Review Article

Emergence and Variations in Disease Ecology of Tick-Borne Bovine Theileriosis in East India

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Abstract

Bovine theileriosis is one of the economically important tick-borne disease (TBD) of bovine limiting livestock production in Eastern India. There has been a massive concern for livestock farmers owing to its involvement in heavy economic losses, often salient in nature, associated with multiple pathogens and difficulty in symptomatic diagnosis. Approximate estimates of annual losses due to these tick-borne diseases in India is about ₹4353.0 crore. The bovines in East India are reported to suffer from theileriosis by two species, i.e. Theileria annulata and Theileria orientalis. Report from AICRP on ADMAS Annual Report 2015-16, NIVEDI Bangalore suggest that highest outbreaks of theileriosis were from Jharkhand in the whole country and moderate reports of the outbreak from Eastern states of Odisha, West Bengal, and Assam. In Chhattisgarh state, the prevalence of theileriosis reported as high as 23.3 % in random samples cattle population. Species difference exists relative to clinical manifestations of tropical theileriosis with exotic cattle and their crosses. Yak is most susceptible animal as compared to Bos indicus, camel and buffalo are considered to be the natural hosts in which the parasite evolved and they may also act as carriers. Pathogenesis in bovine is related to different stages of the parasite in the host and causing damage to lymphoid and red blood cells. Clinical symptoms with a history of the tick infestation can be suggestive of theileriosis. However, definitive diagnosis required laboratory testing using Giemsa stained blood smears (GSBS). Though new modern diagnostic methods have developed, GSBS is the most common diagnostic method in practice. Treatment and control of TBDs can be achieved by the use of biological agents, genetic selection, chemotherapy, and vaccines. Tick control is another crucial strategy to limit TBDs, including theileriosis.

Key words: Climate Change, East India, Emergence, Control, Tick-Borne Diseases, Theileriosis

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Introduction

Tick-borne diseases (TBDs) of bovine are of massive concern to livestock farmers owing to its involvement in economic losses, often salient nature, association with multiple pathogens and difficulty in symptomatic diagnosis. Economic losses due to TBDs attributed to high mortality rates, reduced milk production and loss of body condition due to anaemia and stress. Eastern Region of India including eastern Uttar Pradesh, Bihar, Jharkhand, West Bengal, Assam, Odisha and Chhattisgarh is unique in itself having extensive plains of Indo-Gangetic basin, hill and plateau regions in Jharkhand, Assam and part of West Bengal, coastal regions in West Bengal and Odisha and international borders of Nepal and Bangladesh. It occupies about 21.85% geographical area and supports approximately 31% livestock population of India with about 165 million bovine population. The crossbred cattle population has increased during the past few livestock censuses (Statistics, B. B. A. H. 19th Livestock census, 2012). As per 19th livestock census, the exotic/crossbred milch cattle in the country has increased from 14.4 million to 19.42 million with an increase of 34.78%. This census data also indicate that the livestock population has increased substantially in Eastern states of our country including Uttar Pradesh (14.01%), Assam (10.77%), Bihar (8.56%) and Chhattisgarh (4.34%). The eastern region is also facing adversity of climate change in the recent past with inconsistent monsoon, extreme summer, and winter (Chaliha *et al*., 2002). Report of a convention suggests that the eastern part of the country is prone to disasters like floods, drought, and earthquakes, and climate change has increased the threat of more disasters and it adversely affect animal health (Indo-Asian News Service, 2018). In addition to this, resilience to these climate changes is comparatively less due to socio-economically disadvantage states in East India, making them more dependence on climate variables with low adaptive capacity. As temperature increases, the environment becomes more favourable for the tick's survivability as well as sustainability and the season suitable for tick activity lengthens, so incidence of TBDs are likely to become more common.

