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Original Article

Clinical, laboratory and epidemiological aspects of *Cryptosporidium parvum* and *Cryptosporidium hominis* infection: a integrative review

Aspectos clínicos, laboratoriais e epidemiológicos da infecção por *Cryptosporidium parvum* e *Cryptosporidium hominis*: uma revisão integrativa

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Abstract

Cryptosporidium parvum and *Cryptosporidium hominis* infection causes cryptosporidiosis, which in humans can result in watery diarrhea that is usually self-limited in immunocompetent individuals, but can be chronic and fatal in immunocompromised individuals. To understand and expose current clinical, laboratory and epidemiological data, as well as characteristics of cryptosporidiosis worldwide. This is a literature review by the integrative review method, qualitative and exploratory through the publications selected in the databases: BVS, ScieLO, MEDLINE and LILACS. Inclusion criteria were: publications from the last 6 years and articles in Portuguese, English and Spanish. Exclusion criteria were: research not evidenced in humans and duplicate articles, as well as articles that were not available in full and free of charge. The variables analyzed were cases by regions of the world, transmission mechanisms and symptoms. In this study, 40 articles were submitted. Regarding transmission, the most commonly reported route was the anthroponotic route, being mentioned in 40% of them (16); the zoonotic route was also prominent, being mentioned in 22.5% (9) of the articles. As for the symptoms, diarrhea was the most present, being mentioned in 82.5% (33 articles), other symptoms mentioned were headache 12.5% (5), joint pain 5% (2) and eye pain 5% (2). With regard to laboratory diagnosis, the most commonly used method was polymerase chain reaction (PCR) 75% (30) and modified Ziehl Neelsen staining 22.5% (9). Therefore, it is noticeable that the main complication of cryptosporidiosis is gastroenteritis, whose manifestations range from diarrhea to abdominal cramps. This parasite is widely distributed throughout the world, mainly in developing and underdeveloped countries, transmitted by the oral-fecal route. In addition, it is notable that PCR was the most commonly used laboratory method for diagnosis, which shows that the disease can be easily detected once the symptoms have manifested themselves. In this sense, knowledge about the parasite is necessary for prevention and thus avoid major complications.

Keywords: apicomplexa, *Cryptosporidium* sp., intracellular coccidia.

Resumo

A infecção ocasionada por *Cryptosporidium parvum* e *Cryptosporidium hominis*. causa criptosporidiose, que em humanos, pode resultar em diarreia aquosa, que normalmente é autolimitada em indivíduos imunocompetentes, mas pode ser crônica e fatal em indivíduos imunocomprometidos. Compreender e expor dados clínicos, laboratoriais e epidemiológicos atuais, assim como as características da criptosporidiose no mundo. Trata-se de uma revisão bibliográfica de literatura pelo método revisão integrativa, qualitativa e exploratória por meio das publicações selecionadas nas bases de dados: BVS, ScieLO, MEDLINE e LILACS. Foram adotados como critérios de inclusão: publicações dos últimos 6 anos e artigos em português, inglês e espanhol. Já como critérios de exclusão: pesquisas não evidenciadas em humanos e artigos duplicados, e também artigos que não foram disponibilizados na íntegra e gratuitamente. As variáveis analisadas foram casos por regiões do mundo, mecanismos de transmissão e sintomas apresentados. Deste estudo, foram submetidos 40 artigos. No que se refere à transmissão, a via mais relatada foi a antroponótica, sendo mencionada em 40% deles (16), a via zoonótica também teve grande destaque com

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menção em 22,5% (9) dos trabalhos. Já em relação à sintomatologia, a diarreia foi a mais presente ao ser citada em 82,5% (33 artigos), outros sintomas mencionados foram cefaleia 12,5% (5), dores nas articulações 5% (2) e dores nos olhos 5% (2). Em relação ao diagnóstico laboratorial, o método mais utilizado foi a reação em cadeia da polimerase (PCR) 75% (30) e a coloração de Ziehl Neelsen modificada com 22,5% (9). Portanto, é perceptível que a principal complicação da criptosporidiose é a gastroenterite, cujas manifestações variam entre diarreias e cólicas abdominais. Este parasito é amplamente distribuído por todo o mundo, principalmente em países em desenvolvimento e subdesenvolvidos, transmitido por via oral-fecal. Além disso, é notável que o PCR foi o método laboratorial para diagnóstico mais utilizado, o que mostra que a doença pode ser facilmente detectada uma vez que os sintomas se manifestem. Nesse sentido, é necessário o conhecimento sobre o parasito para a prevenção e assim evitar complicações maiores.

Palavras-chave: apicomplexa, *Cryptosporidium* sp., coccídios intracelulares.

1. Introduction

Cryptosporidium parvum and *Cryptosporidium hominis* are enteric intracellular coccidia protozoa of the Apicomplexa phylum that infect both humans and animals (Korpe et al., 2019). *Cryptosporidium* sp. infection causes cryptosporidiosis, which in humans can result in watery diarrhea can result in watery diarrhea, which is usually self-limiting and does not cause major hemodynamic repercussions in immunocompetent individuals, but can be chronic and fatal in fatal in immunocompromised individuals, which can lead to situations of massive infection, severe dehydration and hemodynamic instability (Tandel et al., 2019).

The route of transmission of the infection is oral-fecal through the ingestion of oocysts. Contaminated food and water are the main means of transmission of the etiological agents. Few oocysts are needed for infection to occur, so, feces from infected humans become infectious in contact with the environment. Basically, the parasite's life cycle begins when the sporulated oocysts are ingested by the host (Sannella et al., 2019). Once ingested, in the lumen of the gastrointestinal system, the oocysts rupture and release four sporozoites, these sporozoites adhere to the apical surface of the intestinal epithelial cells and these sporozoites adhere to the apical surface of intestinal epithelial cells and develop into trophozoites within the parasitophorous vacuole, an intracellular compartment in the host in which the parasite multiplies (Khalil et al., 2017).

These trophozoites reproduce asexually (merogony) and develop into 6-8 merozoites (meront I), which are released and invade neighboring cells to repeat the cycle and increase the number of merozoites. The merozoites can change into type II meronts, releasing type II merozoites to form sexual stages: the microgamont, with microgametocytes inside (male form), or the macrogamont (female form). Then, during fertilization, a microgametocyte fertilizes a macrogametocyte, generating a zygote that can be converted into thick-walled oocysts (80%) or thin-walled oocysts (20%) (Heo et al., 2018).

Thick-walled oocysts are commonly excreted by the host, contaminating soil, water, food and objects, while thin-walled oocysts are mainly involved in autoinfections and the maintenance of a chronic infection, due to their tendency to rupture, leading to their tendency to rupture, leading to chronic diarrhea, hypovitaminosis and even severe dehydration (Heo et al., 2018).

Then, after ingesting the oocysts and the future release of the sporozoites, when they penetrate the intestinal epithelial cells, they cause the common symptoms of the disease, such as mild self-limiting watery diarrhea, as well as abdominal cramps, nausea and vomiting. However, some studies have reported that individuals infected with *C. hominis* can present non-specific extraintestinal symptoms, such as: low-grade fever, myalgia, asthenia, malaise, headache and anorexia. The incubation period is usually between 2 and 10 days and symptoms usually last from 2 days to 3 weeks in healthy adults (Adler et al., 2017).

It is noticeable that cryptosporidiosis is considered to be one of the main causes of diarrhea in individuals living in underdeveloped and developing countries. It is considered one of the most important causes of moderate and severe diarrhea, also associated with mortality among children under 2 years old. The association of diarrhea with cryptosporidiosis has resulted in more than 48,000 deaths, as well as 4.2 million disability adjusted life years (DALYs) in children under 5 years old in 2016. Countries considered underdeveloped and developing have a higher endemicity, with lower levels of hygiene, higher rates of infection at an earlier age and greater associations with individuals with HIV/AIDS (Yang et al., 2021). In view of the importance of cryptosporidiosis in public health, based on the above,this study aimed to carry out an integrative review of the studies of the last six years worldwide on cryptosporidiosis.

2. Methods

This is an integrative literature review, which sought to describe the current scientific knowledge on infections in humans by *Cryptosporidium parvum* and *Cryptosporidium hominis*, using relevant terms referring to the guiding question: "What are the main clinical, laboratory and epidemiological aspects associated with infections by Cryptosporidium parvum and *Cryptosporidium hominis* in different populations and geographic contexts?". The following terms are cited as health descriptors used for the production of this article: "*Cryptosporidium parvum*", "*Cryptosporidium hominis*"; "cryptosporidiosis", "cryptosporidiosis". The Boolean marker used in each cross was the AND.

For the development of this integrative review, the methodological steps recommended by Whittemore et al.

(2023) were adopted: 1) Elaboration of the review question; 2) Search and selection of primary studies; 3) Data extraction from studies; 4) Critical evaluation of the primary studies included in the review; 5) Synthesis of the results of the review and 6) Presentation of the method. The articles, fundamental in deepening the theme, with a survey of scientific data for analysis and interpretation of the results, in the following databases: Virtual Health Library (VHL), Scientific Electronic Library Online (Scielo), Medical Literature Analysis and Retrievel System Online (MEDLINE) and Latin American Literature in Health Sciences (LILACS).

