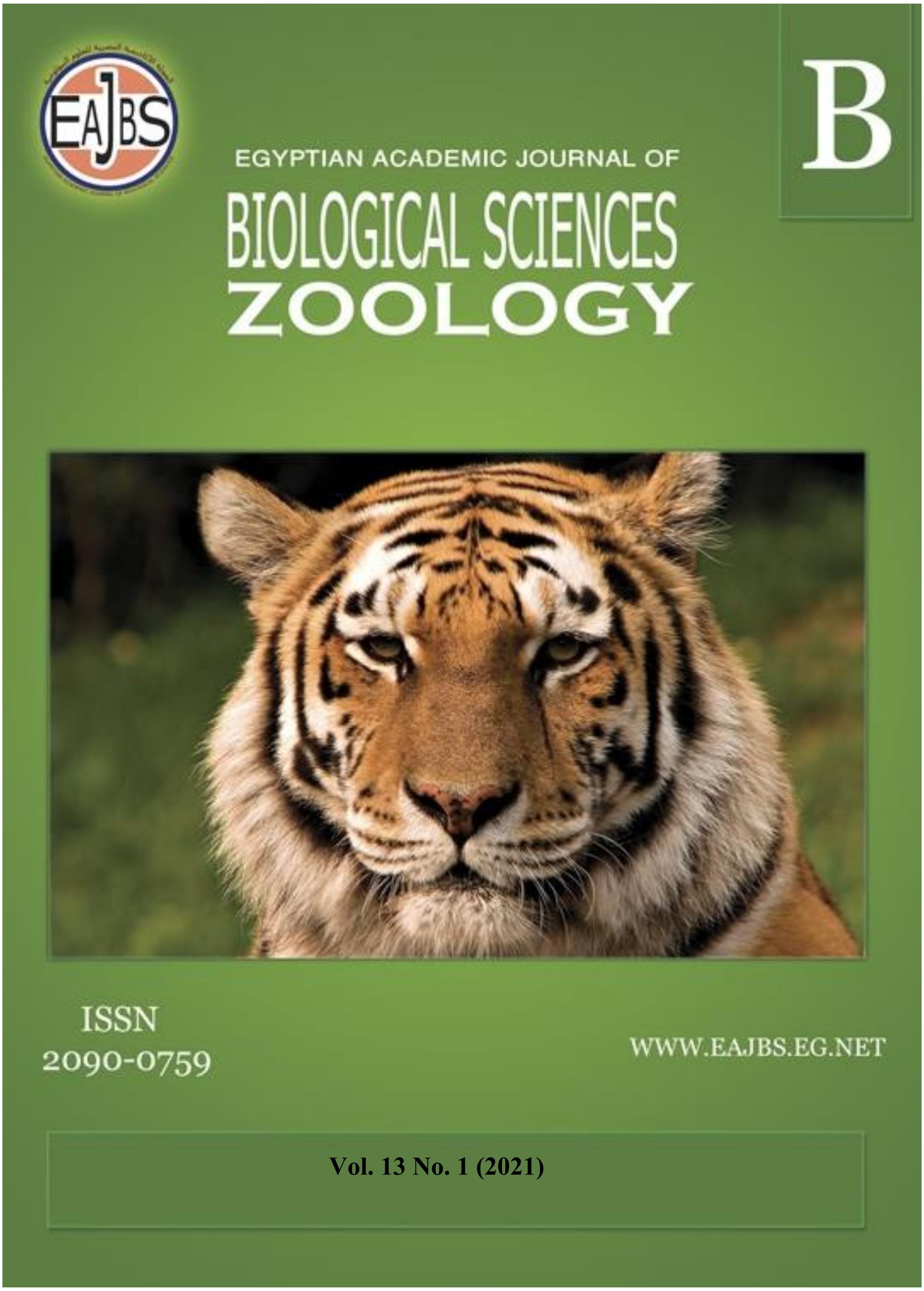

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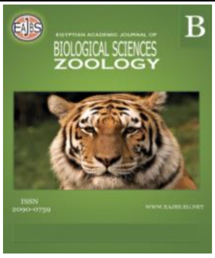

