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Economic importance of ticks and their effective control strategies

Haranahalli Vasanthachar Manjunathachar^{1*}, Buddhi Chandrasekaran Saravanan¹, Manickam Kesavan², Kumaragurubaran Karthik³, Prakashkumar Rathod⁴, Marappan Gopi⁵, Paramasivam Tamilmahan⁶, Bharemaru Lingaraju Balaraju⁴

¹Division of Parasitology, Indian Veterinary Research Institute Izatnagar, Bareilly, Uttar Pradesh 243122, India

²Division of Pharmacology and Toxicology, Indian Veterinary Research Institute Izatnagar, Bareilly, Uttar Pradesh 243122, India

³Division of Bacteriology and Mycology, Indian Veterinary Research Institute Izatnagar, Bareilly, Uttar Pradesh 243122, India

⁴Division of Extension Education, Indian Veterinary Research Institute Izatnagar, Bareilly, Uttar Pradesh 243122, India

⁵Division of Nutrition, Indian Veterinary Research Institute Izatnagar, Bareilly, Uttar Pradesh 243122, India

⁶Division of Surgery Indian Veterinary Research Institute, Indian Veterinary Research Institute Bareilly, Bareilly, Uttar Pradesh 243122, India

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ABSTRACT

Role of livestock in improvement of a country's economy is inevitable. Livestock contributes a lion's share in agricultural sector of developing countries. Several developing countries have adopted the use of exotic germplasm to improve the productivity of their native breeds, which has brought down the disease resistance. Among various problems hindering the growth and productivity of livestock, parasite related problem plays a major role. Tick and tick borne diseases are prevalent in 80% of the cattle population around the globe. They cause various worries to the farmers by transmitting major disease causing pathogens and jeopardize animal health leading to poor production. Ticks transmit various pathogenic agents like virus, bacteria, protozoa and other parasites as well. Many of them are dangerous for the livestock health and some are also zoonotic hence, need to be checked at the initial stages. Control of ticks is the major concern in the present situation as the use of anti-parasitic drugs has led to the current trend of resistance development. Search for an effective alternative method has begun; vaccination will be a better alternative and promising tool for protecting livestock from the tick infestations and thereby tick borne diseases.

1. Introduction

Livestock production is an important integral component of the Indian agricultural production system and plays an imperative role in the development of a country's economy as well as for the food and nutritional security. It also plays an important role in the socio-economic development of the small and medium hold farmers. More than one fourth of the total output of the agricultural sector in India is contributed by the livestock alone[1]. In 2010–2011, 3.37% GDP

was contributed by animal husbandry proving that it is the major sector in Indian economy[2]. The success of livestock industry depends on the health of livestock, with sustained productivity. Animal breeding plans introduced exotic germplasm to increase productivity of the animal, where the disease resistance/health of the animal was least concerned. Susceptibility to the diseases shattered the hope of livestock sector, and these issues are multifactorial in nature. India stands top in the livestock population throughout the world, even though production of milk and meat is 20%–60% lesser in comparison to the world average[3]. Livestock diseases, decreased resistance to the pathogens and lack of an effective disease control strategy were reasons for the production loss apart from the low productivity of Indian animals. Among the top ten diseases of the livestock, four

*Corresponding author: Haranahalli Vasanthachar Manjunathachar, PhD Scholar, Division of Parasitology, Indian Veterinary Research Institute Izatnagar, Bareilly, Uttar Pradesh 243122, India.

Tel: +919528059591

E-mail: manjunathachar632@gmail.com

of them are caused by parasites^[4]. Parasitic diseases are a major concern worldwide not only to the health issues but also in terms of economic status of the country^[5]. Tick and tick borne diseases (TTBDs) rank fourth among the major infections of livestock and latter is regarded as the most important arthropod borne diseases of livestock, humans and companion animals^[6]. For the economic development and achieving food security, increasing the livestock population is a constraint because of scarcity of feed, fodder and pressure on natural resources. Therefore, increasing the standard of animal health through controlling TTBD and increasing disease resistance of the animals are one of the few important passive ways to achieve the maximal animal productivity. Various methods are followed throughout the world to control ticks like use of acaricides, vaccines, biological control, physical methods and recent techniques like RNA interference^[7].

