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Emergence, Diagnosis and Control of Bovine Trypanosomiasis in Indian Subcontinent with Reference to African Countries: A Current Perspective

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Abstract: A large assortment of domestic animal is affected by trypanosomiasis. *T. vivax*, *T. congolense* and *T. brucei brucei* are the trypanosome species found prevalent in sub-Saharan African countries infecting cattle. Whereas, *Trypanosoma evansi* is also believed to cause bovine trypanosomiasis in Asian countries. Trypanosomiasis is indicated severe anemia, emaciation, hyperesthesia, edema, abortion and fever. Methodologies such as direct smear microscopy, serological analysis and molecular techniques are often utilized to confirm infection. Several host and environment related factors are implicated during epizootic events of this disease. Being a vector-borne pathogen, impeding the spread of disease involves extermination of biting flies responsible for its transmission. However, indiscriminate use of pesticidal agents and trypanocidal preparation, have rendered their efficacy reduced. Due to trypanosome endemicity in African region, certain breeds have developed a trypano-tolerance to the clinical manifestation of disease. Authors of this review have endeavored to highlight pathology, etiology and diagnostic techniques pertaining to Bovine trypanosomiasis. Moreover, advancements regarding vector control and therapeutic procedures found effective amongst African countries have also been discussed in the context of Indian Subcontinent.

Key words: Bovine · Polymerase Chain Reaction · Trypanosomiasis · Trypanocidal Drugs · Trypano-Tolerance · Tsetse Fly

INTRODUCTION

Livestock is the primary source of income for the most part of Subcontinent [1]. Pakistan is recognized for its diverse and huge livestock population [2]. A large proportion of dairy livestock is held by small scale farmers [3]. Livestock not only provides sustenance but also draft for crop production. Yet, Pakistani farmers fail to capitalize on their natural resources and optimally utilize their means primarily due to high incidence and poor disease

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management [4]. Amongst those diseases trypanosomiasis is quite notorious for hindering growth in the livestock sector [5]. Trypanosomiasis is a multifaceted disease of protozoa [5]. It is caused due to extra erythrocytic protozoan which is found as several different sub-species of unicellular parasites (trypanosome) in nature [5]. Prevalence of Trypanosomiasis is greatly influenced by high density swarms of tsetse flies affecting herds of cattle grazing on pastoral lands. Tsetse fly population places a constraint and limitation on the ability of farmers to properly exploit grasslands [6]. Multiple trypanosome species have been reported affecting cattle in Asia and Africa, but crucially relevant ones are *Trypanosoma vivax*, *Trypanosoma congolense* and *Trypanosoma brucei brucei* [7, 8]. There are far reaching consequences of this disease in humans and livestock, ranging from dire economic losses for livestock industry to human mortalities. Disease has been specifically declared endemic in the Indian subcontinent with most disease outbreaks resulting in high mortality rates ranging between 20-90%. Thus, this disease has significant socio-economic consequences. The objectives of this review are to evaluate the epidemiological and monetary implications of bovine trypanosomiasis in Pakistan and its surrounding regions. Authors have intended to summarize latest diagnostic and therapeutic strategies against trypanosomiasis.

