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Review on Bovine Trypanosomosis in Ethiopia

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Abstarct: Trypanosomosis is one of the most prevalent protozoal diseases of cattle with greatest effects in terms of serious economic loss and pathogenic impact. In Ethiopia bovine trypanomosis is highly prevalent in the low lands of tsetse infested area. This bovine trypanomosis is mainly caused by three etiological agents,T.vivax, T.congolense and T.brucei. Bovine trypanomosis is transmitted from the infected animal to susceptible host both mechanical and biological vector. Bovine trypanomosis is characterized by enlargement of lymph node, chronic emaciation and others. This disease can be diagnosis by clinical sign, direct and indirect parasitological diagnosis. Once the infection of bovine trypanomosis is happened, it can treat by diminazene aceturate, homidium bromide, homidium chloride, isometamidium and quinapyramine sulphate. Bovine trypanomosis can be controlled by early treatment of infected animal, vector control and others. Thus, it is recommended that an appropriate use of antiprotozoal drugs,integrated prevention and control program should be implemented to eradicate trypanomosis and other protozoal disease.

Key words: Cattle · Epidemiology · Ethiopia · Trypanosome · Trypanomosis · Tsetse Fly

INTRODUCTION

In the developing countries, livestock industry plays an important role that constitutes like milk, meat, for cultivation of land and foreign incomes from skin and hides. Increasing the livestock productivity can have significant impact of achieving food security and alleviating poverty in sub-Saharan Africa as it is important assets especially in the rural small holder house hold economy [1]

Ethiopia possesses the largest livestock population in Africa. The country ranked 8th in the world averaging 23 million between 1995 and 2000, 46 million in 2003 and 44 million in 2004 [1].

Trypanosomosis is a protozoan disease of both human and animals caused by different species of the genus Trypanosomes. Trypanosomosis is the single most important livestock disease in Sub-Saharan Africa (SSA) and is present in 37 countries in that region. More than one third of the land (~9 million km2) is infested by tsetse flies [2].

Trypanosomosis is a complex disease of protozoa that is caused by different species of unicellular parasites (Trypanosome) found in the blood and other tissues of vertebrates include livestock, wild life and people [3]. Bovine trypanosome is one of the disease that caused by this flagellated protozoal parasite belong to the genus trypanosome. Trypanosomosis limited the extension of natural herds particularly in Africa were the presence of the tsetse fly density access to woodland and savanna areas with good grazing potential [4].

Tsetse transmitted trypanosomosis is widely distributed in western and southern lowlands and the river valleys cutting into the central highlands of Ethiopia. It is a major constraint to the utilization of large land resources. Prior to the 1960's trypanosomosis had relatively little impact on the economy of Ethiopia. However, much of the country is tsetse free, because it is either north of the main African "Tsetse belts" or too high, hence too cold to support the fly [3].

As of early 1970's the significance of the disease has increased enormously and is increasing. The loss of fertility caused by drought, overpopulation and overstocking of much land in the marginal, high temperature, low rainfall northern regions lead to the resettlement of the affected rural population and their livestock in more potentially productive areas, many of which are tsetse infested. Furthermore the expansion of

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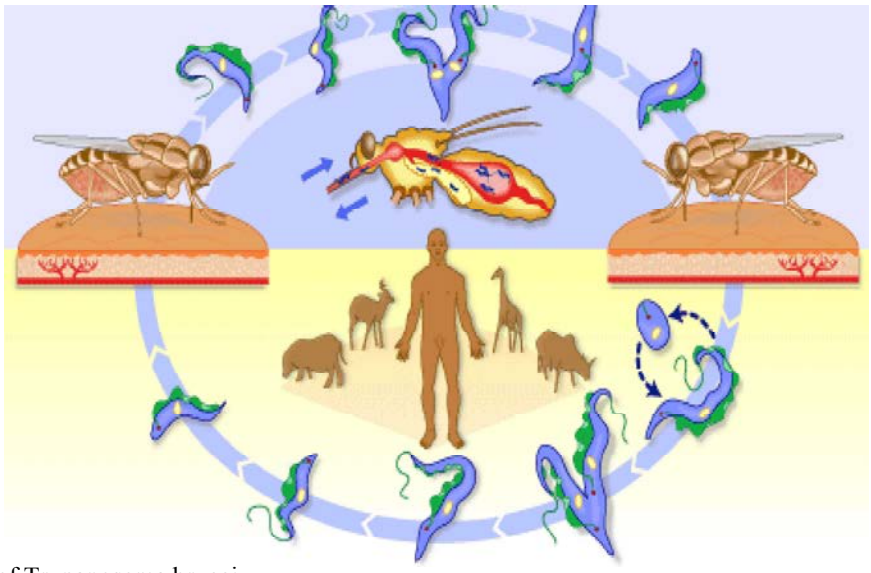