The criteria for inclusion of the pre-selected articles were published articles that addressed infections in humans, written in English, Portuguese or Spanish, available in full, published in the period from 2017 to 2022. However, all monographs, dissertations, theses, incomplete articles, duplicates, and extended abstracts, which deviated from the objective or the guiding question, which did not contain in the title the terms cryptosporidiosis in humans, published in the period shorter than the stipulated (before 2017), in any other language not previously mentioned, were excluded. The articles were organized and tabulated using the Mendeley platform, for later methodological analysis and reading for the construction of the present study.

In this integrative review, one hundred and seventy-two (172) publications were surveyed, being reduced to one hundred and fifty-one (151) after the inclusion and exclusion criteria established during the selection. Next, a critical analysis was carried out, totaling a final of forty (40) articles, which were organized in a flowchart (Table 1).

Table 1. Authorship, title, year and objectives of the articles on clinical and epidemiological aspects of cryptosporidiosis in humans chosen for this review.

Author/Year (published)	Title	Objective
Cunha et al. (2022)	Molecular characterization of *Cryptosporidium* spp. obtained from fecal samples of immunosuppressed patients from Brazil.	Detect and genetically characterize *Cryptosporidium* sp. in kidney transplanted patients and immunosuppressed individuals from an outpatient clinic suspected of having *Cryptosporidium* sp. infection.
Sjöström et al. (2022)	Outbreak of *Cryptosporidium* hominis in northern Sweden: persisting symptoms in a 5-year follow-up	This article aimed to investigate whether the parasite caused post-infectious sequelae for up to 5 years after the outbreak.
Menu et al. (2022)	Cryptosporidiosis outbreak in Amazonia, French Guiana, 2018.	Investigate the outbreak of cryptosporidiosis cases in March 2018 in the village of Maripasoula.
Urrea-Quezada et al. (2022)	Serum IgG Responses to gp15 and gp40 Protein-Derived Synthetic Peptides From *Cryptosporidium parvum.*	The objective of this study was to evaluate humoral immunity, as demonstrated in the recognition of synthetic peptides of the *Cryptosporidium parvum* gp15 and gp40 proteins by serum IgM and IgG antibodies from patients infected (cases) with *Cryptosporidium hominis*, *C. parvum*, and *Cryptosporidium canis*, and uninfected individuals.
Wang et al. (2022)	Molecular detection and genetic characterization of *Cryptosporidium* in kindergarten children in Southern Xinjiang, China.	Assess the genetic characteristics and epidemiological status of *Cryptosporidium* sp. in kindergarten children in Southern Xinjiang, China.
Cossa-Moiane et al. (2021)	High Frequency of *Cryptosporidium hominis* Infecting Infants Points to A Potential Anthroponotic Transmission in Maputo, Mozambique	This study aimed to determine the frequency and risk factors for *Cryptosporidium* sp. infection in children hospitalized in Maputo City through the National Surveillance of Acute Diarrhea.
Guy et al. (2021)	Molecular characterization of *Cryptosporidium* isolates from humans in Ontario, Canada.	Identify the species and subtypes of *Cryptosporidium* sp. in sporadic cases from a random subset of *Cryptosporidium*-positive human stool samples from 2008–2017, submitted to the provincial reference laboratory in specimen collection containers lacking fixative.
Hailu et al. (2021)	Molecular characterization of *Cryptosporidium* spp. from humans in Ethiopia	Determinate the prevalence of *Cryptosporidium* sp. infection and identify genetic diversity of the parasite circulating in the human population living in Wurgissa district and Hawassa in Ethiopia.
Mohammad et al. (2021a)	Genotyping of *Cryptosporidium* species in children suffering from diarrhea in Sharkyia Governorate, Egypt.	Differentiate *Cryptosporidium* species among children suffering from diarrhea in Sharkyia Governorate, Egypt.

Table 1. Continued...

Author/Year (published)	Title	Objective
Mohammad et al. (2021b)	Molecular prevalence of *Cryptosporidium* isolates among Egyptian children with cancer	Evaluate the prevalence of *Cryptosporidium* sp. parasite and its genotypes in children with cancer.
Messa Junior et al. (2021)	Molecular Characterisation of *Cryptosporidium* spp. in Mozambican Children Younger than 5 Years Enrolled in a Matched Case-Control Study on the Aetiology of Diarrhoeal Disease	This study aimed to analyze the diversity and frequency of *Cryptosporidium* species and subtypes detected in stools from children younger than 5 years from the Manhiça district, Mozambique.
Yang et al. (2021)	Molecular Epidemiology of Human Cryptosporidiosis in Low- and Middle-Income Countries.	Carry out a molecular and epidemiological characterization of *Cryptosporidium* sp. in Low- and Middle-Income countries
Yulfi et al. (2021)	Prevalence of *Cryptosporidium* spp. and *Blastocystis hominis* in faecal samples among diarrheic HIV patients in Medan, Indonesia.	Investigate the prevalence of *Cryptosporidium* sp. among diarrheic HIV patients in two different outpatient clinics.
Izadi et al. (2020)	Frequency and Molecular Identification of *Cryptosporidium* Species among Immunocompromised Patients Referred to Hospitals, Central Iran, 2015-16.	This study aimed to genotypes isolated from immunocompromised patients, in four provinces including Chaharmahale Bakhtiari, Isfahan, Markazi and Yazd, central Iran
Hutter et al. (2020)	*Cryptosporidium* spp.: Human incidence, molecular characterization and associated exposures in Québec, Canada (2016-2017).	This study aimed to describe the epidemiology of human cryptosporidiosis in Québec from 2016 to 2017 and to identify possible exposures associated with the disease.
Martinot et al. (2020)	Cryptosporidiosis after treatment with fingolimod: a case report and pharmacovigilance review	Physicians should be aware of this association and screen for *Cryptosporidium* sp. in cases of diarrhea in patients treated with fingolimod. Patients should be aware of this risk and advise to take appropriate measures to avoid such contamination.
Mulunda et al. (2020)	Molecular characterization of *Cryptosporidium* sp. from patients with diarrhoea in Lusaka, Zambia	Determinate the prevalence and genetic characteristics of *Cryptosporidium* sp. in stool samples from patients with diarrhea who presented at the University Teaching Hospital in Lusaka, Zambia.
Hossain et al. (2019)	*Cryptosporidium* infection in rural Gambian children: Epidemiology and risk factors.	Investigate the epidemiology of, and evaluate possible risk factors for, *Cryptosporidium* sp. diarrhea.
Martins et al. (2019)	Surveillance of *Giardia* and *Cryptosporidium* in sewage from an urban area in Brazil.	Investigate the presence of *Giardia* sp. and *Cryptosporidium* sp. in raw and treated sewage from Londrina, Paraná, Brazil.
Nic Lochlainn et al. (2019)	Risk Factors for Sporadic Cryptosporidiosis in the Netherlands: Analysis of a 3-Year Population Based Case-Control Study Coupled With Genotyping, 2013-2016.	Describe the epidemiology of sporadic *Cryptosporidium* sp. infections and to identify risk factors for sporadic clinical infections with *Cryptosporidium* sp. in the Netherlands, to acquire information for control strategies.
Pielok et al. (2019)	Massive *Cryptosporidium* infections and chronic diarrhea in HIV-negative patients.	Describe three cases of middle-aged persons with massive *Cryptosporidium* sp. infection and chronic diarrhea with no immunological abnormalities.
Grossman et al. (2019)	Molecular typing of *Cryptosporidium* in Israel.	Explore and genotype molecular epidemiology of cryptosporidiosis cases.
Sannella et al. (2019)	A retrospective molecular study of *Cryptosporidium* species and genotypes in HIV-infected patients from Thailand.	Molecular characterization of parasite isolates from HIV infected people in Thailand in order to understand the transmission dynamics and the clinical manifestations.
Shaposhnik et al. (2019)	The Prevalence of *Cryptosporidium* among Children Hospitalized because of Gastrointestinal Symptoms and the Efficiency of Diagnostic Methods for *Cryptosporidium*.	Investigate the prevalence of cryptosporidiosis among children admitted to the hospital with gastrointestinal symptoms.
Zheng et al. (2018)	Case Report: Diagnosis of Cryptosporidiosis in Renal Transplantation in a Low-Prevalence Setting.	Describe our institutional experience in diagnosing cryptosporidiosis in a low-prevalence setting and review the literature about management options in the organ transplant population.

Table 1. Continued...

