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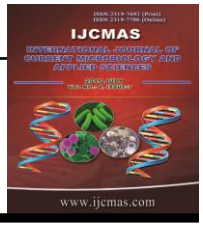

Review Article

Zoonotic significance and Prophylactic Measure against babesiosis

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A B S T R A C T

Babesiosis is a vector borne disease by the different species of genus Babesia, affecting a large no of mammals worldwide. Babesiosis has zoonotic significance all over the world, causing huge loss to livestock industry and health hazards in human population. The primary zoonotic vector of babesia is ixodes ticks. Different species have different virulence, infectivity and pathogenicity. Literature was collected from the individual researchers published papers. Table was made in the MS excel. The present study review for the current knowledge about the babesia species ecology, host specificity, life cycle and pathogenesis with an emphasis on the zoonotic significance and prophylactic measures against Babesiosis. Prophylactic measure against Babesiosis in early times was hindered but due to advancement in research, the anti babesial drugs and vaccines have been developed. This review emphasizes on the awareness of public sector, rural communities, owners of animal husbandry and health department about the risk of infection in KPK and control measure should be implemented. Vaccines of less price tag should be designed to prevent the infection of cattles and human population.

Keywords

Babesiosis, Prophylactic, Tick borne, Vector, Zoonosis.

Introduction

Babesiosis is a tick transmitted disease, infecting a wide variety of wild and domestic animals, as well as humans. Babesiosis is also called tick fever, Texas fever, red water and piroplasmosis caused by different *Babesia* species found in tropical and temperate regions of the world (Criado-Fornelio *et al.*, 2004). Babesiosis is an emerging zoonotic disease having different reservoir host for zoonotic *Babesia* species. *B. microti*, other *Babesia microti* like species and *B. divergens* have zoonotic significance.

At specie level there is considerable confusion about the true number of zoonotic species. Recent studies indicate that *Babesia microti* is a species complex together with at least four named species (US, Munich, Kobe, and Hobetsu) and unknown number of other strains (Goethert *et al.*, 2006; Tsuji *et al.*, 2006; Nakajima *et al.*, 2009). Babesiosis may be asymptomatic estimating that about a third of patients remain asymptomatic (Krause *et al.*, 2003) While in symptomatic cases clinical signs of human Babesiosis are persistent non-periodic high

fever (40–41°C) chills, severe sweats, headaches, myalgia, and lumbar and abdominal pain. Jaundice due to high level of haemolysis, vomiting and diarrhea may also occur. Respiratory, cardiac, renal, or hepatic failure may be present due to release of toxins during haemolysis and because of host immune response (Zintl *et al.,* 2003; Telford *et al.*, 2006; Hunfeld *et al.*, 2008). It is possible that single *Babesia specie* can infect more than one vertebrate host as *Babesia microti* (rodents and men). Babesiosis is transmitted biologically by a vector tick Ixoded species but biting of flies and fomites may also involve in the mechanical transmission of Babesiosis from infected to clinically susceptible animals (Ristic and Levy, 1981).

At the beginning of twentieth century vector borne diseases resulting in the worldwide epidemics affecting thousands of people (Gubler, 1998). Zoonosis emerges in the populations due to the immigration of humans and livestock, lack of public attentiveness and health resources, poverty and changes in the climate (Sumilo *et al.,* 2008). Pakistan being economic country having large rural and developing urban population is also endemic to a large variety of tick vector and insect species (Reisen and Boreham, 1979; Ghosh *et al.*, 2007). In Pakistan more than 70% population of KPK depend on the livestock for their survival. Due to restricted use of tick control measure and denied access to vaccines, the vector borne diseases in the people and livestock industries are common in KPK and FATA regions of the Pakistan. These vectors borne diseases cause morbidity and mortality from the animals acting as a reservoir of zoonotic, vector borne agents (Irwin and Jefferies, 2004; Otranto *et al.,* 2009).

