



## A Review on Bovine Babesiosis in Egypt

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### Abstract:

Bovine babesiosis is a tick-borne hemoprotozoan disease of cattle. It is caused by intra-erythrocytic protozoan parasites of the genus *Babesia*, which affects a wide range of domestic and wild animals and occasionally humans. Several species of the genus *Babesia* are involved, with the two most important species in cattle; are *B. bigemina* and *B. bovis* that are mainly transmitted by ticks through the transovarial route. The disease causes severe economic losses in the cattle industry, mainly associated with the reduction in the production rate and high mortalities. The disease prevails in tropical and sub-tropical areas where overlapping with the vector, one-host tick of *Boophilus species*, exist. Subclinical babesiosis leads to conversion of the affected livestock to chronic carriers, producing a persistent source of infection for tick vectors, and maintaining the natural transmission of the disease. Active disease cases are commonly diagnosed with the traditional geimsa-stained blood smears, although more advanced diagnosis techniques exist including, but not limited to, the molecular and serological methods. The disease is optimally controlled through treatment of affected animals, and prevention of the disease dissemination by eradicating vector ticks. This review, focused on all aspects of the disease from the historical perspectives, biology of the parasite, risk factors, pathogenesis, clinical signs, vector transmitters, diagnosis, prevention and control.

**Key words:** Cattle; *Babesia bigemina*; *Babesia bovis*; Epidemiology; Diagnosis

## INTRODUCTION

Cattle have a great social economic importance in people life because of their milk, meat, hoof, bones and hide production (Saunoucy 1995). Piroplasmid of the genera *Babesia* is a tick borne protozoa, causes a clinical fatal disease of babesiosis and associates with significant losses in the cattle and other farm animals. Thus, the disease represents serious challenges for both animal life and farm economy. Babesiosis as a

tick-borne disease is widespread in tropical and sub-tropical regions which cause anemia, icterus, hemoglobinuria, and death (Wagner et al., 2002). Most affected areas are located between 40°N and 32°S (McCosker 1981). *Babesia spp.* is a protozoan parasite transmitted mainly by *Ixodidae* ticks (Silva et al., 2010) and able to infect erythrocytes of a wide variety of domestic and wild animals (El Moghazy et al., 2014). The most important species in cattle are *B. bovis* and *B.*

*bigemina* (Zintl et al., 2013).

## 2- Historical Perspective

**Victor Babes (1888)** first detected a disease which caused haemoglobinuria in cattle and responsible for the death of 50 thousand cattle in Romania. He recognized them as Bacteria, giving it the naming code of *Haematococcus bovis*, which later changed to that of *Babesia bovis* (Angus 1996). In the United States, (Smith and Kilborne 1893) demonstrated the etiology of cattle Texas fever which caused by *Babesia bigemina*. There they also been the first to detect transmission of *Babesia spp.* from vector to a host by ticks of *Boophilus annulatus* (Smith and Kilborne 1893). Lignie`res (1903) described two forms of *Babesia* as *Babesia bigemina* and *B. bovis* in Argentina. (Hoyte 1961) recognised four species of bovine *Babesia* which are *Babesia bovis*, *B. bigemina*, *B. divergens* and *B. major*. It was widely concluded that *B. bovis* is highly pathogenic than *B. bigemina* (De Vos and Bock 2000).

## 3- Geographical Distribution

Babesiosis is worldwide distributed (Fakhar et al., 2012). Most affected areas are located between 40xN and 32xS where *Boophilus spp.* As the tick vector is commonly occurs. The main important species in cattle are *B. bigemina* and *B. bovis* that are endemic in tropical and subtropical areas. They are reported in Asia, Africa, Central and South America, Australia, and Southern Europe (Uilenberg 1995). *Boophilus annulatus* is the principal vector of *B. bovis* and *B. bigemina* in Turkey (Sayin et al. 1996), Northern Africa (Ndi et al., 1991, Sahibi et al., 1998 and Bouattouret al., 1999), and south Europe (Caeiro 1999). *B. bovis* and *B. bigemina* have the same distribution, nevertheless and in Africa *B. bigemina* is more prevalent than *B. bovis* because of the ability of *Boophilus decoloratus* and *Rhipicephalus*

*evertsi* to transmit the protozoan parasite (Pohl 2013).

## 4- Host Range

It has been found that out of more than one hundred of *Babesia spp.* which infect many types of mammalian host, only 18 species cause the disease in domestic animals. Babesiosis mainly affects cattle, goats, sheep, horses, dogs, cats and human (Hamsho et al., 2015). *Babesia bovis* and *B. bigemina* are found in cattle which are the main reservoir hosts. They also affect water and African buffaloes. They were recently detected in white-tailed deer in Mexico. Animals other than cattle were considered of little epidemiological significance. (CFSPH 2008).