Author/Year (published)	Title	Objective
Cheung et al. (2018)	*Cryptosporidium* diagnosed on endoscopic biopsy in a paediatric patient with inflammatory bowel disease	This study is a case report of a child with cryptosporidiosis diagnosed on endoscopic biopsy.
Mosnier et al. (2018)	Cryptosporidiosis Outbreak in Immunocompetent Children from a Remote Area of French Guiana	Microbiological and epidemiological investigations conducted to establish the presence of a potential epidemic context, determine the etiology, evaluate risk factors, and contribute to elaboration of preventive procedures.
Ng-Hublin et al. (2018)	Comparison of three cryptosporidiosis outbreaks in Western Australia: 2003, 2007 and 2011.	Analyze the outbreaks of cryptosporidiosis that occurred in Australia in the year 2003, 2007, 2011.
Iglói et al. (2018)	Long-term sequelae of sporadic cryptosporidiosis: a follow-up study.	Determine the frequency of occurrence of sequelae following cryptosporidiosis.
Gilchrist et al. (2018)	Genetic Diversity of *Cryptosporidium hominis* in a Bangladeshi Community as Revealed by Whole-Genome Sequencing.	Analyze parasitic genetic diversity as measured by gp60 genotyping in children infected with *Cryptosporidium* sp. over a 2-year period in Bangladesh.
Delahoy et al. (2018)	Clinical, environmental, and behavioral characteristics associated with *Cryptosporidium* infection among children with moderate-to-severe diarrhea in rural western Kenya, 2008-2012: The Global Enteric Multicenter Study (GEMS).	Evaluate the clinical, environmental, and behavioral characteristics associated with *Cryptosporidium* sp. infection among children under five years old with MSD in rural western Kenya.
Mamba et al. (2018)	Lateral Flow Loop-Mediated Isothermal Amplification Test with Stem Primers: Detection of *Cryptosporidium* Species in Kenyan Children Presenting with Diarrhea.	Detection of *Cryptosporidium* sp. in Kenyan Children Presenting with Diarrhea at the pediatric ward of Mbagathi district hospital and from three clinics to evaluate the developed LAMP test.
Franklin et al. (2019)	*Cryptosporidium* infection in a case of appendicitis.	Investigate the influence of *Cryptosporidium* sp. infection in a case of appendicitis.
Casmo et al. (2018)	Occurrence of *Cryptosporidium* spp. and *Cystoisospora belli* among adult patients withdiarrhoea in Maputo, Mozambique.	This study conducted in Mozambique has specifically addressed the occurrence of *Cryptosporidium* sp. and *C. belli* in adult diarrhoeic patients, most of whom had a confirmed diagnosis of HIV.
Steiner et al. (2018)	Species of *Cryptosporidium* Causing Subclinical Infection Associated With Growth Faltering in Rural and Urban Bangladesh: A Birth Cohort Study.	This study investigated the burden of cryptosporidiosis and its impact on child growth in both a rural and an urban site in Bangladesh.
Lilja et al. (2018)	Persisting post-infection symptoms 2 years after a large waterborne outbreak of *Cryptosporidium hominis* in northern Sweden.	This study aimed to determine what were the symptoms that persisted 2 years after the waterborne outbreak of *Cryptosporidium hominis*.
Bednarska et al. (2018)	Prevalence of *Cryptosporidium*, *Blastocystis*, and other opportunistic infections in patients with primary and acquired immunodeficiency.	This study aimed to define the prevalence of intestinal micro-pathogens in hospitalized patients with different immunological statuses and detect the pathogenicity in the patients with *Cryptosporidium* sp. and *Blastocystis hominis*.
Stiff et al. (2017)	Long-term health effects after resolution of acute *Cryptosporidium parvum* infection: A 1-year follow-up of outbreak-associated cases	Describes for the first time sequelae reported by patients up to 12 months after infection with *C. parvum*, which appear to be similar to those described with *C. hominis*.
Khalil et al. (2017)	*Cryptosporidium* species subtypes and associated clinical manifestations in Indian patients.	Study the distribution of *Cryptosporidium* species subtypes in patients with complaints of diarrhea.
Adler et al. (2017)	Symptoms and risk factors of *Cryptosporidium hominis* infection in children: data from a large waterborne outbreak in Sweden.	Describe the duration of symptoms of *C. hominis* infection and the risk factors for such illness in children aged <15 years in a Western setting.

3. Results

Thus, after the search made in the databases, 193 articles were found. In the first analysis, duplicate articles, paid articles, and articles in other languages that were not part of the inclusion criteria were removed. Thus, 9 articles were excluded (2 paid articles, 6 duplicates, and 1 in another language), furthermore, a selection by title was performed, in which 77 articles were excluded because they did not match the research objective. After reading the abstracts, 54 articles were removed and 53 articles on the researched themes were selected to be read in full. After reading the articles, only 40 articles were filtered to be included in this review (Table 2). The most relevant information from the selected scientific papers is presented in the following subtopics:

4. Discussion

From the results presented in table 2, it is possible to identify a series of variables that draw attention and deserve to be mentioned. It is noticeable that there was no exclusion of groups for risk factor in relation to age or sex of patients. There are both female and male patients, plus there are elderly patients (≥60 years old) and infants (≤1 year old) being affected by cryptosporidiosis (Gilchrist et al., 2018; Hailu et al., 2021). The predominant infections were caused by oral-fecal transmission, that is, the ingestion of the protozoan through contaminated surfaces, either objects or food. However, it is worth noting that the articles also reported other, rarer forms of contamination through, for example, barbecued meat and by zoonotic route (Nic Lochlainn et al., 2019). An important consideration is that in most cases, anthroponotic contact was observed as the main route of transmission of the disease, especially in places where not much hygiene was observed, most likely where the first case was through ingestion of unwashed vegetables containing the protozoan, and the following ones through oral-fecal contact with that patient or objects contaminated by the patient (Casmo et al., 2018).

In addition, it is notable that another significant mode of transmission of the protozoan causing cryptosporidiosis is waterborne, thus a range of articles treat it as the main one (Sjöström et al., 2022; Menu et al., 2022; Adler et al., 2017). However, transmission occurs in places with poor sanitation, linked to precarious living conditions, since contaminated water is used as an instrument for ingestion and hygiene. Still, a common risk factor was observed: tap water; possibly the main contamination route for the infected in the reported studies (Menu et al., 2022). It is worth mentioning that cryptosporidiosis contamination peaks may occur due to environmental conditions that may spread contaminated water to the population through the overflow of sewage water, as demonstrated in the article from Londrina, Brazil (Martins et al., 2019). As well as the contamination of approximately 400,000 people in Sweden through the public water supply in 1993 is an example of this (Adler et al., 2017).

Its great worldwide distribution is observable, presenting increasing diversity, with cases that address not only the East, but also the West. There were a large number of articles that highlight the regions of the African continent and the Asian continent (20 articles - 50%), being a fact that it is an endemic disease in these populations. However, one cannot fail to notice researchers done in other continents, such as America or Oceania, which make it clear that cryptosporidiosis affects the whole globe (Ng-Hublin et al., 2018).

Therefore, it was observed that in Australia outbreaks of cryptosporidiosis have been predominantly attributed to the use of contaminated recreational waters and contact with contaminated people, this is confirmed when analyzing that 64% of the study patients reported having swum in a pool, and 16% of the infected patients during the outbreak reported having contact with a person with diarrhea. All these outbreaks were predominantly in the metropolitan area, mainly in children aged 0 to 4 years (Ng-Hublin et al., 2018). A high number of infections in children is observed in most articles (Mosnier et al., 2018; Gilchrist et al., 2018; Yang et al., 2021; Urrea-Quezada et al., 2022). This is mainly due to the lack of understanding that hygiene care is essential to avoid possible contamination, and the neglect of this care, essentially in regions where this type of information is uncommon (Yang et al., 2021).

It is certainly a disease that affects mainly underdeveloped countries that do not have the infrastructure to wash food or purify the water they drink, nor the education to know how to take care of their health, which is why there is a high prevalence of cases in these regions. However, it is observed that this is a disease that does not only affect underdeveloped countries. Thus, there are cases in America, both in developing countries such as Brazil and in developed countries such as Canada (Martins et al., 2019; Cunha et al., 2022; Hutter et al., 2020; Guy et al., 2021). However, as mentioned before, regardless of the region where the studies were carried out, most of them show that the main transmission routes were anthroponotic and through contaminated water. This proves that no country is immune to contamination by this protozoan, no matter how developed it may be.

According to Yang et al. (2021), the epidemiological characteristics of human cryptosporidiosis in emerging countries differ significantly compared to developed countries, due to higher endemicity, low hygiene levels, greater economic vulnerability, and social fragility. Therefore, the occurrence of infections at an earlier age, presence of more frequent outbreaks, and more common association with HIV/AIDS characterize higher prevalence in emerging countries (Hossain et al., 2019; Mohammad et al., 2021b). The prevalence of cryptosporidiosis in HIV-infected persons ranges from 5.6% to 41.6% in South America, 2.6% to 15.1% in Europe, 5.6 to 25.7% in Africa, 3.7% to 45.0% in Asia. In contrast, there is a high frequency of protozoan infection in people of various ages and immune statuses in developed nations, certainly as a reflection of reduced immunity, an issue noted in several articles. In these countries, improved hygiene and improved potable water treatment have probably led to a reduction in exposure to certain oocytes, corroborating a reduction in immunity.

In general, the most common clinical manifestation of cryptosporidiosis is gastroenteritis, gastrointestinal

Table 2. Data collection of published articles included in this integrative review.