Fig. 1: Life cycle of Trypanosoma brucei

tsetse population into higher altitude areas brings them into contact with previously unaffected livestock. Livestock, cattle in particular play a major role in the agricultural economy of Ethiopia [4].

It is a serious constraint to agricultural production in extensive areas of the tsetse fly infested Ethiopian low lands [5]. Over 10 million kilometers of the tropical African is infested by tsetse fly [6]. These wide ranges of the tsetse and trypanosomosis survey were carried out in Didesa and Abay river system. According to Nttic [7] tsetse transmitted animal trypanosomosisstill remain as one of the largest causes of livestock production losses in Ethiopia.

About 15-20% of the land believed to be suitable for livestock production is affected by one to two species of tsetse flies [7]. The effects of trypanosomosis not only the direct losses resulting from mortality, morbidity, infertility of the infested animals and costs of controlling the disease, but also due to indirect losses, which include exclusion of live stock and animal power based crop production from the huge fertile tsetse infected areas. Since, bovine trypanosomosis is highly devastating disease that have great economic impact on the country development [8]. Therefore the objectives of this seminar are

- To review the epidemiological information and economical significance of bovine trypanosomosis with a particular emphasis to Ethiopia live stock sub-sector.
- To give high light on the effective control and preventive strategies against the disease.
- To draw conclusions based on the information available and forward recommendations.

Definition of the Disease: Trypanosomosis (It is also known "Nagana") is a disease complex caused by several species of unicellular protozoan parasites of the phylum Sarcomastigophora, order Kinetoplastida, family Trypanosomatidae and genus Trypanosoma. It is mainly transmitted cyclically by the genus *Glossina* (Tsetse flies), but also transmitted mechanically by several biting flies (*Tabanids, stomoxes*, etc.). The disease can affect various species of mammals but, from an economic point of view, tsetse-transmitted trypanosomosis, is particularly important in cattle. It is mainly caused by *Trypanosoma congolense*, *T. vivax* and, to a lesser extent, *T. brucei brucei* [9].

Etiology: Trypanosomes are flagellated protozoan parasites that live in the blood and other body fluids of vertebrate hosts. They swim in body fluids by flagellum, boring their way between cells. They generally possess a kinetoplast and undergo cyclical development in an arthropod vector. Their biological adaptations, morphology and pathogenicity are fascinating and are being extensively studied. Each of the parasites causes adisease (Now the disease is termedas trypanosomosis rather than trypanosomiasis). [10].

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* [9].

Life Cycle: Most tsetse-transmission is cyclical and begins when blood from a trypanosome infected animal is ingested by the tsetse fly. The trypanosome loses its surface coat, multiplies in the fly, then reacquires a surface coat and becomes infective. *Trypanosoma brucei* species migrate from the gut to the proventriculus to the pharynx and eventually to the salivary glands; the cycle for *T. congolense* stops at the hypopharynx and the salivary glands are not invaded; the entire cycle for *T.vivax* occurs in the proboscis. The animal-infective form in the tsetse salivary gland is referred to as the metacyclic form. The life cycle in the tsetse may be as short as 1week with *T. vivax* or extend to a few weeks for *T. brucei* species [11].

Pathogenesis: Pathogenesis of trypanosomosis in most species is a progressive, but not always fatal disease and the main features are anemia, tissue damage and immunosuppression. Metacyclic trypanosomes are inoculated intradermally as the fly feeds. They multiply at this site provoking a local skin reaction (Chancre), which is most pronounced in a fully susceptible host and may be slight or absent with some strains or species of trypanosomes. Within the chancre, metacyclic parasites change to trypomastigote form, enter the bloodstream directly or through the lymphatics and initiate characteristic intermittent parasitemias. Their behavior thereafter depends largely on the species of trypanosome transmitted and the host [6].