## 5- Etiology and Morphology

Babesiosis is best known as piroplasmosis, tick fever, Texas fever and Red water fever (Sahinduran 2012). The genus *Babesia* belongs to the phylum Apicomplexa, class Sporozoasida, order Eucoccidiorida, suborder Piroplasmorina, family Babesiidae and species *B. bovis* and *B. bigemina* (Allsopp et al., 1994). More, the phylogenetic analysis based on the 18s rRNA was used as the basis for the taxonomical classification of *Babesia* species (Criado-Fornelio et al., 2003). *Babesia bovis* is a small size parasite, located in the center of the RBCs. It measures 1-1.5 x 0.5-1.0 µm, and is found as pairs at an obtuse angle. While, *Babesia bigemina* is a much longer parasite, and found as pairs at an acute angle. *Babesia bigemina* is typically pear-shaped, but many irregular forms are found. It is 3-3.x 1-1.5µm (Soulsby 1986) (Fig 1, 2).

## 6- Transmission of bovine babesiosis

*Babesia* species is transmitted biologically by the tick vector via transovarian transmission which transmits from egg of mother tick (first generation) to the next stage (Demessie and Derso 2015). Bovine babesiosis is transmitted by one host tick vector (*Boophilus spp.*). *B. bigemina* and *B. bovis* are transmitted biologically by *Boophilus*

ticks, in which nymphs and adults transmit *B. bigemina* but only tick larvae transmit *B. bovis* (Esmail et al., 2015). It is also transmitted mechanically by infected needles and syringes, blood transfusion and surgical instruments.

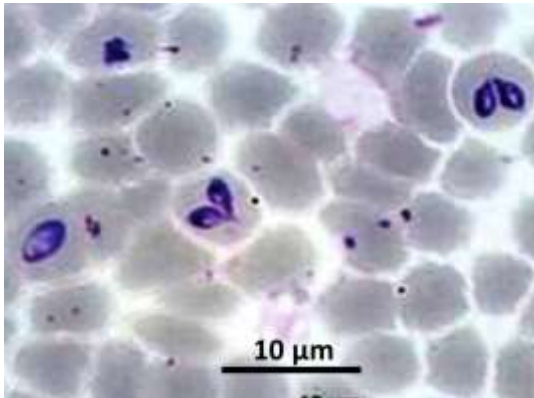


Fig (1): Giemsa stained blood smears from cattle showing *Babesia bigemina*, 100x. (Mosqueda et al., 2012).

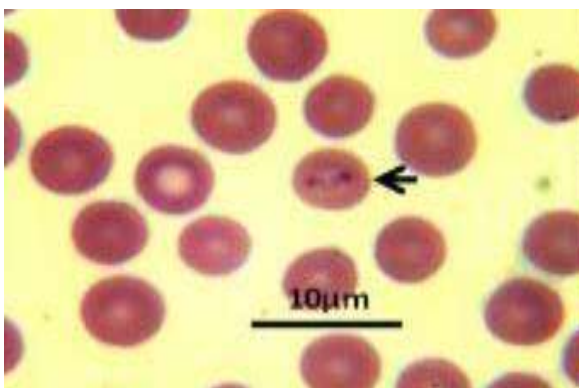


Fig. (2): Blood smear from cattle showing *B. bovis* (arrow), Giemsa stain, 100 x. (El-Bahy et al., 2018).

### 7- Life cycle

Life cycle of *Babesia spp.* divided into three stages as shown in (Plate 1, Otify 2011).

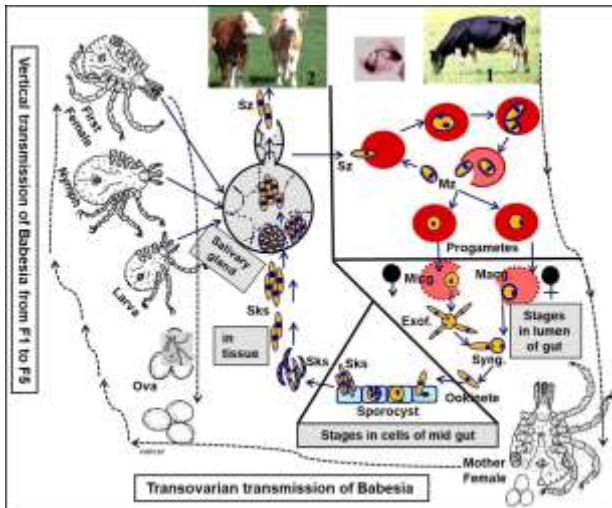
First, inside tick vector (mother tick): This stage is carried out inside the vector gut in the following way: After the ticks suck the blood of an infected animal, red blood cells break and the parasites of *Babesia spp.* will be released. Where most of them die, and the adult phases remain alive. The growth of both female and male gametes is completed in a period of 2-4 days after the ticks take the blood meal.