TBDs of bovine prevalent in the region are dependent on the prevalence of different species of tick. Single species of individual tick can harbour more than one disease causing agents. The susceptible animal can be infected with multiple pathogens at a time, compounding the difficulty in diagnosis, rationale treatment as well as prevention. In eastern India, these include protozoal diseases (Theileriosis and Babesiosis) and one rickettsial disease Anaplasmosis. They are more prevalent and lethal in exotic and crossbred cattle population and milder to subclinical in indigenous cattle and buffalo population, indicating breed as an important risk factor (Jabbar *et al*., 2015). Approximate losses due to these TBDs in India is estimated to be ₹ 4353.0 crore as detailed by Minjauw and McLeod (2003) and reviewed by Narladkar (2018). However, earlier worker report suggests that in India alone, tropical theileriosis causes an estimate loses of ₹ 8427 crore annually (Devendra, 1995). Amongst these TBDs, theileriosis is the most economically significant and challenging disease to diagnose it symptomatically due to similarity posed with anaplasmosis and

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mixed nature of infections. Babesiosis is comparatively easy to diagnose based on its clinical manifestation of red water urine. For better understating of the review on TBDs, we attempted to focus on bovine theileriosis in east India with primary emphasis on its causative agents, vector involved, clinical findings, diagnosis, rationale treatment and control.

Bovine Theileriosis

The bovines in East India are reported to suffer from theileriosis by two species i.e. *T. annulata* and *T. orientalis*. The transmission of T. *annulata* is by infective sporozoites in the saliva of ticks of the genus *Hyalomma.* These are mostly two host ticks, preferring hot and humid climate for completion of their life cycle. *T. orientalis* causing *'oriental theileriosis*is' reported to be transmitted by ticks of the genus's *Rhipicephalus microplus* and *Haemaphysalis* (Fuujisaki, 1992; Lahkar, 1991) and it has also been detected in other arthropods such as mosquitoes and lice, though evidence of transmission by their bite is lacking. In ticks *Theileria sp*. is transmitted only by trans-stadial means, though few researchers have speculated trans-ovarian transmission, lacking conclusive evidence. While *T. annulata*, apicomplexan protozoan is considered to be pathogenic causing a lymphoproliferative disease refered as *'tropical theileriosis*' and *'mediterranean theileriosis'*. Reports of tropical theileriosis from all the seven states of eastern India are documented. It is associated with higher prevalence rate, morbidity, mortality and economic losses to the livestock owners in the region. As per OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals, the mortality rate for tropical theileriosis can vary from 3% to 90% (OIE, 2009), depending on the parasitic strain and the susceptibility of the animals. The disease can occur in any season and month of the year; however, the incidence tends to increase in summer and monsoon coinciding with tick breeding season. Recent reports on the incidence rate of theileriosis from Bihar was reported to be about 31% based on Giemsa stained blood smear (GSBS) (Kala *et al*., 2018). Similarly, higher incidence rate of about 10 % is reported from peri-urban Ranchi of Jharkhand of theileriosis (Singh, 2007) while report from AICRP on ADMAS Annual Report 2015-16, NIVEDI Bangalore (ICAR-NIVEDI., 2016) suggest that Jharkhand state has highest outbreaks of theileriosis in the whole country and moderate reports of outbreak from eastern states of Odisha, West Bengal, and Assam. In Chhattisgarh state, the prevalence of theileriosis was reported as high as 23.3% in random samples of cattle populationbased on GSBS (Naik*et al*., 2016). Similarly, highest number of outbreaks was reviewed based on epidemiological data from states of Orissa followed by Bihar, West Bengal, Jharkhand by Saminathan *et al.* (2016).

Oriental theileriosis caused by T. orientalis is reported to be benignor non-transforming theileriosis. *T. orientalis* is also known as *T. sergenti* and *T. buffeli*. It exerts its primary effect through erythrocytic destruction. The life cycle of *T. orientalis* is similar to that of other Theileria spp. except that the schizonts do not induce transformation and fatal lymphoproliferation. Consequently, schizonts stage of the pathogen

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known as Koch Blue Body (KBB) is not present in Giemsa stained lymph node aspirate smear. Outbreaks of disease due to the benign *T. orientalis* have been reported recently from sates of Assam (Kakati *et al*., 2015a), Odisha (Sahoo *et al*., 2017), Bihar (Kumar *et al*., 2019) in East India and may represent a hidden burden to livestock productivity in regions where this species is endemic.

Host and Clinical Findings

Clinical manifestations in animals suffering from tropical theileriosis may vary (polymorphic) depending on the severity of disease as acute, subacute and chronic. It also depends on the degree of parasitised cells of the host, virulence of the *T. annulata* and risk factors like previous exposure to the disease, physiological state and, species of the host affected and, concurrent infection of other pathogens as well. *T. annulata* can infect cattle (*Bos taurus*; *Bos indicus* and their crosses) and yak (*Bos grunniens*), camel (*Camelus dromedaries*) and water buffalo (*Bubalus bubalis*) (Pieszko, 2015). Species difference exists relative to clinical manifestations of tropical theileriosis with exotic cattle and their crosses. Yak is most susceptible animal as compared to *Bos indicus* (OIE, 2009), camel and buffalo are considered to be the natural hosts in which the parasite evolved and they may also act as carriers.

