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Review of *Cryptosporidiosis* in Calves, Children and HIV/Aids Patients

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Research Article

Abstract

Cryptosporidiosis is among the most important protozoan parasitic diseases of animals and humans importance that commonly causes diarrheal disease in a wide range of vertebrate hosts, particularly, neonatal calves, Children, and HIV/Aids Patients. The host immune capacity is the most important factor affecting both the probability of infection and the severity of the subsequent disease. Commonly, humans and animals get an infection when they contact animal manure and consume food and drink containing Oocysts that contain four Sporozoites within this protozoan. Although the disease has occasionally been reported in adult animals and humans, the severity of the disease is common in neonatal calves, young children particularly in those < 5 years and HIV/AIDS patients. The prevalence of bovine Cryptosporidiosis ranges from 6.25 to 39.65% in different parts of the world and 2.3 to 27.8% in Ethiopia as well. Diagnosis of Cryptosporidiosis is mostly based on the detection of Oocysts from fecal samples. Animals and human sewage discharges are generally considered as the major sources of contamination. At present, there is no effective treatment and vaccines to prevent Cryptosporidiosis in either livestock farms or humans. Thus, the practice of good personal and dairy farm hygiene, prevention of environmental contamination of Oocystsare the best prevention methods in humans and animals. The objective of this paper is to review the current status of Cryptosporidiosis, the zoonotic implication of Cryptosporidiosis in both humans and animals.

Keywords: Calves, Children, Cryptosporidiosis, Hiv/Aids, zoonotic

1. Introduction

Cryptosporidium is a microscopic protozoan parasite of medical and veterinary importance that commonly causes diarrheal disease and inhabits the small intestine of wide range of vertebrate hosts, including humans (Chalmers and Katzer, 2013; Gharpure*et al*., 2019). *Cryptosporidium* was first named and reported by Ernest Edward Tyzzer who observed in the stomachs of mice (peptic glands of laboratory mouse) (Tyzzer, 1907, 1910). Cryptosporidiosis is progressively inviting attention as an emerging zoonotic disease of great public health importance due to its dominant involvement worldwide (Shirley *et al*., 2012). At present

Cryptosporidiosis is estimated and accounted for about 30-50% of deaths in young individuals worldwide and found to be the second - highest reason for diarrhea and deaths in children after rotavirus (Gharpure*et al*., 2019).
Cryptosporidiosis is usually self-limiting and resolves within 2–3 weeks with profuse watery non-bloody diarrhea, weight loss, abdominal pain, anorexia, fatigue, and cramps in immune-competent individuals (Warren and Guerrant, 2008). But, in immune-compromised persons such as HIV and cancer patients, the infection is more serious and can cause prolonged, life-threatening illness (Gharpure*et al*., 2019). Due to the lack of prophylactic and therapeutic measures against the disease, the mortality rate in humans is an emerging public health issue worldwide (Liu *et al*., 2012). The prevalence of Cryptosporidiosisishigher in developing countries 5.9-17%, than in developed countries 0.1–2% (Mumtaz*et al*., 2010).
The infection rate is higher in newborns and children **<**5 years of age owing to limited infrastructure and poor sanitary conditions in developing countries (Chalmers and Davies, 2010). The main reason for Cryptosporidiosis to increase importance was due to the epidemic of HIV/AIDS that created a pool of susceptible people during the 1980s. In calves, the economic importance of Cryptosporidiosis and its role as a major cause of diarrhea and gastrointestinal illness had been reported (Szonyi*et al*., 2010). Commonly, animals and humans acquire the infection when they consume food and drinking containing *Oocysts* of these protozoa which are tolerant to several chemicals and disinfectants as well as chlorine which is frequently used to treat in drinking water, water parks, and swimming pools (Pumipuntu and Piratae, 2018). Commonly in calves and humans, the zoonotic important spp. of *Cryptosporidium* includes *C. parvum, C. andersoni,* and *C.bovis* (Thomson *et al*., 2017). The disease is known to occur widely in the source of drinking water and caused waterborne outbreaks of GIT. Farm animals and human sewage discharges are generally considered as the major sources of surface water contamination with *Cryptosporidium Oocysts*(Painter *et al*., 2015).
Several studies reported that the degree of pathogenicity and virulence is based on host susceptibility to infection (immune status), *Cryptosporidium* species, and ingested *Oocyst* dose. According to Bouzid*et al*. (2013) stated, the infection begins when the ingested *Oocysts* release *sporozoites*, which subsequently attach to and invade the intestinal epithelial cells and promoting its reproduction, besides causing direct injury to epithelial cells and leading to impairment in the absorptive and secretory functions of the gut. As the infection has no pathognomonic symptoms, diagnosis is made conventionally by microscopy after staining fecal smears with the gold standard acid - fast stain (Modified Ziehl-Nelson) for the detection of round *Cryptosporidium Oocysts*(khan *et al*., 2019).
The preventive measures such as regular sanitation of dairy farm, limiting the amount of animal's density in the farms, minimizing contact between calves and other herds by the construction of separate pen, and keeping a short calving period of animals can reduce transmission of Cryptosporidiosis (Thomson *et al*., 2017). The best applicable strategy to prevent transmission of Cryptosporidiosis between humans is a practice of good personal hygiene, including handwashing before preparing and consuming food, after using a toilet and contacting diarrhea patients (children), and some animals or livestock's, raw food, and water must be appropriately cleaned, washing, heated, cooked, or boiled before consumption and drinking, respectively (Pumipuntu and Piratae, 2018).