T. vivax usually multiplies rapidly in the blood of cattle and is evenly dispersed throughout the cardiovascular system, whereas *T. congolense* tends to be aggregated in small blood vessels and capillaries of the heart, brain and skeletal muscle. Both species exert their effect mainly by causing severe anemia and mild to moderate organ damage. The anemia has a complex pathogenesis involving mainly increased erythrophagocytosis, some hemolysis and dyshemopoiesis [12].

Very acute infection with *T. vivax* in cattle causes parasitemias and disseminated intravascular coagulation (DIC) with hemorrhages. Such syndromes resemble a septicemia and anemia may not be severe. *T. brucei* and rarely *T. vivax* have the added capability of escaping from capillaries into interstitial tissues and serous cavities where they continue to multiply. The cerebrospinal fluid is often invaded by *T. brucei* alone or mixed with other species or as a relapse after an apparently successful treatment. Animals chronically infected with any pathogenic trypanosome may develop concurrent and even fatal bacterial, viral and other protozoan infections as a result of immunosuppressant [13].

The pathogenesis of tsetse-transmitted trypanosomosis can be categorized into groups according to the site of host-parasite interaction.

Chancre: The first interaction between trypanosomes and host occur in the skin following a successful feed by an infected tsetse fly. Within a few days of bite, cattle develop a raised cutaneous swelling called a chancre, which is caused by the reaction to multiplying trypansosmes [12].

Lymphadenopathy: Following enlargement of the lymph node draining the chancre, generalized enlargement of lymph nodes and splenomegaly develop. This is associated with marked proliferation of lymphoid cells in the organs. In the medullary cords of lymph nodes and spleenic red pulp there are increases in plasma cells and numerous large active germinal centers are also present [12]. In addition, the red pulp of the spleen, there is an increase in the number of activated macrophages, some of which are engaged in erythrophagocytosis [14].

Anaemia: Plays the major role of pathogenesis of bovine trypanosomosis. The development of anaemia is well recognized sign of trypanosome infection in cattle. The anaemia in bovine trypanosomosis can be divided into two phases based on the presence or absence of trypanosomes, response to trypansocidal drug treatment and pathological findings [15]. These are referred as acute and chronic phases of anaemia.The acute phase anaemia is characterized by progressive anaemia accompanied by parasitaemia [16]. The initial fall in PCV values is associated with the first wave of parasiatemia in the blood. During this period the anaemia is extravascular and is possibly the result of increased red blood cell (RBC) destruction by phagocytosis in the spleen, lungs, haemal nodes and bone marrow [15].

Progressive decrease in PCV takes place over a period of 4 to 12 weeks after infection and may result in death. In general trypanosomosis causes a 40 – 50% drop in PCV. Cattle that survive the acute process progress into phase two, which is a chronic anaemia. This disease syndrome may still result in death, or in either spontaneous recovery or survival with persisting low grade anaemia. This chronic phase is characterized by low and transient parasitaemia or complete absence of detectable parasites in the blood [15].

Tissue Damage: Organs are damaged during the course of infection, some consistently more severely than others. Even though necrosis is not a major feature of bovine trypanosomosis, tissue cell damage and degeneration may be marked. The heart is constantly damaged by all three species of trypanosomes.Other vital organs or systems, which are commonly affected, include the skeletal muscle, central nervous system endocrine organs and reproductive systems [17].

When an animal is infected with trypanosomes, antibodies against the surface coat are produced. However, trypanosomes have multiple genes, which code for different surface proteins; allowing organisms with new surface coat glycoproteins to elude the immune response. This process is called antigenic variation and results in the persistence of these organisms. Antigenic variation has thus far prevented development of a vaccine and permits reinfection when animals are exposed to tsetse carrying trypanosomes with surface coat glycoproteins of a new antigenic type [18].

The pathogenesis of trypanosomosis is however, rather complex and depends on the trypanosome species and the species of the transmitting vector as well as on the resistance of the host. The real cause that leads to the death of the animal is not fully understood. On the one hand it is believed that the parasite releases toxic substances when it is destroyed within the circulatory system which damages the lining of the blood vessels. In some cases the sudden release of large amounts of such toxins triggers a chain of reactions, which produce a shock-like syndrome [19]. Therefore, the damage to the host does not depend on nutrients being taken away by the parasite but rather on the production of toxic substances. With this theory, the typical symptoms of trypanosomosis, such as cachexia, oedema, anaemia and nervous symptoms can be explained [17].