Techniques for Managing Ticks and Tick-Borne Diseases Under Changing Climate; A review

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ABSTRACT

Tick infestation is the main issue for animal health that causes substantial economic losses in the form of mortality and morbidity, particularly in tropical and subtropical countries of the world including Pakistan. The rural economy of Pakistan depends upon on livestock industry which faces the problems of some zoonotic diseases spread by tick infestation. Tick infestation caused Crimean-Congo hemorrhagic fever (CCHF), Lyme disease, theileriosis and babesiosis in wild and domestic animals including humans. Climate change is highly associated with the distribution of ticks and ticks borne-diseases (TBDs). Due to global warming, the temperature of the globe is rising which directly and indirectly affects vector-borne diseases like TBDs. To minimize the ticks and TBDs various approaches have been used in different regions of the world including Pakistan. The need for a review paper is to investigate the impact of climate change on ticks and TBDs in livestock as well as public health in Pakistan. To evaluate the effectiveness, environmentally safe, economically feasible and acceptable tick management approaches, literature was reviewed.

INTRODUCTION

Tick:

Ticks are ectoparasites, which suck the blood of wild and domesticated animals. Ticks are mostly found in a tropical and subtropical region of the world. There are three families of ticks viz. Ixodidae, Argasidae and Nuttalliellidae. The Ixodidae and Argasidae are known as hard and soft ticks, respectively (Ramzan et al., 2019). The hard ticks have scutum or hard plate on the dorsal side of the body and suck more blood while soft ticks lack these features (scutum) and suck less amount of blood. The family, Nuttalliellidae has features in-between with the first two families (hard and soft) (Guglielmone et al., 2010). The families Ixodidae and Argasidae have 700 and 200 species, respectively while Nutteliellaide has only one species (Ramzan et al., 2018).

The main genera of these mentioned families are*Hyalomma, Amblyomma, Rhipicephalus, Ornithodoros, Boophilus, Dermacentor* and *Ixodes*. Both sexes (male and Female) suck the host's blood to fulfill their energy requirement. Ticks can live for a long period of time without bloodsucking depending upon their host availability and species of ticks. Ticks reached their hosts by using the breath, odors, sensing body heat and vibration of their hosts (Ramzan et al., 2018; 2019). Ticks mostly attack the ears, udder and tails of animals. There are three stages of ticks like egg, nymph, larva and adult. After hatching from eggs convert into six legs nymph and six legs then develop into eight legs adult (Montales et al., 2016).

Ticks Distribution:

Ticks and Ticks borne diseases (TBDs) are found almost all over the world like Asia, Europe, Africa, Australia, North and South Americas (Haque et al., 2011; Bilkis et al., 2011; Sajid et al., 2011; Razmi and Ramoon, 2012; Singh and Rath, 2013; Reye et al., 2012; Tiki and Mekonnen, 2011; Elghali and Hassan, 2012; Lohmeyer et al., 2011; Kamau, 2011).

Factors Involved in the Transmission of Vector-borne Diseases:

The main factors involved in the transmission of various tick-borne diseases are deforestation, use of land, habitat loss, reforestation, migration of animals, birds and many other factors which provide suitable conditions for increasing their hosts. The various other factors like Urbanization, tourism, loss of biodiversity, the introduction of alien species, travel and trade are helpful for TBDs transmission. The biotic and abiotic factors are also responsible for the transmission of vector-borne diseases including ticks borne-diseases. The abiotic factors include habitat structure and climate change while biotic consist of host abundance is favorable sites for the protection of tick species. Humans are also involved in diseases by using raw milk of infested animals.

Climate Change and Tick-borne Diseases:

Climate change is the main factor that changes our way of living and the environment. Due to climate change, the need for air condition is increase and resulting in global warming. The temperature of the globe is increasing due to the burning of fossil fuels and the emission of greenhouse gases. The concentrations of chlorofluorocarbons are enhanced due to the emission of these gases and deplete the ozone layers which also contribute to increasing the atmosphere temperature (Dahl, 2013).