Etiology: Trypanosomiasisis a parasitic disease instigated by a unicellular protozoan responsible for instigating serious economic loses in livestock [5]. Causative organism for this ailment is a Trypanosoma belonging to phylum (Sarcomastigophora), of the order (Kinetoplastida) and family (Trypanosomatidae) [7]. *T. vivax, T. congolense* and *T. b. brucei* are the trypanosome species found prevalent in Ethiopia [9], Nigeria [10] and other sub-Saharan African countries infecting cattle [11]. Whereas, a study evaluating prevalence and characterization of *Trypanosoma* species in Cholistan desert of Pakistan discovered the endemicity of *Trypanosoma evansi* amongst the livestock [5]. *T. congolense* belongs to subgenus *Nannomonas* which are poorly developed trypanosomes with a medium-sized marginal kinetoplast. They exhibit limited motion as they lack free flagella and undulating membranes[12]. Subgenus *Duttonella* comprises of a single specie namely, *T. vivax* which is endemic to African and Sub-Saharan areas [13]. Trypanosomes classified in subgenus *Duttonella* possess a large terminal kinetoplast, a separate flagellum along with an unremarkable undulating membrane [14]. Despite its improved motility, this organism is considered to be just mildly pathogenic than *T. congolense* for bovine species. The lessened pathogenic impact of *T. vivax*, it is found to be endemic even in regions free from the scourge of tsetse fly, whereby it is transmitted by indirect means [13]. Mechanical transmission by biting flies, contaminated syringes or surgical instruments is evident in several research dissertations. *T. b. brucei* is classified in the subgenus *Trypanozoon. T. b. brucei* is a stumpy, non-flagellate and extremely polymorphic trypanosome [15].

Outbreaks in the Subcontinent: Most outbreaks in the subcontinent have been associated with camel [16] and equine species. But cases in bovine [17], ovine [18], caprine [19] and canine have been frequently reported as well. Trypanosomiasis has been reported several times across Indian Punjab and Haryana in bovine species [20]. Prevalence of disease has been reportedly significantly higher in Bihar [21] amongst cattle populations than buffaloes. This trend has been similarly reported in some districts of Andhra Pradesh [22] and Karnataka [23].

Life Cycle and Relationship with Tsetse Fly: Diverse species of trypanosomes spend varied amount of time in different parts of a tsetse fly whereby they undergo cyclical development (Fig. 1) [24]. Certain factors such as ambient temperature may also contribute towards influencing a site of trypanosome development. The developmental cycle of *T. vivax* is completed in the proboscis and pharynx [25], while *T. congolense* concludes its development in mid gut and proboscis [26]. Whereby, *T. b. brucei* is much more complex constituting about 3 weeks of development in mid gut and salivary glands [27].

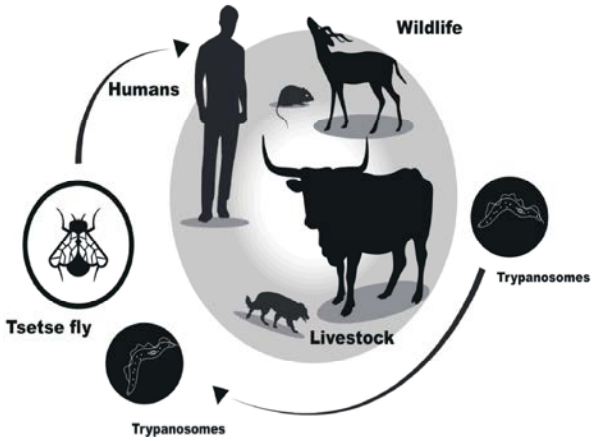

Fig. 1: Trypanosome transmission and relationship with tsetse fly

Pathogenesis: The pathogenesis of trypanosomiasis is quite varied based upon the strain of contagion, the demographics of the host and method of transmission i.e., natural or artificial. Initially, when a fly bites a host only a swelling is observed but later the affected part develops into an ulcerative wound [28]. The wound is called a chancre, which is formed as a result of an immune response elicited due to the deposition of multivariate metacyclic proliferating trypanosomes into the host during the blood sucking process [29]. Prior to trypanosomes entering host`s blood stream, chancre forms a site for their proliferation [28]. As these parasites disseminate across the host`s body, they invade lymph nodes and continue to propagate [30]. Bovine infections attributed to *T. vivax* are repetitively found to cause parasitemia and disseminated intravascular coagulation (DIC) [31]. In certain instances, *T. vivax* and *T. b. brucei* escape from the blood capillaries into intercellular spaces where they keep on multiplying [31]. Occasionally after an animal has completely convalesced from a bout with trypanosomiasis, the cerebrospinal fluid may be invaded by *T. b. brucei* [32]. Animals convalescing from chronic infections of trypanosome may develop secondary viral, bacterial or other protozoan infections as a result of immunosuppression. Trypanosomes are capable of crossing placenta barrier thereby causing some cows to abort.