Metabolic disorders are observed in the host due to a trypanosome-induced hypothyroid status [20] and pituitary dysfunction during trypanosomosis [20]. The ability of trypanosomes to change their surface-coat-antigen continuously leads to the exhaustion of the antibody production of the host leading to immunosuppression [21].

In addition, there is lymphoid enlargement and splenomegally associated with plasma cell hyperplasia and hypergammaglobulinaemia [22]. Acute infections associated with high parasitaemia may lead to the death of an animal still in good body condition. On the other hand, chronic trypanosomosis is associated with progressive emaciation and eventually cachexia. This is usually accompanied by low levels of parasitaemia and death in untreated cases [16].

Epidemiology

Mode of Transmission: Trypanosomosis is a disease, which is cyclically and a cyclically transmitted by different species of tsetse flies and other flies [23]. The tsetse fly becomes infected with trypanosomes when feeding on an infected animal. Once the trypanosomes are ingested they lose the surface coat, develop a mitochondrion and undergo a number of developmental stages before they become infected, once more, for the mammalian host. These developmental stages are known as trypomastigote, epimastigote and metacyclic forms [24].

Although the developmental stages are similar for the three species of trypanosomes, the sites within the tsetse in which they occur are different [25] (Table 1).

Distribution of Bovine Trypanomosis in Ethiopia: The epidemiology of African trypanosomosis is determined mainly by the ecology of the tsetse fly which is found only in tropical Africa [25].

Table 1: Morphological characteristics of trypanosomes and site of development in tsetse fly

Species	Site of development in tsetse fly	Free flagellum	Kinetoplast	Undulating membrane	Size in micrometer	Size & motility in wet film
T. vivax	Proboscis	Present	Large, terminal	Not prominent	20-26	Large, extremely active, traverses the whole field very quickly, pausing occasionally
T. brucei	Mid-gut Salivary gland	Present in all but not in stumpy form	Small, subterminal central	Prominent	15-35	Large, rapid movement in confined areas
T. congolense	Midgut Proboscis	Absent	Medium, subterminal, marginal	Not prominent	9-18	Small, sluggish active, adheres to red blood cells by anterior end

Table 2: Trypanosome species reported in Ethiopia

Trypanosome	Vector	Mainly affected host	Regional distribution
T. congolense	Tsetse	Cattle	Amhara
T. vivax &T. brucei	Tsetse	Cattle	Benshangul-Gumuz, Gambella
Oromiya, SNNPR *T. vivax*	Biting flies	Cattle	All over Ethiopia

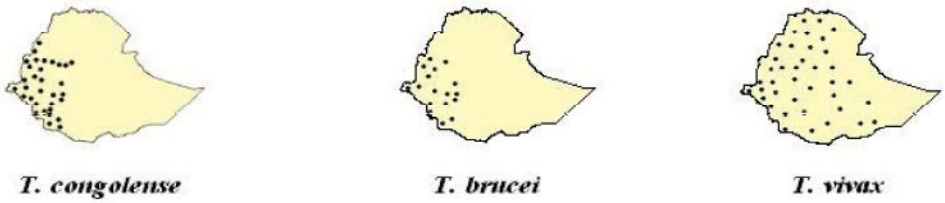

Fig. 2: Distribution of pathogenic trypanosomes in Ethiopia.

Risk Factors

Host Factors: 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* [26].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 [12].

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 [7]. 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 [11].

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 [27].

Importance

Economic-Importance: Tsetse flies infest 10 million square kilometers of Africa involving 37 countries.Hence, nagana is today the most important disease of livestock in the continent. Since nagana is a wasting disease, affected animals are chronically unproductive in terms of milk, meat,manure and traction and the mortality rate can be high. The disease in Africa costs livestock producers and consumers an estimated US$1340 million each year. The anticipated losses due to *T. vivax* in South America exceed $160 million.1 Furthermore, the disease may impact on various immunization campaigns in endemic areas due to the fact that it can cause immunosuppression [28].

