

Epidemiology, Public Health Impact and Control Methods of the Most Neglected Parasite Diseases in Ethiopia: A Review

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Abstract: Toxoplasmosis, leishmaniasis and hydatidosis are the most neglected, an important public health problem and of economic importance, affecting largely the poorest of the poor, mainly in developing countries. Toxoplasmosis is a problematic zoonosis, particularly in vulnerable groups such as pregnant women and immunodeficient patients. *Toxoplasma gondii* was first isolated in the early 1900s from an African rodent (i.e. *Ctenodactylus gundi*). *Toxoplasma gondii* is an obligate intracellular protozoan parasite, infecting humans and almost all warm-blooded animals. Toxoplasmosis is the most common disease complication, next to tuberculosis, among HIV seropositive admissions and deaths in Ethiopia. Leishmaniasis is a major vector-borne disease caused by obligate intramacrophage protozoa of the genus *Leishmania* and transmitted by the bite of phlebotomine female sand flies. Currently, leishmaniasis shows a wider geographic distribution and increased global incidence. Environmental, demographic and human behaviors contribute to the changing landscape for zoonotic cutaneous and visceral leishmaniasis. The primary reservoir hosts of *Leishmania* are sylvatic mammals such as forest rodents, hyraxes and wild canids and dogs are the most important species among domesticated animals in the epidemiology. HIV/AIDS co-infection in the north-western, visceral leishmaniasis focus in Ethiopia has the highest known HIV co-infection rate in the world. Hydatidosis is a major parasitic disease caused by the larval stage of the dog tapeworm *Echinococcus granulosus* and is characterized by the formation of single or multiple cysts (hydatid cysts) varying in size. Dogs are particularly important in zoonotic transmission due to their close relationships with humans. Ethiopia has been noted for a high prevalence of hydatid disease since 1970s during which it was reported that the disease occurs in all parts of the country. Likewise, studies conducted recently in abattoirs of various locations have indicated that hydatidosis is widespread in Ethiopia with great economic and public health significance. Therefore, it is highly imperative public health education to build up public awareness about the sources of infection, control and prevention method for overcoming neglected tropical diseases.

Key words: Ethiopia · Hydatidosis · Leishmaniasis · Neglected · Toxoplasmosis

INTRODUCTION

Toxoplasma gondii is an obligate intracellular protozoan parasite, infecting humans and almost all warm-blooded animals and causing serious zoonotic toxoplasmosis, with a worldwide distribution [1]. While only felidae can act as definitive hosts shedding oocysts, almost all warm-blooded animals can serve as intermediate hosts and harbour tissue cysts in brain or muscles [2]. *Toxoplasma gondii* is one of the most well studied parasites because of its medical and veterinary importance and its suitability as a model for cell biology and

molecular studies with a unicellular organism [3]. Toxoplasmosis is a problematic zoonosis, particularly in vulnerable groups such as pregnant women and immunodeficient patients. *T. gondii* was first isolated in the early 1900s from an African rodent (i.e. *Ctenodactylus gundi*) from which the species name was derived [4, 5]. Major routes of transmission are different in human populations and depend on social culture, eating habits and/or environmental factors [6].

Humans and other animals become infected with *T. gondii* mostly by ingesting undercooked meat of infected animals or by ingesting food or water

contaminated with oocysts [3]. Cats are essential in the life-cycle of *T. gondii* because they are the only hosts that can excrete the environmentally resistant oocysts in nature. The prevalence of *T. gondii* antibodies varies with age, life style of the cat (stray vs. pet), the serological test utilized, the screening dilution and other undefined factors. In general, infection in cats increases with age and the prevalence is higher in stray cats. Infected cats can shed millions of oocysts in a matter of a few days and after sporulation oocysts can survive in the environment for months or even years depending on the moisture and ambient temperature [7].

Humans Can Become Infected Through Three Routes:

(i) uptake of sporulated oocysts from the environment, (ii) consumption of raw or undercooked meat containing tissue cysts and (iii) pre-natal infection [2]. Transmission takes place mainly by ingestion of raw or undercooked meat that contains parasite cysts or by ingestion of oocysts excreted in cat faeces, which can contaminate water and raw vegetables [8].