Epidemiology: The epidemiology of trypanosomiasis is highly dependent on the parasite, vector and host factors. Trypanosomes are multivariate and antigenically diverse exhibiting varied response to chemotherapeutic agents. Epidemic of trypanosomiasis is highly convoluted since the parasites infect a wide array of feral and domestic species which constitute as the reservoirs of disease [33]. Risk of disease in domestic animal increases exponentially with exposure to vector species, density of tsetse flies present, specie and strain of trypanosomes prevalent in the region and source of infection (wild or domestic animals) [33].

Mode of Transmission: Trypanosomiasis is a disease, which is communicated by both definitive and intermediate hosts [34]. Pragmatically, any specie of *Trypanosoma* may be transmitted by birth or may be acquired by exposure to the vector [6]. Once infected, a tsetse fly remains a carrier. Inside the fly, *Trypanosoma* undergoes distinct morphological changes [25]. Trypanosome amastigotes first transform into promastigotes then epi-mastigotes until finally becoming trypomastigotes [35]. This metacyclic stage is capable of infecting mammalian species. Upon feeding on a disease-ridden animal, tsetse fly becomes infected with trypanosomes [28]. As the trypanosomes pass through the proboscis into the mid gut, a number of developmental changes occur including removal of surface coat and mitochondrial development before finally being transmitted to mammalian host during feeding [33].

Risk Factors

Host: Host response towards trypanosomiasis is extremely varied. Mostly, acute incidence of disease is observed following transmission of the infection. However, in certain wild and domestic animal population a balance is established with the parasite. Whereby the host remains a carrier but clinically healthy for a prolonged period of time [28]. Explicitly, certain varieties of African cattle are tolerate trypanosome infections [36]. They accomplish this task by impeding the proliferation of trypanosomes in their body, especially in cases pertaining to *T. vivax*. This phenomenon is identified as trypano-tolerance [37]. In addition to specific genetics, certain environmental factors are responsible for such a phenotypic expression. Therefore, extent of this so-called tolerance is highly varied in different individuals.

Likewise, crossbred Taurine as well as Zebu cattle with higher levels of genetic heterogenicity are more resilient than pure bred zebu cattle [38]. Nevertheless, the indeterminate genotype of Taurine and Zebu population is imperative for extrapolating the true source for trypano-tolerance [39]. Even amongst genetically similar animals, extent of trypano-tolerance may fluctuate and vary based upon certain factors such as stress, malnutrition and the tsetse fly distribution in the region [40]. Sheko, a hump-less breed, residing in eastern parts of Africa exemplifies trypano-tolerance. Sheko breed is indigenous to only certain parts of Ethiopia [41, 42] and is specifically found around the Bench-Maji zone [43].

Environmental Factor: Tramping and extensive grazing of domesticated African bovines across savannas face an imminent risk of being bitten by tsetse flies [25]. Furthermore, the risk is compounded when cattle routes converge on to major bridges or watering holes. Incidence of disease in a specific area is correlated with the density of tsetse population [28]. The presence of tsetse flies in any habitat is highly influenced by climate. In the last century or so, industrial and agricultural developments

have brought about a decline in tsetse population by eliminating their ecosystem [33]. Owing to a lack of appropriate niche, tsetse flies converge wherever game or forest reserves are established. Animals from nearby farms are at high risk of trypanosomiasis [6]. Tsetse flies (*Glossina* spp.), require a temperate habitat which is heavily affected by ecological and climatic perturbations. Any type of climatic extremes, particularly above 36°C and below 10°C can cause high adult fly mortality [44]. A decline in tsetse population is thought to be as a result of prolonged rainy seasons followed by protracted dry seasons. Tsetse flies are negatively affected by high altitude therefore their geographic distribution is limited across equatorial line [25]. Diverse varieties of tsetse flies may flourish on different types of fauna and require specific climatic conditions suitable to their evolutionary requirements. Consequently, a cumulative effect of perfect climate, vegetation and habitat is essential for prevalence of tsetse fly in a region [45]. So, it may be deduced that trypanosomiasis is affected by all the factors responsible for the bloom or decline in tsetse fly population.

