Cryptosporidiosis in HIV Patients _ **A Battle for Survival**

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Abstract- Cryptosporidiosis, a parasitic contamination brought about by Cryptosporidium species, represents a critical wellbeing challenge, especially for vulnerable compromised people, like those living with HIV. The worldwide HIV pandemic has worked with the spread of sharp disease, with Cryptosporidiosis arising as a main source of causing diarrhea and serious sickness among HIV positive people. This review centers around the study of disease transmission and treatment of Cryptosporidiosis in individuals living with HIV (PLHIV). The pervasiveness of Cryptosporidiosis shifts generally from zero to hundred percent relying upon geological district, with higher rates seen in regions with restricted admittance to Antiretroviral Treatment (ART). Transmission of Cryptosporidiosis happens through immediate and round about contact, water conceived pathway and less usually sexual contact and medical care settings. Resistant compromised patients Likely who are with low CD4+ T lymphocyte numbers (<100cells/mm3), are more defenseless against persevering Cryptosporidiosis which can bring about delayed looseness of the bowels, lack of hydration, ailing health and increment mortality. Determination is much of the time affirmed through sub-atomic examine and microscopy and routine testing for Cryptosporidiosis isn't broad in numerous localities. Treatment stays testing as no all-around viable chemotherapeutic specialist exist. Nitazoxanide, the main FDA supported drug for Cryptosporidiosis shows restricted effectiveness in safe compromised people. Workmanship has demonstrated compelling in supporting resistant capability consequently helping control the contamination in a roundabout way. The continuous fight against Cryptosporidiosis in PLHIV highlights the significance of further developing admittance to ART upgrading demonstrative ability and growing more compelling medicines. This Review features the requirement for proceed with examination and general wellbeing mediation to address the worldwide weight of Cryptosporidiosis, especially in assets restricted settings where sicknesses stay generally pervasive.

Keywords- Cryptosporidiosis, HIV, Antiretroviral Treatment (ART), Immune-compromised patients, Nitazoxanide, Epidemiology

I. INTRODUCTION

Humans are fighting against HIV since 1960s. The first case of HIV-1 Detect in 1959 from obscure male in Kinshasa the City of Congo A Scandinavian man visited the west focal Africa was the distinguished patient who have HIV contamination and help in its detection (Esbjörnsson & Joakim,2010). HIV was first recognized in 1983 and has since guaranteed roughly 40.4 million lives overall starting around 2022. This number is faltering, and whenever left uncontrolled, HIV could turn into a worldwide wellbeing emergency (Swinkels et al., 2024). Human immunodeficiency infection (HIV) is the infection which has mechanism against the immune system. AIDS (acquired immunodeficiency syndrome) happens at the most exceptional phase of disorder (Ansyori et al., 2024). HIV mainly effect WBCs and seriously affect the immune mechanism, this makes the patient more vulnerable to other diseases like *tuberculosis*, contamination and some malignant tumor.

Entrepreneurial disorder is the impurity that have the more chances of happening Constantly and serious in those individual with compromised immune system and those patient with HIV (Mawanda & Bashir, 2017). Opportunistic infections are brought about by different microorganisms (infections, microbes, Advancement and parastatical). OI-causing microorganisms extend in different methods for example via air, bodily fluid or in Contaminated food and water. They can responsible medical conditions when an individual's safe framework is debilitated by HIV infection (O'g & Otaqo'ziyevMurodjonAbdulhomid, 2024). Some OIs that individual with HIV might get incorporate are *candidiasis, Salmonella* disease, *toxoplasmosis*, and *tuberculosis* (TB) as shown in Fig. 1. (Antony & Beena., 2017).



Fig. 1: Types of Opportunistic Infections in HIV/AIDS The AIDS scourge, Presently, in its tertiary 10 years, has developed into a into a wide spread illness, that undermines the entire human community. All around the world, about 4 million people living with HIV have *cryptosporidium* contamination from the total 36 million patient if HIV (Wang et al., 2018). The 3 entrepreneurial Protozoans that are often observed in HIV patients are *Pneumocystis carinii, Toxoplasma gondii,* and *Cryptosporidium parvum* (Botero et al., 2003). With an expected 10% chance of contamination in created nations, People living with HIV have higher risk of having Cryptosporidiosis (Ajjampur et al., 2008). Around 30% to 60% of AIDS patients in created countries and 90% of patients in non-industrial nations experience the diarrhea (Ahmadpour et al., 2020)

Around the world, *cryptosporidium* is one of the main sources of looseness of the bowels (Troeger et al., 2017). In immunocompetent people, *Cryptosporidium* disease is generally selfrestricting. Notwithstanding, in patients with compromised safe frameworks, *Cryptosporidium* sp. can be the reason for persistent the diarrhea, cachexia, absence of craving, fever, retching, lack of healthy sustenance and may prompt passing. Disease with *Cryptosporidium* sp. is obtained through ingestion of oocysts in debased food or then again water or by direct contact with contaminated people or creatures (Ryan et al., 2016) (Liu et al., 2016). Subsequently we go over the latest exploration on the *cryptosporidium*, HIV, spread, the study of disease transmission, Clinical discoveries, Pathogenesis, potential treatments in this audit.

Global footprints of cryptosporidiosis in HIV patients

Diarrhea is a major cause of death for children under five globally and is typically a sign of a bacterial, viral, or parasitic infection (Kaiser 2012). The oocysts of parasite in the mouse stomach epithelial cells were first reported by Clarke in 1895 (Current et al., 1991). The first recorded cases of Cryptosporidiosis in humans date back to 1976, while *Cryptosporidium* was first identified in 1907. However, since the early 1980s, when HIV/AIDS first appeared, the parasite has gained widespread recognition as a human infection (Dillingham et al., 2002) (Tzipori and Widmer, 2008).