Diagnosis of toxoplasmosis is performed by isolation of the parasite from patients and more commonly by serological tests. Techniques such as histology, immunohistochemistry, bioassays and polymerase chain reaction (PCR) can be utilized to detect *T. gondii* organisms in tissue samples. While, serological techniques such as the Sabin-Feldman dye test, modified agglutination test (MAT), enzyme-linked immunosorbent assay (ELISA), indirect fluorescent antibody test (IFAT) and immunoblotting can be used to detect *T. gondii* specific antibodies [3].

Disease Status in Ethiopia: There are no reports of clinical toxoplasmosis in animals. Serological surveys indicated a high prevalence of *T. gondii* antibodies in sheep and goats, although these surveys are more than a decade old. Seroprevalence in cattle was low [7]. To our knowledge, there is no report of isolation of viable *T. gondii* from animals (or humans) in Ethiopia. The prevalence recorded in sheep is 54.7% and 26.7% in goats in Nazireth [9]. Recently high percentage of infection was 58.3 in goats at Ambo, Ada'a-Liben and Fentale districts of Central Ethiopia and provided risk in raw meat and milk consumers of the districts [10].

In Humans: The prevalence of *Toxoplasma* and the relative contribution of the various routes of transmission in humans in Ethiopia have not been adequately studied although 80% prevalence of *Toxoplasma* infection has

been reported in different risk groups. Although latent *Toxoplasma* infection has great importance among HIV infected people, it has been poorly studied [11, 12]. Based on a conservative *T. gondii* seroprevalence of 50%, thousands might die of concurrent opportunistic infections, including toxoplasmosis. However, exact figures are not available and most serological surveys are not current [7]. Much medical attention is being focused on the acquired immune deficiency syndrome (AIDS) epidemic in Africa. Ethiopia is the second-most populous nation in the horn of Africa, with over 82 million inhabitants and a high rate of AIDS. The prevalence of latent *Toxoplasma* infection was 93.3% (154/165) among HIV positive and 86.7% (143/165) among HIV negative participants [12].

Control and Prevention: The seroprevalence of latent *T. gondii* infection is high and similar by HIV status. Educating people to prevent acquisition of new *Toxoplasma* infection and minimizing the risk of disease manifestations among HIV-*Toxoplasma* co-infected individuals is important. Two circumstances facilitate human postnatal *Toxoplasma* infection: the ingestion of bradyzoites in infected undercooked meat and the ingestion of oocysts via hands or food contaminated with the feces of infected cats. Hence, the control of human toxoplasmosis consists of avoiding these circumstances. Although the measures apply to everyone, pregnant women and immunodeficient individuals merit special attention, the former because of the possibility of congenital infection and the latter because of the risk of developing a severe case. Sanitary education should be directed particularly toward high-risk populations and it should focus on teaching people to avoid eating raw or undercooked meat and, in the case of food handlers, to prevent their hands from becoming contaminated [13].

Populations at risk should also be taught to prevent infection from oocysts. People who keep cats in their homes, especially young animals that are just beginning to hunt, should dispose of the cat's fecal matter daily and rinse out the receptacles for the feces with boiling water, thus eliminating the oocysts before they have a chance to sporulated and become infective. These cats should be kept indoors and fed canned, cooked, or previously frozen food to keep them from hunting and catching infected rodents and birds and thus becoming infected [13,14]. Good hygiene is important in preventing infections. Kitchen items should be washed with hot soapy water after they have contacted raw meats, raw seafood or unwashed fruits and vegetables. Hands should be

washed after contact with raw meat, soil or sand and before eating or touching the face. Pregnant women and others at risk should wear gloves when gardening and during other soil or sand contact [3].

Litter boxes should be cleaned daily to reduce the risk of oocyst sporulation and rinsed with boiling water. Pregnant women should avoid cleaning the litter box; if this is unavoidable, they should use gloves then wash their hands [14]. Pet cats should be fed only dry, canned, or cooked food. The cat litter should be emptied every day (to prevent sporulation of oocysts), preferably not by a pregnant woman. Gloves should be worn while gardening, while changing cat litter and while handling soil potentially contaminated with cat feces. To prevent foodborne transmission of *Toxoplasma* to humans, meat and other edible parts of animals should not be consumed raw or undercooked, i.e. they should be cooked thoroughly (at 67°C or higher) before consumption. Although freezing alone is not a reliable means of rendering all tissue cysts non-infective, deep-freezing meat (-12°C or lower) before cooking can reduce the risk of infection. In addition, meat should not be tasted during preparation or cooking [3].