2. Literature Review

2.1. Etiology and Taxonomy

Cryptosporidium spp. are classified under the family *Cryptosporidiidae*, sub-order *eimeriorina*, order *eucoccidiorida*, sub-class *coccidiasina*, class *sporozoasida*, phylum *apicomplexa* (Bhat *et al.*, 2013). Currently, 18 names are allied with individual spp. and 26 are considered valid based

on different *Oocysts*site of invasion, morphology, genetic variation, and vertebrate class specificity (Bamaiyi and Redhuan 2017). Among described species of *Cryptosporidium* the most spp. infecting animals and man includes *C. andersoni*, *C. bovis*, *C. canis*,*C. felis*, *C. hominis*, *C. meleagridis*, *C. molnari*, *C. parvum*, *C. scophthalmi*, *C. scrofarum*, *C. suis*,and*C. xiaoi*. Also, four spp. of *Cryptosporidium* are commonly found in calves; *C. parvum*, *C. bovis*, *C. andersoni*and*C. ryanae* but only *C. parvum* is associated with clinical disease in neonatal calves, with older animals showing asymptomatic shedding of *Oocysts*(Thomson *et al*., 2017).

2.2. Life Cycle and Morphology

Members of the genus *Cryptosporidium* complete all developmental stages in a single host which can be divided into an asexual and sexual (Bouzid *et al*., 2013). After ingested, *Oocystsexcysts* in the GIT, release four motile and infective *sporozoites* through a suture in the *Oocysts* wall. The incident of *excystation* can be provoked by low PH in the GIT and body temperature, but other environmental causes may include bile salts, CO_2, and pancreatic enzymes (O'Hara and Chen, 2011).

The *merozoites* derived from type II *meronts* re-infect the epithelium and differentiate into either *macrogamonts* or *microgamonts*. The *microgametes* are released and fertilize a *marogamont* resulting in the only diploid stage of development, producing a *zygote*. The diploid *zygote* undergoes a process similar to *meiosis* and forms either thin or thick-walled *Oocysts*. The previous (thin wall) *sporozoites excysts* in the gut lumen and re-infects the host, while the thick wall excretes in the environment through feces Caccio and Widme, (2014) The auto-infection capacity of the parasite obtained from thin-walled *Oocyst,* which is one of the reasons why the *Cryptosporidium* parasite is so conquering. While the parasite produces many new *Oocysts* in a moderately short time we can explain it as auto-infection (Thomson *et al*., 2017).

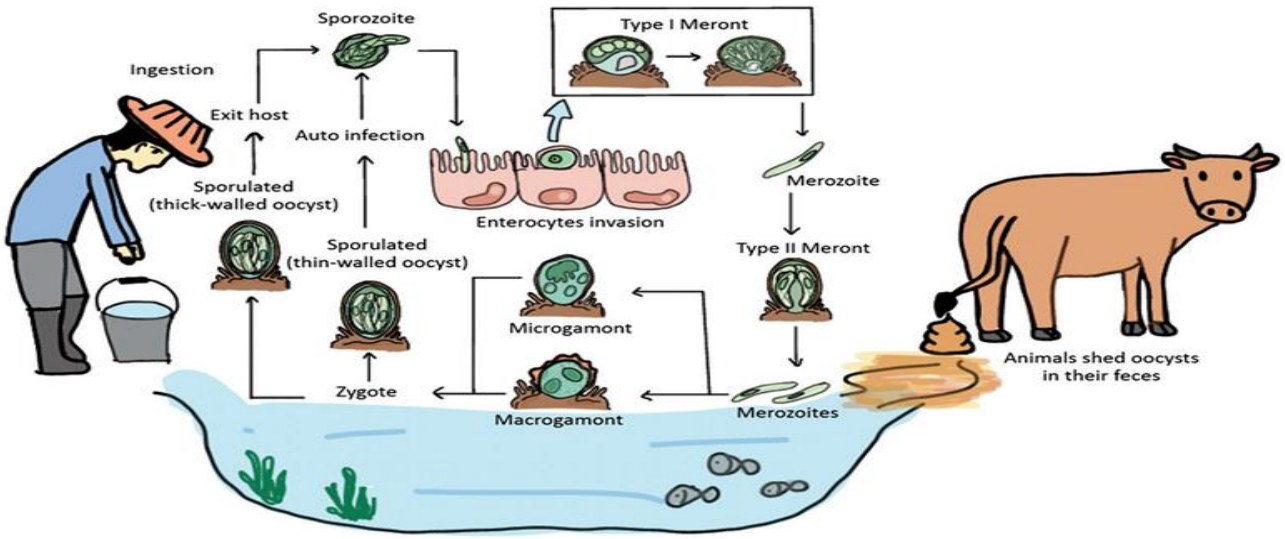

Figure 1: The Life cycle of *Cryptosporidium*
Source: (CDC, 2015)

