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African Animal Trypanosomiasis (Nagana): A Review

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Abstract: African animal trypanosomiasis (AAT) occurs only in Africa in 37 sub-Saharan countries in 10 million square kilometers (a third of the continent). AAT is a disease complex caused by a protozoan *Trypanosoma* in the phylum Sarcomastigophora, order Kinetoplastida, family Trypanosomatidae and genus *Trypanosoma*. There are three species of trypanosome known to be pathogenic to animals: *T. vivax*, *T. congolense* and *T. brucei*. Trypanosomes are known to affect a number of livestock and wild animal species. It is cyclically transmitted by tsetse flies. Tsetse flies are obligatory blood feeders of their hosts. The most easily diagnosed clinical signs include anemia, lymphadenopathy, emaciation and loss of production. AAT significantly reduce production, traction power, causes mortality and morbidity as well as death if left untreated. AAT can be effectively controlled by controlling tsetse flies by using insecticide chemicals. Therefore, the control and prevention of the disease needs a priority to save the losses of poor people of Africa.

Key words: *Trypanosoma* · Sub-Saharan Africa · Tsetse fly · Anemia · Trypanotolerance · Economic Loss

INTRODUCTION

African animal trypanosomiasis (AAT) known as Nagana (Derived from Zulu word to mean to be depressed or unfit) is a parasitic disease that causes serious economic losses in livestock from anemia, loss of condition and emaciation [1]. Many untreated cases are fatal and is found mainly in those regions of Africa where its biological vector, the tsetse fly, exists [2]. It is of great economic importance in Africa as 5-10 million cattle are at risk of infection and 30 million deaths annually [3]. Livestock are the background of socioeconomic system of most of the rural communities in Africa. This can be noted more clearly with those who are adopting the pastoral and semi-pastoral ways of living [4]. Agricultural development is essential for growth across sub-Saharan Africa, employing 65% of the labor force and accounting for 32% of gross domestic product [5]. Diseases of livestock reduce agricultural output by up to 30% in developing countries which equals twice the impact as in developed countries [6].

Trypanosomes are pathogenic, not only for animals but also for man where they cause sleeping sickness. Most species of domestic animals are to some degree susceptible to AAT [7]. African animal trypanosomiasis restricts agricultural development leading to poverty on the African continent despite the availability of prophylactic and curative drugs [8]. In Africa, *Trypanosoma vivax*, *Trypanosoma congolense* and *Trypansoma brucei* are the three most important species of trypanosomes responsible for considerable production losses and livestock morbidity where they occur [9]. The objective of this paper is to review on the general overview of trypanosomiasis.

Etiology: Trypanosomes belong to kingdom animalia, subkingdom protozoa, phylum sarcomastigophora, subphylum mastigophora, class zoomastigophora, order kinetoplastida, suborder trypanosomatina, family trypanomastidae, genus *Trypanosoma*; subgenus nannomonas (*T. congolense*), Subgenus Duttonella (*T. vivax*) and Subgenus *Trypanozoon* (*T. brucei* species) [10]. Flagellated protozoan parasites that live in the blood, lymph and various tissues of their vertebrate hosts: *T. congolense, T. vivax* and to a lesser extent *T. brucei brucei*, *T. uniforme* and *T. simiae* are other, less common tsetse-transmitted species. *T. congolense* and *T. vivax* are mainly intravascular parasites while *T. brucei* has an affinity for tissues. Several types of *T. congolense* can be distinguished by molecular biology; the most

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common and pathogenic one in cattle is the type "Savannah", the other ones (Type "Forest" and "Kilifi" or Kenya coast) are less pathogenic and have different host affinity. Mixed trypanosome infections with two or three species are common. Trypanosomes are blood borne unicellular protozoan parasites dwelling in various body and tissue fluids [11, 12].

Trypanosomiasis: The Disease: Animal trypanosomiasis of African origin is a disease complex caused by one or several of these *Trypanosoma* species, transmitted mainly cyclically by the genus *Glossina* (Tsetse flies), but also mechanically by biting flies such as tabanids and *Stomoxys* in sub-Saharan Africa (Latitudes 10° North to 20-30° South [13]. The tsetse fly (*Glossina*) is responsible for biological (Cyclical) transmission of trypanosomiasis. The first scientific description of African trypanosomes was made at the end of the 19th century and the importance of the tsetse fly in transmission was discovered soon afterwards [14]. African trypanosomiasis (AAT) is an important constraint to livestock production and a threat to food security in sub-Saharan Africa [15, 16].

