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(REVIEW ARTICLE)



Public health risk of *Giardia* and *Cryptosporidium* posed by drinking water, Saudi Arabia

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Abstract

Our review gives information on the health effects and treatment technology that would be useful in dealing with the contamination of drinking water and the health advisory about *Giardia* and *Cryptosporidium* spp., that cause human and animal disease worldwide, and to attract the attention of officials responsible for protecting public health when contamination situations occur, and as guidance to assist people to maintain personal hygiene as well as awareness of contamination with parasites, especially drinking water to protect themselves from parasitic diseases. Cryptosporidium is the first parasite to cause concern to health officials in the world and Giardia which has heightened world concerns because of its severity. Thus, our study focused on the protozoan Giardia and Cryptosporidium are responsible for most water-borne diseases all over the world, as a result of the extent and number of outbreaks of waterborne diseases suggests a significant risk of their potential transmission via drinking water. Therefore, the light was shed on the importance of drinking water quality and its free of pathogenic parasites were preserved to preserve public health, especially, Cryptosporidium spp., and Giardia spp., are important intestinal protozoa of humans, livestock, and wild animals worldwide, resulting in diarrhea which can be fatal and threatening human health worldwide. Many outbreaks among humans have been caused by both the massive *Giardia* and *Cryptosporidium*-associated waterborne outbreak. Such outbreaks pose significant challenges to public health. In the United States, it is estimated that 748,000 cryptosporidiosis cases occur every year. According to the World Health Organization, annually, there are 500,000 emerging giardiasis cases globally.

Keywords: Drinking water; Water-borne parasites; Public health; Cryptosporidium; Giardia

1. Introduction

Clean water, a better environment, and a healthy life are aimed in the development goals by securing safe water, adequate sanitation, and clean environment, which are essential for human life. Moreover, water was recognized as a basic human right by United Nations General Assembly [1]. Therefore, everyone should have access to clean water for their physical health and for a healthy environment. Unfortunately, every day around one thousand children die due to preventable diseases caused by lack of water and sanitation because water, environment, and health are interrelated and they must be taken into account holistically. When the environment is polluted, it increases the parasitic contamination in water. In return, this leads to diseases such as diarrhea, cerebral and corneal diseases and others [2, 3]. Many classes of pathogens excreted in animals and human feces are responsible for waterborne disease. Protozoans

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are known to cause outbreaks disease worldwide and they are very robust in water environments and are strongly resistant to most disinfectants, including chemical procedures. Access to adequate supplies of good quality drinking water continues to be limited among many communities [4]. Previous studies have reported association of the occurrence of oocysts and/or cysts, including those of *Toxoplasma gondii, Cryptosporidium spp., Giardia, and Acanthamoeba* which are the main parasites associated with waterborne diseases [4]. Granulomatous Amoebic Encephalitis (GAE) is a serious human disease that predominantly occurs in immune-compromised individuals. It can be caused by two protozoan pathogens, *Acanthamoeba* spp and *Balamuthia mandrillaris. Acanthamoeba* GAE is a rare infection; it almost always proves fatal with the mortality rate of more than 90% and majority of GAE infections are identified at the post-mortem [5].

Water is the most crucial commodity for life support process in organism. Water is basic and mandatory need for the humans and the entire living creature on earth. Therefore, the consumption of water by human should be safe, easily accessible, adequate and free from any kind of contamination [6]. Pollutants in drinking water and water bodies pose a severe threat to human health as well as aquatic ecosystem, especially pathogens [3].

Consumption of drinking water contaminated is one of the biggest threats to public health. Globally, about 1 to 2 billion people are suffering from a lack of safe drinking water and 30,000 people die every week from contaminated water, more than people died as a result of the war [3, 6]. Drinking water has a range of risks in the form of pathogenic parasites (such as protozoa and helminthes) and if these parasites are not properly disposed of, they can pose a threat to public health and the environment [7, 8]. In a 2017 World Health Organization (WHO)/UNICEF report [7], 29% of the world's population (2.1 billion people) in 2015 lacked access to safe drinking water in their homes and therefore more than 3.4 million deaths from water-borne diseases, making them the cause of disease and death around the world. Most of these deaths are young children, about 4000 children a day. Through the year from 2013/2014, water-borne diseases caused 289 illnesses, 108 hospitalizations and 17 deaths in the United States [7].