Due to climate change, infectious diseases are transmitted into animals and humans through vectors including ticks (Altizer et al., 2013). Ticks most of their lifetime spend in vegetation, environment and depend upon hosts and climate for their survival and development (Dantas-Torres, 2010). Among these factors, climate change is helpful for tick distribution and transmission of the tick-borne pathogen to humans and animals (wild and domestic) (Leger et al., 2013).

Today due to climate change, global warming and tick-borne diseases are becoming the main issue all over the world (Keesing et al., 2010; Estrada-Pena et al., ~ 2012, 2014b; Ogden et al., 2013; Estrada-Pena and de la Fuente, ~ 2014; Parham et al., 2015; Medlock and Leach, 2015; Gilbert, 2010; Randolph, 2010). The Mediterranean spotted fever spread through brown dog ticks due to climate change (Tokarevich et al., 2011). In the north of European Russia has been reported that climate change act as a major driving force for the distribution of tick-borne encephalitis. Similar results have been reported by many workers (Mannelli et al., 2012; Medlock et al., 2013) that climate change is helpful for *Ixodes ricinus* and *Borrelia burgdorferi sensulato* development and survival into various regions of the world especially northern latitudes and altitudes.

Ticks are the second most important vector of diseases after mosquitoes. Ticks transmit viral, protozoal, bacterial and rickettsial diseases in humans and animals like domestic and wild (Yu et al., 2015). There are two ways such as transovarial and transstadial through which diseases transmit into hosts. During transovarial transmission, ticks suck the host's blood while in transstadial, vertical transmission occurs and diseases spread from one stage of a tick to other.

Ticks are the vector of several types of diseases in domesticated and wild animals [86]. The main diseases which transmit through ticks in human are Babesiosis, Colorado tick fever, Ehrlichiosis, Relapsing fever, Rocky Mountain spotted fever, Tularemia and Lyme disease while in animals Anaplasmosis, Babesiosis, Ehrlichiosis, Haemobartonellosis, anemia, Rocky Mountain spotted fever, Lyme disease, Theileriosis, Hepatozoonosis, Cytauxzoonosis and transitory hemoglobin urea (Wu et al., 2013; Naz et al., 2012; Shahzad et al., 2013; Ramzan et al., 2018) globally. Among all these diseases, Crimean-Congo Hemorrhagic Fever (CCHF) is a serious disease with a maximum percent death rate.

Crimean-Congo Hemorrhagic Fever (CCHF):

Crimean Congo hemorrhagic fever (CCHF) is a contagious disease spread by hard ticks belonging to the genus, *Hyalomma* (Ramzan et al., 2018, 2020). It has a wide range and is spread all over the world with an approximately 50% death rate. Its causative agent is the virus belongs to genus and family Nairovirus and Bunyaviridae respectively (Qadir et al., 2017). It is a negative single-stranded RNA virus. The disease spread through direct and indirect contact. It can be spread through biting the infected ticks or contact with blood. The virus transmission can take place from human to human and cells of infected ticks. The main vector of CCHF is *Hyalomma marginatum marginatum marginatum*. Other tick genus such as *Rhipicephalus*, *Ornithodoros*, *Boophilus*, *Dermacentor* and *Ixodes spp*. are the reservoirs of CCHF.

CCHF has been distributed in more than 30 regions of the globe like Africa, Southeast Europe, Middle East and Asia (Qadir et al., 2017). The major hosts of ticks are domestic as well as non-domestic animals including buffaloes, cattle, goats, sheep, birds, rodents and small mammals. All these hosts have some antibody response against tick infection. The migratory birds also carry ticks and become the cause of tick distribution.

Climate change greatly influences the prevalence of ticks borne diseases all over the world. Due to global warming, the prevalence of ticks borne diseases reached the highest and the chance of epidemiology of CCHF increase (Randolph, 2013; Ostfeld and Brunner, 2015). In Pakistan the peak point of CCHF disease has been reported during months of March and May and then in August and October, while in Iran the disease was maximum in August and September. These months are favorable for tick growth and reproduction due to highest temperature.