The disease can affect various species of mammals but from an economic point of view, tsetse-transmitted trypanosomosis is particularly important in cattle, where the disease is referred to as Nagana. It is mainly caused by *T. congolense* (Subgenus *Nannomonas*), *T. vivax* (Subgenus *Duttonella*) and, to a lesser extent, *T. brucei brucei* (Subgenus *Trypanozoon*) [17].

Geographical Distribution: Trypanosomes transmitted by tsetse flies are endemic in a part of sub-Saharan Africa called the tsetse fly belt covering 10 million square kilometers in 37 African countries, which occurs approximately between latitudes 10°N and 20-30°S [11]. Table 1 summarizes the occurrence of trypanosomiasis in some African countries.

A few species of tsetse flies have also been detected in parts of the southwestern Arabian Peninsula. Trypanosomes, particularly *T. vivax,* can spread beyond the tsetse fly belt by animal movements and transmission through mechanical vectors. *T. vivax* has become established in parts of South and Central America and the Caribbean, which are free of tsetse flies thought to be most significant for *T. vivax* [11, 18].

Host Range: African animal trypanosomiasis infects, domesticated and some free-living or captive wild mammals. Wildlife known to be susceptible to infection include ruminants such as South American white-tailed deer, duikers, antelope and African buffalo, wild equids, felids, warthogs, capybaras, elephants, nonhuman primates and various rodents. Cattle, pigs, horses, donkeys, camels, sheep, goats and dogs are infected by trypanosoma. Clinical cases have been seen in a number of species including water buffalo, alpacas, llamas, cats and captive wild ungulates. Reptiles and birds carry their own species of trypanosomes, but *T. vivax* DNA was detected by PCR in crocodiles and monitor lizards in Africa [18].

Table 1: Summary of prevalence of trypanosomiasis.

Country	Prevalence	Author
Benin	6.7%	19
Cameroon	14.3%	20
Cote' Devoir	9.09%	21
Ethiopia	8.12%	22
Kenya	35%	23
Mali	2.8%	24
Nigeria	16.1%	25
South Africa	17%	26
Tanzania	9.3%	27
Uganda	25%	28

Life Cycle and Transmission: Trypanosomes require both vertebrate and invertebrate (Tsetse fly) hosts to complete their life cycle [30]. Tsetse flies usually rest in sheds of forests near potential food areas. They are obligatory blood feeders and sensitive for moving objects, blue objects, carbon dioxide and odors generated from animals. The life cycle of a trypanosome begins when a tsetse fly picks up the trypanosome parasite by feeding from an infected host. Tsetse flies suck up trypomastigote forms of trypanosomes, which lose their glycoprotein surface coats, elongate and multiply in the mid gut of a tsetse fly thereby transforming into elongated procyclic trypomastigotes which transform into epimastigote forms in salivary glands or proboscis of tsetse fly. Epimastigotes produce the infective metacyclic trypomastigotes (Figure 1). *T. vivax* develops in the proboscis while *T. congolense* develops in the mid gut and proboscis. *T. brucei* migrates from the mid gut to the salivary glands within the tsetse fly. Trypanosome species can also be identified based on their location. The epimastigotes multiply and give rise to small infective metacyclic forms of trypanosomes which acquire a glycoprotein surface coat. At this point the tsetse fly becomes infective to the new host it feeds on [31; 32].

When the metacyclic trypanosomes are injected into a susceptible mammalian host, they develop and multiply locally at a site of infection causing skin chancre.

Table 2: Host species of Trypanosomes.

Trypanosome species	Domestic animal affected	Reservoir hosts	Laboratory animal
T. congolese	Cattle, camels, horses, dogs, sheep, goats, pigs	Several group wild mammals	Rats, mice, guinea pigs, rabbits
T. simie	Pigs	Wart hog, bush buck	Rabbits, monkeys
T. godfreyi	Pigs	Wart hog	None susceptible
T. vivax	Cattle, sheep, goats, domestic buffalo, horses	Several group wild mammals	Usually none susceptible
T. uniforme	Cattle, sheep, goats	Wild ruminants	None susceptible
T. b. brucei	Horses, camels, dogs Sheep, goats, cattle, pigs	Several group wild mammals	Rats, mice, guinea pigs, rabbits
T. b. gambiense and	Human sleeping sickness; affect domestic animals	Wild mammals	As for *T. b. brucei* (after initial adaptation
T. b. rhodesianse		(*T. b. rhodesiense*)	where *T. b. gambiense* is concerned
T. evansi	Camels, horses, cattle, dog, domestic buffalo	Wild mammals in Latin America	As for *T. b. brucei*
T. equiperdum	Horses, donkeys, mules	Not known	As for *T. b. brucei* (after initial adaptation

