A Review on Bovine Babesiosis

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Abstract

Bovines can be exposed to different protozoan parasitic diseases among those diseases bovine babesiosis is one of them, which is caused by babesia spp that are a diverse groups of tick born, obligate intraerythrocytic apicomplexan parasite. The most prevalent spp are babesia bovis and babesia bigemina in which the economic loss can be considerable particularly in developing country. Although both morphological and serological differentiation is needed for specific identification of the various diseases producing spp, all can be categorized as being either large or small in size. Bovine babesiosis has a worldwide distribution and largely related to the distribution of vector ticks. Bovine babesiosis also occurs in immune compromised humans. Infections is initiated by inoculation of sporozoites stage parasite and the disease is diagnosed by detection of the babesia spp on giemsa stained blood smears, serological test, or inoculation of spleenoectomized calves with infective blood. The disease can be treated by antibabesial drugs. Therefore, this seminar paper enables us to focus on major pointes of bovine babesiosis and to highlight on the economic and zoonotic significance of bovine babesiosis.

Introduction

Animal disease is one of the important constraints to increase productivity of animals in all parts of the world. Among those disease protozoan diseases have major effects, particularly bovine babesiosisis [14]. In 1893, Americans Thioband Smith Fred Klibone identified the parasite as the causes of Texas fever and also identified the ticks as the agent of transmission, discovery that first introduced concept of arthropods functionally as a disease vectors. Therefore, Bb is an important disease of bovine which caused by members of the genus babesia, which are tick transmitted intraerythrocytic protozoan parasites [19]. Bovine parasites require both a competent vertebrates and non vertebrate hosts to maintain the transmission. Additionally, some spp are zoonotic and affect human health. The most important recent reviews of bovine babesia spp primarily concerns parasites of bovines in tropical and subtropical regions [19].

Worldwide distribution of bovine babesia spp has increased as a result of human cases caused by identical or similar parasites outsides areas where Bb is endemic [2]. The spp of babesia affecting bovines such as, babesia bovis and babesia bigemina are widely distributed and of major importance in Africa, Asia, Australia and central and south America. Babesia divergens is important in some parts of Europe where tick spp the vector babesia [3].

The pathogenic effects are in most infection related direct to lyses of RBC by emerging parasites but other mechanisms including sludging of RBC, haemoglobinuric nephrosis, and release of vasoactive peptide contribute to the signs (fever, haemoglobinuria, anorexia, nervous signs and responsible for death) [14].

Ticks are the natural vector of Bb and the causative parasites persist and pass through parts of their life cycle in the vertebrate host. Contaminated needle, surgical instruments and blood inoculations, aids for sources of infections and transmissions. History of tick bites, movement to an area where Bb is endemic aids for diagnosis analysis. A positive diagnosis requires identification of the babesia spp on giemsa stained blood smears or inoculation of spleenoecontomized calves with infective blood. In chronic cases numbers of parasitized erythrocytes diminishes, becoming as spares to make detection difficult [15]. Control of Bb can be based on through the control of ticks by acaricidal treatment of hosts by using chemotherapy and avoiding areas where or times when ticks are present [9]. Generally, the disease has a huge economic importance due to loss of meat and beef production of infected animals and quality of cattle in endemic areas remains low and death is occurred [12].

Therefore, the objectives of this paper out line are:

- To forward an information on major points of bovine babesiosis including on economic and zoonotic significances.

### Literature review

#### Etiology

The disease Bb, synonymy also called tick fever, cattle fever, Texas fever, piroplasmosis and red water fever which is caused by the protozoan parasite of genus babesia bovis, babesia bigemina and babesia divergens. Other babesia parasites that can infect cattle include babesia major, babesia ovate, babesia oculeatus, Babesia Jakimovi. The bovine spp which are affected by those parasites are cattle, white tailed deer, American buffalo, water buffalo, rein deer, African buffalo [4].

#### Taxonomic classification

Taxonomically, the babesia parasites are positioned as the following series, phylum; protozoa (apicomplexa), subphylum; sporozoa; class; sporozoasida; order; piroplasmodida, family; babesidae and genus babesia [14].