The review intended to discuss the zoonotic significance and prophylactic measure against Babesiosis in KPK Pakistan and in the last suggesting preventive and prophylactic measures in order to minimize the transmission of vectors to humans and animals. Prophylactic measures are also recommended against tick vectors, to reduce the economic loss to livestock industries in KPK.

Historical background

For centuries Babesiosis was known to be a serious hemolytic disease of wild and domesticated animals, chiefly cattles. Victor Babes, a Romanian scientist who 1st reported this disease in the Romania in 1888, by describing the symptoms of haemolysis in the cattle and sheep (Ristic and Levy, 1981). In 1893 Americans Theobald Smith and Fred Kilborne recognized the parasite as the causal agent of this disease, they also describe that ticks are instrumental in the Babesiosis transmission. They reported Babesiosis as the first tick-transmitted disease. Hutcheon in South Africa in 1896 describes the presence of canine babesiosis.

Epidemiology and pathogenesis

The genus *Babesia* causes Babesiosis which is an intraerythrocytic protozoan. There are about more than 100 *Babesia* species in which some are pathogenic to the humans for example *Babesia microti* is causative agent of human Babesiosis in North America while *Babesia divergens* in the Europe also four to five *Babesia* species are reported in other human cases (Oliver Jr *et al.*, 1993). *Babesia bigemina* and *Babesia bovis* cause bovine Babesiosis (Mehlhorn and Kakoma, 1994). *Babesia argentina* is mostly found in the South America (Levine, 1985). Out of 20 *Babesia* species, 5 species are more important in the cattle's. *Babesia berbera* found in the North America and *Babesia* major is slightly smaller than *Babesia bigemina* and transmitted by

Haemaphysalis punctata and prevalent in the United Kingdom and northern Europe (Pumell, 1981). *Babesia equi* and *Babesia caballi* are distributed globally and cause equine babesiosis. Both species can be transmitted by *Boophilus, Hyalomma, Dermacentor*, and *Rhipicephalus* species of tick (Levine, 1985; Friedhoff, 1988). *Babesia canis* and *Babesia gibsoni* are the causal agents of dog piroplasmosis and transmitted by *Rhipicephalus sanguineus* or *Dermacentor reticulatus* ticks (Levine, 1985).

Babesia jakimovi is large specie and it is the causal agent of Siberian piroplasmosis in cattle. It can also infect the tartarean roe deer, Asian elk and reindeer. The symptoms of *Babesia jakimovi* disease are similar to *Babesia bigemina* (Pumell, 1981). *Babesia ovate* is reported in the Japan and it is slightly pathogenic and it is serologically different from *Babesia bigemina* and transmitted by the larvae of *Haemaphysalis longicornis* (Minami and Ishihara, 1980). *Babesia bigemina* and *Babesia bovis* are two economically most important species to the livestock industry in tropical and sub-tropical areas of the world and transmitted by the same tick vector Rhipicephalus also called *Boophilus microplus* (Callow, 1984a,b; Hove *et al.,* 1998). Babesiosis in the dogs is caused by *Babesia canis* first time reported in Itly. Babesiosis in case of *Babesia bovis* characterized by anemia, fever up to 42°C, jaundice, ataxia, anorexia, increased respiratory rate, muscle weakness, depression and difficult to move. While in Babesiosis due to *Babesia bigemina*, cattle do not seem to be as sick as those with *Babesia bovis*, but haemoglobinuria occurs again and again, anemia and jaundice occurs very frequently and death may occur silently. Babesiosis also causes abortion in cattle's and reduces the fertility rate of bulls approximately six to eight weeks (Callow, 1984b).

Pakistan economically depends on the livestock sector, having contribution in 2008 and 2009 to agricultural value (51.8%) and also to national gross domestic product (11.3%) (Mustafa, 2008). From epidemiological studies, it is revealed that Babesiosis in sheep is the third most important disease in Pakistan (Morris, 2009). Babesiosis in Pakistan causes huge economic loss to the livestock industries. Ticks are cosmopolitan in distribution in tropical and sub-tropical areas. Pakistan is tropical country having rich fauna of tick in the number of genera and species, Because of most favorable climatic conditions for the tick's growth and reproduction (Rasul and Akhtar, 1975).