Source: 29

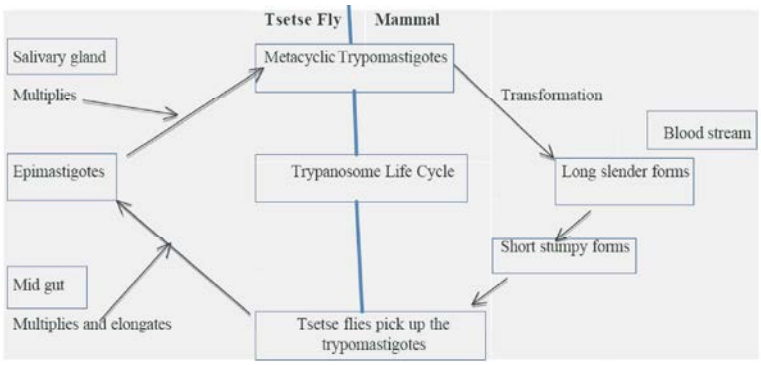

Fig. 1: The life cycle of trypanosoma in the tsetse fly and mammalian hosts.

The mature trypomastigotes are then released into the blood stream through lymph vessels, broken capillaries and tissues where they multiply further by binary fission and can be detected by parasitological examinations. *T. congolense* localize in capillaries and small blood vessels where they attach to vascular endothelial cells. This is enabled by their small size. *T. brucei* and *T. vivax* invade the tissues of various organs where they cause damage [31, 33].

Trypanosomes can also be transmitted by mechanical vectors including surgical instruments, needles, syringes and other biting flies. Trans-placental, venereal, peri-partum transmissions were proven to happen in some circumstances [11, 18].

Risk Factors: Trypanosomiasis is one of the most pathogenic diseases of domestic and wild animals. There is a report that seasonality, altitude and migration practices contribute for the occurrence of trypanosomiasis [34]. Other risk factors like age, species of animals and anemia were significantly associated with the trypanosomiasis occurrence [35]. Body condition was significantly associated with trypanosomiasis in as study conducted in Ethiopia [36]. High density vegetation and human activity (Livestock market and cattle movement) were identified as strong risk factors for infection in cattle [37].

Incubation Period: The incubation period for African animal trypanosomiasis ranges from 4 days to approximately eight weeks. Infections with more virulent isolates have a shorter incubation period [2].

Virulence and Pathogenesis: Nagana only creates severe symptoms in domesticated animals since in wild animals it only causes mild infections and infected animals show no clinical symptoms at all therefore, making them reservoir hosts [38]. The pathogenesis of AAT evolves in two forms, chronic and acute, depending on the susceptibility status of the animal and the virulence of the Trypanosoma strain involved. Acute or chronic stage of the disease may be fatal following a short period of illness; however chronic illness can endure for months to years. In goats acute disease causes high fever, mucous membrane turn pale and there is a rapid weight loss in the affected goat host [11, 39].

The three major features of trypanosomiasis are anemia, tissue damage and immune suppression [40]. Initial replication of trypanosomes is at the site of inoculation in the skin; this causes a swelling and a sore (Chancre). Trypanosomes then spread to the lymph nodes and blood and continue to replicate. *T. vivax, T. congolense* and *T. brucei* are characteristically present in the bloodstream. *T. brucei* is also found extravascular in for example the myocardium, the central

nervous system and the reproductive tract. Lymphoid enlargement and splenomegaly develop associated with plasma cell hyperplasia and hyper gamma globulinaemia, which is primarily due to an increase in IgM. Concurrently there is a variable degree of suppression of immune responses to other antigens such as microbial pathogens or vaccines. Ultimately, in infections of long duration, the lymphoid organs and spleen become shrunken due to exhaustion of their cellular elements [41]. Anemia is a cardinal feature of the disease, particularly in cattle and initially it is proportional to the degree of parasitaemia. It is hemolytic in that the red blood cells are removed from the circulation by the expanding mononuclear phagocytic system. Cell degeneration and inflammatory infiltrates occur in many organs such as skeletal muscle and the CNS, but perhaps most significantly in the myocardium where there is separation and degeneration of the muscle fibers [42].