#### Morphological features of the organism

The morphology of the parasite is typically pyriform but can be round, tetrad, rod shaped, elongated and cigar shaped organism. The tetrad morphology which can be seen with the giemsa staining of thin blood smear is unique to babesia and serves as distinguishing features from plasmidium falciparum, protozoan of similar morphology that causes malaria. Examination of stained blood films shows the organism to be within RBC, almost always singly or as pairs, often arranged at characteristics angle with their narrow ends opposed. Conventionally, the various spp are grouped in to the small babesia whose pyrim form bodies are 1-2.5 µm and large babesia which are 2.5-5 µm long. With Romanowsky dyes the cytoplasm appears blue and the nucleus red. Under the electron microscope the parasite is seen to possess at its blunt and an electron dense apical complex which is thought to be concerned with assisting penetration of the erythrocyte [14]. There are forms of babesia which are sporozoites, trophozoites and merozoites. Sporozoites are infective forms and they are present in the saliva of infective ticks and ticks infect during their blood meal [8]. The agent does not survive outside its host and transmitted through a tick vector, therefore parameters associated with resistance to physical and chemical actions (such as temperature, disinfectants and environmental stress are not as such meaningful [14].

### Table 1: Morphology of bovine babesia spp and their tick vectors.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Morphology</th>
<th>Tick vectors</th>
</tr>
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<tbody>
<tr>
<td>Babesia bigemina</td>
<td>4.5 x 2.5 µm (large, round,</td>
<td>Boophilus anulatus</td>
</tr>
<tr>
<td></td>
<td>pyriform and acute angle)</td>
<td>Boophilus decoloratus</td>
</tr>
<tr>
<td>Babesia bovis</td>
<td>1.5 m x 1.4 m (small, round,</td>
<td>Ixoides spp</td>
</tr>
<tr>
<td></td>
<td>pyriform and acute angle)</td>
<td>Boophilus microplus</td>
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<tr>
<td></td>
<td></td>
<td>Babesia anulatus</td>
</tr>
<tr>
<td>Babesia divergens</td>
<td>1.5 µm x 1.4 µm (small, round,</td>
<td>Ixoides ricinus</td>
</tr>
<tr>
<td></td>
<td>pyriform and acute angle)</td>
<td>Babesia divergens</td>
</tr>
<tr>
<td>Babesia major</td>
<td>2.6 µm x 1.5 µm (similar with</td>
<td>Haemaphysalis punc-</td>
</tr>
<tr>
<td></td>
<td>babesia bigemina but smaller)</td>
<td>tata</td>
</tr>
<tr>
<td>Babesia jacobini</td>
<td>2-4.6 µm x 1.5-2.1 µm (large,</td>
<td>Ixoides ricinus</td>
</tr>
<tr>
<td></td>
<td>round, and pyriform)</td>
<td>Babesia jacobini</td>
</tr>
<tr>
<td>Babesia ovate</td>
<td>4.5 µm x 2.5 µm (large, round,</td>
<td>Haemaphysalis long</td>
</tr>
<tr>
<td></td>
<td>and pyriform)</td>
<td>icorinis</td>
</tr>
</tbody>
</table>

#### Life cycle and development of babesia

Babesia undergoes different developmental stages during their life cycle and their development is almost follow similar patterns in ticks. Babsia spp penetrates erythrocytes of vertebrate hosts and its life cycle is consists of merogony, gametogy and sporogony stages. Sporozoites penetrates the cell membrane of an erythrocytes with the aid of a specialized apical complex, once inside, it transforms into a trophozoite (feeding stage) from which two merozoites develop by process of merogony (binary fusion) or asexually, then in the passage of host blood to the mid gut of the tick vector the development of two population of ray bodies from the gamete (gametocytes) occurs the ray bodies undergo further multiplication and once division is complete a single nucleated ray bodies are haploid and assumed to be gametes emerge from the aggregate and then fuse together in pairs (syngamy) to form zygote [14].