2. Economic impact of TTBD

TTBD affects 80% of world cattle population, and their prevalence is throughout the world, particularly important in tropical and sub-tropical countries causing loss of production^[8]. Vector-borne diseases, directly or indirectly affect the growth of the livestock industry, which is of fundamental importance to rural people in India. They are the source of income to small hold/landless farmers and ensure food supply and income during the quiescent period the agriculture^[6]. Ticks are responsible for a variety of losses, and directly attach to the host ('tick-worry') causing injection of toxins, blood loss, general stress, hide damage and irritation, leading to decrease in productivity in terms of milk, meat *etc.* Indirectly it depresses the immune function and transmits several pathogens^[8–12].

De Castro estimated that the annual global costs associated with TTBDs in cattle amounted between US\$ 13.9 to US\$ 18.7 billion^[9]. In Australia alone, losses due to cattle tick [*Boophilus (Rhipicephalus) microplus (B. microplus) (R. microplus)*] were estimated to be US\$ 62 million and in Brazil losses were around US\$ 2 billion per year. In Africa, tick-borne diseases are considered to be the most important problems in animal production. In India, the economic losses due to TTBDs in animals were calculated as US\$ 498.7 million per annum^[11,13].

Accurate estimation of losses due to TTBDs is very difficult, but they significantly affect the farm income. TTBDs severely affect dairy cows and reduce milk yield. When crossbred Holstein-Zebu cows are infested with an average of 105 ticks, a reduction in 23% of milk yield/day was observed. Losing about ¼ of the income through milk has a significant impact on livestock dependent system^[7,14]. Further, the direct effect of tick infestation on meat and hide industry is much more significant. Frisch *et al.* reported that animals

with an average of 40 ticks/day could lose weight up to 20 kg/year and also diminished hide value by 20%–30%^[15,16]. Further, ticks are major contributors for transmission of important disease causing agents to animals (Table 1). Bovine tropical theileriosis caused by the protozoan parasite *Theileria annulata (T. annulata)*, is transmitted by the tick species of the genus *Hyalomma* worldwide, putting about 250 million cattle at risk to this important protozoan disease^[21]. Estimated loss due to *T. annulata* and tick worry worldwide and India was US\$ 384.3 million and US\$ 57.2 million, respectively^[5,12]. In Sweden, over the past 30 years, increase in *Ixodes ricinus* tick population was recorded^[22,23]. Recently in 2012, Karnataka, India, outbreak of Kyasanur forest disease (KFD), a *Haemaphysalis* tick borne infection has occurred despite routine vaccination, indicating the need of strategic control of the tick vector^[24].

3. Tick control strategies

Tick control demands the attention of researchers because many important livestock diseases are transmitted by ticks and this can be achieved by controlling ticks. To counteract the adverse effects of ticks on animals and humans, various tick control programs were followed in modern livestock practices. The main method among them is the use of acaricides (amidines, benzoyl phenyl ureas, benzene hexachloride/cyclodienes, carbamates, macrocyclic lactones, organophosphates and pyrethroids). Acaricide usage is not sustainable in the long run because the striking ability of ticks becomes resistant. Moreover, acaricide residues in animal food products, undesirable effects on animal health and ecosystem, and the cost involved are other drawbacks of the use of acaricides. So, all these factors warrant the alternate tick control strategies^[7].

Effective control of TTBDs is best achieved through a combination of practices like tick control, prevention of disease through vaccination, and treatment of clinical cases. Tick control methods can be grouped into chemical (using acaricides) and non-chemical methods such as, grooming, pasture spelling (*i.e.*, leaving pastures unstocked to break the tick's life-cycle), endosymbiotic approach, biological control, genetic manipulation, use of biopesticides, herbal acaricides and vaccination with tick antigens. Both the methods of tick control are briefly discussed in this review to provide information regarding conventional and upcoming control strategies to control TTBD.