For that available drinking water must meet drinking water quality standards and does not pose any health risk over a life time [1]. Tap water and also potable water is drinking water that is provided for home use. It is clean and safe to drink or to use in food preparation and others [2]. Therefore available drinking water must meet drinking water quality standards and does not pose any health risk over a life time. Tap water and also potable water is drinking water that is provided for home use. It is clean and safe to drink or to use in food preparation and others [3].

So, the highest priority and goal that all countries seek with the world health organization (WHO) by adopting standards and laws to keep water safe and clean to prevent the spread of the disease as water-borne diseases are the leading cause of death worldwide [9]. In the current review an endeavor has been made to recognize the water pollution based on biological (parasitic) indicator and categorize the drinking water parasites contaminants. A brief discussion on water pollutants, *Cryptosporidium* and *Giardia*, and their impact on environment and human health in Saudi Arabia.

2. Drinking water resources

The sources of drinking water available to the population are diverse and include; water supply network, surface water such as (lakes, rivers, streams, glaciers), groundwater sources (springs or wells) or precipitation (rain, snow) [1]. Springs are often used as sources for bottled waters [10]. Tap water, delivered by domestic water systems refers to water piped to homes and delivered to a tap or spigot. To ensure the safe consumption of any water source, it must receive appropriate treatment and be subject to drinking water quality standards [11]. Water quality is generally assessed by several aspects that affect its quality including; microbiological, physical, chemical (inorganic chemicals, organic compounds) and radiological characteristics and the effect of these characteristics on public health. Detailed water analyses should be carried out to ensure that drinking water should be clear, free from offensive taste or smell, free from chemicals or compounds contaminations that may have adverse effects on health or harmful in long term and free from pathogenic organisms. Most of the serious problems in drinking water especially in developing countries are mainly due to microbiological and chemical contaminations and microbial quality is usually the most important especially pathogenic parasitic contaminants [1].

Saudi Arabia lies in an arid area of the world with severe climatic conditions and an absence of permanent natural water resources such as lakes and rivers. So, one of the main challenges in Saudi Arabia is water scarcity. In order to overcome water scarcity, the Saudi Arabian Government (SAG) is taking drastic measures in revamping its water policies to address Saudi's critical water challenges, substantial investments have been undertaken in seawater desalination, water distribution, sewerage and wastewater treatment. Water is obtained from four distinct sources; non-renewable groundwater from the deep fossil aquifers, desalinated water, surface water and renewable groundwater from shallow alluvial aquifers

Only the last two sources are renewable. Their volume, however, is minimal. Desalinated water is prevalent along the coasts, surface water in the southwest region and groundwater elsewhere. So, about 50% of drinking water comes from desalination plants, 40% from the mining of non-renewable groundwater and only 10% from surface water in the mountainous southwest of the country [12].

3. Parasitic Contamination of Drinking Water

Protozoan parasites were the most frequently identified etiologic agents in waterborne disease outbreak. The waterborne parasites: *Giardia lamblia, Naegleria fowleri, Acanthamoeba* spp., *Entamoeba histolytica, Cryptosporidium parvum, Blastocystis hominis, Toxoplasma gondii, Fasciola* spp., *Schistosoma* spp., *Balantidium coli, Cyclospora cayetanesis, Dracunculus medinensis, Isospora belli,* and *Microsporidia* spp. are cosmopolitan parasites. The waterborne transmission of all these parasites is possible. Surface water supplies used for drinking water are potential sources of contamination [1, 3]. *Giardia lamblia* and *Cryptosporidium* spp. have received great attention in worldwide during the last years because they are the etiological agents of waterborne diseases. The life cycles of *Giardia lamblia* and *Cryptosporidium* are described with a special reference to drinking water technologies aimed at removing these parasites [3].

Water-borne diseases are diseases that are transmitted to humans or animals through water, which usually contain a proportion of pathogenic microorganisms. According to the World Health Organization, 1.4% of people who have suffer from diarrhea caused by contaminated water. Contaminated water (especially groundwater) kills 1.8 million people every year [13]. Most waterborne parasites are transmitted in other ways, such as food and the direct spread from feces to the mouth [14]. According to the definition of the parasite by Centers for Disease Control and Prevention (CDC) [15], is the living organism that lives in or on a host organism and gets its food from or at the expense of its host. There are three types of parasites; one of them is unicellular protozoa that live in intestine, blood or tissue. The second is parasitic worms, such as tapeworms, round worms and finally external parasites like lice and mites.