Pathogen Factor: T lymphocyte triggering factor (TLTF), B- cell mitogen, non-descript enzymes and variant surface glycoproteins (VSG) are produced by living and dead trypanosomes. These biologically active substances are believed to cause trypanosomiasis.

Variant Surface Glycoproteins: In mammals, 107 variant surface glycoprotein molecules coat the surface of trypanosomes [46]. It is common in infectious condition the coat of trypanosome undergoes a change in its antigenic expression of VSG coat. This is done to escape phagocytosis by mammalian immune system [47]. A membrane anchor made up of phosphatidylinositol is used for mammalian cell attachment [48]. These glycoproteins sometimes enter and cause lysis of mammalian erythrocytes [49].

Trypanosome Enzymes: Trypanosoma has the capability to produce enzymes such as phospholipases, protease and sialidases which may be used as pathogenic factors.

Sialidases: Sialidases are proficient in altering erythrocyte surfaces. As a consequence, erythrocytes appear foreign to the animal's immune system. Such a turn of events, thereby causes autoimmune phagocytosis of these red blood cells. Membrane-bound sialidase has been reported in *T. vivax, T. b. brucei* and *T. congolense* infections [50].

Proteases: African trypanosomes release proteases namely serine oligo-peptidases and cysteine proteases into the circulatory system of their diseased hosts. Peptidases are broadly regarded as the foremost virulence factors and prime targets for chemotherapeutic agents in trypanosome infections [51].

Phospholipases: Phospholipases have diverse and substantial biological implications during trypanosome infections. In biological systems Phospholipases and lyso-phospholipases are believed to have been generated by autolyzed trypanosomes [52].

B-Cell Mitogen: Serum-immunoglobulins, especially IgM, surge significantly in trypanosomiasis. A B-cell mitogen is produced by Trypanosomes which anticipates responses to new antigens. B-cell mitogen behaves as non-specific antigen, therefore it stimulates an incoherent immune response from the host making it more favorable for the host to survive [53].

T Lymphocyte Triggering Factor: Lymphocytic triggering factor produced by trypanosomes selectively activate CD8 (+) T lymphocytes, while also stimulating them to release IFN-gamma [54]. These triggering factors are called as trypanokines and are responsible for tempering with host's cytokines system for the advantage of parasite. *T. vivax* produces a higher level of parasitemia in cattle than any other species, which in turn facilitates in its mechanical transmission [53]. Conversely, *T. b. brucei* is seldom noticeable by microscopic examination of blood smear [55].

Zoonotic Importance and Risk of Anthropozoonosis: Though animal and human pathogens are not the same, but in case of *T. brucei gambiense* and *T. brucei rhodesiense* certain animals can intermediately and non- restrictively serve as hosts [56]. Humans can get bit by tsetse flies anywhere with heavy forest coverage or in other rural environments. There haven't been any cases reported of sleeping sickness in Ethiopia since 2000 [57].

Trypano-Tolerance: Investigation has revealed that diverse mammalian hosts respond unpredictably to trypanosome infection. Some hosts are genetically resilient to trypanosome infection both in natural and experimental settings. In case of laboratory mice, BALB/c are vulnerable to trypanosome infection whereas, C57B1/6 mice are quite resistant [58]. This phenomenon has also