3.1. Grooming

Investigation has been carried out in most mammal species to assess the effect of grooming for the control of ticks. It has direct effect on wellbeing via removal of ectoparasites

Table 1

Causative agents, vectors, and distribution of representative tick-borne diseases of animals and humans.

Pathogen	Disease	Principal vectors	Geographical distribution	Host species affected	References		
Protozoa	<i>Babesia bigemina</i>	Cattle babesiosis	<i>Rhipicephalus</i> spp.	Africa, America, Asia, Australia	Cattle, buffalo	10	
	<i>Babesia bovis</i>	Cattle babesiosis	<i>Rhipicephalus</i> spp.	Africa, America, Asia, Australia	Cattle, buffalo	10	
	<i>Babesia ovata</i>		<i>Haemaphysalis</i> spp.	Asia	Cattle	10	
	<i>Babesia ovis</i>	Sheep babesiosis	<i>Rhipicephalus bursa</i> , <i>Rhipicephalus turanicus</i>	Africa, Asia, Europe	Sheep	10	
	<i>Babesia motasi</i>	Sheep babesiosis	<i>Haemaphysalis</i> spp.	Africa, Asia, Europe	Sheep	10	
	<i>T. annulata</i>	Tropical theileriosis	<i>Hyalomma</i> spp.	Eurasia, Africa, Central Asia	Cattle, Camels	10	
	<i>Theileria orientalis</i>		<i>Haemaphysalis</i> spp.	Asia	Cattle, Asian buffalo	10	
	<i>Theileria parva</i>	East coast fever	<i>Rhipicephalus appendiculatus</i>	Africa	Cattle	10	
	<i>Anaplasma marginale</i>	Bovine anaplasmosis	Various	Worldwide	Cattle	10	
	<i>Anaplasma centrale</i>	Bovine anaplasmosis	Various	Worldwide	Cattle	10	
	Bacteria	<i>Ehrlichia bovis</i>	Ehrlichiosis	<i>Hyalomma</i> spp.	Asia	Cattle	17
		<i>Borrelia burgdorferi</i>	Lyme disease	<i>Ixodes pacificus</i> , <i>Ixodes persulcatus</i> , <i>Ixodes ricinus</i> , <i>Ixodes scapularis</i>	USA, Canada, Europe, Asia, Northern Africa	Human	18
	Viruses	<i>Flaviviridae</i> , <i>Flavivirus</i>	Tick borne encephalitis	<i>Ixodes ricinus</i> , <i>Ixodes persulcatus</i> , <i>Haemaphysalis concinna</i> , <i>Haemaphysalis punctata</i>	Europe, Asia	Human	19
<i>Flaviviridae</i> , <i>Flavivirus</i>		KFD	<i>Haemaphysalis</i> spp. (mainly <i>Haemaphysalis spinigera</i> and <i>Haemaphysalis turturis</i>)	Forested areas of the Kyasanur District in India	Human, Monkeys	19	
<i>Asfaviridae</i> , <i>Asfavirus</i>		African swine fever	<i>Ornithodoros moubata</i> , <i>Ornithodoros raticus</i> , <i>Ornithodoros turicata</i> , <i>Ornithodoros coriaceus</i>	Africa, Southern Europe, Caribbean (outbreaks in Brazil, likely imported)	Domestic pigs	19	
CCHF virus		CCHF	<i>Hyalomma marginatum</i>	Asia, Southern Europe, Southern Russia and India	Human	20	
Nematodes		<i>Acanthocheilonema viteae</i>		<i>Ornithodoros tartakovskyi</i>	Asia	Rodents	10

such as lice, fleas and ticks^[25]. The manual removal of ticks is widely practiced in developing countries^[5,26]. But, the drawback of grooming method is that it should be performed on daily basis, if not, pathogens can be transmitted to host by the ticks^[27]. Care should be taken while removing ticks from animals because ticks can also transmit deadly pathogens like Crimean–Congo hemorrhagic fever (CCHF) and KFD to humans which are transmitted by ticks of genus *Hyalomma* and *Haemaphysalis* respectively^[22,28].