Signs and Symptoms:

High fever, joint pain, back pain, stomach pain, and vomiting. Flushed face, petechiae on the palate, jaundice, red throat and eyes are the initial signs and symptoms of CCHF. During unadorned cases, changes occur in mood and sensory perception.

Diagnosis of Crimean Congo Hemorrhagic Fever (CCHF):

Real-time polymerase chain reaction (RT-PCR), antigen-capture enzyme-linked immunosorbent assay (ELISA), immunofluorescence assay (IFA), detection of antibody by ELISA (IgG and IgM) and virus isolation attempts; laboratory tests that are used to diagnose CCHF. During the serious stage of the disease, patient diagnosis can be done by using the combination of detection of the viral antigen (ELISA antigen capture), viral RNA sequence (RT-PCR).

Rocky Mountain Spotted Fever:

Humans are also involved in the distribution of ticks and TBDs. As the human population is increasing the need for sources like land and food also become a major problem for their requirements. The distribution and abundance of ticks and TBDs are highest during the migration of humans, animals and birds from one region of the world to another. During the migration the new sites and hosts available for tick reproduction and development. Deforestation and floods also major factors for the transmission of vector-borne diseases including tick-borne- diseases. Due to the reduction of plants and vegetation, ticks migrate toward the new hosts for the bloodsucking. The people which live close to the animals carried more ticks and TBDs, so animal husbandry also involves in ticks-borne diseases.

Ticks, *Dermacentor variabilis, Dermacentor andersoni, Rhipicephalus sanguineas* and many other tick species are the main vector of Rocky Mountain spotted fever in several regions of the world. This fever is ticks transmitted rickettsial disease in humans through a causative agent, *rickettsia*. This zoonotic disease is also transmitted by horizontally as well as vertically into hosts (Anonyms, 2012). Both nymphs and larvae of ticks attacked on their hosts cause rickettsia in dogs and rodents. It has been reported that fever is transmitted through the immigration of dogs in the Americas (Burlini et al. 2010). It has been reported that April, September, June and July being the peak months of fever. These are favorable months because in the above-mentioned month's temperature reached the peak point.

Signs and Symptoms:

The infested patients showed symptoms like fever, chills, vomiting, lack of appetite, headache, depression, abdominal pain, arthritis-like stiffness when walking and neurological abnormalities. During the severely attacked rashes can be developed on the feet and palms of the hands.

Diagnosis of Rocky Mountain Spotted Fever:

Major laboratory findings are elevated liver enzyme levels, low platelet count and blood sodium concentration. The best method, immunofluorescent antibody assays can apply for diagnosis.

Babesiosis:

Babesiosis is a protozoal disease that caused severe economic losses around the globe including in Pakistan. It is caused by Babesia species in buffaloes and cattle. Ticks species that spread the disease are Rhipicephalus, *Haemaphysalis*, *Dermacentor*and *Ixodes* (Figueroa et al., 2010). The majority of these diseases are found in temperate, subtropical, and tropical countries of the world (Farooqi et al., 2017).

The reasons for the high prevalence of the disease are due to due to the hot and humid season. The temperature, rainfall and relative humidity during summer are favorable conditions for ticks and TBDs development. It has been seen that the disease is maximum in summer and minimum in winter due to low temperature in winter and highest in spring and summer (Haq et al., 2017).

Signs and Symptoms:

It also affects the red blood cells of the patient. Anemia, lack of lethargy, vomiting, weakness, appetite and weight loss are the main signs and symptoms.

Diagnosis of Babesiosis:

The techniques such as enzyme-linked immune-sorbent assay (ELISA), indirect immunofluorescence assay (IFA) and immunoblot can use for the detection of disease.

Theileriosis:

Ticks' species are the vector of several diseases in tropical and subtropical areas of the globe including Pakistan. The climatic condition of Pakistan is suitable for ticks and TBDs such as ovine theileriosis in small ruminants especially cattle and sheep (Farooqi et al., 2017; Ramzan et al., 2018). The climatic condition, directly and indirectly, affects the animals and humans (Irshad et al., 2010; Zulfiqar et al., 2012; Jalali et al., 2013) by ticks borne-diseases.