In Pakistan Hyalomma tick have highest prevalence rate followed by *Boophilus*, *Haemaphysalis* and *Rhipicephalus* in district Kasur (Durrani and Kamal, 2008). In the Khyber Pakhtunkhwa province of Pakistan vector borne diseases is most prevalent due to favourable climatic conditions and poverty (Irwin and Jefferies, 2004; Otranto *et al.,* 2009).

Host specificity and life cycle

Babesias are apicomplexan parasites of the suborder Piroplasmidea of family babesiidae due to their specific invasion in the erythrocytes, multiplication by budding rather than schizogony. The life cycle of all *Babesia* species is approximately similar but slight difference exists because in some species transovarial transmission occur (*Babesia* spp *sensu stricto*) while not in other species (*Babesia microti*). Almost all the *Babesia* species are transmitted by the infected tick bite. The major difference between *Babesia* and *Theileria* is that in *Babesia* during tick infestations the sporozoites directly infect the red blood cells while in *Theileria* they do not readily infect

the red blood cells, but first they invade the lymphocyte or macrophage in which they develop into schizont (Uilenberg, 2006). *Babesia* species require two classes of host, a vertebrate and invertebrate. All *Babesia* species depend on both hosts for their survival because specific tick vector must feed on the vertebrate reservoir in order to attain infectious stage. *Babesia* species generally complete their life cycle in 3-stages.

1-Gamogony (in the tick gut gametes fusion and formation)

2-Sporogony (in salivary glands asexual reproduction occur)

3-Merogony (in the vertebrate asexual reproduction occur)

Infection is directly related to the tick infestation time if it is prolonged then infection rate will be 100 % (Piesman and Spielman, 1982). Ixodes ticks are instrumental in the transmission of babesiosis. Except in the *Babesia meri* in which a non-ixodes tick *Ornithodoros erracticus* acting as a vector. They feed in the fall (May through July) and in spring in nymphal stage, after which they lay eggs, hatched in the larvae in summer (late July), these infected larvae overwinter and moult to become nymphs in the spring again. Finally nymphs molt into adults in the fall and complete the life cycle. Tick responsible for transmission of *B. divergens* to humans is *Ixodes ricinus*. The life cycle of *I. ricinus* complete in 3 years, as larva in the first year, nymphs in the second, and adults in the third. When tick feed on the vertebrate host for 10 hours, the organism can be seen in the ticks in consumed red blood cells after 46–60 hours. Some of the gametocytes develop in arrow head structure in the anterior region called Strahlenkörper or ray bodies. The basic function of this structure is gamete fusion (Kakoma and Mehlhorn, 1993; Rudzinska *et al.*, 1983). Then epithelial cells of the tick gut are penetrated by the Strahlenkörper and start feeding on the epithelial cells after 80 hours of penetration, from where they move to the salivary glands of the tick with the help of haemolymph (Rudzinska *et al.*, 1983).

The development of sporozoites complete in 3 phases in the tick salivary glands. First, they form sporoblast that is a branching meshwork from which new sporozoites develop by budding approximately 5,000 to 10,000 new sporozoites can be develop in the single Sporoblast (Kakoma and Mehlhorn, 1993; Karakashian *et al.*, 1983). In the Second step, the specialized organelles of the new developing sporozoites (micronemes, rhoptries, and double membrane segments beneath the plasma membrane) will form within the meshwork when ticks host start feeding again. Finally, through budding process a mature sporozoite will form which is 2·2 by 0·8µm in size and pear shaped having smooth endoplasmic reticulum, free ribosome's, mitochondria like structures, interiorly located rhoptry and many micromeres (Karakashian *et al.*, 1983). During final hours of attachment and feeding approximately several thousands of sporozoites are deposited around the tick mouth in dermis. Transmission is directly related to the saliva having anti-inflammatory or immunosuppressive pharmacological activity (Ribeiro, 1987).