3.2. Pasture management

To reduce the environmental infestation by ticks, pasture management like rotational grazing, burning the grazed pasture is widely practiced in African countries and Australia^[5,29]. These methods are not feasible in India due to various factors like shrinking pasture land in India, eliminated pasture system of grazing, tick species involved, local geography, pasture, soil type and lack of compliance by farmers^[30]. Mostly animals are let free to graze on forests or wastelands and these lands can act as potential source of parasitic infections including ticks. Pasture spelling and rotation of pastures are not very effective for the control of multi host *Ixodid* spp. [e.g., *Hyalomma anatolicum anatolicum* (*H. a. anatolicum*)] or argasid ticks because of

the long survival periods of the unfed nymphs and adults^[31].

3.3. Biological control

Biological control is a component of an integrated pest management (IPM) system. It is defined as, introduction of one microorganism into the environment of other to obtain control of target parasite. Thereby, it reduces the population growth of the latter below the threshold, above which causes clinical diseases and economic losses. It involves an active human role and is not having any negative effects on the environment, like chemical control methods. Laboratory and field observations have revealed that many tick antagonists play important role in tick control^[32]. Some of them are birds, rodents, shrews, ants, spiders, fungi and plants. Ox peckers, *Buphagus* spp. eat ticks and reduce tick burden on animals. In Africa, chickens (*Buphagus africanus*) are natural predators of ticks^[33]. So raising poultry chicks in the cattle barns greatly reduces tick burden on the infested cattle. Some hymenopterous insects (e.g., *Ixodiphagus* and *Hunterellus* spp.), parasite on nymphal stages of ticks, lay eggs on them and ticks are literally eaten out by the hatching larvae of insect^[33]. The chalcid wasp, *Hunterellus hookeri* has been used to control the American dog tick *Dermacentor variabilis*. Fire ants (*Pheidole megacephala*) and parasitoid wasps (*Ixodiphagus*) are the noteworthy tick predators^[34].

The larval stage of ticks to find their host animals climb over various plants. Some subtropical and tropical plants have acaricidal effects by trapping ticks in viscous fluid secretions and kill them by toxic vapour released from the plant. One example is the *Stylosanthes* spp. (tropical legumes) can kill or immobilize larval ticks and the use of these plants may simultaneously improve pasture quality^[35]. *Brachiaria brizantha* has also been shown to be lethal to *Boophilus* larvae^[36]. *Jatropha curcas* (Linn) leaf ethanolic extract can significantly inhibit the hatching of laid eggs by ticks even at low concentrations^[37]. *Cissus adenocaulis* F, *Cassia didymobotrya* Fresen., *Kigelia africana* (Lam.) Benth. and *Euphorbia hirta* L. have shown good activity against *Rhipicephalus appendiculatus*^[38].

Among all these biological agents, entomopathogenic fungi play uniquely important role in the control of insects. *Aspergillus terreus* fungal spore suspension arrest the oviposition of *H. a. anatolicum* tick^[5]. Recently, it has been demonstrated that, *Metarhizium anisopliae* a soil fungi cause 100% tick mortality within 2 d when tested *in vitro*^[39]. So, fungal biopesticides are one of the important non-chemical methods for tick control^[40]. Finally, as an alternative to chemical control, biological control products are safe to users, animals and the environment. But still biological tick control methods have not been successfully implemented due to their environmental instability, and reduced selectivity on target species.

3.4. Genetic manipulation for tick resistance

The idea of developing tick resistance breeds in control of tick borne diseases is appealing but it is complex in nature. Tick resistance varies from breed to breed and within the breeds. Some individuals in the breed are either consistently more or less resistant than the average for that particular breed^[41]. Further, the degree of resistance to the tick achieved by cattle is an inherited trait. For example, *Bos indicus* (zebu) cattle of tropical regions are resistant to *B. microplus* (one host tick) than *Bos taurus* (*B. taurus*) (European) cattle, which are widespread throughout the temperate regions^[42,43]. For example, zebu (*e.g.*, Sahiwal) and sanga (*B. taurus* × *Bos indicus*), the indigenous cattle breeds of India and Africa, respectively were very resistant to *Ixodid* ticks after their initial exposure. In contrast, European (*B. taurus*) breeds usually remained fairly susceptible. Zebu cattle are more resistant to ticks than European cattle due to their thick movable hides covered with short straight, non-modulated hair, well developed panniculus muscle, sensitive pilomotor nervous system which moves their hides upon the slightest provocation, high density of sweat glands and an efficient erector pili muscle which makes the hair stand up on provocation by ticks and stimulates the secretion of sebum in the hair which is repellent for ticks^[44]. So cross breeding between these breeds were started to exploit