Infection with *Cryptosporidium* species is widespread in many sub-Saharan African developing nations as a result of inadequate hygiene, sanitation, and access to clean portable water (Tiwari et al., 2013) (Zafar et al., 2019). Occurrence of Cryptosporidiosis in HIV patient varies greatly about, from 0% to 100%, with greater rates observed in those who have not begun antiretroviral therapy (ART) (Hunter and Nichols, 2002). A prevalence ratio of 2.6– 21.3% has been reported in Africa, per the 2010 Global Disease Burden Report Cryptosporidiosis is a disease that has ability to characterize AIDS that has high fatality rate more than other diseases (Colford et al., 1966).

Nowadays, Cryptosporidiosis Is primary cause of long-term diarrhea in people living with HIV and a major global source of morbidity and mortality (Khan et al., 2017). People living with HIV (PLHIV) frequently have chronic diarrhea as a major hardship, particularly in underdeveloped nations (Desai et al., 2012). Individuals with less CD4+ T-lymphocyte numbers and those new to antiretroviral medication (ART) were more likely than other patients to have a Cryptosporidium infestation (P <.01). People with low number of CD4+ T-Lymphocytes approximately less than 50 to 100 cells/mm³ may experience diarrhea for several month Which can cause acute dryness, no weight gain and less availability of nutrients, prolonged hospital pause, and even death (Wang et al., 2018). Prolonged diarrhea that is caused by a Cryptosporidium infection in people living with HIV can be potentially fatal, and it is linked to poor antiviral medication absorption and treatment failure in HIV patients (Girma M et al., 2014). In Kenya, persistent diarrhea

accounts for almost 40% of PLHIV mortality (Wanyiri JW et al., 2014). Low CD4+ counts are directly linked to diarrhea, which is the second most common reason for hospital visits in a number of developing nations. In the US, there are about 8500 instances of Cryptosporidiosis recorded each year (Painter JE et al., 2016). However, countries in Brazil and Africa reported 3.5% to 22.4% and about 50% of cases of Cryptosporidiosis among PLHIV-negative individuals with low CD4+ cells, respectively (Squire SA and Ryan U, 2017).

In China, 10.1% of PLHIV cases were found to have Cryptosporidium infections (Wang JL et al., 2016). In Iran, patients who tested positive for HIV were found to have 7.6% of instances of Cryptosporidiosis (Gholami R et al., 2016) and 71.4% of those cases were linked to diarrhea. Asymptomatic cases accounted for 4.3% of Cryptosporidium infection cases in Bangladesh (Ehsan AM et al., 2015) and 28.6% of cases in India (Ajjampur SSR et al., 2010). 12.4% of PLHIV in Malaysia had Cryptosporidium infection (Asma I et al., 2015). In 2006, the incidence of Cryptosporidiosis in PLHIV in Cambodia was found to be 40% in the symptomatic group and 53% in the asymptomatic group. This suggests that the infection with Cryptosporidium was not properly diagnosed (Chhin S et al., 2006). In 2009, it was reported that 4.9% of PLHIV in Indonesia had positive results for either Cryptosporidiosis or Blastocystishominis (Kurniawan A et al., 2009). 5.5% of patients had multiple Cryptosporidium spp. infection in 2013, accounting for Cryptosporidium hominis, Cryptosporidium meleagridis, Cryptosporidium felis, and Cryptosporidium parvum infections, which accounted for 77.7% of HIV-positive cases (Abubakar I et al., 2007). Numerous investigations carried out in Cambodia, Indonesia, Lao People's Democratic Republic, Malaysia, Myanmar, Philippines, Singapore, Thailand, and Vietnam have revealed cases of Cryptosporidium infections in Southeast Asia (Lim YAL et al., 2013). Numerous variables, including as population movements between nearby nations, fast modernization, political and economic development, and population increase, contribute to the spread of infectious illnesses (Lim YAL et al., 2013). These elements, in addition to the rise in AIDS cases in tropical and subtropical regions, are highly favorable for the spread of numerous opportunistic infectious pathogens (Table 1) (Lan GL et al., 2016).

Diarrheal infections continue to be the primary cause of death for children in Pakistan, a developing nation where 64% of the population lives in rural regions. According to reports, around 30.4% of Pakistani rural households lack access to better sanitation (DHS M, 2013-2018). Only in 2015, 1.4 million people died as a result of diarrheal illnesses, according to the WHO. Additionally, research demonstrating how children under the age of five die reveals that diarrhea accounts for 11% of all pediatric deaths (WHO, 2017). Furthermore, a significant frequency of human and animal Cryptosporidiosis was found in several regions of Pakistan, including Ravi and Patoki (73.33%), Karachi (55.0%), Sindh (53.0%), Lahore (25.6%), Skardu (20.8%), and Peshawar (9.0%) as shown in figure.2. These researches used staining and molecular approaches (Shafiq MA et al., 2015) (Ali S et al., 2014) (Raja K et al., 2014) (Nasir A et al., 2009) (Khushdil A et al., 2016) (Mumtaz S et al., 2011).

 Table 1: Prevalence of above-mentioned diseases in different regions

Country/ Regions	Cryptosporidiosis Prevalence in PLHIV or Population		
Kenya	Persistent diarrhea accounts for nearly 40% of PLHIV mortality		
United States	~8500 cases of Cryptosporidiosis annually		
Brazil	3.5% to 22.4% of Cryptosporidiosis cases among PLHIV- negative individuals with low CD4+ counts		
Africa	${\sim}50\%$ of Cryptosporidiosis cases among PLHIV-negative individuals with low CD4+ counts		
China	10.1% of PLHIV cases infected with cryptosporidium		
Iran	7.6% of PLHIV with Cryptosporidiosis; 71.4% of these cases associated with diarrhea		
Bangladesh	4.3% of Cryptosporidium cases were asymptomatic		
India	28.6% of Cryptosporidium cases were asymptomatic		
Malaysia	12.4% of PLHIV had Cryptosporidium infection		
Cambodia	40% of symptomatic PLHIV and 53% 0f asymptomatic PLHIV had Cryptosporidiosis		
Indonesia	4.9% of PLHIV tested positive for either Cryptosporidium or Blastocystishominis		
Southeast Asia	5.5% of patients had multiple Cryptosporidium spp.		