The major TBDs are theileriosis distributed in various regions of the world including Pakistan. It can transmit by many tick genera such as *Amblyomma, Haemaphysalis, Hyalomma,* and *Rhipicephalus***.** It spread by *Hyalomma anatolicum, Theileria annulata* and

Theileria orientalis diseases affected the livestock especially buffaloes and cattle resulting reduction the production (Ghosh and Nagar, 2014). The exotic and crossbreed animals are mostly affected by theileriosis than indigenous animals. It can become fatal for exotic and crossbreed animals if an effective measure is not adopted for its management.

Signs and Symptoms:

Heart failure, anaemia, swelling and enlargement of lymph nodes, Haemorrhages in the ocular and vaginal mucous membranes, jaundice, hyperthermia and Bruxism are the main signs and symptoms of the disease.

Diagnosis of Theileriosis:

Laboratory tests including are ELISA, in a direct polymerase chain reaction (PCR) and immunofluorescence test can also help in disease diagnosis.

Anaplasmosis:

Anaplasmosis is caused by intraerythrocytic rickettsia in tropical and subtropical regions. The huge number of tick species can become the cause of disease spreading in wild and domesticated animals especially *Hyalomma* and *Rhipicephalus* (Camus et al., 2010). This disease is spread by pathogens like *Anaplasma marginale*, a threat for humans and animals. It can cause due to two species of bacteria like *Anaplasma phagocytophilum* and *Anaplasma platys. Anaplasma phagocytophilum* is a zoonotic disease, deer tick and the western black-legged tick are the major vectors of *Anaplasma phagocytophilum. Anaplasma platys* are spread by brown dog tick.

Signs and Symptoms:

Loss of appetite, Lethargy, Lameness, reluctance to move, Myalgia, cough, Neck pain, or neurologic are the signs of *Anaplasma phagocytophilum* while Spontaneous nosebleeds, bruising on the gums and belly are the symptoms of *Anaplasma platys*.

Diagnosis of Anaplasmosis:

The disease can be predicted by checking the thrombocytopenia, elevated liver enzyme levels in the patient body. The serologic tests like immunofluorescence assay (IFA) and enzyme immunoassay (EIA) were performed to diagnose. PCR can be used for diagnosis purposes.

Lyme Disease:

Lyme infectious disease is transmitted by bacteria, *Borrelia burgdorferi* in humans. The main vector of the disease transmission is black-legged tick *Ixodes scapularis* (Nelde et al., 2018). This disease is quickly spreading in various regions of the world including Pakistan due to climate change. The infested ticks bite the person, attached for a long period of time and transmit the pathogen to the person. The disease is distributed all over the world due to changes in climate. There is a positive correlation between temperature and ticks borne-diseases like Lyme disease. It has been seen that disease increases with an increase in temperature. It has been reported that approximately 80% tick population was in the winter than other seasons temperature (Brunner et al., 2012). The disease prevalence was influenced due to climate change (Ramzan et al., 2018)

Signs and Symptoms:

Kidney and heart failure, depression, weight and appetite loss, fatigue, spontaneous and shifting leg lameness are the symptoms.

Diagnosis of Lyme Disease:

Enzyme-linked immunosorbent assay (ELISA) and Western blot tests can perform to diagnose the disease.

The Economic Significance of Ticks and TBDs:

A huge economic loss occurred to animals during a severe infestation of ticks in the form of a drop in milk production, retarded growth, damage to skins, wool, weight and meat reduce and even death of animals. The great losses occur in the form of mortality and morbidity in domestic and wild animals due to tick borne-diseases (TBDs) (Domingos et al., 2013; Kakarsulemankhel, 2011). The performance of animals is also reduced due to the severe attack of tick (Ramzan et al., 2018). The damage is not only caused due to tick bites but also ticks transfer zoonotic pathogens which become a major threat for animals and humans.

Ticks and Ticks Borne-Diseases Management Methods:

The various methods like chemical, biological, Entomopathogenic, Ecological, chemotherapy and vaccination have been adopted for the management of ticks and reduction of losses caused due to ticks borne-diseases in many regions of the world including Pakistan.