genetic resistance. The introduction of zebu cattle (notably Sahiwal cattle) to Australia has revolutionized the control of *B. microplus* in that continent. ‘Belmont Adaptaur’, hybrid was developed by Commonwealth Scientific and Industrial Research Organisation in Australia by crossing Hereford and shorthorn cattle. The Adaptaur bulls showed good resistance to the heat stress, *B. microplus* ticks and internal parasites. Use of resistant cattle as a means of tick control is also becoming important in Africa and America in the control of diseases^[45].

3.5. Vaccination

Although there may be many alternative tick control measures, immunization against ticks at present seems both practical and sustainable due to their cost effectiveness, reduction of environmental contamination and the prevention of drug-resistant ticks caused by repeated acaricide application. There is no effective vaccine against most protozoan and tick vaccines^[46]. Tick antigens are usually regarded as either exposed or concealed antigens. Exposed antigens are those that naturally come into contact with the host immune system during tick infestation *viz.*, antigens from the cuticle, salivary gland and its secretions. Hosts immunized with these antigens are boosted by continuous tick exposure. Concealed antigens are not exposed to the host immune system during tick infestation and therefore repeated immunizations are required to maintain high antibody titers. Most of the concealed antigens are derived from the gut epithelium of the ticks. Concealed antigens are more advantageous since ticks are unlikely to evolve mechanism that counteracts the host immune response, contrarily to an exposed antigen^[47]. Earlier Brossard started tick vaccination experiments with salivary gland extracts of *R. microplus* ticks to immunize cattle and showed partial protection on challenge^[48]. Later in 1986, Kemp *et al.* also documented rejection of *R. microplus* in animals vaccinated with tick extracts^[49]. Subsequently, Willadsen *et al.* identified a concealed antigen from the midgut of engorged female *R. microplus* tick and called it as Bm86^[50]. Immunization with Bm86 showed significant rejection of adult ticks, reduction in engorgement and egg mass. It also showed more than 80% protection against challenge infestations in cattle. Further, Kimaro and Opdebeeck vaccinated cattle with midgut membrane extract of *R. microplus* and showed significant protection after challenging the animals with 20000 larvae^[51]. Subsequently, Rand *et al.* cloned and expressed Bm86 in prokaryotic (*Escherichia coli*) vector^[52]. A 89 kDa glycoprotein of Bm86 that used for vaccination, showed considerable reduction in egg mass and tick rejection by host. Later, Turnbull *et al.* produced glycosylated Bm86, as a vaccine candidate, expressed in eukaryotic vectors *viz.*, *Aspergillus nidulans* and *Aspergillus niger* using the amdS promoter system^[53].

Upon vaccination, this molecule showed a significant immune response against *R. microplus* infestations in cattle. Incorporation of the Bm86 vaccine into IPM programs in Cuba, reduced utilization of acaricides up to 82%[54].

In 1995, Willadsen *et al.* purified the Bm86 protein from *Yeerongpilly* strain and commercialized as TickGARD and combination of Bm86 and Bm91 (glycoprotein located in the salivary gland of *R. microplus*) was marketed in the name TickGARD Plus in Australia, and they studied immune response of TickGARD and TickGARD Plus[55]. The combination vaccine gave a better immune response when compared to Bm86 vaccine alone[56].