Fig. 2: Frequency of Cryptosporidiosis in different areas of Pakistan

Infection pathways: Understanding the spread of disease Direct Transmission

Direct transmission, including animal-to-animal, zoonotic, human-to-animal, and Person-to-Person (*anthroponotic*) transmissions, happens by the fecal-oral pathway from infected hosts (Cama VA et al., 2008) (Casemore D et al., 1985) (Hunter P and Thompson RC, 2005). Human-to-human transmission is commonly defined as less important cases, particularly within family members and in places (Xiao L and Feng Y, 2008) where outbreaks occur, such as hospitals and day care facilities (Glaberman S et al., 2002).A strain of Cryptosporidiosis was diagnosed in children who visited farm was also present in animal and also including veterinary students and scientists when they were working with exposed young calves, provide epidemiological and microbiological proof of animal to human transfer of the disease. In animals, oocysts from contaminated environments are typically consumed by calves to contract Cryptosporidiosis. There are numerous potential causes of infection, such as: (1) contaminated water; (2) contaminated stables; (3) unclean cow udders and teats; and (4) shedding of sick neighbor animals.

Indirect Transmission

Direct transmission occurs when a person comes into touch with water, food, clothing, or other fomites contaminated with *Cryptosporidium* fecally. Indirect transmission can also happen as a result of environmental contamination, which typically entails the spilling of sewage, slurry, or excrement after periods of intense rain (Guerrant 1997) (Hayes et al., 1989) (Jiang J et al., 2005). Data from investigation of intranasal infections of young pig corroborated the discovery of another mechanism of Oocyst transfer via nasal cavity in immune compromised individuals and youngsters (Xiao et al., 2000) (Egger M et al., 1990) (Harari et al., 1986) (Ma P et al., 1984). This method is connected with respiratory symptoms (laryngotracheitis), which may be mild diarrheal.

Waterborne Transmission

Large-scale *Cryptosporidium* outbreaks from the portable water in the 1990s highlighted the importance for strict inspection by health authorities, leading to the development of water quality standards and guidelines. Due to the under recognition of infections and sudden onset, the true load of this illness is not identified. From the 71 drinkable water samples that were examined in and around Chandigarh in 2019, 16% had *Cryptosporidium* oocyst contamination (Tzipori and Ward, 2002). Since *Cryptosporidium* can withstand chlorine and is difficult to filter out, it is the frequent water origin like swimming area are involve in again development of disease. Human infections are common, but their transmission is not well understood (Utaaker KS et al., 2019).

Sexual Transmission

HIV can spread through contaminated bodily fluids, including breast milk, semen ejaculate, vagina moist, and anal fluid. In the world, sexual contact is the most frequent way through which the HIV is spread. HIV is primarily spread through anal or vaginal sex in the US, while it can also spread through vocal sex, parents to children's transmission (in the time of pregnancy, delivery, or breastfeeding), syringe injuries, vital fluid transfusions, and organ transplanting of the 36,801 new HIV infections in 2019, males who sex with males (MSM) accounted for 69%, high-risk heterosexual activity for 23%, and injecting drug users for 7% ((CDC, 2022).

The global AIDS plague is propelled by newly discovered illnesses in females who are fertile. Both parties run the risk of acquiring HIV during condom-free sex, but a woman has higher risk of getting HIV from HIV positive male then from females. HIV can enter the body through the mucous membrane linings of the vagina and the cervical cavity. A simple avenue for transfer across the vaginal mucosa is provided by the fact that HIV-1 cycle of replication and the epithelial dendritic cells of vagina hold it. (Pena-Cruz et al., 2018).

HIV transmission is significantly influenced by sexually transmitted diseases. HIV transmission has thus been demonstrated to be increased by conditions that cause mucosal inflammation, such as *gonorrhea* and *chlamydia*, and *genital ulcer* illnesses, such as *syphilis, cancroid,* and *herpes simplex* infections. It has been demonstrated that trichomonas increases a woman's risk of contracting HIV by 50% (McClelland et al., 2007).

Transmission in the healthcare setting

HIV can infect anyone working in a hospital environment who may come into contact with contaminated medical equipment, surroundings, or bodily fluids. A healthcare worker may be exposed to HIV-positive patient blood, tissue, or other fluid of body a early cutaneous injury, even if you touch the membranes of mucous, or non-intact skin. This increases the risk HIV transmission in healthcare workplaces. Rough estimates place the likelihood of HIV passing on after percutaneous and membrane of mucosa expose to HIV-positive blood at 0.2% and 0.9%, respectively. The danger of HIV transmission by contact between undamaged skin and HIV-positive bodily fluids is essentially nonexistent (CDC, 2020). Unless clearly bleeding, feces, urine, nasal fluid, sweat, tears, sputum, vomitus, and saliva are not regarded as potentially infectious (Bell, 1997).

The kind and intensity of exposure as well as the level of *viremia* are the main variables affecting the likelihood of transmission. Deep wounds, hollow bore needle injuries, and expose to a significant blood volume from an infected person were associated with a higher probability of transmission. The risk of transmission is increased by higher blood (inoculum) titers of HIV, which are observed in people with acute HIV infection or untreated HIV (CDC, 2020).

Transmission through the use of injectable drugs

A person who uses syringes and injections to inject the drugs in HIV patient have high risk of transmitting virus to healthy one. The second most dangerous habit for HIV infection is sharing syringes. Temperature of storage and leftover blood volume were related to HIV survival in syringes. Fifty percent of the syringes that were kept at 4 degrees Celsius for 42 days or more had viable HIV (Abdala et al., 2000).

The CDC has identified several prevention obstacles, including high-risk behaviors including by using same needle and also same syringe sharing for more than one person, participating in unprotected sexual contact, use of medicine, and community factors that restrict the reach to HIV prohibition and care include medium addiction method.

Techniques used for disease decoding

HIV infection diagnosis could be made after a thorough and meticulous examination of the patient's clinical presentation, laboratory results, and previous history including if involve in unprotected mating, use of drugs via veins, blood transfusion, HIV Antibody test, HIV positive family member especially mother or if that person is professionally related to HIV. Pathogenic assays and testing for HIV antibody helps in the authentication of the HIV pathogen detection. (National Health Commission, 2021).