Host Immune Response: The specific immune response to the infecting parasites involves both the humoral and cellular branches of immune systems. In trypanosomosis, parasite growth is primarily controlled through T-cell dependent antibody responses to the variable surface glycoprotein and possibly to other molecules embedded on the surface of the parasites. Cellular immune responses also occur but at the level of immune-suppression directed against B cells. Additionally, a variety of immune-modulatory cytokines like tumor necrosis factor alpha (TNF-á), interferon gamma (IFN-γ), interleukins (IL-10, IL-4, IL-6, IL-12), prostaglandins (PG) and etc are produced during the course of infection. These soluble mediators appear to influence immune activity; changes in their production may represent a means by which microorganisms can alter immune competence. The center of the immune-pathology is the T-cell-independent production of antibodies to the variant surface glycoprotein of trypanosomes, the anti-Variant Surface Glycoprotein (VSG) antibody-mediated phagocytosis of trypanosomes by macrophages and the subsequent profound mal-regulation of the macrophage system [43].

Macrophages after uptake of parasites can mediate immune-suppression and thus serve at least as one key target cell for parasite action [44]. These cells play a key role in controlling B and T cell function [45] and in trypanosomiasis they are activated, undergoing major changes in phenotype and mediator release [46]. In the mammalian host, the whole parasite is covered with a glycoprotein coat of a single molecular species, called the variant surface glycoprotein (VSG). The surface coat of one trypanosome consists of about 107 VSG molecules. The VSG is anchored into the cell membrane via glycosyl-phosphatidyl-inositol (GPI). The GPI lipid, a diacylglycerol (DAG) moiety consisting of two myristic acid chains linked to glycerol, is inserted into the outer leaflet of the trypanosomal cell membrane. The capacity for antigenic variation in African trypanosomes is almost unlimited [47].

Clinical Findings: Most clinical cases in ruminants are chronic, but acute disease, which may be fatal within weeks. The first sign may be a localized swelling (Chancre) intermittent fever, anemia, lethargy, lymphadenopathy, weight loss, hypoglycemia, loss of condition/emaciation, decreases in milk yield, decreased appetite, submandibular edema, cardiac lesions, diarrhea and keratitis or corneal opacity with lacrimation. There may also be abortions, premature births, peri-natal losses and damage to the male reproductive organs (e.g. orchitis and epididymitis) leading to reduced fertility. Trypanosomes can cause immunosuppression and concurrent infections may complicate this disease. Sudden deaths have been reported in small ruminants and deaths are common in untreated animals with chronic clinical signs. Infected animals may show neurological signs [11, 18].

Diagnostic Methods

Wet Blood Films: Wet films are made by placing a droplet of blood (About 2 µl) on a clean microscope slide and covering with a cover-slip (22 × 22 mm). The blood is examined microscopically at ×400 total magnification with condenser aperture, phase-contrast or interference contrast. Trypanosomes can be recognized by their movement among the red blood cells. 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. Final confirmation of the species is made by the examination of the stained preparation [17].

Thin Smear: Thin blood smears are made by placing a small drop of blood (About 3 µl), for example from a microhaematocrit capillary tube, on a clean microscope slide approximately 20 mm from one end and spreading with the edge of another slide. This slide is placed at an angle of approximately 30° to the first slide and drawn back to make contact with the blood droplet [48]. The blood is allowed to run along the edge of the spreader, which is then pushed to the other end of the

Table 3: Trypanosome subgenera or species identification morphological characteristics:

Trypanosoma Species		Size	Undulating Membrane	Free Flagellum	Kinetoplast
T. vivax,		20-27 µm Long	Medium or not Obvious	Present at anterior end, posterior end rounded	Large & Terminal
T. brucei	Long Slender Form	17-30 µm Long & about 2.8 µm Wide	Conspicuous	Present at anterior end, posterior end pointed	Kinetoplast Small & Subterminal
	Short Stumpy Form	17-22 µm Long & about 3.5 µm Wide	Conspicuous	Absent, posterior end pointed	Kinetoplast Small & Subterminal
T. congolense		8-25 µm Long (Small Species)	Not Obvious	Absent, posterior end rounded	Medium & Terminal, Laterally Positioned

Source: 50, 51

slide in a fairly rapid but smooth motion. The blood is thus pulled (by capillary action) by the spreader slide. If the correct amount of blood is used, the slide should be covered with a film of blood with no surplus before the end of the slide is reached and the smear should take the shape of a bullet. The slide is dried quickly by waving in the air. The slide is fixed for 3 minutes in methanol and stained as for thick blood smears. After staining, the slide is washed gently under tap water and allowed to dry (OIE terrestrial manual, 2018). Finally, fields of the stained thin smear are examined with a ×50 or ×100 oil-immersion objective lens [17, 49]. Table 3 shows morphological identification criteria of trypanosome under microscope.