In 1997, Canales *et al.* commercialized rBm86 protein (Gavac™, Heber Biotec S.A., Havana, Cuba) expressed and purified from methylotrophic yeast *Pichia pastoris* in Mexico, Argentina and Columbia and reported an efficacy of 82%[57]. The efficacy of Gavac™ in other *Rhipicephalus* tick species was also checked. It showed 99% efficacy against *Rhipicephalus annulatus* (*R. annulatus*) infestations[58]. It has also showed partial cross protection against *Hyalomma* spp. and *Rhipicephalus* spp. Gavac™ has shown good protection against *R. microplus* and *R. annulatus* infestations in field trials thereby reduced the transmission of babesiosis[59]. Recombinant glutathione S-transferase from *Haemaphysalis longicornis* provided cross-protection to cattle against *R. microplus* infestation[60]. Ubiquitin and subolesin recombinant proteins were compared for immunoprotection against *R. microplus* larvae in cattle. Subolesin immunized animals showed a better response compare to ubiquitin[61].

In India, development of vaccine against ticks is gaining importance but still in growing phase. Several attempts were made to develop an effective tick vaccine. Earlier, crude and purified antigens were used to immunize cattle against ticks. Rajendra Kumar and Singh immunized group of crossbred calves with the whole ground tick antigen, gut antigen and salivary gland antigen obtained from female ticks of *R. microplus* and *H. a. anatolicum* with Freund's complete adjuvant, and they concluded ground tick antigens, and midgut proteins were more immunogenic than the salivary gland glycoprotein[62]. The immunization of cattle using the tick extract supernatant antigen and tick extract antigen showed that, tick extract supernatant antigens were more immunogenic than tick extract antigen antigen[63].

From crude extract of *H. a. anatolicum*, a 39 kDa protein was isolated and immunization using this protein reduced 71.6% of larval and 77.3% of nymphal infestation[64]. Subsequently, six proteins of molecular weight ranging from <43, 43, 47.3, 50.8, 57.5 and 60 kDa were found to be common between *B. microplus* and *H. a. anatolicum* ticks[65]. Later from these two ticks, 29 and 34 kDa proteins were isolated respectively, and confirmed protection for up to 30 weeks[66].

Infestation with multiple tick species may prevent the efficacy of tick vaccines with a narrow spectrum that are

produced with antigens from a single tick species[67]. So developing a universal anti-tick vaccine consisting of one or more common tick antigens capable of triggering protective immune responses against heterologous tick challenges would be both economically and technically attractive[68]. Development of a universal vaccine could therefore afford to rely on highly conserved tick proteins with limited and manageable antigenic variations, which are capable of inducing protective cross-reactive immunity against different tick species. Moreover, finding an antigenic protein conserved between mosquitoes and ticks has boosted the prospects of a pan-arthropod vaccine[69,70].

The mechanism of Bm86 based vaccine for controlling tick infestation relies on polyclonal antibody response against the concealed antigen. The sequence variation in the Bm86 locus of parasites can affect the efficacy of Bm86 based recombinant vaccines. There is an inverse correlation between the efficacy of vaccine and the sequence variations in Bm86 locus. The mutation fixation index in the Bm86 locus was calculated to be 0.1 amino acids per year[71]. Tick population studies in Argentina revealed polymorphisms in the Bm86 gene that resulted in a soluble rather than a membrane-bound protein, making these ticks resistant to vaccination with the original Bm86[72,73]. To overcome this resistance, a new recombinant vaccine based on Bm95, Bm86 homologue was developed. Recently, a Bm86 vaccination trial in cattle involving *R. microplus* and *R. annulatus* infestations, reported overall vaccine efficacy of 60% and 100%, respectively[74], indicating the potential of Bm86 as a component of a multi-species anti-tick vaccine. To develop a universal vaccine, homogeneity of targeted gene among different species/isolates of ticks are essential. Across the globe, attempts were made to identify the Bm86 homologue in different strains/species[75](Table 2).

Table 2

Bm86 homologue identified in other ticks.