A blood sample or saliva sample can be collected for HIV laboratory diagnosis. Tests performed for identification of HIV are

- 1- Rapid test
- 2- NAATs (nucleic acid amplification test)
- 3- Western blot
- 4- Immunoassays (line immunoassay, indirect immunofluorescence assay and ELISA)

When Cryptosporidium infection is suspected, especially request testing for this organism as routine testing for eggs and parasites usually does not include Cryptosporidium. Target pathogens in novel molecular intestinal panel assays typically include Cryptosporidium. Since Cryptosporidium is occasionally secreted in the stool, gather several samples to improve test sensitivity (i.e., gather specimens over three different days).

Additional diagnosing methods consist of molecular test, fast immune chromatographic cartridge assays, microscopy using enzyme immunoassay kits, and modified acid-fast labeling, and microscopy with direct fluorescent antibody, which is regarded as the gold standard. Keep in mind that fast immuno chromatographic cartridge assays may produce untrue positive results; think about using microscope for confirmation.

There are no recognized international standards for diagnosing Cryptosporidiosis. Testing for Cryptosporidium is restricted in several countries to those who are known to have HIV/AIDS; however, adult sample testing is typically contingent upon certain criteria including chronic or watery diarrhea, as well as when clinical suspicion is present. Clinical signs of HIV/AIDS patients differ according to the level of immunological impairment (reviewed in (R.M. Chalmers, 2008) (Huang DB and White AC, 2006) (Hunter PR and Nichols G, 2002). Individuals with CD4 cell number more than 180–200 ml could not exhibit any symptoms or experience self-limiting diarrhea. Nevertheless, individuals having progressed AIDS (CD4 cell number less than 50 per ml), especially in underdeveloped nations. When access to ART is limited, may get acute diarrhea that can last for a several weeks, causing serious malnourishment, weight loss, and prolonged dehydration hospital stays as well as death rates. Furthermore, individuals having progressed AIDS are at higher risk of getting infection outside the digestive tract, especially in the biliary, respiratory and pancreatic systems (reviewed in (Abubakar I et al., 2007). Species of Cryptosporidium are the most isolated microorganisms in the biliary tract of AIDS-related cholangiopathy patients (Chen XM et al., 2002). Lately, there have been cases of cryptosporidiosis in HIV-negative people.

Combating infections: Use of Antibiotics, Antivirals, and Emerging Therapies

HIV/AIDS, also known as acquired immune deficiency syndrome, has become a global health and financial danger, infecting millions of people. It has spread like wildfire. (Zhu et al., 2020). HIV suppresses the immune system, making the body unresponsive to outside stimuli (Laila et al., 2019). The most important strategy for extending life expectancy (KatzIT and

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Maughan-Brown B, 2017), avoiding opportunistic infections (H,BrooksJT et al., 2014) and preventing cancer in people living with HIV (PLWH) is antiretroviral therapy (ART) (Park LS et al., 2018). When ART is used, HIV becomes a chronic manageable illness rather than a deadly one (Altice et al., 2019). Just 60% of HIV-positive individuals are currently receiving antiretroviral medication, despite significant worldwide investment (Ndung'u, T et al. 2019). HIV-positive patients have responded well to antiretroviral therapy (ART); however, there is still no cure and lifelong medicine is required. (Deeks, S.G et al., 2021). Zidovudine, a nucleoside reverse transcriptase inhibitor, was the first successful treatment for HIV. This was authorized in 1987 from the Food and Drug Administration (FDA) (Kemnic TR and Gulick PG, 2024). People living with HIV now having lower rates of morbidity and mortality because to the discovery of antiretroviral therapy (ART) (Vincent, C. C. N., et al., 2021).

The parasite *Cryptosporidium* is an opportunistic one (Gerace et al.,2019) can cause deadly diarrheal illness in immune compromised individuals and small infants (Ryan et al., 2021) and is zoonotic in nature (Pumipuntu N and Piratae S, 2018).

Since there are currently no viable treatments or vaccines, control depends on our ability to comprehend the mechanisms of transmission (Ryan, U et al., 2021). While no proven chemotherapeutic treatment is effective against Cryptosporidium, nitazomamide and parmomycin can be somewhat beneficial in a small number of AIDS patients. Antiretroviral therapy may increase immunological function and accelerate the spread of Cryptosporidiosis. Other therapeutic approaches include nutrient replacement, electrolyte replacement, and supportive therapy (Mohammad et al., 2023). The only medication that has been shown to be beneficial is Nitazoxanide (Huston CD, 2021). Nitazoxanide (NTZ) is the sole medication approved by FDA for the treatment of Cryptosporidiosis. It is a broad-spectrum nitrothiazolebenzamide anti-parasitic chemical (Christopher D Huston, 2021) which shortens the time that adults in otherwise good health shed Cryptosporidium. Sadly, Nitazoxanide is only marginally beneficial for kids, and for AIDS patients, who still receive normal care consisting of antiretroviral therapy to try and rebuild immunity, it is as effective as a placebo (Huston CD, 2021), it has not demonstrated any advantages for immune compromised individuals with HIV and Cryptosporidiosis (PyIroh Tam et al., 2021). An anti-cryptosidal medication clofazimine lowers Cryptosporidium shedding in cases of Cryptosporidiosis. When treating patients with advanced HIV infection for Cryptosporidiosis, clofazimine was ineffective (Huston CD, 2021).