Author/Year	Country	Sample studied	Transmission	Clinical manifestations	Diagnosis and Exams	Treatment and Prognosis
Cunha et al. (2022)	Brazil	11 positive cases with *cryptosporidium* sp./ range 25-75 years old/ male-female.	Not mentioned	Diarrhea.	Stool examination, immunochromatographic test, and real-time polymerase chain reaction (real-time PCR)	Nitazoxanide is the only drug indicated for cases of diarrhea caused by *Cryptosporidium* sp
Sjöström et al. (2022)	Sweden	262 cases positive for *Cryptosporidium* sp./ all ages/male-female.	Transmitted through the public water supply.	Including diarrhea, abdominal pain, nausea, fatigue, joint discomfort and headache.	Study population and data collection, used a written questionnaire which included questions on demographics, onset and symp-toms of cryptosporidiosis, and underlying medical conditions	Five years after the outbreak, 56,5% of the case group and 41,2% of the non-case group reported symptoms during the follow-up period.
Menu et al. (2022)	French Guiana	16 positive cases with Cryptosporidiosis/ 9 children, 6 adults and 1 60 year old man/ male-female.	Contamination of the water network with *Cryptosporidium parvum*.	Fever, diarrhea and vomiting.	Bailanger's concentration method, Kato-Katz technique, modified Ziehl–Neelsen stain, and PCR. and sequencing of the gp60 gene.	Not mentioned.
Urrea-Quezada et al. (2022)	México	39 positive cases with Cryptosporidiosis/ 5 months to 9 years of age/ male-female.	Not mentioned.	Acute gastroenteritis, malnutrition and dehydration.	Microscopic observation of oocysts and PCR sequencing.	Not mentioned.
Wang et al. (2022)	China	8 positive cases with cryptosporidiosis/ 2-6 years old children/ male-female.	Ingestion of oocysts directly from infected human or animals or upon its ingestion with contaminated food/water	Diarrhea-related fatalities.	Stool sample. Nested PCR amplification of an approximately 830 bp partial SSU rDNA gene fragment to screen the samples for the presence of *Cryptosporidium* sp.	Not mentioned
Cossa-Moiane et al. (2021)	Mozambique	*Cryptosporidium* sp. positive in 103 cases/ 0-60 months old/ male-female.	Mainly person to person transmission.	Diarrhea.	PCR method and modified Ziehl-Neelsen. PCR-RFLP targeting SSU rRNA.	Not mentioned
Guy et al. (2021)	Canada	131 positive cases with *Cryptosporidium* sp./ the median age was 23 years/male-female.	Zoonotic transmission and anthroponotic transmission.	Gastroenteritis and/or diarrhea or vomiting.	Microscopic fecal examination, nested PCR followed by Sanger sequencing	Not mentioned

Table 2. Continued...

Author/Year	Country	Sample studied	Transmission	Clinical manifestations	Diagnosis and Exams	Treatment and Prognosis
Hailu et al. (2021)	Ethiopia	86 patients infected by *Cryptosporidium* sp./6–66 years/ male-female.	Zoonotic transmission might be the main route of transmission.	Clinical signs related to the gastrointestinal tract and gastrointestinal symptoms with diarrhea.	Stool samples collected from patients were examined using nested PCR, real time PCR and microscopy.	Not mentioned.
Mohammad et al. (2021a)	Egypt	27 positive cases with cryptosporidiosis/ 1- 15 years/ male-female.	Cryptosporidium infection was more common among children with a history of animal contact.	Diarrhea, abdominal pain, fever, vomiting and flatulence.	Stool culture. The nested PCR was performed targeting *Cryptosporidium* oocyst wall protein (COWP) gene using two consecutive PCR reactions.	Not mentioned
Mohammad et al. (2021b)	Egypt	43 *Cryptosporidium* positive cases/ range 1-12 years old/ male-female.	Not mentioned.	Diarrhea, abdominal colic, systemic fever, vomiting.	Modified Ziehl–Neelsen (MZN) and PCR.	Not mentioned
Messa Junior et al. (2021)	Mozambique	430 patients infected with Cryptosporidiosis/ 0-60 months/ male-female.	Mainly anthroponotic transmission.	Diarrhea.	ELISA; gp60-PCR and/or ssu-PCR..	Not mentioned.
Yang et al. (2021)	Low- and middle-income countries	Total cases not mentioned/Children under 2 years/ Male-female.	Anthroponotic transmission.	Moderate to severe diarrhea and retarded growth.	qPCR and gp60 subtyping.	Comprehensive studies combining genetic, biochemical, and chemical techniques indicated that bicyclic azetidines can kill *C. parvum* in mice by inhibiting the phenylalanyl-tRNA synthetase of parasites.
Yulfi et al. (2021)	Indonesia	13 patients positive for *Cryptosporidium* sp./ Most of them ≥30 years/ male-female.	Fecal-oral route, direct contact from an infected individual or oocyst contaminated-food or water.	Acute and chronic diarrhea for several hours or days.	Microscopic examination and enzyme-linked immunosorbent assay (ELISA) of fecal samples.	Antiretroviral therapy (ART).
Izadi et al. (2020)	Iran	12 positive cases for *Cryptosporidium* sp./ all ages /male-female.	Anthroponotic transmission in the region and zoonotic transmission. But anthroponotic transmission prevails over zoonotic.	Diarrhea.	A two-step semi-nested PCR protocol for the 18S rRNA gene was performed.	Not mentioned

Table 2. Continued...

Author/Year	Country	Sample studied	Transmission	Clinical manifestations	Diagnosis and Exams	Treatment and Prognosis
Hutter et al. (2020)	Canada	201 cases of cryptosporidiosis/ all ages/ male-female.	Anthroponotic transmission and zoonotic transmission.	Diarrhea, abdominal cramps, appetite loss and fatigue.	Nested-PCR amplification and standard questionnaire to carry out an epidemiological investigation.	Not mentioned
Martinot et al. (2020)	Not mentioned	1 case/60 year/male.	Contracted cryptosporidiosis after treatment with fingolimod for multiple sclerosis.	Abdominal pain, diarrhea and fever.	Stool culture, blood examination, modified Ziehl–Neelsen staining method and parasitological examination.	Fingolimod was stopped, and the patient was put on nitazoxanide 500 mg bid for 7 days. A control parasitological examination of the stool performed 2 weeks later was negative.
Mulunda et al. (2020)	Zambia	278 patients were positive for Cryptosporidiosis/ prevalence in 1-4 year children / male and female.	Mainly transmitted through the anthroponotic route.	Diarrhea.	Ziehl-Neelsen and nested PCR	Not mentioned.
Hossain et al. (2019)	Gâmbia	141 positive cases with cryptosporisis/ children below 5 years old/ male-female.	Consumption of stored drinking water and animals (cow, cat, rodents) living in the compound are potential risk factors for *Cryptosporidium* diarrhea. More prevalent in patients with HIV (AIDS).	Severe and prolonged gastrointestinal illness.	Stool sample collection and laboratory testing. TaqMan Array Card (TAC)-based real-time polymerase chain reaction (PCR).	Not mentioned.
Martins et al. (2019)	Brazil	Not mentioned	*Cryptosporidium sp.* are present in raw sewage.	Diarrhea.	PCR-RFLP.	Not mentioned.
Nic Lochlainn et al. (2019)	Netherlands	609 total cases/ range 0-95 years old/ male-female.	Household person-to-person transmission and eating barbequed food were strongly associated with being a case.	Gastrointestinal symptoms (Diarrhea, abdominal pain, vomiting, loss of appetite, weight loss), headache, fatigue, dizziness, eye pain, joint pain	Microscopy or polymerase chain reaction	The median duration of diarrhea was longer for *C. hominis*–infected cases as compared to *C. parvum*–infected cases.

Table 2. Continued...

Author/Year	Country	Sample studied	Transmission	Clinical manifestations	Diagnosis and Exams	Treatment and Prognosis
Pielok et al. (2019)	Poland	3 positive cases with Cryptosporidiosis/ all middle-aged/ 2 male and 1 female.	Not mentioned.	Watery diarrhea, abdominal pains, mild fever, arthropathies, stiffness in the lumbosacral region, eye pain, headache, painful and inflamed joints.	Modified Ziehl–Neelsen staining smears and MAS-PCR.	In two out of three cases, the treatment with trimethoprim/ sulphametoxazole was insufficient. Treatment with nitazoxanide and azithromycin is more effective in the cases described.
Grossman et al. (2019)	Israel	146 confirmed cases with *Cryptosporidium* sp./. majority were young male children under 5 years/ male-female.	Human-to-human transmission.	Diarrhea.	Microscopic examination, antigen detection and qPCR.	Not mentioned.
Sannella et al. (2019)	Thailand	104 positive cases for *Crypstosporidium sp.*/ 20-65 years/ male-female.	Anthroponotic transmission prevails over zoonotic transmission	Diarrhea.	Microscopic examination of fecal samples. PCR amplification of the 18S rDNA gene. Tests with different combinations of primers to amplify fragments of the gp60 gene.	Not mentioned.
Shaposhnik et al. (2019)	Israel	9 positive cases for *Cryptosporidium* sp. /0–14 years/ male-female.	Not mentioned.	Diarrhea, abdominal pain/ contractions, vomiting, and nausea.	Stool culture; PCR test for *Cryptosporidium*; quick antigen test for *Cryptosporidium*; microscopic examination.	Not mentioned.
Zheng et al. (2018)	Singapore	1 case/37 years/ male.	Not mentioned.	Severe acute Bristol 7 diarrhea, up to 10 episodes a day, associated with generalized abdominal discomfort and coryzal symptoms. He was clinically dehydrated.	Stool FilmArray gastrointestinal panel (GIP) nucleic acid-based assay and stool microscopy. Full blood count, liver function test, and C-reactive protein.	Combination oral paromomycin 1 g twice daily and azithromycin 500 mg daily. He remained asymptomatic for 4 weeks following antimicrobial cessation.