R antigen	Tick species	References
Bm95	<i>R. (B.) microplus</i> Argentinian strain	73
Hl86	<i>Haemaphysalis longicornis</i>	76
Bd86-1, Bd86-2	<i>Rhipicephalus (Boophilus) decoloratus</i>	77
Hm86	<i>Hyalomma marginatum</i>	78
Ba86	<i>Rhipicephalus (Boophilus) annulatus</i>	79
Haa86	<i>H. a. anatolicum</i>	75

3.6. Endosymbiotic approach

In endosymbiosis, the symbiont lives within the body of its host or inside the cells of host tissue[80,81]. They are commonly found in arthropods usually in midgut, haemolymph and ovaries of the different arthropod vectors[82]. Arthropod vectors benefit from the symbiosis and symbiosis augments the functional capabilities to facilitate their expansion to novel niches. The beneficial endosymbionts like, *Wigglesworthia glossinidia* in *Glossina*

fly synthesize vitamins that promote their reproduction and *Wolbachia* in arthropod vector is called as “reproductive parasite” since it manipulates the reproduction of the host vector[83,84].

Ticks can harbor a wide range of endosymbiotic bacteria including *Rickettsia*, *Francisella*, *Coxiella*, and *Arsenophonus*, amongst others[85]. Recently, Andreotti *et al.* reported the presence of bacteria of 121 genera in different tissues and stages of *R. microplus*, by using pyrosequencing technique[86]. Among this, most of these were free-living environmental Gammaproteobacteria, Gram-positive cocci and anaerobes without strict association with ticks[87].

Since endosymbiotic organisms are essential for the survival of arthropods including ticks, disturbing the interaction between endosymbiont, vector and pathogen helps in control of vector borne diseases. Determining the molecules crucial for the endosymbiont–vector–pathogen interaction will help in the designing transgene products which will disturb this interaction[88]. For instance, *Wolbachia pipientis* when transfected into *Aedes aegypti* mosquitoes hinders the replication of dengue and chikungunya viruses[89]. So more studies are needed in this emerging field, whose results may have wide applications, including the control of vector borne diseases of humans and animals. Identification and characterization of endosymbiotic microorganisms of ticks results in potential future targets for tick control[6].

3.7. Acaricides

Acaricides play a main role in the control of ticks in spite of their well known drawbacks *viz.*, development of resistance, environmental pollution, and residues in meat, milk, hide, skin and natural toxicity. Acaricides are still the backbone of tick control as they are effective both in the short-term by cleaning ticks off the animal and in the long-term in reducing TTBD[90]. The most commonly practiced method of controlling ticks on livestock is the application of acaricides directly on the animal host[5]. It is important that application should be systematic so that the acaricides will be highly effective against ticks without affecting the host. Acaricides can be applied by dipping, spraying, spot-on, pour-on, horn bands, hand dressing and oral treatments or injections. Insecticide and acaricide ear tags are commercially available in some countries for the control of horn flies, face flies and spinose ear ticks[91].

Chemical compounds effectively kill ticks on livestock which are arsenicals, chlorinated hydrocarbons, organo phosphorous compounds, carbamates, *etc.*, but a number of tick species have developed resistance to these acaricides. Worldwide acaricide resistance was reported for one-host tick, *R. (B.) microplus*[92]. Resistance is usually associated with mutations in genes related to drug susceptibility (target