	Table 2: Therape	utic Drugs & the	eir mechanism o	of action
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Drugs	Mechanism of Action	Patients Group
Nitazoxanide (NTZ)	Inhibits the growth of <i>Cryptosporidium</i> by interfering with pyruvate- <i>ferredoxinoxidoreductase</i> enzyme	Healthy adults, marginally effective in children AIDS Patients
Paromomycin	AminoglycosideantibioticthatinhibitsproteinsynthesisinCryptosporidium	AIDS Patients
clofazimine	Anti-leprosy drug with anti- inflammatory and anti-	Cryptosporidiosis, advanced HIV Patients

	cryptosidal properties; reduces shedding of <i>Cryptosporidium</i>	
Antiretroviral Therapy(ART)	Increase immune function indirectly helping control	AIDS Patients
Azithromycin	Macrolide antibiotic that inhibits bacterial protein synthesis; used to treat several opportunistic infection	azithromycin is not efficient in curing Cryptosporidial infection, it can be used as a safe and effective short-term treatment for symptoms of the disease.
Spiramycin	Macrolide antibiotic with activity against <i>Cryptosporidium</i>	Spiramycin is advised for children who have severe or protracted diarrhea when Cryptosporidium appears to be the etiological cause of the illness.
Supportive Therapy	Focuses on fluid, electrolyte replacement and nutrition to manage symptoms	General Population, especially vulnerable group(Children, Immuno compromised)

Preventive strategies

Following preventive measures and controls can help out to reduce the risk of disease opportunity (Chen et al., 2002):

- 1- Wash hands
- 2- Avoid touching farm animals
- 3- Wash your daily use fruits and vegetables and cook food completely
- 4- Avoid touching pet's stool
- 5- Use caution while utilizing hot tubs and swimming in rivers, lakes, and pools.

6- Use distilled water which is safe for health Take extra care when travelling anywhere else.



Fig. 3: Prevention and control measures for Cryptosporidium and AIDS

II. CONCLUSION

The prevalence of *cryptosporidium* infections in HIV/AIDS patients has increased during the last few decades.

Cryptosporidium is a major problem for patients with HIV/AIDS-related diarrhea, low CD4+ T-lymphocyte counts, and those receiving antiretroviral therapy (ART). The species and subtypes of *Cryptosporidium* seen in HIV/AIDS patients are equivalent to those found in HIV-negative people genetic alteration of the parasite, high-throughput screening of novel or repurposed medications, and generation of optimum.

REFERENCES

- Esbjörnsson, Joakim. "HIV-1 evolution, disease progression and molecular epidemiology of HIV-1 single and HIV-1 and HIV-2 dual-infected individuals in Guinea-Bissau." (2010).
- 2) Swinkels, Helena, Angel JustizVaillant, Andrew Nguyen, and Peter Gulick. "HIV and AIDS." *StatPearls* (2024).
- Ansyori, A.R., Gusvania, A.A., Meidina, A.N., Humaira, N.T., Asmarani, A.Q., Novalina, F. and Turridho, A., 2024. Comprehensive Foundation of Knowledge on HIV/AIDS: Indonesian Case Studies and Applications. Asadel Publisher.
- 4) Mawanda, Bashir. "Prevalence of opportunistic infections among patients attending art clinic at Ruhiira Health Centre Three, Isingiro District." (2017).
- O'g, OtaqoʻziyevMurodjonAbdulhomid. "COMORBID CONDITIONS OF INTERNAL DISEASES IN AIDS PATIENTS." *PEDAGOGICAL REFORMS AND THEIR* SOLUTIONS 1, no. 1 (2024): 49-50.
- 6) Antony, Beena. "Opportunistic Infections in HIV/AIDS: An Overview." *Holistic Approaches to Infectious Diseases* (2017): 217-230.
- 7) Wang ZD, Liu Q, Liu HH, Li S, Zhang L, Zhao YK. Prevalence of Cryptosporidium, microsporidia and Isospora infection in HIVinfected people: a global systematic review and meta-analysis. Parasite Vectors. 2018;11(1):28.
- 8) Botero JH, Castaño A, Montoya MN, Ocampo NE, Hurtado MI, Lopera MM. A preliminary study of the prevalence of intestinal parasites in immunocompromised patients with and without gastrointestinal manifestations. Rev Inst Med Trop Sao Paulo. 2003;45(4):197–200
- Ajjampur SSR, Sankaran P, Kang G. Cryptosporidium species in HIV-infected individuals in India: an overview. Natl Med J India. 2008;21(4):178–84.
- 10) Ahmadpour, E., H. Safarpour, L. Xiao, M. Zarean, K. Hatam-Nahavandi, A. Barac, S. Picot et al. "Cryptosporidiose chez les patients VIH-séropositifs et facteurs de risqueassociés: revue systématique et méta-analyse." *Parasite (Paris, France)* 27 (2020): 27.
- 11) Troeger, Christopher, et al. "Estimates of global, regional, and national morbidity, mortality, and aetiologies of diarrhoeal diseases: a systematic analysis for the Global Burden of Disease Study 2015." *The Lancet infectious diseases* 17.9 (2017): 909-948.
- 12) Ryan, Una, AlirezaZahedi, and Andrea Paparini. "Cryptosporidium in humans and animals—a one health approach to prophylaxis." *Parasite immunology* 38.9 (2016): 535-547.
- 13) Liu, J.; Platts-Mills, J.A.; Juma, J.; Kabir, F.; Nkeze, J.; Okoi, C.; Operario, D.J.; Uddin, J.; Ahmed, S.; Alonso, P.L.; et al. Use of Quantitative Molecular Diagnostic Methods to Identify Causes of Diarrhoea in Children: A Reanalysis of

the GEMS Case-Control Study. *Lancet* **2016**, *388*, 1291–1301. [Google Scholar] [CrossRef] [PubMed] [Green Version]