2.3. Epidemiology

2.3.1. Geographic distribution

Cryptosporidiosis has been recognized as an emerging zoonotic threat worldwide (Brook *et al*., 2008). Various reports indicated that the prevalence of Cryptosporidiosis ranges from 6.25 to 39.65% in calves in different parts of the world (Ayele *et al.,* 2018). However, the prevalence of

Cryptosporidiosisvaries between countries, design of the studies and detection methods used. For instance, according to Wells (2015) stated the prevalence in pre-weaned calves in the UK ranges from 28.0 to 80.0%. Studies from other parts of the world reported prevalence of *Cryptosporidium* infection in pre-weaned calves ranges from 3.4 to 96.6% (Peng *et al*., 2003).

2.3.2. Risk factors

The host immune capacity is the most important factor affecting both the probability of infection and the severity of the subsequent disease. However, the occurrence of Cryptosporidiosis in the calves and humans can be determined by several factors such as age, colostrum feeding, diarrheic and non-diarrheic, hygiene conditions, management practices, feed and water sources, sewage water management, drinking or using untreated water, climate conditions, contact with a suspected animal or human and poor economic status of the families may play a key role in the current prevalence of bovine Cryptosporidiosis (Ayele*et al*., 2018; Khan *et al*., 2019).

According Kvac*et al*. (2014) stated the age-related distribution of *Cryptosporidium* species seen in several host species is due to changes in the gut micro-flora as the animal matures or due to dietary changes that may affect the ability of the parasite to infect the gut. In addition, a seasonal occurrence of infection is occasionally visible, probably in proportion to rainfall peaks, pollution increased from farm or calving and lambing activities. The prevalence of *Cryptosporidium* infection is common in spring relatively with average monthly, in addition to bathing or drinking in surface water possibly a significant risk factor for the disease (Khan *et al*., 2019).

2.3.3. Modes of transmission and sources of infection

Commonly, humans and animals usually get an infection when they contact animal manure and consume food and drink containing *Oocysts* that contain four *Sporozoites* within this protozoan. As a result transmission of the disease can be from animal to human (zoonotic) and human to human or animal to animal (*anthroponotic*) (Abu-Madi *et al*., 2011). In some reports, person-to-person spread is well described, especially in families and in outbreak settings, including institutions such as daycare centers and hospitals (Yoder *et al*., 2010). Commonly direct and indirect routes of transmission of *Cryptosporidium* have been recognized.

The direct transmission is associated with a fecal-oral route by accidental ingestion of the *Cryptosporidium Oocysts* excreted from the feces of the infected host (Gharpure *et al*., 2019). This type of transmission usually emerges in swimming pools, water parks, daycare centers, hospitals, and during anal sexual contact with human feces and this process is frequently raised by sexual intercourse behavior of men who have sex with men through the fecal-oral route (Hellard *et al*., 2003). Moreover, the direct transmission can occur through direct exposure to infected animals, for example, animal health students or animal researchers are infected by direct contact with infected calves (Gharpure *et al*., 2019).

However, the occurrence of indirect transmission can be through of cross-contamination of food-stuff, food materials, drinking water, and many fomites such as clothes and footwear used in livestock farm or wildlife park which have been exposed to the feces of an infected human or animal (Baldursson and Karanis, 2011). The *Cryptosporidium* spp. can infect and live in epithelial surfaces of the intestine in a wide range of vertebrate animals including humans and passed from feces or stool and subsequently contaminate the soil and water sources; pond, river, water, sewage or slurry, even many water containers especially insufficiently treated public water supplies.

An additional mode of transmission is via the inhalation of *Oocysts* which were reported in immune-compromised patients and children (Sponseller *et al*., 2014). Seasonal variation particularly, the high rate of rainfall and flooding events can extremely influence the

transmission and distribution of the disease (Jiang *et al*., 2005). About 60% of deaths were reported as food and a waterborne outbreak of the infection worldwide from 2004 to 2010 years (Baldursson and Karanis, 2011). For instance, from 2009 to 2017, public health officials from many countries voluntarily reported to CDC 444 the infection outbreaks (14.6%) were associated with contact with calves, (12.8%) were associated with contact with infected persons in child care settings. with the 22 food-borne outbreaks, (40.9%) were associated with unpasteurized milk and four, (18.2%) with unpasteurized apple cider. The source of infection and mode of transmission was unknown for (14.2%) outbreaks; the main sites included private homes (28.6%) and (19.0%) in child care (Gharpure *et al*., 2019; Khan *et al*., 2019).