Zoonotic Importance: The animal pathogens do not infect humans, but animals can serve as reservoirs of T. brucei rhodesiense and *T. brucei* gambiense, the causes of human sleeping sickness, which are morphologically indistinguishable from T.brucei brucei.Human infections result from tsetse bites,generally in game parks, forest reserves and along streams or other rural setting [29].

Clinical Findings: There are no pathognomonic signs that would help in pinpointing a diagnosis.The general clinical picture is as follows but there are many variations determined by the level of tsetse challenge, the species and strain of the trypanosome,and the breed and management of the host. Acute episodes last for a few days to a few weeks from which the animal dies or lapses into a sub acute to chronic stage, or the illness may be chronic from the beginning. Chronic cases may run a steady course, may be interrupted by periodic incidents of severe illness, or undergo spontaneous recovery [29].

The basic clinical syndrome appears after an incubation period of 8-20 days. There is fever, which is likely to be intermittent and to last for a long period. Affected animals are dull, anorexic, apathetic, have a watery ocular discharge and lose condition. Superficial lymph nodes become visibly swollen, mucous membranes are pale, diarrhea occasionally occurs and some animals have edema of the throat and underline. Estrus cycles become irregular, pregnant animals may abort and semen

quality progressively deteriorates. The animal becomes very emaciated and cachectic and dies within 2-4 months or longer. Thin, rough-coated, anemic, lethargic cattle with generalized lymph node enlargement are said to have 'Fly-struck' appearance. Furthermore, intercurrent bacterial, viral, or other parasitic infections may mask or complicate the basic clinical syndrome. Immune response to bacterial and some viral, vaccines is also depressed but is restored if trypanocidal therapy is given at the time of vaccination [30].

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 [29].

Clinical Diagnosis: Severity of disease varies with species and age of the animal infected and the species of trypanosome involved. *T. congolense* and *T. vivax* are highly pathogenic for cattle and *T. brucei* infections are generally regarded as being of low pathogenicity. The primary clinical signs are intermittent fever, anaemia and weight loss. Cattle usually have a chronic course with high mortality, especially if there is poor nutrition or other stress factors [31].

Clinical diagnosis was found to have a good sensitivity (78%) but a low specificity (27%) when compared to parasitological tests [32]. From this study, it appears that treatment of cattle based on clinical examination may clear up to 87, 5% or 78% of the cases that would be positive by either molecular or parasitological diagnosis, respectively. Under field conditions, in the absence of simple and portable diagnostic tools or access to laboratory facilities, veterinarians could rely on clinical sings and direct parasitological diagnosis to screen and treat cases of bovine trypanosomosis presented by farmers [32].

Parasitological Diagnosis by Direct Examination

Wet Blood Film: These are made by placing a drop of blood on a microscope slide and covering with a cover-slip. The blood is examined microscopically using an x40 objective lens. Approximately 50-100 fields are examined. Trypanosomes can be recognized by their movement among the RBC. The method is simple, inexpensive and gives immediate results. Depending on the trypanosome size and movements a presumptive diagnosis can be made of the trypanosome species [33]. Final confirmation of the species is made by the examination of the stained preparation. The diagnostic sensitivity of the method is generally low, but depends on the examiner's experience and the level of parasitaemia. Sensitivity can be improved significantly by lysing the RBCs before examination using a haemolytic agent such as sodium dodecyl sulfate [34].

Thick Blood Smear Technique: The method is simple and relatively inexpensive, but results are delayed because of the staining process. Trypanosomes are easily recognized by their general morphology, but may be damaged during the staining process. This may make it difficult to identify the species [35].

Thin Blood Smear Technique: Usually, both a thin and thick smear is made from the same sample. Thick smears contain more blood than thin smears and, hence, have a higher diagnostic sensitivity. While, thin smears allow trypanosome species identification.

Trypanosome species can be identified by the following morphological characteristics (Criteria of the Office International des Epizooties):

Trypanosoma Vivax: 20-27 ìm long, undulating membrane is not obvious, freeflagellum present at the anterior end, posterior end rounded, kinetoplast large and terminal [11].

Trypanosoma brucei is a polymorphic trypanosome species. Two distinctly different forms can be distinguished, i.e. a long slender form and a short stumpy form. Often, intermediate forms, possessing characteristics of both the slender and stumpy forms, are observed. The cytoplasm often contains basophilic granules in stained specimens [11].