Hand Collection/ Ecological Control:

The hand collection method is used as a small scale and common method. The herdsmen have removed ticks with their hands or with the help of forceps. Other strategies like culture can be adopted to minimize the attack and ticks the population in specific areas. In this method, fencing and pasture spelling was used to stop the migration of ticks hosts like rodents, deer and many others. The pasture areas should keep free for some months so that in the absence of hosts at some extent pathogens, ticks have died. Some animals like crossbreeds were considered resistant against ticks and TBDs. The movement control of ticks hosts like birds and livestock's from one region of the world to another during transport, trade and truisms stop the dispersal of ticks and TBDs**.**

Biological Control:

The use of biological agents is another alternative method to chemical control. The biological agents are those organisms that feed to other organisms via parasitism, parasitoids and predation. These agents have been extensively used, nontoxic to human and non-target hosts. The agents can be helpful in the reduction of insecticide resistance. Biological agents such as parasitoid wasps, *Bacillus thuringiensis* bacteria, nematodes, insectivorous birds and deuteromycete fungi including *Metarhizium anisopliae* and *Beauvaria bassiana have been used for the management of tick's population*. Ticks become the food of mammals and birds during their self-grooming. It has been studied that larval black-legged ticks' population was reduced through the consumption of white-footed mice (*Peromyscus leucopus*). The abundance of immature black-legged ticks can be reduced through the predation of wild turkeys (*Meleagris gallopavo*). Turkeys are the host of several tick's species especially *Amblyomma americanum*, With the abundance of turkeys, ticks' number can be reduced. The number of ticks and Lyme disease transmission can be reduced by using the bird, helmeted guineafowl (*Numida meleagris*) as natural enemies. Other important ticks' consumers are oxpeckers (*Buphagus* spp.), pan-African birds, which feed on wild as well as domestic mammals. These birds are predators of both nymphs and adult ticks. A parasitoid chalcid wasp, *Ixodiphagus hookeri*, has been extensively used for the management of the American dog tick, *Dermacentor variabilis*, and the Rocky Mountain wood tick, *Dermacentor andersoni* (Mwangi et al. 1997). The bacteria, *Bacillus thuringiensis* (Bt.) also was ingested by ticks during blood feeding. Both black-legged and American dog ticks have been controlled through Bacillus thrungenesis bacteria.

Biocontrol of Ticks by Using Entomopathogenic Fungi:

Several types of entomopathogenic fungi have been tested against ticks and proved to be helpful to manage. Among them, *Metarhizium anisopliae* and *Beauveria bassiana distributed worldwide* caused maximum ticks mortality in a laboratory as well as field condition (Humber 1992). The fungus damage was varied with geographic regions, species and life stages of ticks. It has been recorded that the highest mortality was seen in engorged female and adult ticks than male and larvae. The fully fed female mass and egg lying capacity have been affected through entomopathogens. Similar results have been observed in field conditions.

Ticks Control by Vaccine:

The attenuated or live blood-derived vaccines have been used against TBDs globally. These vaccines have been used to control babesiosis and anaplasmosis in various regions of the world like Australia, Argentina and Israel. There are three developmental stages sporozoites, schizonts and piroplasms of the pathogen's life cycle in theileriosis. The animals after recovering from *Theileria parva* or *Theileria annulate* infection, get infested with other pathogens (heterologous strains). The immunity in livestock can be produced through the vaccination with parasitic strains. The cattle immunity can be improved by mixing the sporozoite and schizont antigens with the vaccines. Australian *Babesia bovis* and Babesia bigemina attenuated strains are applied to induce the immunity response in livestock in other countries like Africa South America and South-East Asia (Anonyms, 2012). The vaccines also have some limitations like short shelf life, the transmission of other pathogens and deterioration to virulence, maintenance in a cold environment. In some regions of the world, antigens Bm86/Bm95 are used and gave the best control against Rhipicephalus microplus. Another antigen is Bm86, which was tested to control cattle tick Rhipicephalus microplus. The antigen, Bm86 is proved to be effective and suppressed the ticks larval population, their weight, and disturb reproductive capacity of engorged female (Marcelino et al., 2012; Hope et al., 2012; Almazán et al., 2010).