Leishmaniasis: Leishmaniasis is a major vector-borne metazoanosis disease, caused by obligate intramacrophage protozoa of the genus *Leishmania* [15]. The parasite is of great medical and veterinary public health significance; it infects numerous mammal species including humans. Leishmaniasis is transmitted by the bite of phlebotomine female sand flies of the genera *Phlebotomus* and *Lutzomyia*, in the old and new worlds respectively [16]. The species are widespread on all continents except Antarctica. Leishmaniasis is still one of the world's most neglected diseases affecting largely the poorest of the poor, mainly in developing countries; 350 million people are considered at risk of contracting leishmaniasis and some 2 million new cases occur yearly in 88 countries.

The primary reservoir hosts of *Leishmania* species are sylvatic mammals such as forest rodents, hyraxes and wild canids and among domesticated animals; dogs are the most important species in the epidemiology of this disease. In addition to becoming ill, dogs are reservoir hosts for *L. infantum*, one of the two most important organisms in human visceral leishmaniasis [18]. Currently, leishmaniasis has a wider geographical distribution pattern than before and it is considered to be a growing public health concern for several countries. The increase in leishmaniasis worldwide incidence is mainly attributed

to the increase of several risk factors that are clearly manmade and include massive migration, deforestation, urbanization, immunosuppression, the environment, as well as the population movements, may lead to alterations in the range and density of the vectors and reservoirs and consequently, may increase human exposure to infected sand flies [15]. In Ethiopia, the disease affects people living in a significant portion of the country. Recurrent epidemics of visceral leishmaniasis have occurred in Metema and Humera. Following agricultural development in the region, a large number of labor migrants from the highlands were moved to the endemic areas in the late 1970 for crop harvesting. This led to outbreaks of VL, which resulted in high morbidity and mortality [19].

Leishmaniasis is one of the opportunistic infections that attack HIV-infected individuals. Most of the co-infection involves the visceral form. Recently, more notice has been taken of *Leishmania*/ HIV co-infection. Visceral leishmaniasis has a mortality rate as high as 100%, if left untreated and is spreading in several areas of the world due to increase number of AIDS victims. *Leishmania* and HIV co-infections have been reported in 35 out of 88 countries, in which leishmaniasis are endemic [20](Ter Horst *et al.*, 2008). In Africa, particularly Ethiopia and Sudan and Southern Europe, HIV Leishmania co-infection is regarded as emerging disease and as many as 70% adults with VL also have HIV infection [21]. HIV/AIDS co-infection in the north-western VL focus in Ethiopia has the highest known VL/HIV co-infection rate in the world. Approximately, 30% of VL patients are estimated to have HIV [20].

Disease Status in Ethiopia: Economic impact of the disease in Ethiopia is not only limited to high cost of treatment, but also time lost during hospitalization. The disease affects the rural poor community and usually outbreak occurs during harvesting seasons [22]. The MoH estimates the annual burden of VL to be between 4,500 and 5,000 cases. While there is currently no reliable estimate of the prevalence of CL, it has been estimated that the number of CL cases significantly exceeds that of VL (Federal Ministry of Health (FMoH) Ethiopia [23]. Several studies have definitively demonstrated that VL occurs in north western Ethiopia (Humera and Metema), Segen and Woito valleys in Gemu Gofa. Sporadic cases of VL have been diagnosed from Wolkayit Tsegede, Gibdo, Raya, Kobo, Kijawa (Gambella) and Gelana (Sidamo) and Genale (Bale) river basins. Recently, a devastating epidemic occurred in Humera with an estimated annual incidence of 1,500-2,000 cases. Due to high mortality,

occurrence of epidemics and high incidence of the disease in 15-45 age groups, leishmaniasis has become one of the leading health problems in Ethiopia [24].