- 14) Kaiser, L.; Surawicz, C.M. Infectious Causes of Chronic Diarrhoea. *Best Pract. Res. Clin. Gastroenterol.* 2012, 26, 563–571. [Google Scholar] [CrossRef] [PubMed]
- 15) Current WL, Garcia LS. Cryptosporidiosis. *ClinMicrociol Rev.* 1991;4(3):325–58. [PMC free article] [PubMed] [Google Scholar]
- 16) Dillingham RA, Lima AA, Guerrant RL (2002) Cryptosporidiosis: epidemiology and impact. Microbes Infect 4: 1059- 1066. Link: <u>https://bit.ly/2Yp7qCQ</u>
- 17) TziporiS, Widmer G (2008) A hundred-year retrospective on cryptosporidiosis. Trends Parasitol 24: 184-189. Link: https://bit.ly/2Sr1HZe
- 18) Tiwari BR, Ghimire P, Malla S, Sharma B, Karki S (2013) Intestinal parasitic infection among the HIV infected patients in Nepal. J Infect DevCtries 7: 550-555. Link: https://bit.ly/3aYHLU0
- 19) Zafar A, Khan MK, Abbas Z, Abbas RZ, Sindhu ZD, et al. (2019) Human Cryptosporidiosis: An insight into Epidemiology, Modern Diagnostic Tools and Recent Drug Discoveries. 6: 60-70. Link: <u>https://bit.ly/2z2B06q</u>
- 20) Hunter PR, Nichols G (2002) Epidemiology and clinical features of *Cryptosporidium* infection in immunocompromised patients. ClinMicrobiol Rev 15: 145-154. Link: https://bit.ly/2SsTnZb
- 21) Colford JM Jr, Tager IB, Hirozawa AM, Lemp GF, Aragon T, et al. (1966) Cryptosporidiosis among patients infected with human immunodeficiency virus. Factors related to symptomatic infection and survival. Am J Epidemiol 144: 807-816.> Link: https://bit.ly/2KTOZOz
- 22) Khan A, Shaik JS, Grigg ME. Genomics and molecular epidemiology of Cryptosporidium species.Acta Trop. 2017;184:1-14. [PubMed] [Google Scholar] [Ref list]
- Desai NT, Sarkar R, Kang G. Cryptosporidiosis: an underrecognized public health problem. Trop Parasitol. 2012;2:91-98. [PMC free article] [PubMed] [Google Scholar] [Ref list]
- 24) Wang R, Li J, Chen Y, Zhang L, Xiao L. Widespread occurrence of Cryptosporidium infections in patients with HIV/AIDS: epidemiology, clinical feature, diagnosis, and therapy. Acta Trop. 2018;187:257-263. [PubMed] [Google Scholar] [Ref list]
- 25) Girma M, Teshome W, Petros B, Endeshaw T. Cryptosporidiosis and Isosporiasis among HIV-positive individuals in south Ethiopia: a cross sectional study. BMC Infect Dis. 2014;14:100. [PMC free article] [PubMed] [Google Scholar] [Ref list]
- 26) Wanyiri JW, Kanyi H, Maina S, et al. Cryptosporidiosis in HIV/AIDS patients in Kenya: clinical features, epidemiology, molecular characterization and antibody responses. Am J Trop Med Hyg. 2014;91:319-328. [PMC free article] [PubMed] [Google Scholar]

- 27) Painter JE, Gargano JW, Yoder JS, Collier SA, Hlavsa MC. Evolving epidemiology of reported cryptosporidiosis cases in the United States, 1995-2012. Epidemiol Infect. 2016
- 28) Squire SA, Ryan U. Cryptosporidium and Giardia in Africa: current and future challenges. Parasit Vectors. 2017;10:195.
- 29) Wang JL, Li TT, Huang SY, Cong W, Zhu XQ. Major parasitic diseases of poverty in mainland China: perspectives for better control. Infect Dis Poverty. 2016
- 30) Gholami R, Gholami S, Emadi-Kouchak H, Abdollahi A, Shahriari M. Clinical characteristic of the HIV/AIDS patients with cryptosporidiosis referring to Behavioral Diseases Consultation Center, Imam Khomeini Hospital, Tehran in 2013. Iran J Pathol. 2016;11:27-34
- 31) Ehsan AM, Geurden T, Casaert S, et al. Assessment of zoonotic transmission of Giardia and Cryptosporidium between cattle and humans in rural villages in Bangladesh. PLoS One. 2015
- 32) Ajjampur SSR, Sarkar R, Sankaran P, et al. Symptomatic and asymptomatic Cryptosporidium infections in children in a semi-urban slum community in southern India. Am J Trop Med Hyg. 2010
- 33) Asma I, Sim BL, Brent RD, Johari S, Lim YAL. Molecular epidemiology of Cryptosporidium in HIV/AIDS patients in Malaysia.Trop Biomed. 2015
- 34) Chhin S, Harwell JI, Bell JD, et al. Etiology of chronic diarrhea in antiretroviral-naive patients with HIV infection admitted to Norodom Sihanouk Hospital, Phnom Penh, Cambodia. Clin Infect Dis. 2006;43:925-932
- 35) Kurniawan A, Karyadi T, Dwintasari SWW, et al. Intestinal parasitic infections in HIV/AIDS patients presenting with diarrhoea in Jakarta, Indonesia. Trans R Soc Trop Med Hyg. 2009
- 36) Abubakar I, Aliyu SH, Arumugam C, Hunter PR, Usman NK. Prevention and treatment of cryptosporidiosis in immunocompromised patients. Cochrane Database Syst Rev. 2007
- 37) Lim YAL, Mahdy MAK, Surin J. Unravelling Cryptosporidium and Giardia in Southeast Asia. In: Lim YAL, Vythilingam I, eds. Parasites and Their Vectors: A Special Focus Southeast Asia. Vienna, Austria: Springer; 2013
- 38) Lim YAL, Vythilingam I, eds. Southeast Asia: hotspot for parasitic infections. In: Parasites and Their Vectors: A Special Focus Southeast Asia. Vienna, Austria: Springer; 2013. [Google Scholar]
- 39) Lan GL, Yuan ZK, Clements-Nolle KD, et al. Social capital and quality of life among people living with HIV/AIDS in Southeast China. Asia Pac J Public Health. 2016
- 40) DHS M. Demographic and health surveys. Calverton: Measure DHS 2013–2018.
- 41) WHO, 2017:11. <u>http://www.who.int/en/news-room/fact-sheets/detail/the-top-10-causes-of-death</u>

