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Review on Trypanosomiasis: Epidemiology, Diagnosis, Control and Prevention

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Abstract

Trypanosomiasis is a protozoan disease of man and animals, causes by trypanosomes, affecting cattle, buffaloes, camels, sheep, goats, horses, donkeys, mules, pigs, cats, and dogs throughout the world. Disease animals mostly show clinical signs including intermittent fever, anemia, edema, lacrimation, enlarged lymph nodes, abortion, and decreased fertility, loss of appetite, body condition and productivity, early death in acute forms, emaciation and eventual death in chronic forms often after digestive and/or nervous signs. The epidemiology of African trypanosomosis is determined mainly by the ecology of the tsetse fly, which is found only in tropical Africa.Trypanosoma brucei brucei¸ *T. congolense, T. vivax, T. evansi, T. simiae* are all-infective to animals causing African animal trypanosomosis while *T. brucei gambiense* and *T. brucei rhodesiense* are the only species pathogenic to man in Africa Tsetse flies (Glossina spp.) are biological vectors for the trypanosomes that cause African animal trypanosomiasis and transmit these organisms in their saliva. Five species of Glossina (*G. m. submorsitans, G. pallidipes, G. tachinoi des, G. f. fuscipes,* and *G. longipennis)* have been recorded from Ethiopia. The prevalence and distribution of the disease depend on the itsrisk factors example host factors (Wild animals those used as the reservoir of the disease, Tsetse fly (Glossina) species present used for transmission of disease, domestic animals and human factor) , environmental factors and pathogen factors**.** Control of the disease can be achieved by two ways; typanosomiasis drug and tsetse control. Control of trypanosomosis in the enzootic area involves control of tsetse fly population, prophylactic treatment, and good husbandry of animals at risk and use oftrypano-tolerant animals. The current initiatives like progressive control pathways, which are stepwise approaches for the reduction, elimination, and eradication of human and animal diseases,are highly recommended.

Keywords: Control, Diagnosis, Epidemiology, Prevention, Trypanosomosis

1. Introduction

Trypanosomiasis is a protozoan disease of man and animals, causes by trypanosomes, affecting cattle, buffaloes, camels, sheep, goats, horses, donkeys, mules, pigs, cats, and dogs throughout the world (Mirshekar *et al*., 2019; Sumbria *et al*., 2014). Trypanosomosis is the primary hemoparasitic condition caused by unicellular protozoan parasites and reproduces in the bloodstream, lymphatic vessels, and tissue, together with cardiac muscles and the central nervous system. It is one of the greatest barriers to animal production in Africa that is likely to

increase the productivity of domestic livestock(Hundessa *et al*., 2021).

The disease is affecting millions of livestock in Africa, the Americas and Asia as well as of humans in Africa and Latin America (Kennedy,2013., Gonzatti *et al*., 2014). Trypanosomoses refer to a group of vector-borne parasitic diseases caused by protozoa of the genus Trypanosoma. Trypanosoma brucei brucei¸ T. congolense, T. vivax, T. evansi, T. simiae are all-infective to animals causing African animal trypanosomosis while T. brucei gambiense and T. brucei rhodesiense are the only species pathogenic to man in Africa. There are over 60 million people in endemic areas all over the world (Karshima *et al*., 2016).

The occurrence and spread of trypanosomiasis in African livestock are determined primarily by the degree of contact between the domestic animal and Glossina, while transmission by other blood sucking Diptera is usually of secondary importance. In turn, the role of tsetse-flies as vectors of 'nagana' is closely related to the source of their food, represented chiefly by wild ungulates a significant proportion of which are symptom less carriers of trypanosome that are pathogenic to domestic stock (Degneh *et al*., 2021).

The direct and indirect agricultural and livestock production annual loss due to trypanosomosis in Ethiopia is estimated at around 200 million USD (FAO, 2010) and the diseaseis still among the most important diseases limiting livestock productivity and agricultural development due to its high prevalence in the most arable and fertile land of Western and South Western part of the country.

The objective of this review is:

- To provide updated information on the livestock trypanosomosis with particular emphasis on the Epidemiology and control of the trypanosomiosis disease in Ethiopia.