The zygote develop into kinets that escape in to the tick haemolymph in the gut cells, schizogony occurs with the formation of polyplod kinites, thus transovarian transmission occur with further development occurring in the larval stage, kinets enter the salivary gland and are transformed in to multinucleated stages (sporogony asexual reproduction and then breaks up to form sporozoites [14].

#### Epidemiology and geographical distribution

Epidemiologically, the distribution of the causative protozoa of Bb governed by the geographical and seasonal conditions of the tick vectors that transmit the diseases [14]. Bovine babesiosis can be found where ever the tick vectors exist; it is most common in tropical and subtropical areas. Babesia bovis and babesia bigemina are particularly important in Asia, Africa, central and south America, southern Europe and Austria. Though babesia bovis is usually found in the same geographic areas with babesia bigemina slightly some differences in their distributions [1]. Bb is present in Ethiopia but their significance in terms of mortality and production loss and the degree of en-
zootic stability are not known. However the relatively uncon-
trolled movements of live stock from Sudan, where this disease
and their vector are found, suggest there is a considerable risk
of the disease being introduced [11].

Figure 1: Life cycle of bovine babesia parasites.

N.B:Sz: schizontes; Sg: schizogony; Z: Zygote; k: Kinets; G: Gametogony;
M: Merozoites T: Trophozoite; Ts: Trophozoites.

Source of infection and transmission

Viable babsias are present only in the blood stream of
animals in the active condition of the infection. Ticks are the
natural vector of babesia and the causative parasite persist and
passes their life cycle in the vertebrate host. Contaminated needle
and surgical instruments, direct inoculation of blood, biting flies, blood contaminated fomites and carriers or recovered animals can also be source of infection and aid for transmission of the disease. Inside the ticks babesia zygotes multiply as vermicular which invade many of the ticks’ organs including the ovaries. Babesia bovis parasites usually become infective within 2-3 days after larval stages of ticks attaches. Babesia bigemina matures in approximately 9 days after larval ticks’ attaches and it is only transmitted by nymph and adult and babesia divergens can be transmitted by (adult, larval, and nymph) [14]. Babesia spp in ticks is transmitted either by transovarian or by stage to stage transmission. The former is the only mode of transmission for one host tick since following the attachment of the tick development stages occur on the same animal. With 2 or 3 host tick, stages to stages transmitting infection which they acquired as nymph or nymph during the same with infection acquired larvae [14].

Risk Factors
Host Factors

Breeds, age, immune status, indoor and outdoor keeping
and stress are the major host factors of Bb disease. Bos indicus
breeds of cattle are much more resistance to babesiosis than
bos Taurus breed. Zebu and Afrikaner cattle have higher resis-
tance to babesia bovis than British and European breeds. The severity of Bb increase with age, Calves from naïve dam are highly susceptible to infection and clinical illness from birth to 2 month of age at which time they develop an innate resistance that persisted to about 6 month of age calves from immune dam receives antibodies via the colostrums. The greatest infec-
tion rate is occurring in the 6-12 months in animals. In housed
cattle, the level of antibodies in the patient are at their lowest
when the cattle come out of the barn in the spring and gradu-
ally increase as they are exposed to vector ticks [14].

In endemic area two features are important in determining
the risk of clinical disease; calves have a degree of immunity
related both the colostrums derived antibodies and age that
persists for 6 months and animals that recover from babesia
infection are generally immune for life [19].

Environmental Factors

There are seasonal variations in the prevalence of clinical
babesiosis. The greatest incidence occurring soon after the reach peak level of the tick population. For example in England
babesiosis is largely a disease of spring, summer and autumn
for this reason, temperature, humidity and rainfall are impor-
tant factors [15].

Pathological factors

Virulence of strains, level of tick challenge, antigenic varia-
tion, are the most important pathological factors. Many intra-
erythrocytic hemparasites survive the host immunity system
through rapid antigenic variation, which has been demonstrat-
ed for babesia bovis. The molecular basis for antigenic variation
in babesial parasites and its possible connection with cytoad-
erherence sequestration have been occurs [14].