2.4. Clinical Signs

2.4.1. Clinical signs in calves

Although the disease has occasionally been reported in adult animals, the severity of the disease is common in neonatal calves young children, particularly in those < 5 years,, enteritis is usually seen in 1-3 week old calves, in general, infected animals with the infection cryptosporidiosis may suffer from profuse watery diarrhea, lethargy, dullness, and dehydration as well in some cases death can occur (Thomson *et al*., 2017). The incubation period usually 5-8 days, range 2-12 days after ingestion of infective *Oocysts* frequently, diarrhea starts approximately 3-4 days and lasts for about 1-2 weeks or most clinical cases are self-limiting within 1-2 weeks and *Oocysts* shedding not constantly related with diarrhea but depends on initial face dose and occurs between 4-12 days post-infection (Zambriski *et al*., 2013). Observational studies found that calves infected with *C. andersoni* show reduced body weight and milk yield in adult cows (Ralston *et al*., 2010).

2.4.2. Clinical signs in human

The disease is common in young children, particularly in those < 5 years, but the disease can also affect healthy people of any age. In different regions; most clinical problems are recognized as a major concern as a result of the transmission of the infection through inhalation and increasing cases of immune-compromised individuals and children. In recent years the infection has been found to not only affect the GIT tract but also cause respiratory symptoms in man (Sponseller *et al*., 2014). The infection causes severe profuse watery diarrhea, dehydration which may result in poor growth rate and high mortality in children (Gharpure*et al*., 2019). According Pumipuntu and Piratae (2018) stated the infection is a long-lasting debilitating diarrheal infection that is usually acute and self-limiting in immune-competent individuals at the same time can be life-threatening to the immune-compromised person, especially in HIV/AIDS and patients who received immune-suppressive drugs. Also, *Cryptosporidium* spp. has been isolated from HIV/AIDS cases with the prevalence of 19-34% from 1996 to 2009 in Thailand (Berger, 2017).

2.5. Pathogenesis

Several studies reported different degrees of pathogenicity and virulence among *Cryptosporidium* species and isolates of the same species as well as evidence of variation in host susceptibility to infection. The *Oocysts* contain up to 4 sporozoites that are bow-shaped attaches (Ryan *et al*., 2004). As few as 2 to 10 *Oocysts* can initiate an infection (Chen *et al*., 2003). The parasite is located in the brush border of the epithelial cells of the small intestine. Okhuysen and Chappell, (2002); Bouzid*et al*. (2013) stated that the infection begins when the ingested *Oocysts* release *sporozoites*, which subsequently attach to and invade the intestinal epithelial cells in a membrane-bound compartment promoting its reproduction causing direct injury to epithelial cells or indirect damage through the effect of inflammatory cells and

cytokines recruited to the site of infection, leading to impairment in the absorptive and secretory functions of the gut. *Oocysts* are mainly located in the jejunum and terminal ileum and bind on the apical surface of the intestinal epithelium hence; the parasite can cause damage to the microvilli where it attaches (Bouzid *et al.,* 2013). As a consequence, they are "intracellular but extracytoplasmic" (Ryan *et al*., 2004). According to FDA, (2009) there is the difference in infectivity based on *Cryptosporidium* species ingested and *Oocyst* dose, for the species that commonly infect humans, *C. hominis* and *C. parvum* the lowest infectious dose has been calculated to be 10 *Oocysts*, although, in reality, one *Oocysts* could be sufficient to cause infection in humans through direct or indirect routes of transmission.
Among *Cryptosporidium* spp. which infects bovine *C. andersoni* inhabits the digestive glands of the abomasum and infects the microvillus border of the gastrointestinal epithelium in adult calves and post weaned calves. The infected host excretes most *Oocysts* during the first week (Ryan *et al*., 2004). *Oocysts* can be excreted for weeks after diarrhea subsides from infections by *C. parvum* (Sponseller *et al*., 2014). The immune system reduces the formation of Type 1 *merozoites* as well as the number of thin-walled *Oocysts* (Ryan *et al*., 2004). This helps prevent autoinfection. B cells do not help with the initial response or the fight to eliminate the parasite (Chen *et al*., 2003). Several studies have been tried to determine the factors responsible for the initiation, establishment, and perpetuation of *Cryptosporidium* infection. Thus far specific virulence factors for *Cryptosporidium* have not been characterized however, putative virulence factors for the infection have been identified as genes involved in the initial interaction processes of *Cryptosporidium Oocysts* and *sporozoites* with host epithelial cells, including excystation, gliding motility, attachment, invasion, *parasitophorous* vacuole formation, intracellular maintenance, and host cell damage (Fayer *et al.* 2009; Wanyiri and Ward, 2006).