been reported in certain breeds of cattle namely, *Bos taurus* (N'Dama breed) indigenous to West Africa which is fairly impervious to trypanosomiasis when compared with *Bos indicus* (zebu breed). Moreover, N'Dama`s legendary resilience towards trypanosomiasis may be attributed to their continued bout with the parasite for several centuries [38].They have developed a unique adaptation which helps them fend-off trypanosome proliferation and tolerate anemia. The mechanism by which these hosts are able to tolerate African trypanosomiasis is complex and thus, is not well understood. It is supposed to involve a robust immune response against the parasitic antigen and production of special cytokines which eliminate the pathogen [38]. Several studies report that there is a difference in cytokine production between resistant and susceptible hosts. Studies show that trypano-tolerant hosts elicit a stronger antibody production than the susceptible ones. In trypano-tolerant mice there was an increased production of interleukin (IL) 10 and IL-14 coupled with a stronger antibody response to trypanosome VSGs during infection [39].

Clinical Finding: Trypanosomiasis cannot be diagnosed by manifestation of specific pathognomonic signs or lesions. Prevalence of disease is predicated upon a myriad of factors. Difference in tsetse fly population and pathogenicity of the endemic strains serve as limiting factors for trypanosomiasis [59]. Clinical phase is often acute in nature with symptoms lasting from a few days to a few weeks. Whereas, incubation phase can last for about 20 days. Animal is dull, depressed and anorexic while experiencing intermittent fever [60]. There is watery ocular discharge and condition of the animal continues to waste away. Superficial lymph nodes become visibly swollen, mucous membranes are anemic and occasional diarrhea is observable. In some animals, throat and brisket regions are edematous [59]. Reproductive cyclicity is impeded while pregnant animals infected with trypanosomiasis may abort fetuses [61]. Semen quality is affected deleteriously as well. Most animals suffering from chronic type of the disease become hide-bound with apparent signs of severe malnutrition [62]. This type of appearance in conjugation with the presence of swollen lymph nodes is said to be having a "fly struck" appearance. Moreover, immune system is compromised to such a degree that vaccinations fail to achieve desirable immunogenicity unless trypanocide drugs are administered [63].

Diagnosis: Without performing confirmatory diagnoses of trypanosomiasis, disease transmission and pathogenesis can never be properly studied [5]. It is only possible after establishing cases of confirmed trypanosomiasis that we can implement chemotherapeutic and monitoring practices against the incidence for the aforementioned disease [59]. Several diagnostic and serological tests are available with different sensitivities and specificities for trypanosome to establish an undisputable diagnosis and study disease distribution across the geographical lines [60]. In certain situations, clinical signs offer a much more reliable source for trypanosomiasis diagnosis than parasitological analysis. However, it has been discovered that while clinical diagnosis offers good sensitivity (78%) it compromises the specificity (27%) of the results.

Parasitological Diagnosis

Wet Blood Film: It is the method which employs a simple smear technique whereby a drop of blood is placed on a glass slide and covered by a cover slip. Then the slide is observed under 40X microscopic magnification. Trypanosomes are observed as extra-erythrocytic bodies. It is a monetarily feasible solution to a wide spread problem. By diagnosing and pre-emptively screening cases of trypanosomiasis, we may control the spread and prevalence of the disease in a region [64].

Thick Blood Smear: Parasites are diagnosed based on their morphology but are often damaged due to process of staining or inefficiency of the observer [65].

Thin Blood Smear: Both thin and thick smear methods employ same principle of Trypanosoma identification though in case of thin blood smears even a specific specie of trypanosome may be distinguished [66]. *T. vivax* is observable with a large terminal kinetoplast under a microscope. It has free flagellum at anterior border while its posterior end is rounded. It has an inconspicuous undulating membrane and a size of 20-27 µm [67]. Unlike *T. vivax, T. b. brucei* has multiple morphological types whereby a long slender form with a length of 17-30 µm and a short stumpy form with length of 17-22 µm and is observed under light microscopy [68]. It has a medium sized kinetoplast that is terminally positioned and commonly measured between 8-25 µm. Furthermore, flagellum is mostly absent in *T. congolense* [66].

Hematocrit Centrifugation: A (70 x 1.55mm) heparinized capillary tube is filled with blood and sealed at both ends. Capillary tube is placed in a centrifuge where blood is allowed to separate. Buffy coat is examined beneath a dark field microscope for the presence of trypanosomes [69].