The north-western VL focus in Ethiopia covers the Semi-arid Metema and Humera plains in Tigray and Amhara regional states bordering Sudan. A marked increase occurred during the 1970s, when migrants from the non-endemic highlands began to arrive in the area to harvest crops on the large-scale agricultural schemes introduced at the time. In 2005, an outbreak of VL in Libo Kemkem woreda, a highland area of Amhara regional state, was identified. By 2007, around 2,450 primary cases and 120 deaths had been reported, since the outbreak began in 2003 [22]. The north-western VL focus in Ethiopia has the highest known VL/HIV co-infection rate in the world. Approximately, 30% of VL patients are estimated to have HIV [21]. The south west foci include the Omo plains, Aba Roba plains and Weyto River Valley in Southern Nations and Nationalities People's Region—all areas of lowland savannah with low rainfall. The lower Omo plains are the oldest known VL focus in Ethiopia. The other main focus in the southwest occurs in the lower course of the Rift Valley, most notably, the Segen (Aba Roba focus) and Weyto valleys in the drainage basin of the Chew Bahir Lake, near Konso woreda. The Aba Roba focus has a particularly high VL endemicity and high population immunity, with 36.4% testing positive with the leishmanin skin test [24].

Cutaneous leishmaniasis occurs in highlands of Ethiopia. Transmission occurs in Cuttaber (Dessie), Aleku (Wellega) and Ochollo (Gemu Gofa). In Ochollo, the overall prevalence of localized CL was 3.6-4.0%, with a peak value of 8.55 in the 0-10 years old age group. Sporadic cases of CL have been diagnosed from many localities in the northern, central and southern high lands of Ethiopia. CL transmission in Ethiopia is zoonotic, with the rock hyrax acting as the main reservoir [19]. Cutaneous form has been extensively studied in the western highlands and lake areas of the Rift Valley. The main areas of transmission include the Ochollo focus in the Rift Valley escarpment above Lake Abaya, the Kutaber area in the eastern Ethiopian plateau near Dessie, the Aleku area of Wollega zone, the south-west highlands of Bale and Sidamo and the Sebeta area near Addis Ababa [25].

Control strategies and prevention measures: Since antileishmanial vaccines are still being developed, the current control strategies for leishmaniasis rely on case management (case detection and treatment), vector and reservoir control. Attention has been mainly focused on

prevention strategies of visceral leishmaniasis, the form with the highest fatality rate. Nevertheless, prevention strategies should be also considered for cutaneous leishmaniasis, which is also a major burden for certain areas, with serious psychosocial effects. The integrated analysis of parasite genetics, parasite virulence factors, host immune responses, host genetics, as well as socioeconomic and environmental risk factors, will provide a better understanding of the interplay between these different factors and the risk of developing the disease [26].

Control of reservoir hosts: On the other hand, new tools have been developed for the surveillance and control of zoonotic VL, based on the control of the canine domestic reservoir. Culling of infected dogs is not considered an acceptable measure, both for ethical reasons and the low impact of this measure in situations of permanent transmission [15]. Active case detection, surveillance and effective treatment, accompanied by measures for preventing reinfection, depending on the coverage achieved, should reduce or eliminate the parasite load and reduce transmission. The elimination of stray and feral dogs is justified for many reasons connected with health, the environment and conservation. Before control activities begin, the distribution and frequency of the infection in dogs should be determined [27]. Control of hyraxes around villages may reduce the transmission of East African cutaneous leishmaniasis caused by *L. aethiopica*. Elimination of hyraxes within 1km of settlements is thought to be effective in reducing transmission [28].

The aim of a vector control program is to reduce or interrupt transmission of disease. An effective strategy for reducing human leishmaniasis is to control sand fly vectors, especially in domestic and per domestic transmission habitats. A number of control methods are available, including chemicals, environmental management and personal protection. Health education is a core element in implementation of any disease prevention and control programme. Multidisciplinary working groups should be established [27].

Echinococcosis /Hydatidosis: Echinococcosis/hydatidosis is a zoonotic disease that occurs throughout the world and causes considerable economic losses and public health problems in many countries [29]. The disease caused by *Echinococcus granulosus*, cystic echinococcosis and is one of the neglected zoonotic diseases recognized. It represents a significant global human disease burden in resource poor pastoral

communities [30]. This multi host parasite is prevalent all over the world and annually, the economic loss in livestock due to this parasite is significant [31]. Hydatidosis or larval *Echinococcus* is defined as the cystic stage of *Echinococcus*, a very small tapeworm of dogs and canids. At its intermediate stage, it forms cysts in the internal organs, especially in liver and lungs and some infections can be fatal in humans if the cyst ruptures and causes anaphylactic shock [32, 33].