Trypanosoma brucei (Long slender form): 17-30 ìm long and about 2.8 ìm wide,undulating membrane is conspicuous, free flagellum present at the anterior end, posterior end pointed, kinetoplast small and subterminal. *Trypanosoma brucei* (Short stumpy form): 17-22 ìm long and about 3.5 ìm wide, undulating membrane is conspicuous, free flagellum absent, posterior end pointed, kinetoplast small and subterminal [11].

Trypanosoma congolense: 8-25 ìm (Small species), undulating membrane notobvious, free flagellum absent, posterior end rounded, kinetoplast is medium sizedand terminal, often laterally positioned. Although *T. congolense* is considered to bemonomorphus, a degree of morphological variation is sometimes observed [36].

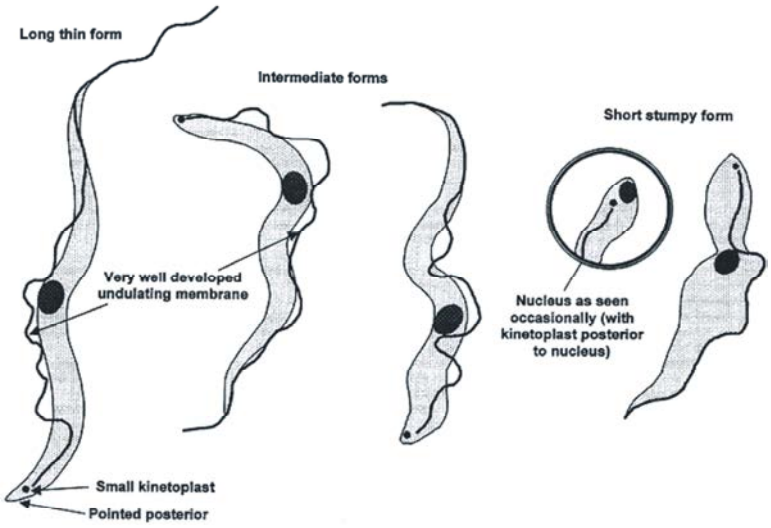

Fig. 3: different forms *of Trypanosoma brucei*

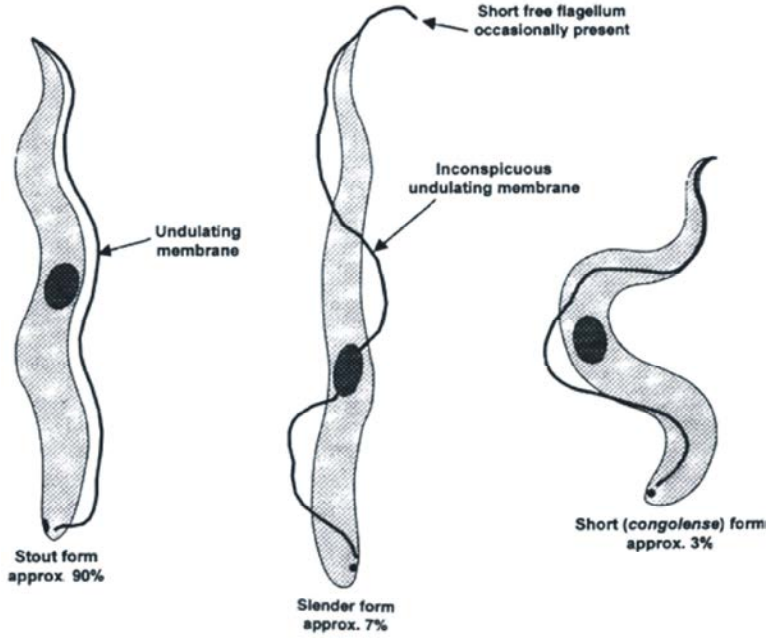

Fig. 4: different forms *of Trypanosoma congolense*

Parasitological Diagnosis by Indirect Diagnosis

The Indirect Enzyme-linked Immunosorbent Assay (ELISA): The binding ofanti-trypanosomal antibodies to the antigen is shown by a conjugate of antibovine immunoglobulins labelled with an enzyme, which can be visualized by adding an appropriate chromogenic substrate (i.e. the interaction between enzyme and substrate will create a colour). Usually solubilized antigens obtained from disrupted trypanosomes (Successive freezing and thawing cycles or ultrasound) are used and the soluble antigens are coated in the wells of microtrays [37].