Serological Diagnosis

Indirect Enzyme Linked Immunosorbent Assay (ELISA): A sandwich ELISA is performed whereby a micro titer plate containing 96 wells coated with antigen is tittered with anti-trypanosome antibodies which are labelled with an enzyme. The reaction between the substrate and an enzyme creates a visible reaction affirming anti-antibody reaction [70]. Mitochondrial heat shock proteins are being studiously examined by scientists for the identification of *T. congolense*.

Indirect Fluorescent Antibody Test: The procedure is financially laborious and it cannot be performed in field conditions. However, this test's sensitivity cannot be denied [71].

Antigen-Detecting Tests: Several underlying factors are indicated for ineffectiveness and non-reliability while testing circulatory trypanosome antigens. It is noteworthy to consider that the reactivity and specificity of antigens used in Ag-ELISA is yet undefined [72]. Consequently, false positives are a norm while considering these tests. Another important aspect is the possible immunogenic interference by the host's defense mechanism thereby contaminating the integrity of blood samples influencing host-agent relationship.

Molecular Diagnosis: Polymerase chain reaction (PCR) is highly specific and effective tool for diagnosis of trypanosomiasis. Over the decades, specie-specific testing kits have been developed which identify particular genetic markers and can distinguish different subgenus. In case of animal pathogen namely, *Trpanosoma evansi* a PCR predicated upon identification of RoTat 1.2 VSG has proven extremely useful [73]. However, some other trypanosome species such as *Trpanosoma equiperdum* and *Trpanosoma brucei brucei* which are very closely related, cannot be specifically identified [73]. With the help of PCR extremely low concentrations of contagion's DNA material may be amplified and detected resulting in pre-emptive diagnosis. Recently, a new methodology involving expression site associated genes 6 and 7 has been developed for diagnosis of *Trypanosoma brucei gambiense* [74]. Concomitantly, serum resistance-associated gene (SRA) was used to confirm *Trypanosoma brucei rhodesiense* [75]. PCR has also been quite helpful in gene splicing and phylogenetic analysis of trypanosome species hailing from different parts of the world. In a prior investigation spliced-leader gene obtained from infected animals in Brazil was detected by PCR amplification of an intergenic spacer sequence which had an uncanny similarity with West African *T. vivax* stocks [76]. The only limitation of this process is a need for specie specific hybridization probes [77].

Control and Treatment: Scientists have attempted to control and eradicate trypanosomiasis for more than a hundred years but most efforts have proven to be futile.

Tsetse Vector Control: Decades ago, when vector and disease interaction was discovered the only feasible method believed to control bovine trypanosomiasis was the elimination of the vector [45]. To that end, clearing unnecessary and wild vegetation along with pesticidal spraying of bushes was believed to be the most pragmatic option. But such a policy was flawed as it involved destruction of valuable resources. Furthermore, large scale use of insecticidal aerosols caused irreparable damage to the ecosystem [57]. Consequently, a two-pronged policy has fervently been implemented which involves setting up targets and traps for capturing and elimination of tsetse flies while the other method is to use pour-on insecticides on the Tsetse fly hosts to act as fly repellants thereby impeding propagation of trypanosomiasis [28]. Sterile Insect Technique (SIT) has also proven to be quite effective in efforts to eradicate trypanosomiasis. Evolution has made tsetse fly very adept to its ecological niche consequently severe actions must be undertaken to force its extinction [78]. Because of the vector`s resilience to traditional control methods and its endemicity, tsetse flies prove to be ideal candidates for traps and targets [14]. Flies are chemotactically attracted to these traps whereby they receive a lethal dose of pesticide and die. Traps and targets are only as effective as well they are employed. Setting up traps in high tsetse density areas during their active hours during the day yield the most effective outcome. The rationale behind treating an animal with insecticides is similar to that of baited traps and targets [25]. Variations of such techniques have been used in central Africa and some parts of India with immense success. Synthetic pyrethroid insecticides such as deltamethrin have been extensively