Drinking contaminated water and eating unclean foods or undercooked meat is one of the most common sources of parasites. Eating these meats can lead to intestinal tapeworms. Drinking contaminated water can lead to scabies, a skin disease. Very strong and contagious, accompanied by severe itching and a rash that looks like pimples [16]. There are many diseases that cause unexplained weight loss, and parasitic infection is one of them. Tapeworms cause weight loss because a large intestinal worm is eating your food, and weight loss is often accompanied by anorexia and upset stomach. The most common symptoms associated with parasites are those that mimic irritable bowel syndrome. Intestinal parasites may cause abdominal pain, bloating, diarrhea, itching, bowel obstruction and anemia. No symptoms may be one of the symptoms. It's frightening, but it's true. Some parasitic infections produce zero symptoms. Experts and doctors recommend a series of blood tests, fecal tests, X-rays, or colonoscopy. Some may be tired but worth it. That parasites cause a very serious disease. Worms can also grow in the human body up to 35 centimeters in length and lead to intestinal obstruction. Humans suffer from a large number of parasites, which cause some of the most important diseases in the world. Therefore, waterborne protozoan pathogens always receive attention because they cause infection and disease in humans and animals. Thus, controlling of waterborne transmission is a real challenge, because it is difficult in some pathogens to remove their eggs, oocysts or cysts by the process of filtration or disinfection due to the fact that it is resistant to the disinfection process [1]. Several species of protozoan pathogens may be transmitted to humans through the drinking water route associated with many health risks. Giardia lamblia and Cryptosporidium spp., transmitted by drinking water in Saudi Arabia (Table 1), and Table 2. Shows the Giardia lamblia and Cryptosporidium spp., cases in Saudi Arabia.

Protozoa	Region / province	References
Giardia lamblia	Tabuk	[17]
	Jeddah and Makka	[18]
	Rafha	[19]
Cryptosporidium spp.,	Tabuk	[17]
	Jeddah and Makka	[18]
	Altaif	[20]
	Rafha	[19]

Table 1 Giardia lamblia and Cryptosporidium spp., transmitted through drinking water in Saudi Arabia.

Protozoa	Region / province	References
Giardia lamblia Dammam and Alkhobar		[20]
	Abha	[21]
	Riyadh	[22]
	Jeddah	[23]
	Makkah	[24, 25, 26]
	Al-Madinah	[27]
	Riyadh	[28]
	Al-Taif	[29]
	Afif	[30]
	Hail	[31]
	Riyadh	[32]
Cryptosporidium spp.,	Dammam and Alkhobar	[20]
	Jeddah	[23]
	Makkah	[24, 25, 26]
	Al-Madinah	[27]
	Riyadh	[28]
	Al-Taif	[29]
	Hail	[31]
	Najran	[33]

Table 2 Giardia lamblia and Cryptosporidium spp., cases in Saudi Arabia.

4. Drinking water quality and standard specifications for drinking water

Since ancient times, there are criteria for drinking water quality when the taste and smell of water change, and the treatment methods were boiling water or exposure to sunlight, filtering through coal to remove suspended substances (coagulation) during the Greek civilization. This was followed by the establishment of the first water supply network in Rome, Greece, Carthage and Egypt during the Roman civilization and a simple progress in treatment by filtering water through cloth [34]. In Scotland in 1804, the first public water facility was built to supply the city with filtered water. Sand filtration was regularly used in Europe.

As a result of scientists' awareness that, diseases could be spread by pathogens in the public water supply [34], and discovery of microorganisms in water. In 1855, epidemiologist Dr. John Snow proved that cholera was a water-borne disease, and both scientists (Louis Pasteur, Joseph Lister and Robert Koch) confirmed the microorganisms transmitted through water [34, 35]. By the beginning of the 20th century, the main concern in water treatment was the elimination of pathogenic microbes using filtration. Disinfectants were used and chlorination became essential for the elimination of pathogenic microbes in water. United States of America was first used chlorine in 1908 as a major disinfectant and at the same time Europeans used ozone in treatment [34].