In *Babesia divergens* and other large *Babesia* species transmission is transovarian in which the zygote also called ookinete, enters in haemolymph from where they may invade the fat bodies or nephrocytes. The ookinete undergo second cycle of division forming secondary ookinete which invade

the ovaries and insure transovarial transmission (Telford *et al.,* 1993). In the vertebrate hosts the sporozoites first go to lymphocytes forming multinucleate schizonts in *Theileria* and in some *Babesia* species (Meldrum *et al.,* 1992). Schizonts undergo the budding process forming merozoites which lyses the host cell. The merozoites or sporozoites of *Babesia* species without forming pre-erythrocytic stage penetrate the erythrocytes and form parasitophorous vacuole. This vacuole will later on disintegrate exposing the parasite with single membrane which is different from the plasmodium species having host membrane along with its own (Rudzinska, 1976). In the host red blood cells the merozoites change in trophozoites, these trophozoites form a large number of merozoites which destroy host red blood cells, causing haemoglobinuria and at this time four parasites can shape Maltese cross form. The trophozoites have the capacity to form gametocytes but at that time trophozoites do not reproduce but only grow in size (Mehlhorn *et al.,* 1980; Rudzinska *et al.,* 1979). The gametocytes change to gametes in the tick gut prior to leave the red blood cells.

Laboratory analysis

For the diagnosis two methods are used microscopy and PCR. Thin blood smears stained with giemsa in which organisms are darkly stained ring like with light blue cytoplasm. The organism may be seen in different forms that are simple rings (annular), paired or pyriform, single pear shaped trophozoites but rarely in Maltese cross (tetrad form). Patients with mild infections are not diagnosed microscopically so remain untreated, for such low grade infections more sensitive techniques are required, such as PCR which is a molecular technique. In this sequence of amplified fragments is analyzed and then compare to a database of already known sequence which enables the identification of the infecting organism. So patients are parasitemic which have known Babesial DNA. DNA presence is an indication of an active infection most studies shown that microbial DNA is cleared from blood in absence of microbial replication (Kain *et al.,* 1993; Nocton *et al.,* 1994; Krause *et al.,* 1998).

Prophylactic measures

Chemophylaxis

Drugs against trypanosomes are also used for babesiosis. Infection in cattle's can be controlled by regular treatment with tickicide. Imidocarb is the drug of choice in bovine babesiosis. Acarcicides are also frequently use drug against bovine Babesiosis (Levine, 1973). First successful treatment against *Babesia bigemina* was trypan blue to indicate the type of infection.

They recommend treatment for *Babesia divergens* is clindamycin and oral quinine in order to resist hemolysis and to prevent renal failure while for *Babesia microti* infections drugs such as hydroxynapthoquinone derivatives (atovaquone), chloroquine, tetracycline, Primaquine, sulfadiazine and pyrimethamine are recommended (Rowin *et al.,* 1982).

In humans Imidocarb has not approved. Pentamidine and cotrimoxazole are also used for *Babesia divergens* treatment (Farwell *et al.,* 1982). For *Babesia bigemina*, *Babesia bovis*, *Babesia jakimovi* and *Babesia ovate* diminazene diaceturate (3-5 mg/kg), Imidocarb (1-3 mg/kg), amicarbalide (5-10 mg/kg) and quinuronium are used. Drugs used for the *Babesia caballi* and *Babesia equi* Imidocarb is used in different dosage for example 2 mg/kg twice a day and 4 mg/kg four times at interval of 72 hours, respectively (Kuttler, 1981).

Vaccine

Vaccines comprising live, attenuated strains of *Babesia bovis*, *Babesia divergens* and *Babesia bigemina* are formed from the infected animal's blood or from *in vitro* culture. Vaccines are provided either in chill or frozen form. Live *Babesia* vaccines are not completely safe. A single dose can provide lifelong immunity against Babesiosis (Barriga, 1994; Callow *et al.*, 1997; Palmer and McElwain, 1995). In 1964 by adaptation in splenactomized calves attenuated strain vaccine for *Babesia bovis* was prepared (Callow, 1971), but attenuated vaccines are most problematic, including the transmission of bovine leukosis virus an enzootic agent (Wright, 1991).