researched as topical repellents against tsetse flies owing to their high efficacy and low toxicity in bovines [61]. Though topical use of insecticides provided adequate protection against tsetse flies in African regions, similar regiments when employed across the subcontinent appeared to interfere with endemic stability of cattle to several tick-borne diseases. Agents like citronella [79], chlorpyrifos [80], amitraz [81], piperonyl butoxide [82] and cypermethrin [83] can be used in different combinations and proportions as pour-on fly repellents. Sterile Insect Technique (SIT) involves sustained and systemic release of sterile insects among the indigenous target population. When these sterilized males copulate with native females, they render such females infertile for the rest of their lives. Such techniques when repeated throughout several tsetse fly generations cause an acute decline in their indigenous population.

Vaccination Against Trypanosomiasis: Trypanosomes are covered by a dense coat of variant surface glycoproteins that stimulate antibody production in the host which in turn makes development of vaccine quite cumbersome. Outer coat evolves and mutates effectively to survive incursion from the host`s immune system. Despite several advancements in the field of immunology, no reliable regiment against antigen switching is available to this day [53].

New Tsetse Repellent Technology: Cutting edge research at the International Centre of Insect Physiology and Ecology (ICIPE), Kenya, has yielded several revolutionizing discoveries for the control of trypanosomiasis [84]. The most groundbreaking technology is predicated on development of potent phenolic repellents. Tsetse flies use kairomone to locate its host, the phenolic derivatives act as olfactory antagonist of kairomone [85]. Consequently, reducing tsetse challenge by almost 80 percent. The olfactory irritants such as 2-methoxy 4-methylphenol may be practically utilized by a repellent dispenser hanging around an animal's neck capable of releasing a constant rate of agent periodically. Another study revealed how body odor constituents such as δ-octalactone, guaiacol, geranylacetone, hexanoic and pentanoic acid of waterbuck are capable of repelling tsetse flies (*G. morsitans* and *G. pallidipes*), when extracted and topically applied across bovine hides [85].

Ethno-Veterinary Remedies Against Trypanosomiasis: Although reasonable efficacy of conventional allopathic medication against both endo- and ecto-parasitic diseases have been thoroughly documented [86]. Consequently, decades of research into ethno-veterinary claims have yielded certain favorable outcomes. *Syzyium quinensis, Boswellia dalzielli, Cissus populnea, Lawsonia inermis* and *Terminalia avicennoides* are some plant species that were scientifically proven to mitigate clinical manifestation of trypanosomiasis. Moreover, several other herbs namely, *Sterculia setigera, Adansonia digitata, Afzelia africana, Pseudocedrela kotschi, Khaya senegalensis, Prosopis africana, Tamarindus indica and Lancea kerstingii*were also found to be quite efficacious [86]. The leaves and stumps of these plants were often macerated to extract their essence. Which was subsequently administered to individuals suffering from trypanosomiasis. A prior study involving infected rats treated with ethanolic extract of *Tithonia diversifolia* was quite promising [87]. Some of these plants including *Nauclea latifolia*was processed to obtain a preparation capable of producing anti-hepatotoxic effects when used in adequate dosages [88]. Elixir made from Sorghum bicolor and *Telfaria occidentalis* reconstituted at a concentration of 4 mg/100ml of distilled proved effective in anemic rabbits [89].

Trypanocide Drugs: Drug control of animal trypanosomiasis relies essentially on drugs such as Homidium chloride and Homidium bromide, Diminazene aceturate [90], Isometamidium chloride and Quinapyramine sulphate. Most of the trypanocide drugs are believed to be effective only against *T. vivax* and *T. congolense*. Though Quinapyramine sulphate possesses significant efficacy against *T. brucei* and *T. evansi* as well [91].