Only small quantities of sera and conjugate are used. An ELISA reading instrumentwill quickly give the optical density (OD) of each well (Showing quantitatively theintensity of the interaction between the enzyme and the substrate), thus helping tospeed up the processing of large numbers of sera.Various ELISA systems have been constructed exploiting different reagents fordetection of antibodies, but still require laboratory and field validation studies to befurther assessed for their capacity to improve diagnosis of African trypanosomosis [27].

Recently, the ability to use mitochondrial heat shock protein 70 (MTP) of*T.congolense* as a diagnostic antigen

was examined by Boulange *et al*. [38] andwith encouraging results, but the technique still needs to befurther validated and evaluated for natural infections in cattle [37].

Antigen-Detecting Tests: These tests have been developed for the detection of circulating trypanosomalantigens, but are not reliable [39,]. Consideration of why the Ag-ELISA fails to detect trypanosomal antigen(s) in serum samples isworthwhile and must take into account the following five factors: (1) the reactivity ofthe reagents (Number of available epitopes of the antigenic target); (2) the specificityof the reagents; (3) the nature of the test sample, e.g. the compartmentalisation of trypanosomes between plasma, serum and red blood cells; (4) possible interference by immune complexing and (5) the biology of the host/trypanosome relationship to gainan understanding of the fluctuations in trypanosomes in the systemic circulation [27].

Polymerase Chain Reaction (PCR): Molecular biology provides tools for sensitive and specific diagnosis based on DNA sequence recognition and amplification. The polymerase chain reaction (PCR) permits identification of parasites at levels far below the detection limit of the commonly used parasitological techniques. PCR assays for trypanosome detection have been developed using species specific DNA hybridisation probes. This method requires either prior knowledge of the species to be found or the use of several probes for each sample to be tested [28].

Prevention, Control and Treatment

Treatment: If detected early,Trypanosomosis can be treated with trypanocidal drug for therapeutic and prophylactic purpose. Therapeutic drugs for includes diminazene aceturate,homidium bromide and homidium chloride.Prophylactic drugs for cattle include homidium bromide,homidium chloride and isometamidium [40].

Diminazene Aceturate: Have remarkable curative properties. It is very active, stable and easy to use and have very toxicity. These advantages make it a practical and risk free trypanocides. Diminazene solution can only be kept for two to three days. It is injected subcutaneously in cattle (Slight localreactions possible) or intramuscularly (Very rapid absorption) at a dose of 3.5 mg/kg live weight for treating *T. vivax* and *T. congolense* infections. Infections due to *T. brucei* can be treated in cattle with the dose of 7mg/kg. Diminazene derivatives bind to DNA and interfere with parasite replications. This class of drugs has tendency to accumulate in tissue, therefore half life is very long, which may lead to residual problems in food producing animals [31].

Quinapyramine Sulphate: Quinapyramine methyl sulphate is sold in the form of white powder that dissolves easily in water. It is prescribed as a curative drug for cattle and small ruminants and is given subcutaneously as a 10% aqueous solution at dose 5mg/kg. It was used in all the African countries, giving excellent result for cattle trypanosomosis (Especially *T. congolense*); it was slightly less successful against *T. vivax*. It causes appreciable systematic reactions and intramuscular injection cause painful local reactions leading to discomfort or lameness. Trypanosomes resistant to this compound should be treated with dimenazene [10].

Homidium: Homidium salts are effective against *T. vivax* infections in cattle, but less so against *T. congolense* and *T. brucei*. Their limited and protective activity in cattle depends on severity challenge and may last three to five weeks. Homidium resistant trypanosome can be controlled by diminazene or isometadium [32].

Isometamidium: Isometamidium is a phenanthridine aromatic amidine with a narrow therapeutic index which has been marketed for both a prophylactic and therapeutic trypanocidal agent. Isometamidium chloride is used as curatively at lower dosage rates and prophylactically at higher dosage rates. It is usually prepared as red powder easily soluble in water. It is used in a 1 or 2% aqueous solution and administered by deep intramuscular injection at the rate of 0.25-1mg/kg, depend on drugs resistant risk. Strain of trypanosomes resistant to isometamidium and other phenanthridine appear frequently, but they remain susceptible to diminazene aceturate. It is given to the animal at dose rate of 0.51mg/kg and it will be protected for two to four months depending on the extent infections risk [40].