2. Literature Review

2.1. Aetiology

Trypanosomes are protozoan parasites in the family Trypanosomatidae. African animal trypanosomiasis is caused by those organisms that are transmitted by tsetse flies but do not ordinarily affect humans. Three most important species are *Trypanosoma congolense* (subgenus Nannomonas*), T. Vivax* (subgenus *Duttonella)* and *T. Brucei* subsp. Brucei (subgenus Trypanozoon). There are three variants of *T. Congolense*, called the savannah, forest and kilifi (or Kenya Coast) types. African animal trypanosomiasis can also be caused by *T. (Nannomonas) simiae, T. (Pycnomonas) suis, T. (Nannomonas) godfreyi* and *T. (Duttonella) uniforme*, and possibly by additional unnamed trypanosomes. Trypanosomes species encountered are *Trypanosoma vivax, T. Congolense, T. Brucei, T. Simiae,* and *T. Evansi*, with the first three being the most widespread in cattle (Njiru *et al*., 2005).

African Animal Trypanosomiasis (AAT) is caused by several trypanosomes species, including *T. Congolense, T. Vivax, T. Godfreyi, T. Simiae*, and *T. Brucei* (Ahmad *et al*., 2016).Three species of trypanosomes are recorded in Ethiopia. These are *T. Congolense, T. Vivax* and *T. Brucei. T. Vivax and T. Congolense* are the main pathogens of cattle. Trypanosomosis outside “tsetse belt” is caused by mechanically biting flies; the main etiological agent of mechanically transmitted trypanosomosis is *T.vivax*. Two related parasites, *T. Brucei subsp. Gambiense* and *T. Brucei rhodesiense*, cause human African trypanosomiasis, which is also known as sleeping sickness. The primary distinction between this disease and African animal trypanosomiasis is that these two organisms can evade the innate resistance humans possess against other tsetse-transmitted African trypanosomes. (Desquesnes and Davila, 2002).

2.2. Transmission and life cycle

Trypanosomiasis is transmitted mechanically by biting insects (tsetse flies and hematophagous flies) and iatrogenic means using the same needle or surgical instrument on more than one animal, at sufficiently short intervals that the blood on the needle or instrument does not dry without properly disinfecting the instruments. It is well known that carnivores may be infected with *T. evansi* and *T. brucei* by ingesting meat or organs from infected animals, as long as these are still sufficiently fresh to contain live trypanosomes.Transmission of *T. evansi* in Latin America by the bites of vampire bats is common.All trypanosome species are occasionally transmitted congenitally, from the mother to the offspring, either through the placenta while the foetus is still in the uterus, or when bleeding occurs during birth. Congenital transmission of *T. Vivax*, for example, has been observed in Latin America as well as in Africa, but its real importance is not well known. Venereal transmission is the normal means by which dourine of equines, caused by *Trypanosoma equiperdum*, is propagated (Desquesnes,2004).

Tsetse flies (Glossina spp.) are biological vectors for the trypanosomes that cause African animal trypanosomiasis and transmit these organisms in their saliva. Trypanosomes must develop for one to a few weeks in the fly before they reach the infective stage. *T. vivax* has the shortest cycle. Trypanosomes can also be transmitted by mechanical vectors including surgical instruments, needles, syringes and other biting flies (CFSPHIICAB, 2018).

The parasite is found in both intra and extravascular fluids of multiple hosts (Alanazi *et al*., 2018). It is transmitted mechanically by *hematophagous* flies (*Tabanus, Chrysops, Atylotus, Lyperosia, Haematopota,* and *Stomoxys*). Trypanosome life cycles can be considered relatively complex and divided into two stages in the tsetse fly and inside the mammalian. Firstly, the life cycle of the Trypanosome inside the mammalian host lifecycle begins when the tsetse fly injects the metacyclic forms into the mammalian host and then starts the adaption phase adapted for life the bloodstream inside a tsetse. The metacyclic form is morphologically characterized, including differentiating and proliferating into long, slender bloodstream forms known as trypomastigote forms (infective form) (Dyer *et al*., 2013) . From the blood, it can enter into different body fluids, such as lymph and cerebrospinal fluid, and can enter the placenta. The parasite will migrate to the organs from the fluids, particularly the brain and central nervous system (CNS). On the other hand, events occurring inside the vector begin when the tsetse fly takes a blood meal, and the parasites are in bloodstream trypomastigote forms, migrate to the midgut. Next, once they arrive in the midgut, trypomastigote forms start to differentiate; via the oesophagus, proboscis, and hypopharynx, they migrate to the salivary gland, where they are able to multiply, and some of them can transform into infectious met acyclic forms (Sharma *et al*., 2009).