Resulting in World Health Organization (WHO) has identified several properties that characterize pathogens transmitted by drinking water which are called waterborne pathogens [36]. There are several characteristics to judge water-borne pathogens: 1) Have the ability to grow in the environment—Cause acute and chronic diseases; 2) They often stick to suspended solids in water, and their concentration changes so that the risk of injury cannot be predicted from their average concentration in water; 3) The disease caused by exposure to the pathogens depends on the dose, invasion and virulence of the pathogen, and the immune status of person; 4) Have the ability to reproduce/multiply

inside the host and can reproduce in foods, beverages, drinks or warm water systems, and this increases the risk of infection; 5) Pathogens do not show a cumulative effect unlike many chemical agents.

Consumption of drinking water contaminated with microbes is one of the biggest threats to public health. Due to the health problems facing the world caused by pollution resulting from population activities on the various components of the environment such as air, soil, food and especially water pollution. To ensure the health of the citizen, the World Health Organization (WHO) has been active in issuing and developing water quality standards through its guidance. The first published report of drinking water quality guidelines and testing methods in 1958 and European drinking water standards in 1961. Guidelines for drinking water quality were issued in 1963 by WHO, followed by several guidelines for drinking water quality and development. In 1974, the United States established the US Environmental Protection Agency (EPA), which is responsible for setting drinking water standards as a result of growing concern about waterborne diseases [1, 37]. The drinking water quality guidelines of the World Health Organization (WHO) cover various aspects that cause harm to health, including physical, chemical, biological and radiological aspects. The World Health Organization (WHO) provides guidance to all the international community for use by governments to set their own national standards [35].

Protecting public health is the main objective of the World Health Organization through its guidance that is useful in providing documented basics that are useful in setting national standards for drinking water quality, health risks and impacts associated with drinking water contaminants, best options for managing drinking water and disease prevention and control. International standards drinking-water (1958) is the oldest edition, followed by the second edition in 1963, the WHO did not established guidelines for parasites. WHO recommended guidelines for parasites starting in 1971 with the development of the following editions. In 1998, the WHO did not establish any new guidelines for the parasites. In guidelines for drinking-water quality [1], the WHO established guidelines for the parasites. This edition considered many recommendations according to drinking-water safety including parasites hazards, which continue to be the important concern in both developing and developed countries. The following table shows the developing of drinking water standards for parasites according to WHO guidelines (Table 3), and Table 4. Shows the available guidelines according to parasitic standards adopted in some countries.

WHO/year	Guideline	Reference
1970	Water circulating in the distribution system, whether treated or not, should not contain any organism that may be of faecal origin.	[38]
1971	Water circulating in the distribution system, whether treated or not, should not contain any organism that may be of faecal origin.	[39]
1984	Drinking water should not contain any pathogenic intestinal protozoa.	[40]
1985	Drinking water should not contain any microorganisms known to be pathogenic, Helminthes should be absent from drinking water.	[41]
1993	It is not possible to set guideline values for pathogenic protozoa, helminthes, and free-living organisms, other than that these agents should not be present in drinking-water.	[42]
1996	It is not possible to set guideline values for pathogenic protozoa, helminthes, and free-living organisms, other than that these agents should not be present in drinking-water.	[43]
1997	Drinking water should not contain any microorganisms known to be pathogenic, helminthes should be absent from drinking water.	[44]
2004	The infective stages of many helminthes, such as parasitic roundworms and flatworms should be absent from drinking-water.	[45]
2008	The infective stages of many helminthes, such as parasitic roundworms and flatworms should be absent from drinking water.	[46]
2018	Drinking-water "shall be free from any micro-organisms and parasites which, in numbers or concentrations, constitute a potential danger to human health.	[47]