site resistance), increased metabolism or sequestration of the acaricide, or reduced ability of the acaricide to penetrate through the outer protective layers of the tick’s body. Metabolic resistance is due to increased metabolism of acaricides and thereby reduced sequestration in the tick. Mainly cytochrome P450s, esterases, and glutathione S-transferases enzymes are generally involved in metabolic resistance[93]. Use of arsenic was the first effective method for controlling ticks and tick-borne diseases, and was used in many parts of the world until resistance to the chemical became a problem[94]. Later on, it was replaced by chlorinated hydrocarbons, but they were very persistent in soil and very toxic to many other arthropods and host animals. Persistence and the tendency for organochlorines to be bio concentrated into living tissue and subsequently passed through the food chain to end the use of these chemicals. So, organophosphates were introduced around 1950, as a replacement for the chlorinated hydrocarbons. Pyrethroid an organic compound similar to natural pyrethrins produced by the flowers of pyrethrums (*Chrysanthemum cinerariaefolium* and *Chrysanthemum coccineum*) were introduced in 1960s. They gained wide acceptance and currently the synthetic pyrethroids are the most used pesticides. They are non-toxic to mammalian hosts and produce instant knocking-down of arthropods. First generation pyrethroids are environmentally non-persistent than second generation compounds. Currently they are being used as insect repellents in household sand for killing arthropods in agriculture and on livestock species. But, resistance to organophosphates and pyrethroids, were recorded in several parts of world[11,86,95]. Formamidine acaricide (Amitraz), plays an important role in the control of the southern cattle tick, *B. microplus*, in countries where resistance to both organophosphate and pyrethroid pesticides reached unacceptable levels[96]. In recent years, formamidine (amitraz) resistance to *B. microplus* populations was reported from Colombia, South Africa, Brazil and Mexico[97]. Currently, the macrocyclic lactones (avermectins) group compounds are effective, against both cattle ticks and other parasites[98]. They were discovered in 1978. Due to 30–40 d withholding period for milk from animals treated with the avermectins, they are unsuitable for use on dairy cows. In 1980s, a new class of neuro-active insecticides with less mammalian toxicity and greater toxicity on arthropods was introduced in market. Their usages were greatly restricted due to their environmental persistence and toxicity to wildlife, aquatic invertebrates, birds and bees.

To counteract acaricide resistance, combinations of powerful acaricides are being used worldwide. Products combined with different active components are available in an attempt to include a diverse number of mechanisms of action, to reduce the emergence of acaricide resistance[99,100]. But several ticks developed multidrug resistance. To avoid

multidrug resistance, new generation acaricides targeting metabolic pathways or bio-molecules synthesis pathway should be generated and these acaricides should be kept in reserve to meet out any emergency situations expected to arrive by the multi-acaricide resistant tick population in future[5,7].

3.8. Integrated control system

Tick control programmes basically depend on the advantages and disadvantages of specific technical approaches. Chemical acaricides, if correctly applied, are efficient and cost effective, however improper use leads to chemical resistance and chemical residues in food which is a public health issue. In biological control methods, cost, efficacy, manufacture, application and stability present serious challenges. Lack of efficacy with current anti-tick vaccines may be a stand-alone question. So there is no single, ideal and affordable solution available at present for the control of ticks. Integrated control is a systematic application of two or more technologies in an environmentally compatible and cost-effective manner to control pest population. Initially in Australia, tick vaccine *i.e.* TickGARD coupled with short term acaricide usage in the name of IPM package was started. It gave an acceptable level of parasitic control[10]. Further similar experiments were carried out in Cuba and Mexico. It not only reduced the chemical usage but also reduced the risk of chemical resistance[72]. Therefore, it is necessary to explore the possible combination of tick control strategies with other available methods in an area to reduce the tick populations and to combat TTBDs in livestock system.

4. Conclusions

The risks of TTBDs are increasing worldwide, which is a major constraint on livestock production system. Ticks cause great economic losses to livestock throughout the world by parasitizing wide range of vertebrate hosts, and transmit a wider variety of pathogenic agents than any other group of arthropods. In the area of tick control, currently, tick control programmes rely mostly on rapid-acting acaricides both on and off the host. Continuous use of these chemicals is often accompanied by serious drawbacks; the foremost important is the development of resistance, environmental contamination and, in farm animals, contamination of milk and meat products with drug residues. Sometimes ticks will develop multiple classes of acaricide resistance, by continues use of same drug over a long period. So identification of novel effective acaricidal compounds is essential to combat increasing resistance rates and concern for the environment and food safety but, the production cost will be more. Reduction in transmission

of TTBDs by vaccination is well documented. But the availability of vaccines against ticks throughout the world is very scanty. The ability to induce an effective, sustained immunological response is crucial but needs improvement. Recent advances in vector biotechnology area open new opportunities for identification and vaccine development. Making tick infestation treatment cost effective and reducing the chemical residual effect on animals and environment sustainable, strategic integrated methods will play a good role in livestock production system.

Conflict of interest statement

The authors declare that they have no conflict of interest.

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