2.3. Epidemiology and Tsetse infestationin Ethiopia

Animal trypanosomoses of African origin (ATAO) are known under several disease names that are associated with one or several *Trypanosoma* species involved. “Nagana” is a disease complex caused by one or several Salivarian trypanosomes belonging to subgenera Nan-nomonas *(Trypanosoma congolense, T. simiae* and *T. godfreyi)* Duttonella (*Trypanosoma vivax* and *T. uniforme*; the occurrence of the latter needs to be confirmed) and Trypanozoon (*Trypanosoma brucei brucei, T. brucei gambiense* and *T. brucei rhodesiense*) “Surra” is a disease caused by *T. evansi*, and “Dourine” is caused by Trypanosoma equiperdum (sometimes referred as *T. brucei evansi* and *T. brucei equiperdum*, due to their phylogenetic relations) (Wei *et al*.,2011).

Nagana are mainly cyclically transmitted by flies of the genus Gloss (tsetse flies). Their geographical distribution is determined by the geographical distribution of the tsetse fly, which is restricted to specific areas of Africa. Tsetse flies have been reported to occur in an area

estimated to be 10 million km2 in size, in 37 countries, in humid and sub-humid sub-Saharan part of Africa (from latitude 10° N to 20°–30° S and in some limited areas of the Arabian Peninsula. The epidemiology of African trypanosomosis is determined mainly by the ecology of the tsetse fly which is found only in tropical Africa (Getachew, 1991).

These areas are mainly found in the Southern, Southwestern, and Western parts of the country**.** Many of the areas are the most suitable for livestock and crop production. To date, five species of Glossina (*G. m. submorsitans, G. pallidipes, G. tachinoi des, G. f. fuscipes,* and *G. longipennis)* have been recorded from Ethiopia. The tsetse flies transmit four species of trypanosomes: *Trypanosoma congolense, T. vivax, T. brucei brucei,* and *T. rhodesiense*(Tsegaye *et al*., 2020).

2.3.1. Host factor

Wild animals: Natural hosts for at least 30 species, including greater kudu *(Tragelaphus strepsiceros), warthog (Phacohoerus aethiopicus), bushbuck (Tragelaphus scriptus),* bush pig *(Potamochoerus porcus),* African buffalo *(Syncerus caffer),* African elephant *(Loxodonta africana),* white rhinoceros *(Ceratotherium simum),* black rhinoceros *(Diceros bicornis),* wild Equidae, lion *(Panthera leo*), leopard *(Panthera pardus)* and various rodents, usually show no clinical signs as host and parasite are in equilibrium, eormous reservoir of trypanosomes (Desquesnes , 2004).

Tsetse fly (Glossina): biological vector of 23 species in sub-Saharan Africa between latitudes 14°N and 29°S are competent, but primarily *G. morsitans, G. palpalis and G. fusca* o Grouped according to preferred habitat: savannah, riverine and forest remain infected by trypanosomes for life. Trypanosome life cycle involves cyclical development in the tsetse fly, taking up to three or more weeks depending on trypanosome species and ambient temperature (Desquesnes, 2004)

Domestic animals: incidental hosts; Trypanosomes can infect all domesticated animals; cattle are the most important economically; *T. congolense*: cattle, pigs, goats, sheep, horses, and dogs;*T. vivax*: cattle, horse, sheep, and goats;*T. brucei brucei:* cattle, horses, dogs, cats, camels, sheep, goats, and pigs (Desquesnes, 2004).

Human: Sleeping Sickness caused by*T. brucei gambiense* and *T. brucei rhodesiense* are the only species pathogenic to man in Africa. Trypanosomiasis in humans has been poorly reported over the years, despite affecting an alarming number of persons. A very small number of human infections caused by *T. b. brucei*, *T. vivax* and *T. congolense* have been reported. Two clinical cases of sleeping sickness in people infected with *T. b. brucei* or *T. congolense* were diagnosed by PCR-based confirmation of the organism's identity (OIE, 2018).

The effect of infection varies with the host in that most wild animal and some domestic ones establish a balance with the parasite and remain as clinically normal carriers for long periods. Specifically, some breeds of cattle indigenous to Africa can tolerate light to moderate challenge with tsetse flies by limiting the multiplication of trypanosomes in their blood and by apparently warding off the infection, especially *T. vivax*. This phenomenon is called trypanotolerance, it is both genetic and environmental in origin and the level of tolerance varies. Crossbreeds of indigenous Taurine and Zebu animals are also more tolerant than purebreed zebu. However, due to the uncertain genetic makeup of animals within these so-called breeds and crossbreeds, the level of trypanotolerance may also vary with individual animals within a given category and it can be overcome by heavy tsetse challenge, malnutrition, or other stress factors (Loses, and Ikede, 2002).