2.6. Diagnosis

2.6.1. Microscopic method of examination

The symptoms of Cryptosporidiosisare not pathognomonic, therefore; laboratory verification is required to confirm the diagnosis. Since the most common symptom of cryptosporidiosis is watery diarrhea, the differential diagnosis for Cryptosporidium includes viral, bacterial, and parasitic enteric pathogens associated with acute diarrhea such as rotaviruses, coronaviruses, Escherichia coli, and Salmonella spp Giardiasis, amebiasis, Crohn disease, inflammatory bowel disease, irritable bowel syndrome. Detection is made conventionally by microscopy after staining fecal smears with Modified Ziehl-Nelson with the sensitivity of about 75% for detection of the round, sporulated *Oocysts*of 4 to 5 µm in size (khan *et al*., 2019).
The Modified acid-fast*Ziehl-Nelson* stains is the gold standard stain for the detection of *Cryptosporidium* species is classically performed by staining a methanol fixed thin smear of fecal material with undiluted Carbol-fuchsine solution for at least 15 minutes. Subsequently, the slide is rinsed in tap water and placed in an acid-alcohol solution to remove the stain, while acid-fast structures will resist the acid-alcohols destaining action. After rinsing again, the slide is placed for a short period in a counter-staining product, such as methylene blue, providing contrast between background material and acid-fast structures. The slide is rinsed once more and after the slide has been air-dried, it can be examined using x40 eyepieces and an oil-immersion objective of x100 magnification (Wanyiri and Ward, 2006) Cryptosporidium *Oocysts* will appear as pink stained, round to oval structures of about 4 to 6 µm in diameter, containing distinct internal structures (Figure2).

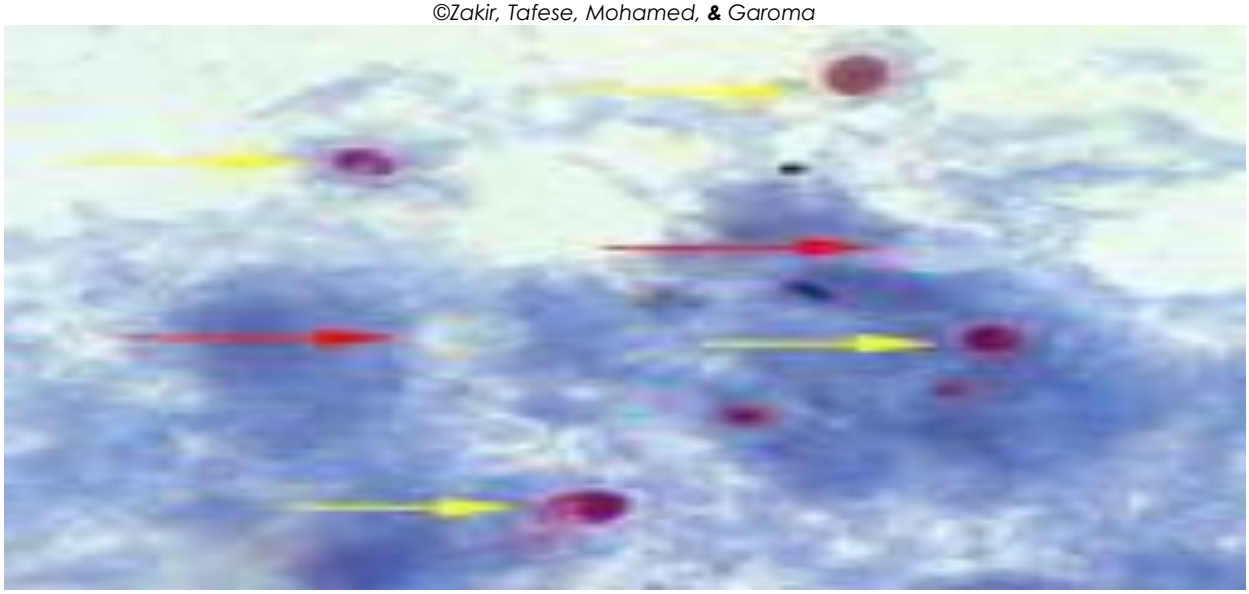

Figure 2: Oocystsof Cryptosporidium spp. stained by: the modified Ziehl-Neelsenstain.
Source: (Chalmers and Davies 2010)

2.6.2. Antigen detection method

Antigenic-based simple and rapid chromatographic lateral flow immunoassay has got more efficiency for detection of *C. parvum*from buffalo and crossbred calves as compared to modified Ziehl-Neelsen staining (Singla *et al*., 2012).

2.6.3. Immunological and molecular method of examination

The immunological approaches like direct immunofluorescence, enzyme-linked immune-sorbent assay, and immune-chromatography for the detection of *Cryptosporidium Oocysts*are useful but inherit the limitation of species identification (OIE, 2008). So those molecular methods are used to identify *Cryptosporidium* species/genotypes in human and non-human hosts (Rieux*et al*., 2014). Molecular methods for detecting *Cryptosporidium* in clinical specimens are more sensitive than conventional microscopy (Chalmers and Katzer 2013). Currently, polymerase chain reaction has transformed the field of diagnosis in the parasitological study of *Cryptosporidium* ssp. Different workers from different parts of the world reported the advantages of PCR for the detection of *Cryptosporidium* in clinical and environmental samples. The most well-described advantages of PCR includes sensitivity, ease of use, ability to analyze large numbers of samples at one time, relatively low cost, ability to differentiate species and strain types (Bhat*et al*., 2014; Pumipuntu and Piratae, 2018).