Fertilization process ended with the formation of zygote that is spherical in the beginning, then it turns into a motile form known as ookinete that begins the next stage of direct division. Ookinetes penetrate the mother tick to form large numbers of sporocysts that lead to the explosion of stomach cells, after which motile sporokinetes spread in the internal fluid (haemolymph) and various body organs, such as ovarian cells. Then the sporokinetes divide inside these tissues before and during the deposition of masses of tick's eggs. Then a new wave of division begins within the larvae after they hatch.

The second stage involves the development of the parasite within the new generations of ticks. After larvae emerge from eggs, the sporokinetes begin its activity leading to the multiple divisions within the tissue of the larva. The larval adhesion to the animal's body begins its salivary gland in the rapid growth of salivary secretion. At this stage, sporozoites reach the cells of the salivary gland and saliva. Sporozoites penetrate the red blood cells to begin the division stage in the animal when larva takes blood meal. It is worth noting that the sporozoites do not all reach the salivary gland, but rather numbers remain in the tissue of the larva, and after the larva has molted, it turns into a nymph. In the same way, the adult tick can transmit the parasite through its eggs to new generations, and this method is repeated for several generations, which is best known as the transovarian transmission.

In the third and final stage, the development of parasite inside the host animal after being infected is concluded as follows. Sporozoites enter the animal's body with tick saliva, they begin to penetrate the red blood cells, and then turn inside them into a small circular or oval shape that has one nucleus, known as trophozoites. Asexual multiplication occurs by binary fission forming schizont. After the completion of the growth of divisions within the red blood cells, the RBCs are destructed, and then each division penetrates into

a new red blood cell, and grows inside it in the same way as the previous, and ends with the hemolysis of the affected cells.



**Plate. (1)** A generalized life cycle for *Babesia* spp. in cattle and the tick vector *Boophilus* spp. (Otify 2011).

1 (first infected cow- donor), 2 (new infected cows- receptors), Sz (Sporozoite), Mz (Merozoite), Micg. (Microgamete), Macg. (Macrogamete), Exof. (Exoflagellation), Syng. (Syngamy), Sks (Sporokinetes), F1 (First female) and F5 (Fifth generation female).

## 8- Vector transmitters

Tick infestation in cattle is one of the major constraints to the livestock industry which adversely affects bovine productivity, mainly by transmission of serious pathogens (Menshawy et al., 2018). Ticks act as vectors for many protozoa as *Babesia* spp. which has a great hazard effect on livestock health resulting in economic impact for farmers (Hoogstraal and Kaiser 1958). *Boophilus* spp. especially male can transfer between cattle in close proximity and this can lead to decrease prepatent period (6–12 days) for *B. bigemina* (Callow and Hoyte 1961), but it is 12–18 days after attachment of tick to animal (Callow 1984). While the larval stage only is responsible for transmission of *B. bovis*

(Mahoney & Mirre 1979) and the prepatent period is generally 6–12 days (Callow 1984). High temperature stimulates larval tick's attachment which enables transmission of *B. bovis* immediately and lead to shortened prepatent periods (Dalglish and Stewart 1982).

## 9- Epidemiology of the bovine babesiosis

It depends on numbers of factors and these include:

9.1. Age of the host, the infection rate is low among young animals because of innate resistance which enhanced by maternal antibodies that transfer to calves via colostrum. This resistance is declined gradually leaving animal with high susceptibility to disease (Fadly 2012).

9.2. Breed of the host, *Bos taurus* breeds of cattle are more susceptible to babesiosis than *Bos indicus* (Radostits et al., 2007). Also, native breeds are more resistance to babesiosis than foreign breeds. Because of the nature exposure of tick populations for long time which developed either an innate resistance or an innate ability to develop a good immune response to the tick (Wodaje et al., 2019).

9.3. The immune status of the host. In endemic areas, young animals acquire immunity passively from colostrum of dam so often suffer only transient infections with mild signs. These infections are sufficient to stimulate active immunity and become carrier for long time. Active immunity is responsible for the persistence state of the carrier and premunity. These animals lose their infection either naturally or by chemotherapy but still retain a solid immunity (Taylor et al., 2007). Benavides and Sacco (2007) classified *Bos taurus* into three different phenotypes according to susceptibility to *B. bovis* infection as: susceptible animals which have severe clinical signs that lead to death, intermediate animals which have mild clinical signs and resistant animals which rarely

demonstrate clinical signs.