Hematocrite Centrifuge Technique: The Woo or (Haematocrit centrifuge technique) (HCT), as described by Woo [52] is widely used for the diagnosis of animal trypanosomosis. It is based on the separation of the different components of the blood depending on their specific gravity. First, fresh, usually ear vein blood (About 70 µl) is collected into heparinized capillary tubes and one end of the capillary tube is sealed with cristaseal. The sealed capillary tubes are placed in a microhaematocrit centrifuge with the sealed ends pointing towards the outside. Trypanosome movement can first be detected using the ×10 lens. The HCT is more sensitive than the direct examination techniques. In the case of *T. vivax* infections, the sensitivity of the Woo methods approaches 100% when the parasitaemia is >700 trypanosomes/ml blood. Trypanosomes become very difficult to detect when the parasitaemia is lower than 60 trypanosomes/ml blood [53]. The Buffy coat technique (BCT) or Murray method [54] represents an improved technique for the detection of trypanosomes for which the capillary tube is cut with a diamond pencil, 0.5 mm below the buffy coat, to include the top layer of RBCs. The Buffy coat and the uppermost layer RBCs are extruded on to a clean microscope slide. The preparations are examined with a dark-ground or a phase-contrast microscope with a ×40 objective lens. Result shows, *T. vivax* is large, extremely active, traverses the whole field very quickly, pausing occasionally. *T. brucei v*arious sizes, rapid movement in confined areas, undulating membrane traps the light into "Pockets" moving along the body. *T. congolense* is small, sluggish, adheres to RBCs by anterior end [17].

Thick Smear: These are made by placing drops of 5-10 µl blood on a clean microscope slide and spreading it over an area of approximately 2 cm in diameter, using the corner of another slide [55]. The thickness of the resultant film should be such that, when dry, the figures on a wristwatch dial can just be read through it. The film is dried thoroughly by rapidly waving in the air and, without fixation, is de-haemoglobinized by immersion in distilled water for a few seconds and dried before staining. A dry smear should be kept dry and protected from dust, heat, flies and other insects. It is stained for 30 minutes with 4% diluted giemsa stain in phosphate buffered saline, pH 7.2. Staining time and stain dilution may vary with stain and individual technique. The stained smear is then washed with buffered water and examined at ×500 to ×1000 total magnification [11, 17].

Molecular Tests: New tools developments by molecular biologists now make it possible to characterize trypanosomes both in the vectors and in the hosts. The use of molecular biological tools, in particular the Polymerase Chain Reaction (PCR), introduced an exceptional sensitivity and especially the possibility of characterization at the specific level. This had been impossible previously [55].

Specific highly repetitive nuclear DNA sequences (Also called satellite DNA, presenting 10,000-20,000 serial repeats in the genome) can be amplified for *T. vivax* and three types of *T. congolense* [55, 56]. Similar to

parasitological examinations, a concentration technique by centrifugation allows enrichment of blood samples; it is therefore recommended to carry out the DNA preparation step on Buffy coats. Due to the multiplicity of these taxon-specific primers in tsetse flies or cattle, a complete Trypanosome species identification requires three to six or more PCR tests be carried out per sample, which considerably increases the cost of diagnosis [57]. The PCR procedure is extremely sensitive, but false-positive results may occur as a result of contamination of samples with trypanosome DNA. False negative results may also occur when the specificity of the primers is too high, so that not all isolates of a particular trypanosome species are recognized [58].

Serological Diagnosis: A presumptive diagnosis can be made after trypanosomes are observed by direct microscopic examination of blood, lymph nodes (e.g., smears of needle biopsies), edema fluid or tissues collected at necropsy [18]. Commonly performed serological tests include IFAT which involves fixation of live trypanosomes using a mixture of 80% cold acetone and 0.25% formalin in normal saline for the preparation of trypanosomal antigens [59].