Table 3 WHO drinking water guideline according to parasitic standards

Country	Guideline	Reference	
Saudi Arabia	Drinking water should be free from any pathogenic protozoa. There is no acceptable value for <i>Cryptosporidium</i> in drinking water.		
Jordan	Drinking water should be free of all phases of pathogenic primary organisms (protozoa), and pathogenic intestinal worms. Free living organisms (nematode): No stage of nematode should exceed one organism per liter.	[49]	
Oman	Drinking water shall be completely free of parasites and insects, their egg, larvae, sacs or parts.	[50]	
Emirates	Drinking water shall be free at all times from parasites, insects and their eggs, larvae, protozoa including amoeba.	[51]	
Egypt	Protozoa, pathogenic nematodes of all phases must not be detectable when microscopic analysis of samples is conducted.	[52]	
Palestine	Drinking-water should be devoid of pathogenic protozoa and pathogenic nematodes of all phases.	[53]	
Sudan	Pathogenic intestinal protozoa must not be detectable in any 100 ml sample.	[54]	
Syrian Arab Republic	Drinking water should be free from protozoa - worms - mosquito and their phases.	[55]	
Lebanon	Drinking water shall be free from insects, or their eggs, larvae, vesicles or parts of them or primary organisms, including amoeba.	[56]	
Yemen	Drinking water shall be free from insects, or their eggs, larvae, vesicles or parts of them or primary organisms, including amoeba.	[57]	
Qatar	No standard value set for <i>Cryptosporidium</i> but the GSO standard refer to microbes of faecal origin and that they should not be present in the water.	[58]	
Pakistan	Drinking water shall be of such a quality that it will not present a risk to the health of the consumer (absence of pathogenic microorganisms).	[59]	
Kuwait	Drinking water should be completely free from parasites and insects, their eggs, larvae, and primary animals, including amoebas.	[60]	
USA	Maximum contaminant level goal of <i>Cryptosporidium</i> and <i>Giardia lamblia</i> is Zero.	[61]	
Canada	Enteric protozoa: <i>Giardia</i> and <i>Cryptosporidium</i> must be minimum 3 log removal and/or inactivation of cysts and oocysts.	[62]	
Australia	No guideline value is set for <i>Cryptosporidium</i> and <i>Giardia</i> due to the lack of a routine method to identify human infectious strains in drinking water If such a guideline were established; it would be well below 1 organism per liter.	[63]	
UK	Water does not contain any parasite.	[64]	
China	Pathogenic microorganisms should not be contained in the drinking water.	[65]	
European Union	Water intended for human consumption shall be clean if it meets all the following conditions: -it is free from any micro-organisms and parasites and from any substances which, in numbers or concentrations, constitute a potential danger to human health.	[66]	
Japan	Water to be supplied through water supply services must not containing organisms or substances that indicate or are suspected to indicate contamination by pathogenic organisms	[67]	
India	Drinking water shall be free from, parasites <i>.Cryptosporidium</i> and <i>Giardia</i> shall be absent in 10 liters of water when tested.	[68]	
Malaysia	Drinking water must be clear and free from all harmful organisms.	[69]	
East Africa	<i>Cryptosporidium</i> and <i>Giardia</i> should be absent from drinking water.	[70]	

Table 4 Drinking water guideline according to parasitic standards in different countries

5. The Treatment of Drinking Water

Water quality control is a real challenge as water plays an important role in the transmission of parasite pathogens. The application of modern water treatment processes had a major impact on water-transmitted diseases, and these processes provide barriers or lines of defense between the consumer and waterborne disease. This review provides an overview of the drinking water treatment processes. The most common treatment process train for surface water supplies conventional treatment consists of disinfection, coagulation, floculation, sedimentation, filtration, and disinfection [3, 71].

The destruction or prevention of growth of parasite pathogens is essential to control the infectious disease transmission. There are various methods of disinfection and factors affecting the disinfectants. Disinfection is most commonly accomplished by heat, chemicals, filtration, or radiation. Inactivation of parasite pathogens is a gradual process that involves a series of physicochemical and biochemical steps, and the thermal destruction of microorganisms is influenced by several factors that include water, fat, salts, sugars, pH, and other substances. Numerous factors determine the effectiveness of disinfectants such as temperature, pH, dissolved chemical substances, presence of particulate matter, and organic detritus. Halogens-such as chlorine-are the most commonly used disinfectants for treating drinking water. Chloramines are used to disinfect drinking water. Ozone is a powerful oxidizing agent, and the effectiveness of ozone as a disinfectant is not influenced by pH and ammonia. The ultraviolet disinfection is used for water treatment in the pharmaceutical, cosmetic, beverage, and electronic industries in addition to municipal water and wastewater application. Photoreactive dyes and radiations (gamma and high energy radiations) can also be used to inactivate microorganisms either directly, or indirectly; however, a number of factors influence the effectiveness of radiation such as type of organism, composition of the medium, or presence of oxygen [3, 72].