Homidium: Homidium has limited effectiveness against most trypanosome species and its efficaciousness varies heavily, depending on severity of disease prevalence in a region. In regions of west Arica where resistance towards Homidium Chloride has yet not developed it may be administered at a dose rate of 0.1mg/kg. While in regions exhibiting higher endemicity, a dose rate of 1mg/kg is recommended [92].

Quinapyramin Sulphate: It is a drug of choice for small ruminant trypanosomiasis but its efficacy in cattle has also been reported. It can be administered sub-cutaneously at dose rate of 5mg/kg [93]. In recent research models Quinapyramin sulphate was reported to be significantly efficacious in *T. congolense* infections than *T. vivax* ones.

Diminazene Aceturate: It can be administered sub-cutaneous or intramuscularly at the dose rate of 3.5 mg/kg in cattle for the treatment of infection caused by *T. congolense* and *T. vivax* while for *T. b. brucei*, 7 mg/kg is required. Diminazene is known to be an effective trypanocide drug which has a tendency to accumulate for long period of time in subject's tissues [92].

Isometamidium: It has been used in field conditions as a prophylactic as well as trypanocide drug. At higher dosages, it is quite efficacious for prophylactic purposes against trypanosomiasis. It is administered at a dose rate of 0.25-1mg/kg intra muscularly in ruminants. Some strains of trypanosomes resistant to Isometamidium have been discovered which can be treated with Diminazene aceturate at dose rate of 0.5-1mg/kg [92]. The resistant strains of trypanosomes have disseminated across the rural planes of Africa. In most situations the root cause behind trypanosome resistance has been attributed to less than therapeutic dose administration of trypanocide drugs which imparts trypano-tolerance to certain pathogenic strains of trypanosomes. In recent years, drug resistant animal Trypanosomes continue to become a huge problem [94]. New strategies such as sanative treatment, increased dosages, repetitive treatments and use of complexes have to be employed for efficacious treatment [91].

CONCLUSIONS AND RECOMMENDATION

The impact of trypanosomiasis on economy and demographics of a rural society have been rarely studied. The monetary expenses involved with diagnosis and therapy pertaining to trypanosomiasis have compounding repercussions on underdeveloped agronomies. Authors have endeavored to present a concise review regarding the pernicious nature of the aforementioned parasite. The causative agent is widely spread around the world and may infect several hosts species. Trypanosoma species may spread through an unlimited number of vectors any propagate through a wide range of host species. In African countries, bovine trypanosomiasis is the main constraint of livestock production and rural development. Over the years, this disease has resulted in serious economic losses, especially in western and southwestern parts of Ethiopia. Bovine trypanosomiasis is difficult to confirm with diagnostic testing. However, from a practical standpoint diagnosis of bovine trypanosomiasis mainly relies on obsolete parasitological diagnostic techniques. Earlier methods of controlling trypanosomiasis involved bush clearing strategies and elimination of game animals on which tsetse flies fed. These methods are environmentally unfriendly and less effective. The current initiatives to control trypanosomiasis are mainly based on tsetse fly control (area-wide integrated pest management). The sterile insect technique has been practiced in Ethiopia for the last 10 or more years and resulted in significant tsetse fly reduction where it has been employed. Such techniques could possibly be employed in Subcontinent countries as well to control spread of trypanosomiasis. However, a major hinderance in vector control strategies is the fact that most of outbreaks reported in India and Pakistan have been due to *Trypanosoma evansi* which has lost dependence upon tsetse flies for its propagation. Further investigations are warranted to clarify the role of *T. evansi* for causing trypanosomiasis in cattle, especially in Asian countries. Bovine trypanosomiasis can be treated by both the prophylactic and curative drugs. The extensive and indiscriminate use of pesticides against flies has made them tolerant to their lethal effects. Thereby causing farmers to opt for even deadlier and toxic preparations. A similar situation has been seen in the case of trypanocide drugs. Whereby their improper usage has rendered them in effective. Therefore, unchecked use of such drugs should be curbed and effective prophylactic measures should be developed to mitigate the spread of this disease.

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