Chemical Control:

The best strategy which has been used for the control of the tick population is acaricides. Tick's abundance can be reduced by applying the insecticides in the field where the tick's population is highest. This strategy has been used in many regions like USA, Australia, Southern Africa and Pakistan. The chemicals like querosene, sulphur and lard have been used against ticks (Domingos et al., 2013). The main chemical which has been used for the management of ticks and TBDs by various workers, dinotefuran, permethrin, pyriproxyfen, imidacloprid, deltamethrin, fipronil and methoprene (Horak et al., 2012) are reasonable.

All these chemicals are applied either orally, dermally and medicated to animals. Carbaryl and chlorpyrifos both were used extensively for controlling ticks population but have a residual impact on non-target organisms. These chemicals were given the best control of ticks and TBDs for several weeks as well as months (Fourie et al., 2010). The chemical was applied directly to livestock via cattle and sheep dips. The application of pesticides to wildlife has been proved an effective tool in the reduction of ticks and TBDs. The spray or insecticides with the help of some spray applying device have been tested against deer. For this purpose, a 4-poster deer feeder has been used against deer ticks, which attract the deer toward the corn. The deer rub the ears, neck with poster and insecticides which applied on the poster attached with their ears and necks, resultantly reduction in ticks and TBDs. Another strategy such as cardboard with insecticides has been used and gives the best control of ticks and TBDs on rodents.

Other devices such as bait tubes also tested against mice ticks and gave batter control. The other device, a plastic box containing fipronil and a hole for rodent entry has been used. Ticks number reduces when mice enter into a box containing fipronil. The use of chemicals (Acaricides) has an advantage as well as a disadvantage. The inappropriate use of acaricides has some residual impact on livestock’s health, resultantly residues remain in milk and meat. The acaricides have negative environmental impacts. The ticks resistance occurred due to excessive use of the acaricides against ticks and TBDs (Abbas et al., 2014).

Future Sustainable Control Methods:

The methods which we discussed above in this review paper have been extensively used but have some advantages and limitations. The excessive use of the chemical is cause ticks resistance, environmental pollution and public health threat. The use of acaricides becomes fatal for young animals. Acaricides, directly and indirectly, affect the animals, residues remain in livestock's body, meat and milk and cause diseases in humans through milk and meat or other products. The acaricides are affecting the non-target hosts. To avoid all these negative effects on humans as well as livestock, and alternative ticks control strategy, genetically ticks resistance livestock's breed should be reared. Such types of breeds carry fewer ticks and the chance of disease transmission is reduced. Anti-tick grasses should be adopted to minimize the effect of ticks on animals as well as human health. The vaccination measure should be adopted regularly to control the tick population. The migration of birds, animals through trade, tourism and free movement of livestock near or on the border should be banned. Another best control method that should be adopted is entomopathogens like targeted site fungi, which directly as well indirectly reduce the tick's number and has no harmful impact on livestock's health. In our opinion, we can overcome the burden of ticks and TBDs by using genetically modified organisms (GMOs).

Conclusion:

The review shows that climate change has a close relationship with ticks and TBDs. Both ticks and TBDs are highly linked with biotic and abiotic factors like temperature and host availability. Habitat loss, deforestation, reforestation, removal of vegetation and global warming tightly associated with ticks and TBDs. The season (summer and spring) has a positive impact on the prevalence of the tick population. The different methods are used for ticks management like chemical, biological etc. Every method has some advantages and limitations. As other studies showed, chemical (acaricides) methods are extensively used for ticks control but have some residual impact on animal's health. An effective and alternative control method should be adopted to get rid of ticks and TBDs. For the reduction and get rid of ticks and TBDs should use theMouse Targeted Devices (Tick Tubes) as well as Deer Targeted Devices (4-Poster Bait Stations). The entomopathogenic agents and ticks resistance breed are alternative approaches against ticks and TBDs.We should educate the formers and give information about ticks and TBDsand their management. The traditional method which has been adopted by many workers should be promoted.

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