2.7. Treatment

Although several drug and drug combinations such as rifaximin, azithromycin, and paromomycin have been tried against Cryptosporidiosis, unsatisfactory and the same results were observed (Bamaiyi and Redhuan,2017). However currently, few products are approved in the UK for the treatment or prevention of Cryptosporidiosis in livestock or humans nevertheless, they are not very effective, and in most cases will only reduce the duration of shedding and have little or no effect in immune-compromised patients (Thomson *et al*., 2017).

2.7.1. Treatment in calves

In calves, prevention and treatment of Cryptosporidiosis can be made by Halofuginone lactate drug but cannot be used in animals have shown signs of diarrhea for > 24 hours (does not completely prevent or cure disease) but can reduce *Oocysts* shedding and the duration of

diarrhea, as a prophylactic measure the drug should be given within 48 hours of birth and as a therapeutic agent, within 24 hrs of the onset of symptoms (Thomson *et al*., 2017). Additionally, according to Viu *et al.* (2000) stated, several infected calves treated with 100 mg/kg paromomycin twice daily for 11 days significant reductions in the severity of diarrhea *Oocysts*shed less than untreated calves were observed. Furthermore, a few *coccidiostats*, such as decoquinate have been tested against *Cryptosporidium* in neonatal calves with limited or no reduction in *Oocysts*(Moore *et al*., 2003). However, more recent studies that have evaluated novel BKIs as a potential treatment for bovine Cryptosporidiosisshowed that experimentally infected calves treated with BKIs had a reduction in *Oocysts* shedding when compared with untreated controls (Lendner *et al*., 2015).

2.7.2. Treatment in human

The only anti *Cryptosporidial* agent which has been approved for the treatment of Cryptosporidiosis in humans by the US FDA is Nitazoxanide. This is the most effective drug for treating patients who are infected with *Cryptosporidium species* but it is not commercially available, the drug is not effective with the less immune response of the host so that it cannot be used effectively in immune-compromised patients or animals (Bamaiyi and Redhuan, 2017). Few reports studied the effect of nitazoxanide against clinical infections of *Cryptosporidium* in animals which verified that nitazoxanide could decrease *Cryptosporidium Oocysts* excretion. However, presently it is not approved for use in calves (Pumipuntu and Piratae, 2018). In HIV patients *Cryptosporidium* causes high loss of fluid due to profuse and watery diarrhea. Fluid loss is especially prominent in debilitated individuals who are unable to drink; utmost attention needs to be paid to correct electrolyte abnormalities and prevent dehydration with intravenous or (ORS) (De Hostos *et al.,* 2011). The main treatment approach is oral rehydration whenever possible; however, intravenous fluids that include sodium, potassium, glucose, and bicarbonate may be required in severe cases (Florescu and Sandkovsky, 2016). ORS-based treatment is a highly efficacious and cost-effective way to counteract the effects and relieve some of the symptoms associated with acute secretory diarrheas such as that caused by *Cryptosporidium*, however, the use of ORS in poor and rural areas remains quite low since treatment is labor-intensive and requires large volumes of ORS to maintain hydration (Zwisler *et al.,* 2013).

Individuals should be encouraged to start ORS early to prevent even initial dehydration. Optimum nutritional support should include a trial of oral nutritional supplements before considering total parenteral or intravenous hyper-alimentation. Nutritional supplements containing 24 medium-chain fatty acids may be better absorbed in patients with small intestinal injury and mal-absorption (Manyazewal *et al*., 2018). Although there is no effective therapy for Cryptosporidiosis in HIV-infected persons, there is an effective strategy for managing *Cryptosporidium* that appears to be immune reconstitution with Highly Active Anti-Retroviral Therapy (HAART) (Miao, 2000). While HAART should increase patient's CD4+ above risk verges, the concomitant target of the opportunistic infection remain important to prevent ongoing morbidity Antiretroviral therapeutic intervention, has a dramatic effect on Cryptosporidiosis and leading to the recovery of the CD4+ count in AIDS patients, is a that (Miao, 2000; Maggi *et al*., 2000).

In a study of two patients with Cryptosporidiosis, both were free from the parasite within 24 weeks after starting antiretroviral therapy. This finding was confirmed in another, larger study, where all patients have taken antiretroviral agents showed clinical recovery (Maggi *et al*., 2000). Two patients subsequently relapsed after the therapy was stopped. It was noted that the resolution of diarrhea seemed to be related to an increased CD4+ cell count rather than a decrease in viral load. These findings give further support to the observation that cellular immunity is of paramount importance in clearing Cryptosporidiosis (Morpeth and Thielman, 2006).

2.8. Prevention and Control Measures of Cryptosporidiosis

Reducing the burden of the disease is challenging as a consequence of environmentally stable *Oocysts*, low infective dose and high levels of excreted *sporulated Oocysts*, the *Oocysts* are resistant to many disinfectants and infection may be transmitted to a group of susceptible hosts very quickly. The only drug licensed for the treatment of the disease by (FDA) is restricted to humans (Chalmers and Giles, 2010.