Table 2. Continued...

Author/Year	Country	Sample studied	Transmission	Clinical manifestations	Diagnosis and Exams	Treatment and Prognosis
Cheung et al. (2018)	Not mentioned	1 case/6 years/ male	Not mentioned	Vomiting and cramping abdominal pain.	C reactive protein, erythrocyte sedimentation, gram stain. Biopsy and colonoscopy.	He required fluids to maintain his hydration status .3-day course of nitazoxanide 200 mg twice daily and was subsequently discharged on day 17.
Mosnier et al. (2018)	French Guiana	14 cases positive for *Cryptosporidium sp./ 4,5-38 months/male-female*.	Direct/waterborne human contacts.	Diarrhea, vomiting and weight loss.	Fecal samples were screened for intestinal parasites using a centrifuge-sedimentation technique and a modified Ziehl-Neelsen stain was performed on sediments from the Ritchie's concentration.	Oral or intravenous rehydration. All patients recovered after oral or intravenous rehydration
Ng-Hublin et al. (2018)	Australia	404 (2003), 607 (2007) and 355 (2011) patients infected by *Cryptosporidium* sp./ mainly 0-4 years old children/ male-female.	Mainly by contamination with infected water.	Not mentioned.	Molecular typing of human fecal samples and sequencing the gp60 gene.	Not mentioned.
Iglói et al. (2018)	Netherlands	. 308 cases of Cryptosporidiosis/ range 0 to 80 years old/ male-female.	Not mentioned	Dizziness, headache, fatigue, weight loss, diarrhoea, loss of appetite, abdominal pain, joint pain, eye pain, vomiting	A follow-up questionnaire 4 months after diagnosis.	"As there is no treatment for cryptosporidiosis, the focus should be on preventive measures.". Gastrointestinal and non-gastrointestinal symptoms were still occurring as sequelae.
Gilchrist et al. (2018)	Bangladeshi	240 infected patients with cryptosporidiosis/ children below 2 years old/ male-female.	Not mentioned	Diarrhea.	Multiplex quantitative polymerase chain reaction (qPCR) and Sanger sequencing (GENEWIZ).	Not mentioned.
Delahoy et al. (2018)	Kenya	195 *Cryptosporidium sp.* positive cases/ 0-60 months old/ male-female.	Person-to-person transmis- sion is likely the predominant route for *Cryptosporidium*.	Persistent diarrhea and decreases in height-for-age z-scores in children. Some children had fever and other required intravenous rehydration	Stool culture.	Nitazoxanide can treat cryptosporidiosis in immunocompetent children 1–11 years old. Among those with 60-day follow-up information, 9 patients died by the time of follow-up.

Table 2. Continued...

Author/Year	Country	Sample studied	Transmission	Clinical manifestations	Diagnosis and Exams	Treatment and Prognosis
Mamba et al. (2018)	Kenya	39 positive cases with Cryptosporidiosis/ children aged 5 years or below/ male-female.	Not mentioned.	Diarrhea	Stool culture. Genomic DNA was processed from the preserved specimen using the QiAmp® DNA Stool Mini Kit (Qiagen, West Sussex, United Kingdom) as per the manufacturer instructions with slight modifications.	Not mentioned
Franklin et al. (2019)	Not mentioned	One case/ 39 years old/ Woman.	Not mentioned.	Progressively worsening abdominal pain and non-bloody diarrhoea for a week.	Stool PCR testing and abdominal CT.	Patient underwent laparoscopic appendectomy and was discharged the following day. The patient was treated as an outpatient for the *Cryptosporidium* infection with nitazoxanide (Alinia) 500 mg every 12 hours for 10 days. Following the 10-day course of nitazoxanide, the patient reported no further symptoms.
Casmo et al. (2018)	Mozambique	36 confirmed cases by *Cryptospor* sp./ 17-73 years old/ male-female.	The main route of *Cryptosporidium* transmission in the present study population was human to human (direct or via food and water).	Diarrhea.	HIV testing, stool samples with modified Ziehl-Neelsen, PCR targeting of the small subunit rRNA (SSU rRNA).	TMP/SMX prophylaxis of the occurrence of this parasite in HIV-infected individuals.
Steiner et al. (2018)	Bangladesh	275 patients with cryptosporidiosis/ gestational age < 7 months/ male-female.	Not mentioned.	Diarrhea.	Stool samples and qPCR.	Most Cryptosporidium infections occurred in absence of diarrhea, 317 infections were phenotypically subclinical.

Table 2. Continued...

Author/Year	Country	Sample studied	Transmission	Clinical manifestations	Diagnosis and Exams	Treatment and Prognosis
Lilja et al. (2018)	Sweden	215 positive cases of cryptosporidiosis/ 3-79 years old/ male-female.	Waterborne outbreak.	Diarrhea, headache, fatigue, abdominal pain, joint pain and nausea.	Follow-up questionnaire.	The health consequences of *Cryptosporidium* infection persist even longer than indicated in previous reports, outbreaks cases were more likely to have gastrointestinal and joint-related symptoms and had a larger number of symptoms up to 11 months after the initial infection compared to non-cases.
Bednarska et al. (2018)	Poland	4 patients infected with different *Cryptosporidium* sp. / under and above 18 years old/ male-female.	Not mentioned	Diarrhea.	Ziehl-Neelsen; a nested-PCR protocol.	One patient received matched unrelated stem cell transplantation and a liver transplantation.
Stiff et al. (2017)	United Kingdom	54 cases positive for *Cryptosporidium* sp./all ages /male-female.	Not mentioned.	Weight loss, abdominal pain, diarrhea, eye pain, joint pain, fatigue and symptoms consistent with irritable bowel syndrome (IBS).	Rome process, examination or clinical investigations	The study suggests persistence of gastrointestinal sequealeup to a year after acute cryptosporidiosis.
Khalil et al. (2017)	India	43 confirmed cases of Cryptosporidiosis/ 3-35 years/ male-female.	Anthroponotic transmission.	Abdominal pain, fever, general malaise, nausea, vomiting and diarrhea.	Microscopic and Polymerase chain reaction (PCR).	Not mentioned.
Adler et al. (2017)	Sweden	529 patients answered the questionnaire/ Below 15 years old/ Male-female.	Cryptosporidiosis from drinking contaminated water.	Watery diarrhea, headache, abdominal pain, asthenia and fever.	Questionnaire.	The mean duration of diarrhea was 7.5 days and no differences in duration were found between male and female children or between different age groups.

complications, such as abdominal pain, nausea, vomiting, and especially diarrhea. Because it is a protozoa, fevers, muscle aches, fatigue, loss of appetite, and tiredness have also been widely reported (Khalil et al., 2017; Iglói et al., 2018; Lilja et al., 2018). Rare and nonspecific symptoms observed in other studies such as the development of tuberculosis, eye pain, arthropathy: inflamed and painful joints and lumbosacral stiffness, and lymphadenopathy were highlighted. The accumulation of the parasite in the upper respiratory tract can lead to the development of sinusitis, laryngitis, or even rhinitis due to the aggression that occurs in the mucosa of these regions. However, all the symptoms mentioned were observed in immunosuppressed patients; normally, the clinical history is considered self-limited; however, in massive infections, more severe and persistent symptoms are observed (Pielok et al., 2019; Nic Lochlainn et al., 2019).

Notwithstanding, the reported symptoms, an extremely rare case of a secondary appendicitis for cryptosporidiosis was reported in a 39-year-old white woman, after an examination detected a large number of parasites in the cecal appendix causing inflammation. The patient presented to the emergency department with abdominal pain in the right lower quadrant and diarrhea for one week. Her stool tested negative for *Clostridium difficile*, *Giardia lamblia,* and *Cryptosporidium* sp. After an abdominal CT (computed tomography) scan was performed, she was diagnosed with appendicitis, but during histological preparation, clusters of small basophilic spherical bodies were noted, which indicated *Cryptosporidium parvum* (Franklin et al., 2019).