Parasite pathogens produce cysts, oocysts or eggs that are highly resistant to water disinfection and are difficult to remove. The most effective way to remove or inactivation of protozoal cysts and oocysts is filtration with coagulation and flocculation followed by disinfectants [1]. Filtration acts as a stable and effective barrier for parasite pathogens. Rapid filtration does not effectively remove parasite pathogens while slow sand filters can be very effective in removing parasite pathogens contamination from water. However, diatom filtration has been shown to be more effective in reducing the concentration of *Cryptosporidium* oocytes and *Giardia* [73]. However, [74] did not ensure that filtered water was free of water-related protozoa. Therefore, high levels of disinfection or more effective disinfection procedures were necessary to protect humans from waterborne protozoa such as *Cryptosporidium* and *Giardia* [75].

Following filtration a disinfectant needs to be added to the water, and the ideal disinfectant must meet the following requirements: Effective in removing pathogens, produce a disinfectant residual, do not produce unwanted products, can be easily, safe to handle and suitable for large scale use and be cost-effective. Not all disinfectants currently meet all these requirements. Chlorine remains the main chemical used for this purpose worldwide. It is a powerful disinfectant and effective in short contact times as well as easy to apply. Nevertheless, it has several disadvantages: ineffectiveness against protozoa, loss of effectiveness [76]. Jarroll et al. [77] determined that *Giardia* cysts had been relatively resistant to chlorine inactivation. *Cryptosporidium* is one of the most resistant microorganisms in the water. Chlorine dioxide is an effective disinfectant against *Giardia* and *Cryptosporidium* (about 90% inactivation of cysts and oocysts) [78]. Ozonization and ultraviolet disinfection are used as additional methods of disinfection. When used in combination with chlorination, they increase its efficiency and reduce the number of chlorine-containing reagents added [79].

It is important to consider adequate water treatment is required because of the low infectious dose for *Giardia*, the wide-spread prevalence of infection in humans and a variety of animals, and the resistance of *Giardia* cysts to environmental conditions and water disinfectants. Studies demonstrate that *Giardia* cysts can be effectively removed or inactivated by commonly used water filtration technologies and most disinfectants. Both disinfection and filtration are recommended to effectively protect against the waterborne transmission of *Giardia*. Filtration can make disinfection effective by reducing cyst levels, disinfectant demand, and particles that may interfere with disinfection effectiveness. A combination of water filtration and disinfection operated under optimum conditions can protect against waterborne transmission of giardiasis. If water sources are also subject to contamination with *Cryptosporidium*, it should be remembered that disinfection levels used to inactivate *Giardia* cysts may not be sufficient to inactivate *Cryptosporidium* oocysts [80].

Unfiltered water systems caused the majority of waterborne giardiasis outbreaks have occurred in , emphasizing the need for water filtration to reduce waterborne risks. The filtration technologies most frequently used to remove microbial contaminants and particles that cause turbidity are: conventional filtration, direct filtration, slow-sand filtration, diatomaceous earth (DE) filtration, and membrane filtration. Conventional and direct filtration, when operated under appropriate coagulation conditions, can remove 3 to 4 log10 (99.9% to 99.99%) of *Giardia* cysts [80].

6. Conclusion

Access to safe drinking water is a fundamental human right. There is a need for safe drinking water to preserve life, maintain public health and reduce diseases. More than 80% of diseases are caused by contaminated drinking water, so, a large number of the population is at risk of water pollution, and for this, guidelines and standards for drinking water quality have been developed to ensure that people have access to safe drinking water. Major waterborne cryptosporidiosis and giardiasis outbreaks associated with contaminated drinking water have been linked to evidence of suboptimal treatment. *Cryptosporidium parvum* oocysts are particularly more resistant than *Giardia lamblia* cysts to remove and inactivation by conventional water treatment. Nowadays, the relationship between environmental conditions and actions of organisms is being researched and becoming clearer. More research on the relationship of water, environment, and health is needed. Results of such research can help us understand the relationship and take measures of protection before the point of no return. The light was shed on the importance of drinking water quality and its free of pathogenic parasites were preserved to preserve public health, especially, *Cryptosporidium* spp., and *Giardia* spp., are important intestinal protozoa of humans, livestock, and wild animals worldwide, resulting in diarrhea which can be fatal and threatening human health worldwide.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflict of interest

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