Susceptible animal suffering from a peracute form of tropical theileriosis may die within a week to fortnight from the day of tick bite or within 3-5 days of onset of fever which may be as high as 107°F and/ or enlargement of the peripheral lymph nodes. Other symptoms may not be visible in this form of disease. GSBS will also be negative for the piroplasms; however, KBB may be the distinctive feature in lymph node aspirate smear (Gill *et al*., 1977).

In acute form of tropical theileriosis, cardinal signs recorded in susceptible infected animals are enlarged peripheral lymph nodes, most easily appreciated at pre scapular region and high fever (103-107ºF) coinciding with lymph node enlargement. Other symptoms reported may vary from lachrymation, nasal discharge, respiratory distress manifested as dyspnea, drop in milk yield, persistent inappetence, anaemia, pale eye as well as vaginal mucous membranes, and rare icterus (Sudan *et al*., 2012). Unusual rare symptoms reported are mastitis (unpublished observation), conjunctivitis, corneal opacity, nodule formation on skin (Gharbi *et al*., 2017), convulsions and nervous symptoms. The affected animal may die or recover and become a carrier.

T. orientalis infected animals mostly do not show any symptoms and remain as an asymptomatic carrier. However, reports from Assam indicates that most symptoms of tropical theileriosis (high body temperature, lachrymation, nasal discharge, swollen lymph nodes and hemoglobinuria) are also evident in reported cases of *T. orientalis* positive susceptible animals (Kakati *et al*., 2015b).

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Pathogenesis and Post Mortem Findings

Pathogenesis in bovine is related to different stages of the parasite in the host and causing damage to lymphoid and red blood cells. Theileria parasites are the only intracellular eukaryotic parasites capable of reversibly transforming host cells (Pain *et al*., 2005). However, *T. orientalis* lacks this mechanism. The primary pathogenesis in oriental theileriosis is related to the destruction of RBCs and resulting anaemia. The sporozoite stage is incubated by the tick by its feeding on the host. Sporozoites invade the lymphoid cells for about 10-15 days before transforming into schizonts stage. The schizonts stage parasitise and proliferate in the lymphocytes. Further, they invade and damage the lymphoid system and are detected as KBB by Giemsa staining of lymph node aspirate impression smear from dead animals. Then schizonts convert into merozoites and merozoites invades RBCs and form spiroplasms, destroying RBCs.

Post-mortem findings are related to the pathogenesis of the organism and organs affected. Lymph nodes and spleen may be oedematous with enlargement and haemorrhages. The gall bladder may be distended. One of the most characteristic and consistent post-mortem findings is punched out ulceration in the abomasums of the affected animals. There may be evidence of haemorrhages on endocardium, pericardium, and epicardium. In few animals manifested with pulmonary involvement, gross observation of congestion, oedema, and emphysema in the lungs may be evident. Similar lesions are also reported in *T. orientalis* infected animals (Aparna *et al*., 2011).

Diagnosis

Clinical symptoms as described above with history of the tick infestation can be suggestive of theileriosis, however definitive diagnosis demands laboratory testing. Most commonly and traditionally practiced laboratory diagnostic test is the microscopic examination of blood and lymph node aspirate.

Microscopic Examination

Microscopic diagnosis of bovine theileriosis relies on the detection of microschizonts, commonly known as Koch's Blue body (KBB) in Giemsa stained lymph node aspirate smears and piroplasms in RBCs of peripheral blood of live animals in GSBS. However, in *T. orientalis*, only piroplasms in RBCs by GSBS can be of some diagnostic value, and that too differentiation as *T. orientalis* from *T. annulata* cannot be made. Impression smears of lymph node and spleen from dead animals can also be attempted for post mortem diagnosis and correlated with other post mortem lesions.

However, the method is insensitive and often of no significance for carrier animals due to low level of the parasitemia in the blood sample and inability to differentiate between species, making it an unreliable technique for accurate results (Gul *et al*., 2015). It is also usually limited to the acute phase of the disease when the parasitemia is high enough to be detected microscopically.