Also addressed in another article were three massive *Cryptosporidium* sp. infections in HIV-negative patients with no history of recent travel. They reported symptoms such as: lymphadenopathy, intense peristaltic movements, arthralgia, watery diarrhea (sometimes with blood), high fever, which lasted for at least 4 weeks. After being negative in bacterial culture tests, these patients underwent colonoscopy, where lesions were observed in the large intestine with changes referring to massive cryptosporidiosis, which, after eradication of the parasite, the symptoms disappeared. Thus, all these statements indicate the need for parasitological examination of feces in cases of chronic diarrhea in which etiologic agents are not detected, but not only in HIV-positive individuals (Menu et al., 2022).

When it comes to the samples obtained, there have been numerous studies addressing this issue, mainly from the analysis of fecal samples from patients using Ziehl-Neelsen staining by microscopy and/or PCR, all with the purpose of determining the prevalence of the most frequent species and genotype infecting the population. What can be observed about the species was that - while in some studies performed, for example: study of fecal samples from 190 children ≲5 years old, a higher infection by *C. hominis* was observed (72.6%, n = 138/190 patients), consequently a lower amount of infected by *C. parvum* (22.6%, n = 43/190 samples) and by another not so common species *C. meleagridis* (4.2%, 8/190 samples), in other studies, the characterization revealed a higher amount of patients infected by *C. parvum*, 35 patients from a total of 47 (74%) and a lower amount by *C. hominis*, 11 patients (23%) (Messa Junior et al., 2021; Hutter et al., 2020). In another article, the population of immunosuppressed patients was approached, in which fecal samples were obtained from patients over 15 years of age, with or without gastrointestinal symptoms, from 346 patients, but only 12 showed the parasite, where 11 were contaminated by *C. hominis* and 1 by *C. parvum* (Izadi et al., 2020).

Still on molecular characterization, the main method used for genome sequencing studies was DNA extraction directly from the fecal sample, followed by nested or semi-nested PCR targeting the small ribosomal RNA subunit (SSU) and glycoprotein 60 (gp60) genes. A study conducted on 129 samples from infected people of all ages, revealed five more species in patients: *Cryptosporidium ubiquitum* (n = 5), *C. felis* (n = 2), C. *meleagridis* (n = 1), *C. cuniculus* (n = 1) and *C. muris* (n = 1). After subtyping the gp60 gene of the samples, 5 allelic families and 17 subtypes of *C. hominis* and 3 allelic families and 17 subtypes of *C. parvum* were revealed, with the most frequent subtype of *C. hominis*: IbA10G2 (n = 5/24 22.3%) and of *C. parvum*: IIaA15G2R1 (n = 57/91 - 62.4%) (Guy et al., 2021). Other studies have reported genetic diversity of the protozoan in human stool samples from Argentina, Brazil, and Peru, identifying mainly *C. hominis* subtype IbA10G2, thus concluding that it is the predominant subtype in South America (Menu et al., 2022); this subtype was also reported to be prevalent during cryptosporidiosis outbreaks in Australia (Ng-Hublin et al., 2018).

Some articles separate the families by an enumeration, being *C. hominis* - "I" and its families: "Ia", "Ib", "Ic", "Id", "Ie"... As for *C. parvum*, because it is another species, its numbering is different - "II" and its families: "IIa", "IIb", "IIc"... After the family, we have the subtype. In another genome sequencing study, performed with 146 samples from Mozambican children under 5 years old, 117 were from *C. hominis*, being the families "Ia" (n = 41) and "Ie" (n = 40) the majority, with the prevalence of subtypes, respectively, IaA23R1 (n = 37) and IeA11G3T3 (n = 39), besides 29 samples from *C. parvum*, with the "IIc" family (n = 25) being the main one found in the samples, with the subtype IIcA5G3 (n = 25) prevalent and unique (Messa Junior et al., 2021). These data prove the wide variety of genotypes capable of infecting humans and causing an infection, and the need to guard against these protozoa.

In view of the forms of pharmacological treatment to combat human cryptosporidiosis, the following pharmacological classes can be seen in the articles analyzed: Antiparasitic (Nitazoxanide) (Martinot et al., 2020; Cheung et al., 2018; Pielok et al., 2019; Delahoy et al., 2018; Franklin et al., 2019; Cunha et al., 2022), macrolide antibiotics (Azithromycin) (Zheng et al., 2018; Pielok et al., 2019), aminoglycoside (Paromomycin) (Zheng et al., 2018), antimicrobials (Trimetropin/ Sulfamethoxazole) (Casmo et al., 2018) and antiretroviral treatment (ART) (Yulfi et al., 2021) in cases of HIV positive or suspected patients, however, it was not possible to identify a therapeutic plan in common with all articles.

Thus, it is possible to verify the different therapeutic approaches evidenced in the articles, such as: the use of Nitazoxanide, the main drug used for the treatment, (500 mg) 1 time a day for 7 days, in which it was observed

that there was remission of the parasite load at the end of treatment1; on the other hand, another article used a combination of Paromomycin (1g) 2 times a day and Azithromycin (500 mg) 1 time a day, with remission of symptoms and parasite load over 4 months of treatment. Thereby, it is worth emphasizing the importance of parasitological examination methods in order to provide an adequate therapeutic approach, as well as to reduce damage complications from the use of inappropriate medications (Zheng et al., 2018).

5. Conclusion

Therefore, it is noticeable that the main complication is gastroenteritis, whose manifestations range from diarrhea to abdominal cramps. Some studies reported that some patients also presented joint and eye pain. This parasite has shown greater virulence by immunodeficient individuals, especially when talking about self infection by its life cycle, being widely distributed throughout the world, especially in developing and underdeveloped countries. The transmissibility happens mainly in the oral-fecal way, through contaminated food and/or water, although zoonotic transmission is also reported in studies. Analysis of patient stool using Ziehl-Neelsen staining by microscopy or PCR were the most commonly used diagnostic criteria in the research. For the articles that mentioned genome sequencing methods, there was a great heterogeneity, in view of the large number of different approaches that were used: qPCR, Sanger Method, ELISA, gp60-PCR, ssu-PCR, PCR-RFLP.

Although many articles did not mention the patient's form of treatment, most of them reported the use of nitazoxanide as the drug of choice, in addition to other therapeutic approaches in order to treat the patient's symptoms, such as hydric replacement. Antiretroviral therapy for HIV patients and antibacterials, such as azithromycin, were also associated.

Accordingly, cryptosporidiosis presents itself as a global disease, which needs extreme attention, mostly in immunocompromised patients; in view of this, it is necessary to have a more thoughtful look at cryptosporidiosis and its effects worldwide.

References

ADLER, S., WIDERSTRÖM, M., LINDH, J. and LILJA, M., 2017. Symptoms and risk factors of *Cryptosporidium hominis* infection in children: data from a large waterborne outbreak in Sweden. *Parasitology Research*, vol. 116, no. 10, pp. 2613-2618. http://doi.org/10.1007/s00436-017-5558-z. PMid:28776228.

BEDNARSKA, M., JANKOWSKA, I., PAWELAS, A., PIWCZYNSKA, K., BAJER, A., WOLSKA-KUSNIERZ, B., WIELOPOLSKA, M. and WELC-FALECIAK, R., 2018. Prevalence of *Cryptosporidium, Blastocystis*, and other opportunistic infections in patients with primary and acquired immunodeficiency. *Parasitology Research*, vol. 117, no. 9, pp. 2869-2879. http://doi.org/10.1007/s00436-018-5976-6. PMid:29946765.

CASMO, V., LEBBAD, M., MAUNGATE, S. and LINDH, J., 2018. Occurrence of *Cryptosporidium* spp. and *Cystoisospora belli* among adult patients with diarrhoea in Maputo, Mozambique. *Heliyon*, vol. 4, no. 9, e00769. http://doi.org/10.1016/j.heliyon.2018.e00769. PMid:30211333.

CHEUNG, D.A., LANGSHAW, A. and RIVERA-RIVERA, E., 2018. *Cryptosporidium* diagnosed on endoscopic biopsy in a paediatric patient with inflammatory bowel disease. *BMJ Case Reports*, vol. 2018, pp. bcr-2017-222015. http://doi.org/10.1136/bcr-2017-222015. PMid:29378737.

COSSA-MOIANE, I., COSSA, H., BAUHOFER, A.F.L., CHILAÚLE, J., GUIMARÃES, E.L., BERO, D.M., CASSOCERA, M., BAMBO, M., ANAPAKALA, E., CHISSAQUE, A., SAMBO, J., LANGA, J.S., MANHIQUE-COUTINHO, L.V., FANTINATTI, M., LOPES-OLIVEIRA, L.A., DA-CRUZ, A.M. and DEUS, N.D., 2021. High frequency of *Cryptosporidium hominis* infecting infants points to a potential anthroponotic transmission in Maputo, Mozambique. *Pathogens*, vol. 10, no. 3, pp. 293. http://doi.org/10.3390/pathogens10030293. PMid:33806380.

CUNHA, F.D.S., JANN, H.W., LUGON, J.R., PERALTA, J.M. and PERALTA, R.H.S., 2022. Molecular characterization of Cryptosporidium spp. obtained from fecal samples of immunosuppressed patients from Brazil. *Revista da Sociedade Brasileira de Medicina Tropical*, vol. 55, pp. e0555-e2021. http://doi.org/10.1590/0037-8682-0555-2021. PMid:35416875.