- 42) Shafiq MA, Maqbool A, Khan UJ, Lateef M, Ijaz M. Prevalence, water borne transmission and chemotherapy of cryptosporidiosis in small ruminants. Pak J Zool. 2015;47: 1715–1721
- 43) Ali S, Mumar S, Kalam K, Raja K, Baqi S. Prevalence, clinical presentation and treatment outcome of cryptosporidiosis in immunocompetent adult patients presenting with acute diarrhea. J Pak Med Assoc. 2014; 64: 613–618.
- 44) Raja K, Abbas Z, Hassan SM, Luck NH, Aziz T, Mubarak M. Prevalence of cryptosporidiosis in renal transplant recipients presenting with acute diarrhea at a single center in Pakistan. J Nephropathol.2014; 3: 127–131. 10.12860/jnp.2014.25
- 45) Nasir A, Avais M, Khan MS, Ahmad N. Prevalence of Cryptosporidium parvum infection in Lahore (Pakistan) and its association with diarrhea in dairy calves. Int J Agric Biol. 2009; 11: 221–224
- 46) Khushdil A, Murtaza F, Chattha MN. Cryptosporidiosis among children of district Skardu, Pakistan.J Ayub Med Coll Abbottabad. 2016; 28: 575–577
- 47) Mumtaz S, Ahmed J, Ali L, Hussain H. modified acid fast staining: a better diagnostic tool in chronic diarrhea due to cryptosporidiosis. J Ayub Med Coll Abbottabad.2011; 23: 72–74.
- 48) Cama VA, Bern C, Roberts J, Cabrera L, Sterling CR, Ortega Y, Gilman RH, Xiao L. 2008. Cryptosporidium species and subtypes and clinical manifestations in children, Peru.Emerg. Infect. Dis. 14:1567–1574
- 49) Casemore D, Sands RL, Curry A. 1985. Cryptosporidium species a "new" human pathogen. J. Clin. Pathol. 38:1321– 1336
- Hunter P, Thompson RC. 2005. The zoonotic transmission of Giardia and Cryptosporidium. Int. J. Parasitol. 35:1181– 1190
- 51) Xiao L, Feng Y. 2008. Zoonotic cryptosporidiosis.FEMS Immunol. Med. Microbiol. 52:309–323
- 52) Glaberman S, Moore JE, Lowery CJ, Chalmers RM, Sulaiman I, Elwin K, Rooney PJ, Millar BC, Dooley JS, Lal AA, Xiao L. 2002. Three drinking-water-associated cryptosporidiosis outbreaks, Northern Ireland.Emerg. Infect. Dis. 8:631–633
- 53) Guerrant R. 1997. Cryptosporidiosis: an emerging, highly infectious threat. Emerg. Infect. Dis. 3:51–57
- 54) Hayes EB, Matte TD, O'Brien TR, McKinley TW, Logsdon GS, Rose JB, Ungar BLP, Word DM, Wilson MA, Long EG, Hurwitz ES, Juranek DD. 1989. Large community outbreak of cryptosporidiosis due to contamination of a filtered public water supply. N. Engl. J. Med. 320:1372– 1376
- 55) Jiang J, Alderisio KA, Xiao L. 2005. Distribution of Cryptosporidium genotypes in storm event water samples

from three watersheds in New York. Appl. Environ. Microbiol. 71:4446–4454

- 56) Xiao L, Alderisio K, Limor J, Royer M, Lal AA. 2000. Identification of species and sources of Cryptosporidium oocysts in storm waters with a small-subunit rRNA-based diagnostic and genotyping tool. Appl. Environ. Microbiol. 66:5492–5498
- 57) Egger M, Mäusezahl D, Odermatt P, Marti HP, Tanner M. 1990. Symptoms and transmission of intestinal cryptosporidiosis. Arch. Dis. Child. 65:445–447
- 58) Harari M, West B, Dwyer B. 1986. Cryptosporidium as cause of laryngotracheitis in an infant. Lancet i:1207doi
- 59) Ma P, Villanueva TG, Kaufman D, Gillooley JF. 1984. Respiratory cryptosporidiosis in the acquired immune deficiency syndrome. Use of modified cold kinyoun and hemacolor stains for rapid diagnoses. JAMA 252:1298–1301
- 60) Tzipori S, Ward H. 2002. Cryptosporidiosis: biology, pathogenesis and disease. Microbes Infect. 4:1047–1058
- 61) Utaaker KS, Joshi H, Kumar A, Chaudhary S, Robertson LJ. Occurrence of Cryptosporidium and Giardia in potable water sources in Chandigarh, Northern India. J Water Supply Res Technol (AQUA) 2019;68:483–94
- 62) CDC, 2022
- 63) Pena-Cruz, V., Agosto, L. M., Akiyama, H., Olson, A., Moreau, Y., Larrieux, J. R., ... & Sagar, M. (2018). HIV-1 replicates and persists in vaginal epithelial dendritic cells. *The Journal of clinical investigation*, 128(8), 3439-3444.
- 64) McClelland, R. S., Sangaré, L., Hassan, W. M., Lavreys, L., Mandaliya, K., Kiarie, J., ... & Baeten, J. M. (2007). Infection with Trichomonas vaginalis increases the risk of HIV-1 acquisition. *The Journal of infectious diseases*, 195(5), 698-702.
- 65) CDC, 2020
- 66) Bell, David M. "Occupational risk of human immunodeficiency virus infection in healthcare workers: an overview." *The American journal of medicine* 102.5 (1997): 9-15.
- 67) CDC, 2020
- 68) Abdala N, Reyes R, Carney JM, Heimer R, survival of HIV-1 in syringes: effects of temperature during storage external icon. Subst Use Misuse. 2000;35(10):1369-1383
- 69) National Health Commission. Diagnosis of AIDS and HIV infection. (2019-01-02) Available from: <u>http://www.nhc.gov.cn/wjw/s9491/201905/6430aa653</u> 728439c901a7340796e4723/files/84dffca4fb2c4293abb6be4 d5353f924.pdf. Accessed September 20, 2021.
- 70) R.M. Chalmers *Cryptosporidium*: from laboratory diagnosis to surveillance and outbreaks Parasite, 15 (2008), pp. 372-378<u>View at publisherCrossrefView in ScopusGoogle</u> <u>Scholar</u>