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Serological Examination

Serological tests such as the indirect immunofluorescent antibody test (IFAT) and enzyme-linked immunosorbent assay (ELISA) can be used to detect circulating antibodies. IFAT is considered gold standard test by OIE. However, cross-reactivity with antibodies directed against other *Theileria spp*. limits the specificity of the IFAT. ELISA can also be used for serodiagnosis and epidemiological study of bovine theileriosis. ELISA is easy to perform, capable of screening large sample in a short period of time and less labour-intensive (Mohammed, 2007). However, there are possibilities of cross-reactivity and may suffer from specificity. Recombinant protein has been tried for the development of these diagnostic ELISA. Most commonly used recombinant proteins are immunodominant surface proteins (TaSP) along with TaD and TaSE showing some promising potential (Seitzer *et al*., 2008). Few commercial ELISA kits are available and marketed in India for undertaking such study.

DNA Based Examination

PCR

Molecular diagnosis of haemoprotozoan diseases involves multi-modality PCR-based diagnostic procedures. PCR based diagnosis has the advantage of being very sensitive and specific to the level of strain; capable of diagnosis using a minimal amount of bio-material. However, the main disadvantage is time consuming qualitative procedure and cost involvement. Availability of sequenced parasite genes in the public domain has made it possible. Most common target genes for diagnosis of *T annulata* are *18s ribosomal RNA* gene, *tams-1* gene, sporozoite surface protein (*tasp*) gene, and *cytochrome III*gene and for *T. orientalis* are *mpsp gene* and *18s rRNA gene*.

Loop-Mediated Isothermal Amplification (LAMP)

Loop-mediated isothermal amplification (LAMP) is a simple technique that amplifies DNA with high sensitivity and rapidity under isothermal conditions (Notomi *et al*., 2000). It is a sensitive, specific and less time-consuming method. It uses DNA polymerase that has low sensitivity to inhibitors and the set of four primers to recognise six different sequences on the target gene. LAMP test has been attempted and developed for the detection of some *Theileria spp*. using targeted *Cytochrome B gene* (Chaouch *et al*., 2018), PIM and *p150 genes* (Thekisoe *et al*., 2010), *p33 gene* (Wang *et al*., 2010), *18S rRNA* and ITS (Liu *et al*., 2012, 2013).

Real-Time PCR

The real-time PCR (qPCR) technique is sensitive and quantitative. This property makes qPCR an appropriate method for early disease diagnosis and parasite quantification. Real-time quantitative PCR

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based on the *tasp*, 18s rRNA and *tams* genes has been used for detection of the *T. annulata* parasites (Dandasena *et al*., 2018) probe based on *mpsp* gene for *T. orientalis* (Bogema *et al*., 2015).

Differential Diagnosis

Tropical theileriosis may be confused with the other theilerioses (*oriental theileriosis*) that may occur in this region. Confirmation can only be made by tick identification and molecular diagnosis of pathogen species using specific primers amplification as discussed above. Other TBDs can also cause trouble in the diagnosis of tropical theileriosis. However, meticulous GSBS examination can give fruitful results. TBDs which should be considered before confirmation of tropical theileriosis is babesiosis and anaplasmosis. Typically, clinical babesiosis is consistently associated with red water urine and responds very well to diminazene aceturate and imidocarb treatment. Arthropod-borne haemo-protozoan like trypanosomiosis and viral malignant catarrhal fever should also be considered for differential diagnosis.

Treatment

Treatment and control of TBDs can be achieved by the use of biological agents, genetic selection, chemotherapy, and vaccines. The most effective and conventionally used method of control and treatment is through the use of effective chemotherapy which is capable of killing the parasites without harming the host. However, the first part is achieved by few chemotherapeutic agents but not the second part, as many of these have toxic side effects (Cheesman, 2000).