DELAHOY, M.J., OMORE, R., AYERS, T.L., SCHILLING, K.A., BLACKSTOCK, A.J., OCHIENG, J.B., MOKE, F., JARON, P., AWUOR, A., OKONJI, C., JUMA, J., FARAG, T.H., NASRIN, D., PANCHALINGAM, S., NATARO, J.P., KOTLOFF, K.L., LEVINE, M.M., OUNDO, J., ROELIG, D.M., XIAO, L., PARSONS, M.B., LASERSON, K., MINTZ, E.D., BREIMAN, R.F. and O'REILLY, C.E., 2018. Clinical, environmental, and behavioral characteristics associated with *Cryptosporidium* infection among children with moderate-to-severe diarrhea in rural western Kenya, 2008–2012: The Global Enteric Multicenter Study (GEMS). *PLoS Neglected Tropical Diseases*, vol. 12, no. 7, e0006640. http://doi.org/10.1371/journal.pntd.0006640. PMid:30001340.

FRANKLIN, H., GLOSEMEYER, K. and HASSOUN, A., 2019. *Cryptosporidium* infection in a case of appendicitis. *BMJ Case Reports*, vol. 12, no. 8, e230419. http://doi.org/10.1136/bcr-2019-230419. PMid:31383686.

GILCHRIST, C.A., COTTON, J.A., BURKEY, C., ARJU, T., GILMARTIN, A., LIN, Y., AHMED, E., STEINER, K., ALAM, M., AHMED, S., ROBINSON, G., ZAMAN, S.U., KABIR, M., SANDERS, M., CHALMERS, R.M., AHMED, T., MA, J.Z., HAQUE, R., FARUQUE, A.S.G., BERRIMAN, M. and PETRI, W.A., 2018. Genetic diversity of *Cryptosporidium hominis* in a Bangladeshi community as revealed by whole-genome sequencing. *The Journal of Infectious Diseases*, vol. 218, no. 2, pp. 259-264. http://doi.org/10.1093/infdis/jiy121. PMid:29514308.

GROSSMAN, T., KEN-DROR, S., PAVLOTZKY, E., VAINER, J., GLAZER, Y., SAGI, O., PERETZ, A., AGMON, V., MARVA, E. and VALINSKY, L., 2019. Molecular typing of *Cryptosporidium* in Israel. *PLoS One*, vol. 14, no. 9, e0219977. http://doi.org/10.1371/journal.pone.0219977. PMid:31479457.

GUY, R.A., YANTA, C.A., MUCHAAL, P.K., RANKIN, M.A., THIVIERGE, K., LAU, R. and BOGGILD, A.K., 2021. Molecular characterization of *Cryptosporidium* isolates from humans in Ontario, Canada. *Parasites & Vectors*, vol. 14, no. 1, pp. 69. http://doi.org/10.1186/s13071-020-04546-9. PMid:33482898.

HAILU, A.W., DEGAREGE, A., ADAMU, H., COSTA, D., VILLIER, V., MOUHAJIR, A., FAVENNEC, L., RAZAKANDRAINIBE, R. and PETROS, B., 2021. Molecular characterization of *Cryptosporidium* spp. from humans in Ethiopia. *PLoS One*, vol. 16, no. 6, e0253186. http://doi.org/10.1371/journal.pone.0253186. PMid:34115820.

HEO, I., DUTTA, D., SCHAEFER, D.A., IAKOBACHVILI, N., ARTEGIANI, B., SACHS, N., BOONEKAMP, K.E., BOWDEN, G., HENDRICKX, A.P.A., WILLEMS, R.J.L., PETERS, P.J., RIGGS, M.W., O'CONNOR, R. and CLEVERS, H., 2018. Modelling *Cryptosporidium* infection in human small intestinal and lung organoids. *Nature Microbiology*, vol. 3, no. 7, pp. 814-823. http://doi.org/10.1038/s41564-018-0177-8. PMid:29946163.

HOSSAIN, M.J., SAHA, D., ANTONIO, M., NASRIN, D., BLACKWELDER, W.C., IKUMAPAYI, U.N., MACKENZIE, G.A., ADEYEMI, M., JASSEH, M., ADEGBOLA, R.A., ROOSE, A.W., KOTLOFF, K.L. and LEVINE, M.M., 2019. *Cryptosporidium* infection in rural Gambian children: epidemiology and risk factors. *PLoS Neglected Tropical Diseases*, vol. 13, no. 7, e0007607. http://doi.org/10.1371/journal.pntd.0007607. PMid:31348795.

HUTTER, J.A., DION, R., IRACE-CIMA, A., FISET, M., GUY, R. and DIXON, B., 2020. *Cryptosporidium* spp.: human incidence, molecular characterization and associated exposures in Québec, Canada (2016-2017). *PLoS One*, vol. 15, no. 2, e0228986. http://doi.org/10.1371/journal.pone.0228986. PMid:32053684.

IGLÓI, Z., MUGHINI-GRAS, L., LOCHLAINN, L.N., BARRASA, A., SANE, J., MOOIJ, S., SCHIMMER, B., ROELFSEMA, J., PELT, W.V. and KORTBEEK, T., 2018. Long-term sequelae of sporadic cryptosporidiosis: a follow-up study. *European Journal of Clinical Microbiology & Infectious Diseases*, vol. 37, no. 7, pp. 1377-1384. http://doi.org/10.1007/s10096-018-3268-9. PMid:29730717.

IZADI, S., MOHAGHEGH, M.A., GHAYOUR-NAJAFABADI, Z., AZAMI, M., MIRZAEI, F., NAMDAR, F., MOHEBALI, M., WANNIGAMA, D.L. and HEJAZI, S., 2020. Frequency and molecular identification of *Cryptosporidium* species among immunocompromised patients referred to hospitals, Central Iran, 2015-16. *Iranian Journal of Parasitology*, vol. 15, no. 1, pp. 31-39. http://doi.org/10.18502/ijpa.v15i1.2524. PMid:32489373.

KHALIL, S., MIRDHA, B.R., PANDA, A., SINGH, Y., MARKHARIA, G. and PAUL, J., 2017. *Cryptosporidium* species subtypes and associated clinical manifestations in Indian patients. *Gastroenterology and Hepatology from Bed To Bench*, vol. 10, no. 4, pp. 311-318. http://doi.org/10.22037/ghfbb.v0i0.1086. PMid:29379597.

KORPE, P.S., GILCHRIST, C., BURKEY, C., TANIUCHI, M., AHMED, E., MADAN, V., CASTILLO, R., AHMED, S., ARJU, T., ALAM, M., KABIR, M., AHMED, T., PETRI JUNIOR, W.A., HAQUE, R., FARUQUE, A.S.G. and DUGGAL, P., 2019. Case-control study of *Cryptosporidium* transmission in bangladeshi households. *Clinical Infectious Diseases*, vol. 68, no. 7, pp. 1073-1079. http://doi.org/10.1093/cid/ciy593. PMid:30192924.

LILJA, M., WIDERSTRÖM, M. and LINDH, J., 2018. Persisting post-infection symptoms 2 years after a large waterborne outbreak of Cryptosporidium hominis in northern Sweden. *BMC Research Notes*, vol. 11, no. 1, pp. 1-5. http://doi.org/10.1186/s13104-018-3721-y. PMid:30165888.

MAMBA, T.S., MBAE, C.K., KINYUA, J., MULINGE, E., MBURUGU, G.N. and NJIRU, Z.K., 2018. Lateral flow loop-mediated isothermal amplification test with stem primers: detection of *Cryptosporidium* species in kenyan children presenting with diarrhea. *Journal of Tropical Medicine*, vol. 2018, pp. 7659730. http://doi.org/10.1155/2018/7659730. PMid:29681951.

MARTINOT, M., ABOU-BACAR, A., LAMOTHE, M., TEBACHER, M.A., ZADEH, M.M., DALLE, F., FAVENNEC, L., COSTA, D., BRUNET, J. and SELLAL, F., 2020. Cryptosporidiosis after treatment with fingolimod: a case report and pharmacovigilance review. *BMC Infectious Diseases*, vol. 20, no. 1, pp. 257. http://doi.org/10.1186/s12879-020-04988-7. PMid:32228484.

MARTINS, F.D.C., LADEIA, W.A., TOLEDO, R.D.S., GARCIA, J.L., NAVARRO, I.T. and FREIRE, R.L., 2019. Surveillance of *Giardia* and *Cryptosporidium* in sewage from an urban area in Brazil. *Revista Brasileira de Parasitologia Veterinária*, vol. 28, no. 2, pp. 291-297. http://doi.org/10.1590/s1984-29612019037. PMid:31188950.

MENU, E., MOSNIER, E., COTREL, A., FAVENNEC, L., RAZAKANDRAINIBE, R., BLANCHET, D., DALLE, F., COSTA, D., GAILLET, M., DEMAR, M. and LAVAL, F.D., 2022. Cryptosporidiosis outbreak in Amazonia, French Guiana, 2018. *PLoS Neglected Tropical Diseases*, vol. 16, no. 1, e0010068. http://doi.org/10.1371/journal.pntd.0010068. PMid:35100286.