2.8.1. Prevention and control in calves

The *Oocysts* of *Cryptosporidium* are very difficult to eliminate from the environment. The preventive measures that can reduce transmission of bovines Cryptosporidiosis are effective farm management practices or frustrating to reduce fundamental risk factors by prevention of the environmental contamination through, regular removal of feces and contaminated bedding from calving areas and calf houses, combined with steam-cleaning and disinfection with a suitable disinfectant such as Hydrogen Peroxide based disinfectants can help to reduce the environmental buildup of *Cryptosporidium Oocysts*.

Also, limiting the amount of animals density in the farms or stocks, minimizing contact between personnel, calves, and other herds, keeping young animals or susceptible hosts that have a high risk of infection separated from adult animals, and keeping a short calving period of animals which may decrease the opportunities for *C. spp*. to spread within animal herds (Thomson *et al*., 2017). At present, there are no commercially available vaccines to prevent Cryptosporidiosis in either farm livestock or humans. However, several attempts to develop such a vaccine have been made, some of which were partially successful under experimental conditions. Calves that immunized with killed (γ-irradiated or lyophilized*)* showed a reduction in *Oocysts* shedding and diarrhea than non-immunized calves (Jenkins *et al*., 2004). As, the disease frequently arises in the first week of life, trying to immunize the neonatal calves is doubtful to be successful as this will not give enough time to persuade important immune reply before infection hence, immunizing of pregnant cows can produce antibodies against infection which can be passed via colostrum to their calves and thus, calves receiving colostrums from cows vaccinated in this method with recombinant *C. Parvum* were reported to protect against diarrhea and also had reduced *Oocysts* shedding, then those calves received colostrum from non-vaccinated cows (Innes *et al*., 2011).

2.8.2. Prevention and control in human

The best applicable strategy to prevent transmission of *Cryptosporidium* species between humans is a practice of good personal hygiene, including handwashing before preparing and consuming food, after using a toilet and contacting with diarrhea patients (children), and some animals or livestock's, raw food and water must be appropriately cleaned, washing, heated, cooked, or boiled before consumption and drinking, respectively (Pumipuntu and Piratae, 2018). More than that, patients who have diarrhea symptom should understand not to swim in a public swimming pool, public water park, or river for preventing transmission to others, and people who swim in a swimming pool, water park, or river should recognize a potential risk of disease infection if they swallow the water (Rossle and Latif, 2013). Moreover, inhuman living areas, livestock husbandry, and their drinking water, the destruction of *Cryptosporidium Oocysts* can be managed by heat or chemical disinfection such as hydrogen peroxide, sterilization processes using steam, ethylene oxide, chlorine dioxide, ozone (O^3), and ultraviolet light. However, all of the chemical disinfection can be used to prevent and control the occurrence of Cryptosporidiosis and to reduce mortality and morbidity rate in both infected in humans and animals (Ghazy *et al*., 2016).

2.9. Public Health Importance of Cryptosporidiosis

Cryptosporidiosis is progressively inviting attention as an emerging zoonotic disease of great public health importance due to its dominant involvement in worldwide mainly, in developing countries with limited infrastructure and poor sanitary conditions (Shirley *et al*., 2012). Globally, Cryptosporidiosis is estimated and accounted for about 30-50% of deaths in young individuals and found to be the second-highest reason for diarrhea and deaths in children after rotavirus (Gharpure *et al*., 2019).

Cryptosporidium spp. that infects immune-competent and immune-compromised humans include, *C. andersoni*, *C. hominis*, *C. parvum*, *C. meleagridis*, and *C. muris* but, the majority humans cases are caused by either the zoonotic species *C. parvum* or the human-adapted species *C. hominis*, these two species account for > 90% of human infections worldwide (Chalmers *et al*., 2009). Frequently, people at risk of exposure for Cryptosporidiosis are people who swim regularly in pools with insufficient sanitation, veterinarian, child-care workers, parents of infected children, people caring for other people with Cryptosporidiosis, backpackers, and campers who drink untreated water, petting farms, and open farms with public access including, swimmers who swallow water from contaminated sources, people handling infected calves, people exposed to human feces (Walker, 2018). In immune-deficient individuals, the illness may cause death as a result of prolonged diarrhea, which does not respond to antibiotic treatment. Nevertheless, infection of immune-competent people with the infection has a propensity to cause self-limiting diarrhea (Gharpure *et al*., 2019). Moreover, children less than four years of age and the elderly are extremely susceptible to disease but, young adults are less susceptible A child tends to acquire the infection shortly after, or during weaning (Chalmers *et al*., 2009). In 2010, it was confirmed that diarrhea accounted for 10.5% of the 7.6 million deaths of children under the age of 5 years hence, diarrhea caused by the infection can result in a large number of deaths (Liu *et al*., 2012).