Recombinant vaccines BM86 and BM95 are also prepared to compensate the problems created by the use of attenuated vaccines. In early history living parasites are used in livestock management for Babesiosis for a long period of time (Callow, 1971, 1979). Recombinant vaccines are also developing from surface antigens of sporozoites in which apical complex proteins are important so these antigens are protective in Babesiosis infection (Palmer and McElwain, 1995; Wright *et al.*, 1992). The scenario for recombinant vaccine is still challenging (Brown *et al.*, 2006). SBm7462 is a synthetic anti-Boophilus microplus vaccine derived from the tick intestinal protein. SBm7462 is 43 amino acid residues are derived from the BM86 protein structure. A killed vaccine for *B. divergens* has been prepared from the blood of infected calves (Zintl *et al.*, 2003). Still no Commercial subunit vaccine is prepared.

Discussion

Babesiosis caused by the intraerythrocytic parasite of the genus *Babesia*, gaining the world attention as an emerging zoonosis (Kakoma and Mehlhorn, 1993). Babesiosis has a cosmopolitan distribution, mostly endemic to tropical and subtropical regions of the world and affecting a large variety of mammals and a small no of bird species. Transmission route is by the infected ixodes tick bite, other routes might be transplacental, intrauterine, blood transfusion and organ transplant (Phipps and Otter, 2004). All *Babesia* species replicate in the vertebrate red blood cells and called as piroplasmosis due to the pear shape structure. *Babesia* parasite requires two proficient hosts, a vertebrate and non-vertebrate for transmission (Kakoma and Mehlhorn, 1993). Human Babesiosis is caused by one of the species of *Babesia* having distinctive geographical distribution depending on the competent hosts. In North America first human case was diagnosed from California (USA) in 1966 (Scholtens *et al.*, 1968), but the causal organism similar to the *Babesia duncani* or *Babesia specie* CA-type, but in Massachusetts (USA) in 1969 *Babesia microti* was diagnosed as the most familiar parasite responsible for human Babesiosis in North America (Western *et al.*, 1970), transmitted by the *Ixodes scapularis*. *Babesia microti* is a rodent borne piroplasm which intermittently transmitted by the other newly documented species of *Babesia* called WA_1 piroplasm. The primary reservoir of *Babesia microti* is white-footed mouse (*Peromyscus leucopus*) but this disease is also caused by the similar *Babesia* species, in short tailed shrews, Eastern cottontail rabbits and Eastern chipmunks (Anderson *et al.*, 1991; Stafford *et al.*, 1999; Telford and Spielman, 1993).

Within the last decade, cases of human Babesiosis have increased (Persing *et al.*, 1995). *Babesia microti* is the primary cause of human Babesiosis in North America, but

four other species have been reported responsible for human Babesiosis including *Babesia duncani*, *Babesia* sp. CA-type, *Babesia* sp. MO1, and *Babesia* sp, TN1 from a patient in Tennessee (64, 65and 66). Babesiosis is the most common disease which is frequently transmitted by the blood transfusion (Young *et al.,* 2012). In Canada no infection has reported transmitted by the tick fauna, but transfusion transmitted cases of *Babesia microti* are diagnosed. Blood transfusion is responsible for the sporadic cases in the non-endemic areas as in the Texas, California, Washington, and Georgia (Kain *et al.,* 2001). Probably from 1980 to 2010, 70–100 infections are transmitted through transfusion in the United States (Leiby, 2011).