Antibody-detection enzyme-linked immunosorbent assay (ELISA) [60] has been further developed for use in large-scale surveys of bovine trypanosomosis [61, 62]. Recommendations have been made that allow antigen production and standardization of the test on a local basis [63]. ELISAs using *T. congolense* or *T. vivax* pre-coated microtitre plates have been developed that have the advantage of a standardized denatured antigen, which can be stored for long periods at room temperature [64].

Differential Diagnosis: Acutetrypanosomosis with fever may be confused with babesiosis, anaplasmosis, theileriosis (East coast fever), haemorrhagic septicemia and anthrax. Also for chronic trypanosomosis with anaemia and emaciation, helminthosis, malnutrition and other haemoparasitoses can be taken as differential diagnosis [11, 18].

Post Mortem Lesions: Post-mortem lesions are nonspecific and are usually related to anemia and the prolonged antigen-antibody response. The lymph nodes and spleen are enlarged in the acute stage and petechiae are frequently found on serosal surfaces, particularly in the peritoneal cavity [18]. Commonly seen postmortem lesions are: emaciation and serous atrophy of fat, enlarged lymph nodes, liver and spleen, excessive fluid in the body cavities and subcutaneous edema, petechial hemorrhages, lymphoid tissue may be atrophic in the terminal phases as the animal is too debilitated to mount an immune response and severe myocarditis is common [11].

Trypanotolerance: Some cattle breeds are gifted to be resistant to trypanomiasis. The indigenous cattle of Africa are the product of generations of natural selection and survival of the fittest. Trypanosomosis has taken its toll on cattle in tsetse areas over the centuries. It is only in this century that drugs or tsetse control has afforded some protection. The degree of trypanotolerance found amongst African cattle is a reflection of the severity of tsetse challenge to which they have been exposed and the length of time over which that exposure has taken place [65]. The selection of trypanotolerant breeds of cattle can lessen the impact of trypanosomiasis. Trypanotolerant cattle breeds known to exist in Africa are: Sheko breed, Savannah Short horn, N'Dama breed, dwarf West African short horn, Orma Boran and Muturu breed [65-67].

Treatment and Prevention: In endemic areas of Africa, African animal trypanosomiasis can be controlled by reducing or eliminating tsetse fly populations with traps, insecticides and other means and by treating infected animals with antiparasitic drugs. Animals given good nutrition and rested are more likely to recover rapidly than undernourished and stressed animals. No vaccines are available for trypanosomiasis [2]. Veterinarians who encounter or suspect African animal trypanosomiasis need to follow their national and/or local guidelines for disease reporting [18]. The search for new therapeutic (And ideally prophylactic) compounds is an urgent priority. Several efforts are underway to develop new compounds for both HAT and AAT and this, combined with recently described developments in compound identification means that a compound(s) to target both diseases will hopefully become available in the next [15]. Commonly used therapeutic drugs for trypanosomiasis are diminazene aceturate (Berenil) and quinapyramine-methyl sulfate while prophylactic preparations include isometamidium chloride quinapyramine sulphate and quinapyramine chloride [68].

Trypanocidal Drug Resistance: Tsetse-borne African animal trypanosomosis (AAT) greatly influences livestock distribution and significantly slows livestock productivity in sub-Saharan Africa. While a number of

control methods targeting the vector tsetse are in field application, treatment with the few available trypanocides continues to be the most widely applied control method. Unfortunately, improper and frequent use of these few available drugs, accelerated by poor veterinary service delivery, promotes trypanosome drug resistance [69]. Trypanocides are probably the most commonly used veterinary drugs in sub-Saharan Africa. It is estimated that 35 million doses of trypanocides are used annually in Africa where about 50-70 million animals are at risk of getting trypanosomosis [70, 71]. However, the use of drugs to treat and control trypanosomosis is fraught with a number of problems including paucity of available drugs, trypanosome drug resistance development [8, 72].

Currently, curative drugs like diminazene aceturate and prophylactic drug isometamidium chloride are widely used in all African countries since half a century which led to drug resistance [73]. According to various reports, multiple drug resistance is increasing such as in Ethiopia [74], Ivory Coast [75], Senegal [76], Togo [77] and Burkina Faso [78].