Control and Prevention: The control of trypanosomosis in enzooticcountries involves control of tsetse fly population, prophylactic treatment, good husbandry of animals at risk and use of trypanotolerant animals. Control of tsetse has been successfully attempted, but reinvasion is frequent if the land is not properly utilized. The earliest methods involved bush clearing and elimination of game animals on which tsetse feed. More recent methods

involved the use of insecticides applied strategically in the form of ground and aerial spraying over large expanses of land [20].

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, areapplied directly on the animal in the form of spray or pour-on formulation.Other effective methods involve targets impregnated with insecticides andtraps that attract and catch tsetse. These are simple and cheap and can beconstructed and maintained by local communities. Furthermore, they do notpollute the environment and are suitable for both small- and large-scale fanning [38].

Another method is the sterile maletechnique. Since the female tsetse onlymates once in a lifetime, this technique is theoretically able to eradicate a targeted tsetse species in areas where other methods have been used to reduce its density. But, it is expensive. Finally, itshould be stated that development of the land for agriculture, industries, highways,etc. will effectively destroy the habitat for tsetse flies [29].

Attempts at trypanosomosis controlhave 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 aheavy tsetse challenge.The prophylacticeffect is supplemented by the development of antibodies and the total periodof protection may be as long as 5 months.However, it is customary to give four or five treatments per year [39]. 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 tsetsetrapping and pour-on applications) with strategic treatment of exposed animals (Chemotherapy and chemoprophylaxis) along with use of trypanotolerant animals when feasible [29].

CONCULUSIONS

Bovine trypanosomosis is a serious protozoal disease that has great economic impact throughout the world,especially in the developing country like Africa.In Ethiopia bovine trypanosomosis is the main constraint of livestock production. This constraint in the livestock production leads serious economic impact on the country development.Bovine trypanosomosis (Nagana) is found in the low land of Ethiopia,especially in the “tsetse belt” like rift vally,omo, borena,metekel zone of Benshangul Gumuz region. Bovine trypanomosis is mainly caused by three etiological agents,*T.vivax,T.congolense*,and *T.brucei*.Bovine trypanosomosis is transmitted from the infected animal to susceptible host both mechanical and biological vector.

The main biological vector is tsetse fly that found in the tsetse belt. *T.vivax* can be transmitted from the infected animal to susceptible host by both mechanically and biologically,but *T.congolense* mainly transmitted biologically.Bovine trypanomosis show chronic emaciation, enlargement of lymph node, aneamia and loss of production. Bovine trypanomosis can be diagnosis by clinical sign, direct parasitological diagnosis and indirect parasitological diagnosis. The direct parasitological diagnosis includes:-wet blood film, thick blood smear,thin blood smear and parasitological concentration technique. The indirect parasitological diagnosis include:-ELISA, PCR. Bovine trypanosomosis can be treated by both the prophylactic and curative drugs. The drug that used for the treatment of bovine trypanosomosis includes:-Diminazene aceturate,Homidium and Quinapyramine. This disease can be controlled by early treatment, vector control. Based on this, the following recommendations are forwarded:

- Effective control, prevent and treatment of bovine trypanomosis is conducted by applying proper management (Restriction of pasture grazing in the tsetse belt), vector controland treatment of the infected animal.
- Exotic breeds are susceptible to bovine trypanosomosis and local breeds (Zebu) are resistant to bovine trypanomosis. But they low production than exotic breed. Therefore,in order to get maximum production and disease resistant breed, use cross breed for animal husbandry.
- In endemic areas detailed study must be performed to know the communities perception to control the trypanosomosis and other protozoal disease.
- Detection of drug resistance trypanosome which are economically important.
- Restriction of cattle movement from an infected area to the disease free area and vice versal to prevent and control of further expansion of bovine trypanosomosis and other protozoal diseases.
- Animal health professional and owner should be aware of the effect of bovine trypanosomosis and other protozoal diseases.

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