Transovarial transmission for *Babesia microti* has not been reported while large *Babesia* species, for example *Babesia divergens* transovarially transmitted. A *Babesia* species formally called *Babesia duncani* was morphologically similar to the *Babesia microti* identified in Washington and California in 1990s (Conrad *et al.,* 2006). Important cases have been reported in immunocompromised, splenectomized and blood transfusion acquired individuals (Herwaldt *et al.,* 2011). From the Phylogenetic analysis, it is evident that it is a separate clade from other *Babesia* species (Charles *et al.,* 2012). For *Babesia duncani* yet no reservoir and tick vector is identified (Persing *et al.,* 1995). In 1992, a rare case of human Babesiosis caused by new specie MO1 was reported in Missouri in splenectomized patient. The natural host for MO1 is lagomorphs and a vector is *Ixodes dentatus*. Phylogenetic analysis on the fragment of an 18s rRNA fragment to indicate that this parasite was initially resemble to the *Babesia divergens* but subsequent analysis showed that MO1 is distinct from the *Babesia divergens* (Holman *et al.,* 2005; Holman, 2006).

The primary cause of human Babesiosis in Europe is *Babesia divergens* and its related zoonotic species called EUI, also known as *Babesia venatorum* reported in Europe. In Asia approximately four zoonotic *Babesia* species with rare infection have been identified in Korea, Korea, Japan, Taiwan, India and China (Wei *et al.,* 2001; Arai *et al.,* 2003; Marathe *et al.,* 2005; Kim *et al.,* 2000). Cattles are the natural host for *Babesia divergens* their infection have been prevalent in Europe and possibly in North Africa (Kim *et al.,* 2000). In 1992 a *Babesia divergens* like species have been identified from the Canary Islands, Spain (Olmeda *et al.,* 1997). In 1998 another human pathogen was reported and diagnosed as EUI (European union-1) in Itly and Austria. The most familiar vector for *Babesia* species EU1 is *Ixodes ricinus* (Herwaldt *et al.,* 2003).

In Africa a number of *Babesia* species have been reported from domestic and wild animals but due to deficiency of human Babesiosis cases sequence analysis, no reservoir for zoonotic Babesiosis is known in Africa (Mazyad *et al.,* 2010).

Bovine Babesiosis is caused by the two most prevalent *Babesia* species (*Babesia bigemina* and *Babesia bovis*) in the tropics and subtropics of the world. Bovine Babesiosis causes most serious economic loss to the livestock industry, endangering half a billion cattle across the world. *Babesia bigemina* and *Babesia bovis* are primarily transmitted by *Boophilus microplus*, also transmitted by the principal vectors such as *Boophilus annulatus* and *Boophilus decoloratus*. *Babesia bigemina* is a large pear shaped body jointed at acute angle in mature infected red blood cell. While the *Babesia bovis* is a small pleomorphic *Babesia* rounded single body or pear shaped jointed at obtuse angle. Transmission is by the feeding of the

nymphal and adult ticks. Calves are virtually resistant to the *Babesia*. *Babesia bovis* causes more severe clinical signs as compared to *Babesia bigemina* (Riek, 1968). For bovine babesiosis, Imidocarb are the drug of choice which can prevent clinical infection up to 2 months, but dosage are different for different species depending on the status of infected host (Kuttler, 1981). Some *Babesia* species are nonpathogenic while some causes mild clinical infections, for example *Babesia* major is nonpathogenic in nature but can lead to death in the splenectomized calves while *Babesia ovate* is mildly pathogenic in nature and have similar chemophylaxis as *Babesia bigemina* (Minami and Ishihara, 1980).

Babesia ovis, is a small *Babesia specie* of goat and sheeps causing mild infection mostly inconsiderable but the symptoms of infection are just like of *Babesia bigemina*. In swine Babesiosis is caused by the two important species, the large one is called *Babesia trautmanni* and a small one *Babesia* perroncitol having no resemblance in the sign of disease to cattle. In Africa their reservoir are wild pigs (Bush pigs and warthogs) but these species are frequently nonpathogenic so they are often ignored (Kuttler, 1981). In wild canids and dogs piroplasmosis is caused by *Babesia gibsoni*, the disease is characterized by the intermittent fever, haemoglobinuria, anemia and ultimately death. Vaccination is done against canine babesiosis; most commonly used recombinant vaccine rP50t is effective to create protective immunity (Fukumoto *et al.*, 2003).