E. granulosus and *E. multilocularis* are the most important members of the genus in respect of their economic loss, public health significance and their geographical distribution. Approximately 60 to 70% of *E. granulosus* cysts occur in the liver and 20 to 25% in the lungs. The remaining cysts can be found almost anywhere in the body including the bones, kidneys, spleen, muscles, central nervous system (CNS) and behind the eye [33]. The definitive host is infected by ingestion of offal containing fertile cysts and the intermediate hosts are infected by ingesting contaminated feeds and water with dog feces contains egg of the parasite [13, 34].

Different studies have shown that cystic echinococcosis (*E. granulosus*) represented considerable economic and public health significance in different countries [35, 36]. Present estimates suggest that cystic hydatid disease, caused by *E. granulosus*, results in the loss of 1 to 3 million disability-adjusted life years per annum. The annual cost of treating cases and economic losses to the livestock industry probably amounts to 2 billion US\$. Alveolar echinococcosis caused by *E. multilocularis*, results in the loss of about 650,000 disability adjusted life years per year as reported by WHO [30]. Echinococcosis causes collateral economic damages to the poor rural farmers because it affects livestock. This occurs as result of condemnations of the affected organs such as the liver. Echinococcosis also leads to poor animal health and production, which ultimately leads to economic losses to livestock owners. Infection with *E. granulosus* results into 10% reduction in the life performance of the animal in terms of meat quality, fiber production, milk production and number of surviving offspring.

Echinococcosis has worldwide distribution, but is more important in developing countries where there is poor sanitation and people live in close proximity with each other and animals. CE is endemic in East Africa especially in nomadic pastoral tribes. A close interaction of dogs and human beings can increase the risk of transmission of CE especially where hygiene and sanitary conditions are poor. Echinococcosis is one of the

neglected diseases especially in the developing countries and hence given less attention. Peoples practices, attitudes and knowledge about echinococcosis plays a significant role towards its spread, yet little is known about these in Uganda especially among the pastoral communities [30].

In Africa, hydatid disease is reported more commonly in cattle, which are communally owned or raised on free range and associated more intimately with domestic dogs. Hydatidosis in domestic ruminants inflicts enormous economic damage due to the condemnation of affected organs and lowering of the meat, milk and wool production. In Ethiopia, hydatidosis have been known and documented as early as 1970s. Hydatidosis is the major cause of organ condemnation in most Ethiopian abattoirs and leads huge economic losses [37, 38].

Certain deeply rooted traditional activities could be commonly described as factors substantiating the spread and high prevalence rates of the disease. These include the wide spread back yard animals slaughter practice, the absence of rigorous meat inspection procedure and the long standing habit of most Ethiopian people to feed their dogs with condemned offal which in effect facilitate the maintenance of the perfect life cycle of *Echinococcus* [36]. Despite the large efforts that have been put into the research and control of echinococcosis, it still remains a disease of worldwide significance. In some areas of the world, cystic echinococcosis caused by *E. granulosus* is a re-emerging disease in places where it was at low levels [33].

Disease Status in Ethiopia: Ethiopia has a high prevalence of hydatid disease since 1970s and was reported in all parts of the country. However, the situation of cystic echinococcosis in humans is not well documented and explored so far in the country. Clinical and serologic tests conducted among the Dassanetch and Nyangatom pastoralist tribes of the southern western part of the country revealed the prevalence of 4.8% palpable abdominal cysts, 15% hepatomegally and 31.7% positive hydatid skin test. A prevalence of 0.5% - 0.7% in Hamar pastoralist tribes of southwest Ethiopia and 1.8% in Borana [39, 40] and 1.6% have been reported in southern parts of Ethiopia [41]. A mean annual incidence rate of approximately 2.3 cases per 100 000 per year was also reported in Bahir Dar by Kebede *et al.* [42] in 4 year retrospective study. In another retrospective study by Kebede *et al.* [36], of the six zonal hospitals in Tigray region diagnoses of 8 cases of human hydatidosis since 2008 were reported. Three cases of cerebral hydatidosis

were also reported by Aseffa *et al.* [43]. From 1995 to 2005, 234 patients and 137 patients seen with hepatic hydatidosis from 1994 to 2006 at Tikur Anbessa Hospital were operated for hydatid disease at Tikur Anbessa hospital in Addis Ababa [44, 45]. Very few retrospective and case reports of cystic human hydatidosis also indicated the relevance of the disease in the human population of the country.