Buparvaquinone, second-generation hydroxynaphthoquinone was initially used as an anti-malarial drug (Hudson *et al*., 1985). The first report of the effective anti-theilerial activity of the hydroxynaphthoquinones came in the late 1980s (McHardy*et al.*,1976) and indicated that effective treatment for theileria infection is possible. After this discovery, many hydroxynaphthoquinones was tested against theileriosis (Minami *et al.*, 1985; Dhar *et al*., 1988). Among this parvaquone and buparvaquone were reported to be the most effective. Buparvaquinone is an antiprotozoal drug related to parvaquone and atovaquone with novel features that make it a favourable compound for the therapy and prophylaxis of all the forms of theileriosis (McHardy *et al*., 1985). Buparvaquinone, currently the most effective anti-theilerial drug for cattle and buffalo. It is recommended for the treatment of clinical theileriosis @2.5 mg/kg b.wt., often a second dose may be necessary (Mishra *et al*., 1993). Alternatively, a single dose of 5 mg/kg b.wt. is more effective (Singh *et al*., 1993). Other anti-protozoal drugs like halofuginone lactate (1.2 mg/kg b.wt., orally), oxytetracycline (20-30 mg/kg b.wt., IM/IV for 3-5 days) or long-acting oxytetracycline @ 10 mg/kg b.wt., IM repeated after 72 hours are reported to be of some effect in bovine theileriosis. Future study can be taken up on chalcones, namely, trans-chalcone and chalcone 4 hydrate on bovine theileriosis. It has shown promising results *in vitro* studies on *Babesia* spp. and *T. equi* (Batiha *et al*.,2019).

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In addition to the primary therapeutic agent, supportive therapy should include emergency treatment like blood transfusion in clinical cases with haemoglobin less than 4.0 gm% and parasitemia found in more than 5% of RBCs. Role of furosemide (Dantas-Torres and Otranto, 2017) and antibiotics effective against respiratory tract such as fluoroquinolones have shown potential in bovine theileriosis with pulmonary involvement. Recent reports suggest that marbofloxacine is more preferred as an antibiotic treatment in cases of tropical theileriosis that suffered from respiratory illness and recovery rate was comparatively higher in group complicated with respiratory illness given combination therapy of buparvaquone with marbofloxacin (Al-Hosary *et al*., 2010).

Medicinal plants with some value as the anti-theilerial effect has been reviewed (Farah *et al*., 2014; Al-Snafi, 2016). Flowers of *Calotropis procera* (commonly known as Akman, Mudar, Aakonda, Akon) is a wild plant found in this eastern region of India. It can be effectively used to treat subclinical bovine theileriosis (Durrani *et al*., 2009; Siddiqui *et al*., 2017). *Peganum harmala* (commonly known as Harmal or Wild rue) is a bushy herb found in upper Gangetic plain, western Bihar. Extract of *Peganum harmala* can also be used to treat bovine theileriosis at the dose of 5 mg extract /kg per day intramuscularly for 5 days (Mirzaei, 2007) and water extract @ 7mg/kg b.wt., for 3 days (Saleem *et al*., 2014).

Nano lipid-based drug delivery systems can be attempted to overcome the challenges encountered with failure in treatment or resistance and unwanted toxicity in the treatment of parasitic diseases. Sodium alginate nanoparticles, self-nanoemulsifying drug delivery system (SNEDDS) has been tried for delivery of quinpyramine sulfate and buparvaquinone (Manuja *et al*., 2016; Smith *et al*., 2018). Solid lipid NPs (SLN) loaded with buparvaquone (BPQ) for targeted delivery in theileriosis was reported to be a promising approach for targeted and improved delivery (Soni *et al*., 2014).

Control

Exotic cattle and their crosses and indigenous dairy breeds like Sahiwal and Gir require prophylactic vaccination and strategic tick control program for prevention from TBDs. Zebu cattle and to some extent buffaloes usually do not require tick control program and also less susceptible to TBDs. However, lice control program should be considered in buffaloes. In India, only one vaccine is commercially available for use by farmers in the name of Rakshavac T®. It is a live schizont grown in lymphoblast cell culture and attenuated by prolonged *in-vitro* passage. It claims to have immunity for up to 3 years. The recommended dose is 3 ml by the subcutaneous route and should be given to calves above two months of age. However, it has limited use in the Eastern region of the country. The main reason for its limited use is the high cost of vaccination and storage requirement of liquid nitrogen for the vaccine. Vaccines can be made from either the sporozoite or the schizont. It has been suggested that the most economical way to control theileriosis in India is to vaccinate calves and to reserve buparvaquinone for treating clinical cases.