2.3.2. Environmental Factors

The density of tsetse population in the area and the level of their contact with the host, will determine the level of infection. Trekking of cattle through tsetse-infested vegetation is a risk nomadic farmer's face from time to time and the risk is even greater where cattle routes converge,

for example, at major bridges or watering holes. Agricultural and industrial developments generally lead to a lowering of tsetse density by destroying its habitat, whereas the establishment of game or forest reserves provides large numbers of preferred hosts or a suitable habitat for tsetse, respectively. Herds located near such reserves are therefore at a higher risk (NTTICC, 2002).

2.3.3. Pathogen Factors

In cattle, *T. vivax* generally produces a higher level of parasitemia than other species. And since, its life cycle in the tsetse is also shorter; *T. vivax* is more readily transmitted than the others when animals are newly introduced into a tsetse infested area. Higher parasitemias also facilitate mechanical transmission. On the other hand, *T. brucei* is rarely detectable by direct examination of cattle blood, even though infection can be confirmed through other diagnostic methods (Rebeski *et al*., 1999).

2.4. Clinical signs

Disease is classically acute or chronic, and is affected by poor nutrition, concurrent diseases, and other stressors. Trypanosomosis in cattle is usually chronic – some may slowly recover but usually relapse when stressed. The most important clinical sign is non-regenerative anaemia, and the most common reason animals are unable to function normally. The major clinical signs are: •intermittent fever , anaemia , oedema, lacrimation , enlarged lymph nodes, abortion, decreased fertility, loss of appetite, body condition and productivity , early death in acute forms ,emaciation and eventual death in chronic forms often after digestive and/or nervous signs When tsetse challenge is high, morbidity are usually also high. All three species of trypanosomes will eventually cause death in their hosts unless treated (OIE, 2018).

2.5. Economic and Zoonotic Importance

Direct losses caused by trypanosomiasis are due to the presence of the disease in livestock populations; They include production and reproduction losses resulting from mortality, morbidity and infertility and the costs of implementing and running trypanosomiasis control operations. Indirect losses are due to the risk of the disease; They include the exclusion of ruminant livestock production from tsetse infested areas, reduced livestock production levels due to restricted grazing, and reduced crop production due to exclusion or limitation of draught power.(Tesfaye *et al.*, 2012., ILRAD, 1993)

Trypanosome transmitted by Tsetse fly continues to be a major constraint in livestock production. It is also a major risk of infection in humans. The disease greatly affects social, economic, and agricultural development of communities in tsetse infested areas (Efa, 2021) . The direct and indirect agricultural and livestock production annual loss due to trypanosomosis in Ethiopia is estimated at around 200 million USD (FAO, 2010; Degneh *et al*., 2021).Based on an estimation of the market price of animals that died due to trypanosomosis, about 1,132 ETB (US$ 102.0) per year per household was lost as a consequence of trypanosomosis-triggered mortalities.About 21.13 ETB (US$ 1.9) was spent on average forone animal (large ruminant) for the treatment of trypanosomosis per annum(Tesfaye *et al.*, 2012).
Human African trypanosomiasis (HAT), or sleeping sickness, is caused by *Trypanosoma bruceigambiense*, which is a chronic form of the disease present in western and central Africa, and by *Trypanosoma brucei rhodesiense*, which is an acute disease located in eastern and southern Africa. The rhodesiense form is a zoonosis, with the occasional infection of humans, but in the gambiense form, the human being is regarded as the main reservoir that plays a key role in the transmission cycle of the disease (Simarro, 2014).
Humans are normally not susceptible to the trypanosomes that cause African animal trypanosomiasis. The trypanolytic activity of apolipoprotein L-I (apoL-I), found in human blood, is thought to be the major innate defense mechanism. Genetic defects in apoL-I have been detected in some people who were infected by trypanosomes not expected to be pathogenic for humans (e.g., *T. evansi*, which causes surra). Partial resistance of *T. vivax* and *T. congolense* to human serum has also beendemonstrated in the

laboratory under certain conditions (CFSPHIICAB, 2018).

2.6. Prevalence of the Trpanosomiasis in Ethiopia

Ethiopia, as part of the sub-Saharan Africa, shares a substantial loss from the disease. At least 10 million cattle, 6.1 million sheep & goats, 1 million camels and 1.2 million equine in the country are under direct exposure to the disease (MoARD, 2004). The following table shows the prevalence trypanosomiasis in some parts of Ethiopia

Table 1:- Prevalence trypanosomiasis in some parts of Ethiopia

Region/area	Zone/woreda	Prevalence	typ	Reference
Ethiopia		*21*	*T.evansi*	Zeleke and Bekell, (2021)
Oromia	Yabello and Gomole	3.19	*T. Congolenses T. vivax*	Oljirra Rafu *et al*., (2019)
Afar	Asayita and Dubti	4.5	*T. evansi*	Bekalu *et al*., (2020)

2.7. Diagnosis

A disease may be diagnosed on the basis of the clinical signs, by demonstration of the causative organism or by reactions to diagnostic tests. In some situations, the clinical manifestations of trypanosomosis, particularly anaemia may provide sufficient grounds for a putative diagnosis. Diagnosis refers to methods for detecting infection, either by identifying the parasites themselves or by interpretation based on the results of other diagnostic tests (Radostitis *et al*., 1994).

