhang L. *C. cayetanensis* infection in humans: biological characteristics, clinical features, epidemiology, detection method, and treatment. Parasitology 8. 2019;1–11.
61. Madico G, Gilman RH, Miranda E, Cabrera L, Sterling CR. Treatment of Cyclospora infections with co-trimoxazole. The Lancet. 1993;342:122–3.
62. Sturbaum GD, Ortega YR, Gilman RH, Sterling CR, Cabrera L, Klein DA. Detection of *C. cayetanensis* in wastewater. Applied and Environmental Microbiology. 1998;64:2284–6.
63. Carter MJ. Enteric ally infecting viruses;pathogenicity, transmission and significance for food and waterborne infection: Journal of Applied Microbiology. 2005;98:1354–80.
64. Hussein EM, Ahmed SA, Mokhtar AB, Elzagawy SM, Yahi SH, Hussein AM El-Tantawey F. Antiprotozoal activity of magnesium oxide (MgO) nanoparticles against *C. cayetanensis* oocysts. Parasitology International. 2018;67:666–74.
65. El Zawawy LA, El-Said D, Ali SM, Fathy FM. Disinfection efficacy of sodium dichloroisocyanurate (NADCC) against common food-borne intestinal protozoa: Journal of The Egyptian Society of Parasitology. 2010;40:165–85.
66. www.dpd.cdc.gov/dpdx/HTML/Frames/AF/Cyclosporiasis/body_ Cyclosporiasis_sporul.htm/; 2023(accessed 29.05.2023).