Feline vector borne diseases have been emerged in the recent years and attain worldwide geographical distribution. Feline Babesiosis is less common than the canine Babesiosis and little work is done. Climatic factors, especially temperature leading to its high prevalence. *Babesia felis* is mostly prevalent in the domestic cats of India and Africa. In feline Babesiosis younger cats are more susceptible as compared to the adults due to low immunity and a cat which is free roaming in nature are also more susceptible (Ghosh *et al.*, 2007). Feline Babesiosis is more prevalent in the humid seasons (July-August) and different seasons have different concentrations of ticks. The concentration of disease is equal in both male and female while in the *Babesia canis* the disease susceptibility is different in male and females. Canine Babesiosis is caused by two important species having differential size; *Babesia gibsoni* is small in size than *Babesia canis*. In case of canine Babesiosis males are more susceptible to the disease than females because male dogs are involved in organized fighting, while other studies reported that susceptibility sex ratio is same (Martinod *et al.*, 1986). The zoonotic significance of the parasitic infection is dependent on the availability of accurate and significant diagnostic techniques.

Molecular techniques, significantly PCR (polymerase chain reaction) play an important role in the diagnostic, characterization of parasites and in the control measure of the zoonosis. Common method used for the diagnosis is microscopy but in case of low parasitemia this method is botched. In order to detect low parasitemic cases more accurately molecular diagnostic methods PCR and ELISA (Enzyme Linked Immunosorbent Assay) are used. Several prophylactic measures have been adopted including chemophylaxis and vaccines for the treatment of babesiosis. Vaccines are used in order to provide lifelong immunity because a single dose of an effective vaccine can induce both innate and acquired protective immunity.

Table.1 Recognized *Babesia* species in the world of the domestic animals

S.No	*Parasite*	Vertebrate host	Tick Vector	Geographical distribution
1	*Babesia bovis* (syn *B.argentina*)	Cattles and deer	*Boophilus annulatus, B. microplus, Ixodes* spp suspected	Cosmopolitan/worldwide
2	B.*bigemina*	Cattles	*Boophilus annulatus, B. microplus* and *B. decoratus*	Cosmopolitan/worldwide
3	*B.divergens*	Cattles	*Ixodes ricinus*	Northern Europe and United kingdom
4	*B.ovate*	Cattles	*Haemaphysalis longicornis*	Japan
5	*B.microti*	Cattles	*Ixodes scapularis*	North America
6	*B.gibsoni*	Dogs and wild canids	*Rhipicephalus sanguineus* or *Dermacentor reticulates*	Worldwide
7	*B.major*	Cattles	*H. punctata*	United kingdom and Northern Europe
8	*B.jakimovi*	Cattles and wild ruminants	*Ixodes ricinus*	Siberia
9	*B.caballi*	Horses	*Dermacentor, Hyalomma* and *Rhipicephalus* species	Worldwide
10	*B.equi*	Horses	*Dermacentor* and *Hyalomma*	Worldwide
11	*B.motsi*	Sheep and goats	*Dermacentor silvarum* suspected, *R. bursa* and *Haemophysalis* spp	Sothern Europe, middle East, former soviet union, South east Asia and Africa
12	*B.ovis*	Sheep and goats	Suspected *Ixodes ricinus* and *D. reticulatus, R. bursa*	Southern Europe and middle east
13	*B.trautmani*	Swine	*R. sanguineus* and *Dermacentor* suspected, *Boophilus* and *Hyalomma*	Soviet union, southern Europe and Africa
14	*B.perroncitoi*	Swine	Unknown	Soviet union, southern Europe and Africa
15	*B. felis*	Cats, lion, leopard	*Haemophysalis* spp	Africa and India
16	*B. occultans*	Cattles	*Hyalomma marginatum*	Africa
17	*B. canis*	Dogs and wild canids	*Rhipicephalus sanguineus* or *Dermacentor reticulatus*	Worldwide