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Efforts have been made to develop subunit vaccines because of the limitations of available live vaccines as discussed above. Infections with *T. annulata* induce only low levels of antibody against sporozoite antigens; however, antibodies capable of fully neutralising the infectivity of sporozoites *in vitro* have been detected in animals after repeated sporozoite challenge (Nene and Morrison, 2016). Monoclonal antibodies with neutralising activity have been produced for *T. annulata* by immunising mice with sporozoites, and most of these Mab recognizes sporozoite surface antigen (SPAG-1) (Williamson *et al*., 1989). *T. annulata* sporozoite surface antigen (SPAG-1) and polymorphism in this antigen have been attempted as a candidate antigen for subunit vaccine (Katzer *et al*., 1994; Boulter *et al*., 1999).

Tick control is another important strategy to limit TBDs including theileriosis. Tick control has been attempted using tick vaccine restricted to limited pathogen transmission, chemical control, biological control, and natural products. Chemical acaricides including topical, oral and parenteral formulation are available for use. Most commonly used chemical acaricides are (George *et al*., 2004) enlisted in Table 1. However, the continuous use of chemical control is responsible for the development of acaricide resistance in ticks (Abbas *et al*., 2013). There has been attempt to develop herbal acaricidal to counter this problem and has been reviewed exhaustively by Ghosh *et al*. (2007); Adenubi *et al*. (2016) and Banumathi *et al*. (2017). In eastern India, plants extracts of *Calatropis*, and tea are being used as traditional medicine for the treatment of heamoprotozoan diseases of cattle. However, they do have a limitation of complete treatment and prevention of recurrence.

Table 1: Different groups of acaricides used for tick control

	Group	Chemicals	Use	Mode of Action	Limitation
1	Organophosphates compounds	Coumaphos, Diazinon, Dioxathion	Topical	Act by contact with the parasite; Inhibits acetylcholinesterase, paralyses the ticks and knockdown effect. (Ravindran *et al*., 2018; Fukuto, 1990)	Tend to accumulate in tissues or milk.
2	Carbamates	Carbaryl	Topical	Inhibits acetylcholinesterase, paralyses the ticks and knockdown effect. (Fukuto, 1990)	-Do-
3	Synthetic pyrethroids	Permethrin, Deltamethrin, Cypermethrin, Flumethrin	Topical	Altered nerve function due to an effect on voltage-gated sodium channels on nerves, prolonging the time of opening of sodium channels. Also effective against flies (Palmquist *et al*., 2012)	Resistance development & prolonged residual activity.
4	Amidines	Amitraz	Topical	Interaction with octopamine receptors in the nervous system of the ticks, causing an increase in nervous activity (Roder, 1995). No residues are found in meat or milk	Prolonged residual activity is of short duration.
5	Macrocyclic lactones	Ivermectin, Moxidectin, Doramectin	Oral, subcutaneous and pour on	Inhibition of glutamate-activated chloride channels, which occur in the muscle and nerves of arthropods (Doan *et al*., 2013).	Expensive and residues in animal products are recorded.
6	Benzoylphenylureas	Difluorobenzo ylurea	Pour on	Growth regulator and does not kill ticks. Acts by inhibition of the cuticle formation during insect development (Tfouni *et al*., 2013).	Long residual life in tissue and milk.

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Conclusion

Bovine theileriosis is one of the economically important tick-borne diseases in Eastern India. Salient nature, association with multiple pathogens and difficulty in symptomatic diagnosis make the disease more serious. The bovines in East India are reported to suffer from theileriosis by *T. annulata* and *T. orientalis* which are two different species with different epidemiology and pathogenicity. Past studies indicate reports of only one species (*T. annulata*) in the region, but now emergence of new species *T. orientalis* in many States of Eastern India indicates its spread and emergence. The main reason may be due to increase in susceptible crossbred cattle, access to trans-state and trans country borders for animal trade, climate change conducive to survival as well as multiplication of ticks and availability of specific modern diagnostic techniques in disease diagnosis. Clinical symptoms with a history of the tick infestation can be suggestive of theileriosis; however, definitive diagnosis required laboratory testing using Giemsa stained blood smears (GSBS). However, molecular diagnosis based on species-specific primer amplification can differentiate the species of pathogens. The challenge to treat and control of TBDs using biological agents, genetic selection, chemotherapy, and vaccines requires refinement. Tick control is another crucial strategy to limit TBDs including theileriosis. Focused and basic research is required to develop tick vaccines and drug delivery system for cattle which can strategically release acaricidal drugs for an extended period.

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