2.11. Epidemiology of Cryptosporidiosis in Ethiopia

2.11.1. Epidemiology of Cryptosporidiosis in calves in Ethiopia

In Ethiopia, there were over 50 million calves are raised under a variety of agro-ecological zones. However, a few research works have been done on Cryptosporidiosis in calves in different parts of the country. A cross-sectional study that had been undertaken on 40 dairy farms in the central part of Ethiopia reported a 17.6% prevalence of the *Cryptosporidium* infection (Abebe *et al*., 2008). An additional cross-sectional study in Haramaya, eastern Ethiopia estimated the prevalence of Cryptosporidiosis in calves 27.8% (the study not only in calves) (Regassa *et al.,* 2013). Moreover, recently Ayele *et al.* (2018) reported, *Cryptosporidium* infection is common in the northwest of Ethiopia, out of the 360 examined calves, *Cryptosporidium Oocysts* were recorded in 67 (18.6%) calves its prevalence found to be 18.6%. Molecular characterization of *Cryptosporidium* isolates from nine regions and the central part of the country confirmed the existence of four species: *C. parvum, C. andersoni, C. bovis and C. ryanae* in the Ethiopian calves (Wegayehu *et al*., 2016. Therefore, depending on existing reports of bovine Cryptosporidiosis the prevalence ranges from 2.3 to 27.8% in Ethiopia (Ayele *et al*., 2018 Abebe *et al*., 2008, Regassa *et al*., 2013).

2.11.2. Epidemiology of human Cryptosporidiosis in Ethiopia

Different studies show the significance of the disease in children and HIV/AIDS patients and reported contamination of drinking water, contact with calves, and poor personal hygiene as risk factors of Cryptosporidiosis. Difference reports in the country indicated that the prevalence of Cryptosporidiosis was varying between 7.3% and 12.2% in apparently healthy children. Studies

on patient children reported prevalence ranging from 5.6-14.8%. Most of the study shows the prevalence of Cryptosporidiosis is relatively higher in the patient than healthy children. The occurrences of infection are higher in HIV patients in that non using an antiviral treatment. Accordingly, the prevalence in HIV patients on-ART medication varied from 0% to 28.4%, whereas the studies on HIV/AIDS patients without ART showed prevalence ranging from 15.2 to 40.3%. Although there is a shortage of molecular-based data of Cryptosporidiosis in humans, some reports have been documented in Ethiopia. According to the studies Cryptosporidiosis is prevalent in humans and highlighted the potential zoonotic importance of other species encountered in humans in Ethiopia. The occurrence of Cryptosporidiosis in humans had been reported from different parts of Ethiopia (Table 3).

Table 1: Summary of studies on human Cryptosporidiosis in Ethiopia

Study Area	Study group	Prevalence	References
Jimma Hospital	Under-5 children	3.3%	Kibru and Mekete,(2000)
LegeDini, East Ethiopia	Normal children	12.2%	Ayalew*et al*. (2008)
Nine regions	Different age	7.6%	Adamu *et al.* (2010)
Pawi District	Normal children	8.1%	Tigabu*et al.* (2010)
North Shewa Zone	Normal children	7.3%	Wegayehu*et al*. (2013)
Yirgalem Hospital	Patients children	14.8 %	Getaneh et al. (2010)
Addis Ababa & its environs	HIV+& farm public	9%	Manyazewal, (2017).
Nekemte Hospital	HIV+ non-ART HIV+ on-ART	25.5% 8.4%	Dufera*et al.* (2008)
Southwest Ethiopia	HIV+	16 %	Mariam *et al*. (2008)
Adama, Afar and DireDawa	HIV+ non-ART HIV+ on-ART	17.5% 1.7%	Adamu and Petros (2009).
Hawasa Hospital	HIV+	20.1%	Assefa *et a*l. (2009)
TikurAnbessa	HIV+	0.0%	Adamu *et al.* (2014)
Asella Hospital	HIV+	26.9%	Kifle *et al.* (2019)
Yirgalem Hospital	HIV+ non-ART HIV+ on-ART	17.7% 40.3%	Girma *et al.* (2014)
Hawasa Hospital	HIV+ non-ART HIV+ on-ART	15.2% 11.7%	Shimelis *et al.* (2016)
EHNRI, Addis Ababa patients	Patients children	7.2%	Endeshaw *et al.* (2007)

3. Conclusion and Recommendations

In general, the risk factors like poor personal and dairy farm hygiene, drinking river water source, drainage of farm liquid wastes to a river, not using ART, occupation (farm attendance), contact with calves are the most contributing factors for the prevalence of cryptosporidiosis in both human and animals. Currently, there is no available treatment and there are no vaccines available to prevent *cryptosporidiosis* in either farm livestock or humans.

Therefore, based on the above conclusions the following recommendations are suggested:

- Regular testing for the cleanness of water should be done by the concerned body.
- Awareness creation for communities about efficient personal and dairy farm hygiene and avoiding manure drainage to river water.
- Collaboration b\n multidiscipline should be adopted to achieve effective control and prevention of Cryptosporidiosis.
- Further studies should be done, for the identification of *Cryptosporidium* spp. circulating b\n humans and domestic animals.

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