The humoral response to Babesial infections especially to *Babesia microti* has limited importance in protection. Antibodies have a short period of protection and have better effect on the free parasite then in the infected red blood cells (Morgan, 2000). Imidocarb is administering intramuscular or subcutaneously while it becomes toxic when given intravenously, side effects include salivation, muscle tremor, colic and irritation at the location of inoculation (Wood, 1971). Vaccination is best prophylactic measure having live, attenuated, dead whole parasite, crude parasite extracts and recombinant vaccines. Live vaccines are not safe because the vaccine strain can itself cause infection. In order to lessen the virulence of live vaccine, it should be continuously passed through the splenectomized calves (Taylor *et al.*, 1983).

Protective antigens either alone or in combination are the basis of recombinant vaccines. Although the attenuated vaccines are good, but due to co-transmission of other enzootic agents such as bovine leukosis virus and short shelf life these attenuated vaccines give no reliable results. So the recombinant vaccines are made from the surface antigens of sporozoites particularly from apical complex proteins due to their host cell penetration capacity. The rhoptry associated proteins (RAP-1) which are encoded by a multigene family. RAP-1can induces the production of the $CD+_4$ and Th_1 cells to provoke partial immunity against babesiosis. Vaccines used against tick vector *Boophilus microplus* is BM86. In case of reinfestation of the tick, the combined therapy of Acarcicides along with BM86 is used while in the case of resistance to BM86. BM95 are used along with the BM86 which can protect the animals that are resistant to the immunization with BM86.

Antigens are also used to improve the vaccines efficacy (Garcia-Garcia *et al.*, 2000). SBm7462 is a synthetic anti-Boophilus microplus vaccine derived from the tick intestinal protein. SBm7462 is 43 amino acid residues is derived from the BM86 protein structure and encapsulated synthetic Spf66 peptide was used to compare with the SBm7462 because of the similarity in size and synthetic procedure. The controlled release system such as PLGA microspheres allow a continuous and pulsable release of encapsulated antigens. SBm7462 vaccine capsulated in the 50:50 PLGA microspheres promote an immune response which is better to the immune response promoted this peptide emulsified in saponin. The saponin is an excellent adjuvant that gave the best response to the SBm7462 peptide (Igartua *et al.*, 1988). In Pakistan, especially the province KPK is endemic for the entomological vectors for various diseases. The most lethal and common, acquiring the attention of researchers is babesiosis, which also have the public health significance. In KPK, a major proportion of population has residence in countryside where people life expenses are totally reliant on the animals. The livestock in rural areas are suffering from different vector born diseases, including Babesiosis, thelioriosis, rickettsiosis and viral hemorrhagic fever due to no control measures and awareness in the public sector against these diseases (Irwin and Jefferies, 2004; Otranto *et al.*, 2009).

Conclusion and future recommendation

From the current study it is revealed that 17 different species of *Babesia* are found in different domestic livestock (Table 1) throughout the world. *Hyalomma* tick has the highest prevalence rate in Pakistan followed by *Boophilus, Haemaphysalis* and *Rhipicephalus*. Vaccines are available for a few species of *Babesia*.

It is highly recommended after the above

discussion that various control strategies should be adopted in order to prevent the day by day increasing losses to livestock industry and human population against the zoonotic and veterinary pathogens. Community education campaigns should be started in rural areas of KPK to bring awareness in the people about the health hazards to humans and animal husbandry, created by the different zoonotic species of *Babesia*. Vectors ticks eradication programs should be started and train the people how to get rid from these vector borne disease having a zoonotic effect on the whole community. Prophylactic measures should be taken, including easily available cost free drugs and vaccines. Such vaccines should be designed having high efficacy and less price tag, so they can be affordable for the rural population.

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Competing interests

The authors declare that they have no competing interests.

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