- 71) Huang DB, White AC. An updated review on Cryptosporidium and Giardia. Gastroenterol Clin North Am 2006; 35:291–314; viii.
- 72) Hunter PR, Nichols G. Epidemiology and clinical features of Cryptosporidium infection in immunocompromised patients. Clin Microbial Rev 2002; 15:145–154.
- 73) Abubakar I, Aliyu SH, Arumugam C, Usman NK, Hunter PR. Treatment of cryptosporidiosis in immunocompromised individuals: systematic review and meta-analysis. Br J Clin Pharmacol 2007; 63:387–393.
- 74) Chen XM, Keithly JS, Paya CV, LaRusso NF. Cryptosporidiosis. N Engl J Med 2002; 346:1723–1731.
- 75) Zhu, QingshuangMPHa; Fang, PengzhongMDb; Zhao, YadongMPHa,c; Dai, DingmeiBSa; Luo, XiaofengPhDa,*. How about the quality and recommendation on prevention, diagnosis, and treatment of HIV/AIDS guidelines developed by WHO: A protocol for systematic review. Medicine 99(52):p e23638, December 24, 2020. | DOI: 10.1097/MD.00000000023638
- 76) Laila, Umme, et al. "Role of medicinal plants in HIV/AIDS therapy." *Clinical and Experimental Pharmacology and Physiology* 46.12 (2019)
- 77) KatzIT, Maughan-Brown B.Improved life expectancy of people living with HIV: who is left behind?*Lancet HIV* 2017;4:e324–6
- 78) H,BrooksJT,BensonCA et al.; HIV Medicine Association of the Infectious Diseases Society of America. Prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: updated Guidelines from the Centers for Disease Control and Prevention, National Institutes of Health, and HIV Medicine Association of the Infectious Diseases Society of America *Clin Infect Dis*2014;58:1308– 11.
- 79) Park LS, TateJP, Sigel K, et al. Association of viral suppression with lower AIDS-defining and non-AIDSdefining cancerincidence in HIV-infected veterans: a prospective cohort study *Ann Intern Med* 2018;169:87–96.
- 80) Altice, F., Evuarherhe, O., Shina, S., Carter, G., &Beaubrun, A. C. (2019). Adherence to HIV treatment regimens: systematic literature review and meta-analysis. *Patient Preference and Adherence*
- 81) Ndung'u, T., McCune, J.M. &Deeks, S.G. Why and where an HIV cure is needed and how it might be achieved. *Nature* **576**, 397–405 (2019).
- 82) Deeks, S.G., Archin, N., Cannon, P. *et al.* Research priorities for an HIV cure: International AIDS Society Global Scientific Strategy 2021. *Nat Med* 27, 2085–2098 (2021).
- Kemnic TR, Gulick PG. HIV Antiretroviral Therapy. [Updated 2022 Sep 20]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-
- 84) Vincent, C. C. N., et al. "Adherence to Antiretroviral Therapy among HIV/AIDS in Federal Medical Centre, Owerri." Journal of Pharmaceutical Research International 33.57A (2021)
- 85) Gerace E, Lo Presti VDM, Biondo C. *Cryptosporidium* Infection: Epidemiology, Pathogenesis, and Differential Diagnosis. Eur J MicrobiolImmunol (Bp). 2019 Oct 22;9(4):119-123. doi: 10.1556/1886.2019.00019. PMID: 31934363; PMCID: PMC6945992.

- 86) Ryan, U.; Zahedi, A.; Feng, Y.; Xiao, L. An Update on Zoonotic *Cryptosporidium* Species and Genotypes in Humans. *Animals* 2021, 11
- 87) Pumipuntu N, Piratae S. Cryptosporidiosis: A zoonotic disease concern. Vet World. 2018 May;11(5):681-686. doi: 10.14202/vetworld.2018.681-686. Epub 2018 May 23. PMID: 29915508; PMCID: PMC5993756.
- 88) Ryan, U.; Zahedi, A.; Feng, Y.; Xiao, L. An Update on Zoonotic *Cryptosporidium* Species and Genotypes in Humans. *Animals* 2021, 11
- 89) Mohammad, Fatima Ibrahim, DoaaAbdAlabasMuhammedRidh, and Osamah Faisal Kokaz. "A General Review on Cryptosporidium Parvum: Pathogenesis, Diagnosis and Treatment." World Journal of Current Medical and Pharmaceutical Research (2023)
- 90) Huston CD. The Clofazimine for Treatment of Cryptosporidiosis in HIV-Infected Adults (CRYPTOFAZ) and Lessons Learned for Anticryptosporidial Drug Development. Clin Infect Dis. 2021 Jul 15;73(2):192-194. doi: 10.1093/cid/ciaa425. PMID: 32277815; PMCID: PMC8427724
- 91) Christopher D Huston, 2021, The Clofazimine for Treatment of Cryptosporidiosis in HIV-Infected Adults (CRYPTOFAZ) and Lessons Learned for Anticryptosporidial Drug Development, *Clinical Infectious Diseases*
- 92) PyIroh Tam, S L M Arnold, L K Barrett, C R Chen, T M Conrad, E Douglas, M A Gordon, D Hebert, M Henrion, D Hermann, B Hollingsworth, E Houpt, K C Jere, R Lindblad, M S Love, L Makhaza, C W McNamara, W Nedi, J Nyirenda, D J Operario, J Phulusa, G V Quinnan, L A Sawyer, H Thole, N Toto, A Winter, W C Van Voorhis, Clofazimine for Treatment of Cryptosporidiosis in Human Immunodeficiency Virus Infected Adults: An Experimental Medicine, Randomized, Double-blind, Placebo-controlled Phase 2a Trial, *Clinical Infectious Diseases*, Volume 73, Issue 2, 15 July 2021
- 93) Christopher D Huston, The Clofazimine for Treatment of Cryptosporidiosis in HIV-Infected Adults (CRYPTOFAZ) and Lessons Learned for Anticryptosporidial Drug

Development, *Clinical Infectious Diseases*, Volume 73, Issue 2, 15 July 2021

94) 94) Chen XM, LaRusso NF. Cryptosporidiosis and the pathogenesis of AIDS-cholangiopathy. Semin Liver Dis 2002; 22:277–289.

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