Parasitological Diagnosis by Direct Examination such as wet blood film, thick blood smear technique and thin Blood Smear Technique: (OIE, 1982) and Parasitological Diagnosis by Indirect Diagnosis such as the Indirect Enzyme-linked Immunosorbent Assay (ELISA) (Bannain *et al*., 2003)., and Polymerase Chain Reaction (PCR) (Kukla *et al*., 1999).

2.8. Treatment

If detected early, Trypanosomosis can be treated with the trypanocidal drug for therapeutic and prophylactic purposes. Therapeutic drugs include diminazene aceturate, homidium bromide and homidium chloride. Prophylactic drugs for cattle include homidium bromide,homidium chloride and isometamidium (Achenef and Bekle, 2013).

2.9. Control and Prevention

Having established that tsetse/trypanosomiasis problem exists, the question of which strategy to implement depends on technical feasibility, availability of resource and cost effectiveness of different approaches. On the technical sides, the number of animal or human to be treated or protected with drugs etc. will be important. Control method can be divided into 2 main type typanosomiasis drug and tsetse control (Naessens, 2006).

The control of trypanosomosis in enzootic countries involves control of tsetse fly population, prophylactic treatment, and good husbandry of animals at risk and use of trypanotolerant animals. Control of tsetse has been successfully attempted, but re invasion is frequent if the land is not properly utilized. More recent methods involved the use of insecticides applied strategically in the form of ground and aerial spraying over large expanses of land (Getachew, and Eley, 1993).

As tsetses are sensitive to insecticides and no resistance has developed, considerable successes were achieved in some countries. However, spraying insecticides is costly and harmful to the environment. These harmful effects are considerably reduced if the insecticides, for example, synthetic pyrethroids, are applied directly on the animal in the form of spray or pour-on formulation. Other effective methods involve targets impregnated with insecticides and traps that attract and catch tsetse. These are simple and cheap and can be constructed and maintained by local communities. Furthermore, they do not pollute the environment and are suitable for both small- and large-scale fanning (Boulange *et al*., 2002).

Attempts at trypanosomosis control have also been directed to prophylactic dosing with chemicals such as suramin, prothridium and isometamidium. Prophylaxis is used along with other methods in areas where there is a heavy tsetse challenge. The prophylactic effect is supplemented by the development of antibodies and the total period of protection may be as long as 5 months. However, it is customary to give four or five treatments per year (Eisler *et al*., 1998). The productivity response to this pattern of treatment is good if general husbandry is also adequate. The downside of this approach is that it has reportedly led to drug resistance in many countries. In the absence of a vaccine, control methods must combine reduced exposure to the vectors (Large scale tsetse trapping and pour-on applications) with strategic treatment of exposed animals (Chemotherapy and chemoprophylaxis) along with use of trypanotolerant animals when feasible (Radostitis *et al*., 1994).

Another way by which control of tsetse fly populations can be accomplished is via successive mid-air insect repellent spraying to target adult vector. This should be done during the developmental stage of tsetse flies from pupal stages in the ground, the use of insecticides as traps may be of immense help when treating cattle (Auty *et al*., 2012).

Sterile male release techniques is used by sterilization of male by chemicals or gamma radiation is thoroughly studied and defined, this method in Ethiopia performed by NTTICC which released sterile male flies (SIT) 2,076,569 and 1,578,640 in 2018 and 2019 respectively (unpublished report from NTTICC, 2019).

3. Conclusion

Livestock trypanosomosis is still serious challenge and results in economic losses in in the world particularly in Africa and it is justifiable to conclude the trypanosomiasis and its vectors (tsetse) are greatest constraints to livestock production in most areas of the western and sout west part of Ethiopia. In Ethiopia the diseases posing a significant impact on the country's development. In many studies the diagnostic techniques mainly depend on the less sensitive parasitological techniques. Spatial and temporal distribution of the disease has very limited information in the country. The various initiatives to control trypanosomosis have mainly been based on chemotherapy and vector control. Some of the challenges in the process of control of trypanosomosis include failure to produce effective vaccine, trypanocidal drug resistance, poor funding interest for research and development in the area.

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