Pathogenesis

The principal pathogenic effects of infection with bovine spp
are intravascular hemolysis by initiated inoculation of sporozo-
ites stage parasites in to the blood stream during blood meal.
The vasodilatation accompanied by increased vascular perme-
ability leading to circulatory stasis and shock. A further patho-
genic effect of the organism intravascular coagulation and sub-
sequent fatal pulmonary thrombosis has been demonstrated in
claves infected with the bovine babesia [14].

Cerebral babesiosis caused by sludging of erythrocytes in
cerebral capillaries. In bovine spp the organism causes hemo-
lytic anemia so an infected animal will show pale mucous mem-
brane, initially as the label of bilirubine (a bi product of RBC ly-
ses) continue to increase, the visible mucus membrane become
yellow in color, hemoglobinuria, fever of 40.5°C develop due to
replace of inflammatory by products [18].

Clinical features

Bovine diseased by babesia parasites shows a clinical signs
after incubation periods of 2-3 weeks, animals with advanced
babesiosis have a low exercise tolerance, collapse and older ani-
imals are more actually affected. Clinical babesiosis is rare in cat-
tle younger than 6 months. There is abortion, fever, depression, anorexia, and increased respiration rate muscle tremor, reluctance to move, haemoglobinuria, occasionally cerebral disarrangement (such as circling, head pressing, mania and convulsion). Anemia and jaundice develop steadily with babesia bovis but much more precipitously with babesia bigemina. Babesia bigemina affected animals may exhibit irritability and aggression but not show the central nervous signs. Babesia diverge exceptional causes which are spasm of the anal sphincter causing the passage of pipe stem feces [14].

The minimum infective dose required to produce overt disease is thought to be 1000 parasites inoculated intra venous. Even an animal which recover spontaneously erythrocyte count packed cell volume and hemoglobin level continue decline steadily after patency [19]. Subclinical infections are quite common and usually missed by the farmer and limitation. Affected animals have low parasitemia may suffer milled fever and anorexia and make uneven full recovery and brain anorexia resulting from severe anemia may cause behavioral changes. Death usually attributed to cardiac failure or hepatic and renal insufficiency [19].

**Diagnosis**

Diagnosis of Bb can be accompanied by the clinical signs and by using the history of the cases where animals are located in enzootic areas where boophilus ticks occur [17].

**Direct blood smear**

There are thin and thick blood smear and those smears are done by giema stained smears of capillary blood, microscopic examination can detected parasitemia of 105 in thin blood film and 106 in thick blood film. Thick blood smears are 10x more sensitive and are more reliable for the detection of very low babesia bovis infection [17]. Differentiation is good in thin films. This technique is usually adequate for detection of acute infection, but not for detection of carriers where the parasitemia are mostly very low and the identification and isolation can be improved by a florescent dye [14].

**Inoculation test**

Sub inoculation of blood to susceptible spleenoectomised calves is highly sensitive techniques for direct detection of babesia infection. In transmission test 50-100ml of blood dose injected into the recipient either SC or IV [14].

**Culture of Babesia**

Babesia from the blood of carrier animals can be isolated using in vitro culture techniques in erythrocytes. The parasite could be isolated 9 month after the acute babesiosis phase and can be susceptibly sub cultured, cryopreserved and resuscitated using culture medium; preservation of live protozoa can be effective by cryopreservation by a medium containing infected bovine erythrocyte and simple culture media in special machinery for long period and in large quantity [13].

**Molecular detection**

Polymerase chain reaction (PCR) detection and identification, this technique allows identification of bovine babesia spp following specific application of the parasite DNA (deoxy ribose nucleic acid) by nested PCR the parasite spp is identified by PCR restriction fragment length polymorphism. PCR and DNA probe used to detect specific parasitemia at very low level of infection. DNA probe have added advantage to detect protozoa in necropsy specimens in ticks tissue. The PCR is more use full because of their high sensitivity which makes them ideal for detection of carriers animal [14]. PCR base techniques are reported to be as much as 1000x more sensitive than microscope with detection (1 parasite in 109 RBC), it is useful as confirmatory tastes and in some cases for regulatory tasting [5].