MESSA JUNIOR, A., KÖSTER, P.C., GARRINE, M., NHAMPOSSA, T., MASSORA, S., COSSA, A., BASSAT, Q., KOTLOFF, K., LEVINE, M.M., ALONSO, P.L., CARMENA, D. and MANDOMANDO, I., 2021. Molecular characterisation of *Cryptosporidium* spp. in Mozambican children younger than 5 years enrolled in a matched case-control study on the aetiology of diarrhoeal disease. *Pathogens*, vol. 10, no. 4, pp. 452. http://doi.org/10.3390/pathogens10040452. PMid:33918893.

MOHAMMAD, S.M., ALI, M.S., ABDEL-RAHMAN, S.A., MOUSTAFA, R.A. and SARHAN, M.H., 2021a. Genotyping of *Cryptosporidium* species in children suffering from diarrhea in Sharkyia Governorate, Egypt. *Journal of Infection in Developing Countries*, vol. 15, no. 10, pp. 1539-1546. http://doi.org/10.3855/jidc.14367. PMid:34780378.

MOHAMMAD, S.M., ALI, M., ABDEL-RAHMAN, S.A., MOUSTAFA, R.A. and SALAMA, M.A., 2021b. Molecular prevalence of *Cryptosporidium* isolates among Egyptian children with cancer. *Journal of Parasitic Diseases: Official Organ of the Indian Society for Parasitology*, vol. 45, no. 3, pp. 746-753. http://doi.org/10.1007/s12639-020-01345-y. PMid:34475656.

MOSNIER, E., MARTIN, N., RAZAKANDRAINIBE, R., DALLE, F., ROUX, G., BUTEUX, A., FAVENNEC, L., BROUSSE, P., GUARMIT, B., BLANCHET, D., EPELBOIN, L., GIROUIN, C., MARTIN, E., DJOSSOU, F., NACHER, M. and DEMAR, M., 2018. Cryptosporidiosis Outbreak in Immunocompetent Children from a Remote Area of French Guiana. *The American Journal of Tropical Medicine and Hygiene*, vol. 98, no. 6, pp. 1727-1732. http://doi.org/10.4269/ajtmh.17-0609. PMid:29692312.

MULUNDA, N.R., HAYASHIDA, K., YAMAGISHI, J., SIANONGO, S., MUNSAKA, G., SUGIMOTO, C. and MUTENGO, M.M., 2020. Molecular characterization of *Cryptosporidium* spp. from patients with diarrhoea in Lusaka, Zambia. *Parasite*, vol. 27, no. 53, pp. 53. http://doi.org/10.1051/parasite/2020050. PMid:33048665.

NG-HUBLIN, J.S.Y., COMBS, B., REID, S. and RYAN, U., 2018. Comparison of three cryptosporidiosis outbreaks in Western Australia: 2003, 2007 and 2011. *Epidemiology and Infection*, vol. 146, no. 11, pp. 1413-1424. http://doi.org/10.1017/S0950268818001607. PMid:29974834.

NIC LOCHLAINN, L.M., SANE, J., SCHIMMER, B., MOOIJ, S., ROELFSEMA, J., PELT, W.V. and KORTBEEK, T., 2019. Risk factors for sporadic cryptosporidiosis in the Netherlands: analysis of a 3-year population based case-control study coupled with genotyping, 2013–2016. *The Journal of Infectious Diseases*, vol. 219, no. 7, pp. 1121-1129. http://doi.org/10.1093/infdis/jiy634. PMid:30395258.

PIELOK, Ł., NOWAK, S., KLUDKOWSKA, M., FRACKOWIAK, K., KUSZEL, L., ZMORA, P. and STEFANIAK, J., 2019. Massive *Cryptosporidium* infections and chronic diarrhea in HIV-negative patients. *Parasitology Research*, vol. 118, no. 6, pp. 1937-1942. http://doi.org/10.1007/s00436-019-06302-0. PMid:30976968.

SANNELLA, A.R., SUPUTTAMONGKOL, Y., WONGSAWAT, E. and CACCIÒ, S.M., 2019. A retrospective molecular study of Cryptosporidium species and genotypes in HIV-infected patients from Thailand. *Parasites & Vectors*, vol. 12, no. 1, pp. 1-6. http://doi.org/10.1186/s13071-019-3348-4. PMid:30867022.

SHAPOSHNIK, E.G., ABOZAID, S., GROSSMAN, T., MARVA, E., ON, A., AZRAD, M. and PERETZ, A., 2019. The prevalence of *Cryptosporidium* among children hospitalized because of gastrointestinal symptoms and the efficiency of diagnostic methods for *Cryptosporidium*. *The American Journal of Tropical Medicine and Hygiene*, vol. 101, no. 1, pp. 160-163. http://doi.org/10.4269/ajtmh.19-0057. PMid:31115293.

SJÖSTRÖM, M., ARVIDSSON, M., SÖDERSTRÖM, L., LILJA, M., LINDH, J. and WIDERSTRÖM, M., 2022. Outbreak of *Cryptosporidium hominis* in northern Sweden: persisting symptoms in a 5-year follow-up. *Parasitology Research*, vol. 121, no. 7, pp. 2043-2049. http://doi.org/10.1007/s00436-022-07524-5. PMid:35451705.

STEINER, K.L., AHMED, S., GILCHRIST, C.A., BURKEY, C., COOK, H., MA, J.Z., KORPE, P.S., AHMED, E., ALAM, M., KABIR, M., TOFAIL, F., AHMED, T., HAQUE, R., PETRI JUNIOR, W.A. and FARUQUE, A.S.G., 2018. Species of cryptosporidia causing subclinical infection associated with growth faltering in rural and urban Bangladesh: a birth cohort study. *Clinical Infectious Diseases*, vol. 67, no. 9, pp. 1347-1355. http://doi.org/10.1093/cid/ciy310. PMid:29897482.

STIFF, R.E., DAVIES, A.P., MASON, B.W., HUTCHINGS, H.A. and CHALMERS, R.M., 2017. Long-term health effects after resolution of acute *Cryptosporidium parvum* infection: a 1-year follow-up of outbreak-associated cases. *Journal of Medical Microbiology*, vol. 66, no. 11, pp. 1607-1611. http://doi.org/10.1099/jmm.0.000609. PMid:28984243.

TANDEL, J., ENGLISH, E.D., SATERIALE, A., GULLICKSRUD, J.A., BEITING, D.P., SULLIVAN, M.C., PINKSTON, B. and STRIEPEN, B., 2019. Life cycle progression and sexual development of the apicomplexan parasite *Cryptosporidium parvum*. *Nature Microbiology*, vol. 4, no. 12, pp. 2226-2236. http://doi.org/10.1038/s41564-019-0539-x. PMid:31477896.

URREA-QUEZADA, A., BALMACEDA-BACA, R., GARIBAY, A., HERNÁNDEZ, J. and VALENZUELA, O., 2022. Serum IgG responses to gp15 and gp40 protein-derived synthetic peptides from *Cryptosporidium* parvum. *Frontiers in Cellular and Infection Microbiology*, vol. 11, pp. 810887. http://doi.org/10.3389/fcimb.2021.810887. PMid:35127561.

WANG, T., WEI, Z., ZHANG, Y., ZHANG, Q., ZHANG, L., QI, F.Y.M. and ZHAO, W., 2022. Molecular detection and genetic characterization of *Cryptosporidium* in kindergarten children in Southern Xinjiang, China. *Infection, Genetics and Evolution*, vol. 103, pp. 105339. http://doi.org/10.1016/j.meegid.2022.105339. PMid:35840104.

WHITTEMORE, R., KNAFL, K. and MULARSKI, C.R., 2023. The theoretical integrative review: a researcher's guide. *Nursing Inquiry*, vol. 30, no. 4, e12517. http://doi.org/10.1111/nin.12517. PMid:37637334.

YANG, X., GUO, Y., XIAO, L. and FENG, Y., 2021. Molecular epidemiology of human cryptosporidiosis in low- and middle-income countries. *Clinical Microbiology Reviews*, vol. 34, no. 2, e00087-19. http://doi.org/10.1128/CMR.00087-19. PMid:33627442.

YULFI, H., ROZI, M.F., ANDRIYANI, Y. and DARLAN, D.M., 2021. Prevalence of Cryptosporidium spp. and Blastocystis hominis in faecal samples among diarrheic HIV patients in Medan, Indonesia. *Medicinski Glasnik*, vol. 18, no. 1, pp. 55-61. http://doi.org/10.17392/1271-21. PMid:33307637.

ZHENG, S., KO, K.K.K., CHAN, K.S. and VENKATACHALAM, I., 2018. Case report: diagnosis of cryptosporidiosis in renal transplantation in a low-prevalence setting. *The American Journal of Tropical Medicine and Hygiene*, vol. 100, no. 1, pp. 78-80. http://doi.org/10.4269/ajtmh.18-0651. PMid:30457100.