Likewise, studies conducted recently in abattoirs of various locations have indicated that hydatidosis is widespread in Ethiopia with great economic and public health significance [38]. CE was also reported in humans from the different regions of Ethiopia; northern, central and southern parts of the country [36]. Most of the studies of hydatidosis in Ethiopia were done on cattle, sheep and goats. Despite the large efforts that have been put into the research and control, it still remains a disease of worldwide significance. It remains persistent and re-emerging problem in countries of low economic status where a resource for an intensive control program is limited [46].

Control and prevention: Cystic hydatidosis continues to be a substantial cause of morbidity and mortality in many parts of the world. Elimination is difficult to obtain and it is estimated that using current control options and achieving such a goal will take around 20 years of sustained efforts [47].

Veterinary public health is listed out strategies for overcoming neglected tropical diseases in the report entitled working to overcome the global impact of neglected tropical diseases launched by WHO [30]. This neglected tropical diseases report which was well received by the public health and donor communities that provides technical information on these diseases. Annual surveillance of infection rates in dogs, livestock and humans is critical for establishing a pre-intervention baseline and assessing the efficacy of control programmes [30].

At present, conventional control measures consist of educating the rural population and its control; centralizing the slaughtering of animals for food in units with veterinary control; ensuring sanitary conditions for slaughtering done on ranches and preventing dogs' access to raw viscera; reducing the number of dogs on the ranches and treating them for *Echinococcus* on a regular basis. Recently, joint and coordinated implementations of these health measures, both medical and veterinary have resulted in noteworthy improvement in the results of the control campaigns [13, 32].

Supervised treatment of owned dogs four to eight times a year with praziquantel is the single most important intervention. Dog registration must be handled sensibly. Imposing a fee is likely to discourage registration and increase the number of free-roaming dogs without a responsible owner. Use of inhumane methods for dog elimination may elicit opposition from communities to the entire control programme. Dog reproduction control and other measures for reducing the carrying capacity of the environment for dogs, such as eliminating food and water sources, are viable sustainable alternatives to dog elimination [30].

Avoiding close contact with dogs that may carry the eggs of the parasite on their tongues or coats and avoiding ingestion of raw vegetables and water that may have been contaminated with the feces of infected dogs [13]. All fruits and vegetables, particularly those picked in the wild should be washed thoroughly to remove any eggs. Fences should be placed around vegetable gardens to keep animals, especially dogs and other canids. The hands should always be washed after handling pets, farming, gardening or preparing food and before eating. Untreated water from sources such as lakes may also contain *Echinococcus* eggs and should be avoided. Regular surveillance with serological tests can be helpful in high-risk populations such as laboratory personnel working with eggs, or children who have been exposed to the feces of infected dogs [33].

Health education can increase participation and maintain the continuity of long-term control, especially in the consolidation phase. Health education is a basic component of any programme for control of *E. granulosus* and should be closely linked to and co-ordinated with all phases of the campaign. Health education requires the motivation and participation of various population groups. Educational programmes at schools and personal visits of dog owners, farmers and other involved groups are of special significance. Continuing evaluation of the impact and the limitations should be undertaken and modifications should be made as and when indicated [32].

One of the latest developments in control attempts is immunization or formulation of vaccines for intermediate hosts. A recombinant antigen vaccine designated as EG95 has been developed. Trials carried out in sheep in Australian and Argentina has shown that the vaccine confers high degree of (96-100%) protection against different isolates of *E. granulosus* [32]. However, the vaccine has no effect on cysts and many of the older livestock already infected will remain a source of infection for dogs and the dogs will continue to infect humans [48].

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