**Serological diagnosis**

There are many serological tests for laboratory diagnosis of Bb among those:

- IFAT (immune fluorescent antibody test),
- complement fixation test and
- ELISA (enzyme linked immune sorbet assay) are widely used.

IFAT has been a popular test used to distinguish between babesia spp and to demonstrate the presence of antibodies in populations. Diagnostic measures through antibody testing are also particularly useful for identifying serum prevalence in asymptomatic individuals. Due to the transmissibility of babesia through blood transfusion, IFAT would be an effective means of screening for the disease in blood donation. IFAT used to demonstrate the presence of antibodies in population [14]. Complement fixation test of babesia antigen is effective but approximately 100 days after infection the complement fixation antibodies drop below reliable diagnostic level [16].

ELISA system using a crude antigenic preparation of babesia bovis has been standardized for the detection IGM antibodies with a specificity of 94% and sensitivity of 100%. Specific IGM antibodies against babesia bovis first appeared on the 11th day post with infected blood. A competitive ELISA is an accurate, reliable, easily standardized and high throughout method for detection of haemoparasite infection. The gene encoding babesia bovis rhpwy associated protein was used to develop the assay. The competitive ELISA accurately differentiated animals with babesia bovis specific antibodies from uninfected animals and from animals with the antibodies against other tick born hemoparasites (sensitivity 98.5% and specificity 98.7%) [14].

One problem associated with all serological tests for babesiosis is that the relationship between antibody titers, the presence of parasites and the state of protective immunity is not clear. Antibodies may persist for long periods after the disease has cleared giving no information as to when an infection was acquired and resulting in an overestimate of disease prevalence. In addition antibody titers may be observed in the absence of parasites or after acquisition of sterile immunity [19].

**Necropsy Finding**

There are numerous pathological lesions appeared on different organs of the body such as varying degree of congestion, pallor or jaundice, blood is usually watery and urine is red, subserosal hemorrhages are common particularly on the heart and intestine, spleen is enlarged with a soft pulp, liver enlarged and brown or yellow with gallbladder filled with thick, granular bile [7]. There is degeneration of the kidney, liver and lung are often emaetous and congested. The abomasal and intestine mucosa may be iceric with patches of subserosal hemorrhage. There are subepicardial and sub endocardial petechial hemorrhage. Gray matter in the brain has a characteristics cherry pink color, postmortem finding in cattle that die per acutely are character-
Differential Diagnosis

Bovine babesiosis resembles other condition that cause fever and hemolytic anemia, enzootic hematuria, trypanosomiasis, enzootic bovine pyleonephritis, thleriosis, parturient hemoglobinuria, bacular hemoglobinuria, leptospirosis and copper poisoning [14].

Treatment and Prognosis

A variety of drugs have been used to treat Bb among those diminuzine aceturate and imidacarb dipropionate are common choices of drugs imidacarb dipropionate given 5-6.6 mg/kg sc or IM twice, 14 days apart or 7.5 mg/kg, SC or IM once. Metronidazole has given 25 mg/kg, orally for 2-3 weeks and other clindamycin hydrochloride, pentamidine isentinate, parvaquina and niritazones are also [14].

Supportive therapy: including blood transfusion, sodium bicarbonate therapy, fluid therapy, corticosteroids, antioxidants, anti-inflamatory drugs and long acting oxytetracycline 20mg/kg may reduce the severity of bb if treatment begins before and after infection. After the onset of hemoglobinuria or cerebral signs the prognosis is poor, acute cases with PCV value above 12% usually respond well to treatment. The prognosis is decreased for cases with PCV values below 10% and successful treatment depends on early diagnosis and prompt therapy [15]. To aid erythropoiesis in recovered animals’ nonspecific supportive therapy is recommended involving the use of iron preparation and fluid replacement [19].