Trypanosomiasis in the Wild Animals: Distinct epidemiological situations that affect trypanosomiasis in the wildlife include zones where people and livestock are absent, areas where people and livestock have been recently introduced into wildlife zones, areas where people and livestock reside in tsetse-infested zones and where large game animals are absent and areas where people and livestock are present at the edge of wildlife interfaces. Game-people-livestock interfaces gets attention due to increasing population pressure and agricultural development and the concomitant disappearance of suitable tsetse habitat outside protected areas such as national parks, game reserves and forest reserves [79, 80].

The wild animals which are the tsetse fly's natural hosts do not seem to be seriously affected by trypanosome infection [81]. The occurrence of trypanosomiasis (*T. vivax*, *T. congolense*, *T. brucei*, *T. b. rhodesiense*) in wild animals such as water buck, lion, greater kudu and bush buck was discussed. Risk actors like host, parasite species and habitat were significantly associated with the occurrence of trypanosomiasis in wild animals [82].

Vaccination: Currently, because of the phenomenon of antigenic variation, no vaccine is available.

Public Health Importance: The trypanosomes that cause African animal trypanosomiasis are not considered to be pathogenic for humans; however, disease might be possible in people with certain genetic defects [2]. Human African trypanosomiasis (HAT) (sleeping sickness) is a parasitic disease caused by a protozoan parasite belonging to the genus *Trypanosoma* and species *T. brucei* types: *T. b. rhodesiense* and *T. b. gambianse*. Approximately 60 million people are exposed to the disease and 500,000 were infected [83]. In Latin and Central America, *T. cruzi* is the cause of chagas disease and is transmitted by kissing bugs from infected people to healthy ones [84, 85].

Economic Importance: Trypanosomiasis causes direct loss due to mortality, morbidity, reduced milk production, reduced traction power and loss of condition [70]. Nagana causes an economic loss of both direct and indirect means more than US$ 4.5 billion per year in agriculture. It also leads to a reduction in food production, low milk yield as well as decreased livestock reproduction rate either through mortality, abortion and low growth rates as well as effecting fertility on domesticated animals in affected countries in Africa [86, 87]. The acute hemorrhagic syndrome caused by some *T. vivax* strains has a mortality rate of 6-35%, but, in general, *T. vivax* is considered to be less pathogenic for cattle than *T. congolense*. Some of the savannah type strains of *T. congolense* are among the most virulent isolates [18].

Morbidity and mortality rates for African animal trypanosomiasis are influenced by an animal's general health, as well as the strain and dose of the infecting organisms. In susceptible cattle or small ruminants, some strains can result in 50-100% mortality within months, especially when poor nutrition or other factors contribute to debilitation. In Africa, trypanosomiasis is now mostly a disease of high morbidity but low mortality in regions where sick animals are treated with trypanocidal drugs. Epizootics with high morbidity and mortality rates can be seen occasionally when susceptible livestock are introduced into endemic regions or when tsetse flies spread into an area where cattle are naive. However, such outbreaks seem to be infrequent. Peri-natal mortality due to abortions and neonatal deaths can exceed 50% in some outbreaks, even if mortality rates in adults are not high. Chronically affected animals may be slow to recover after treatment [18]. Trypanosomiasis also causes infertility and exclusion of ruminant livestock production from tsetse

infested area [88]. Indirect losses due to trypanosomiasis include costs for chemotherapy, control, awareness creation, transportation and social impacts [89].

CONCLUSION

African animal trypanosomiasis is cyclically transmitted by tsetse flies. Animal trypanosomiasis needs sustainable control measures to prevent serious economic losses. It causes mortality, morbidity, reduced livestock production and loss control expenditure. Annually, AAT causes many billions of US dollars to be lost through both direct and indirect means in 37 African countries. AAT affects ruminants, swine, camels, equines and carnivores, but the heaviest burden on subsistence livestock keepers in sub-Saharan Africa is caused by bovine trypanosomosis. Tsetse-transmitted trypanosomosis is also listed by the World Organization for Animal Health (OIE) as a notifiable disease.

Recommendations:

- In order to effectively control AAT, tsetse flies need to be controlled using insecticides.
- AAT should be therapeutically treated with diminazene aceturate and isomethamidium chloride in endemic areas.
- Tsetse infestation needs progressive control approach to manage reinvasion to the controlled areas.
- In the control and management of tsetse and trypanosomiasis, coordination and good collaboration of different actors is mandatory to get the desired result.
- Correct diagnosis of trypanosomiasis in the field helps for proper treatment of sick animals.
- The overall regulation of a country should focus on proper drug handling and usage to prevent trypanocidal drug resistance.

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