Economic Importance

Bovine babesiosis is the most economically important disease because of direct loss of production and restriction of movement of cattle for trade by quarantine laws. Many animals die or undergo a long period of covalence entailing, loss of meat milk, treatment and control costs. The morbidity and mortality rates and the losses associated with bb in animals spp are difficult to determine because of the y exist as enzootic disease in areas where they occur [14].

Zoonotic implication

Human babesiosis is caused by different babesial spp that have distinct geographic distribution based on the presence of competent host. Persons who have frequent contact with animal are highly prone to the disease [10]. Babesia divergens and babesia microti are the most known zoonotic bovine babesia parasites. Human cases of babesia divergens infection have been reported in France, Britain, Ireland, Spain, Sweden, Switzerland, the former Yugoslavia and the former USSR. Babesia divergens is the primary cause of human babesiosis in Europe resulting inn fatality rates of 42% among persons who have been spleenectomized and 5% among those with intact spleen. Babesia represents potential threat to the blood supply for transfusion since asymptomatic infection in human are not uncomon and spread has been reported from various countries using the micro aerophilous stationary phase culture techniques the parasite perforates in a settled layer of RBC [14].

During the incubation period of 1-3 weeks patients frequently complain of general weakness and discomfort. Acute illness appears suddenly with hemoglobinuria as the presenting symptom [19].

Subsequent non specific clinical presentation can be easily confused with malaria; jaundice due to severe hemolysis accompanied by persistent non periodic high fever (40-41 oc), shaking, chill, intense sweating, headache, abdominal pain, vomiting and diarrhea may also present and hemoglobin and hematocrit is decreased dramatically. The liver may be moderately enlarged and painful. In the most severe cases patients develop shock like symptoms with renal failure induced by intravascular hemolysis and pulmonary edema. Human babesiosis can be treated with anti malarial drugs such as chloroquine, quinine. A mild infection was resolved after the use of pentamidine and cotrimoxazole [19].

Prevention and control measures

Vector control

Acaricide application, controlled range burning, cultivation, prolonged pasture rest uses of repellents, control of stock movement, raising, cattle, resistant to ticks, are major methods. The common acaricides are chlorinated hydrocarbons, carbamates, organophosphate, natural and synthetic pyrethrins and avermectin (dips or spray). In recent years several other measures of acaricides application has developed including pour on and spot on [16].

Parasite control

Immunization of susceptible stocks, chemo prophylaxis treatment of infected animals mostly imidacarb is used and vaccination are major parasite control methods. The most common forms of immunization consist of inoculating live organism (virulent or attenuated) into susceptible calves to induce a state of pre immunization [16].

Generally, control of tick born babesiosis is based on:

- Tick control through acarical treatment of host
- Chemotherapy of infected host
- Test and slaughter of infected animals
- Quarantine of infected animals [9].

Conclusion and recommendation

Generally, bovine babesiosis is a considerable tick born disease in which older bovines are more susceptible than that of younger with great public health significance. Bovine suffers from babesiosis frequently have a history of recent movement to tick infected pasture either through grazing management or often purchase. Intravascular which is initiate by inoculation of sporozoites stage parasites into blood stream during blood meal, will result sever pathogenic effect of the babesia spp. The great complexity of the relationship between causal agents, vector and host severely hindered the efforts towards the production of a safe, long lasting, solid protection induce vaccine. A better understanding of some anomalies of parasites epidemiology such as a low incidence of babesia infections even areas where bovine babesiosis is endemic will lead to improved control mechanism. Introduction of effective prophylactic treatment and vaccination could enables for decline of the disease.

Based on the above conclusion the following recommendation are forwarded:

- Appropriate prophylactic, antibabesial drug treatment and vaccination with improved pasture management should be maintained.
- Veterinarians, private sectors and government should create awareness for clients about the disease characteristics and how they can manage their animals as well as themselves.

- Since ticks play a pivotal role in the transmission of bovine babesiosis they should be controlled and prevented by applying appropriate chemicals and keep animals movement where ticks population are prevalent.

- Further study on the epidemiology of the disease, the biology and ecology of the ticks are useful in planning and programming control strategies.

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