9.4. The virulence of *Babesia* strain. *B. bovis* is more pathogenic than *B. bigemina* (CFSPH 2008). Many blood parasites survive the host immune system through rapid antigenic variation which has been demonstrated for *B. bovis* and *B. bigemina* (Bock et al., 2004).

9.5. Stress factors, the prevalence of babesiosis is affected by seasonal variation which also is influenced by the peak of the tick population. From the climatic factors, air and temperature is the most important because of its effect on tick activity; higher temperatures increase its occurrence (Menshawy et al., 2018). *Babesia* spp. infection in cattle reaches peak in the summer season (El Bahy et al., 2018).

## 10- Clinical signs

The clinical signs and pathogenesis vary with the age of the animal, the species and strain of the parasite. Affected animals suffered from fever which present for several days before the beginning of other clinical signs (OIE 2010), that included loss of appetite, cessation of rumination, labored breathing, emaciation, sometimes massive intravascular haemolysis which produce progressive hemolytic anemia, various degrees of jaundice (Icterus) from paleness in mild cases to severe yellow discoloration of conjunctival and vaginal mucous membranes in more progressive cases haemoglobinuria. Other signs include, accelerated heart and respiratory rates, ocular problems and drop in milk production. The fever during infections in some cases causes abortions of pregnant cattle (Abdel Aziz et al., 2014). Coffee colored urine is the characteristic clinical feature of babesiosis (De Vos and Potgieter 1994)

## 11- Diagnosis

**Detection of active cases of babesiosis based mainly on a number of diagnostic techniques as follow:**

1. Direct microscopic examination, Giemsa stained thin blood smears has been considered the traditional and golden method of identifying the agent in infected animals. It is a cheap, easily and available method in all laboratories also possibly even in the field (Nayel et al., 2012) and is a good technique for species differentiation. It is adequate for detecting cases of acute infection but less effective in low parasitemia and in carrier animals.

2. Serological examinations, Indirect fluorescent antibody test (IFAT) and enzyme linked immunosorbent assay (ELISA) are capable of detecting antibodies of *Babesia* in sub-clinical infections (El-Fayomy et al., 2013), and to avoid drawbacks of microscopic examination. These tests are of low sensitivity due to the occurrence of false-positive and false-negative results and cross reactions make species diagnosis difficult, and in most cases fail to differentiate between chronic and acute infections (Mahmoud et al., 2016). Nevertheless, these methods easy to do but requires a good quality antigen which is difficult to obtain (Mosqueda et al., 2012). (Anon 2008) described a complement fixation (CF) test to detect antibodies against *B.bovis* and *B.bigemina*.

3. Molecular diagnosis, polymerase chain reaction (PCR) is more sensitive and specific technique which offers an alternative approach for the detection of babesiosis (AbouLaila et al., 2010) and been able to identify the parasite in the early stage of the disease.

## 12- Prevention and control

Control of babesiosis is mainly based on the immunization, chemoprophylaxis and tick eradication or by a combination of these approaches (Suarez and Noh 2011). The three methods must be integrated to reach to the best results of controlling the disease and to avoid breed resistance and enzootic stability. Chemoprophylaxis is not a viable for long time, so immunization is an alternative effective method to face outbreaks of babesiosis either using live or

dead whole parasite and isolated parasite antigen (Yusuf 2017). Cattle which recover from a primary *Babesia* infection or that have been immunized with attenuated parasites are resistant to challenge infection. Second, immunization of cattle with native *Babesia* antigen extracts or culture-derived supernatants containing secreted *Babesia* antigens elicit protective immunity against both homologous and heterologous challenge (Radostits et al., 2007). Animals should also be treated with an acaricide that able to prevent tick attachment especially in endemic areas. Repeated treatment of cattle with acaricides in areas of high challenge; such treatment may require to be carried out twice weekly in order to kill the tick before the infective sporozoite develop in the salivary gland (Urquhart et al., 1996). In endemic areas, where all indigenous cattle are infected as calves, no control is usually necessary. Maintenance of the enzootically stable state is dependent on exposure of calves to the infection while they are most resistant. If the challenge is still sporadic, continual vaccination of the calf crop from year to year may be necessary (El Sawalhy 2012). Reduced tick numbers will decrease time risk of babesiosis due to the reduced natural exposure of animals. Affected animal should be treated as soon as possible with a suitable treatment to control babesiosis in some areas of the world (Kuttler 1981). The indiscriminate use of anti-*Babesia* prophylactic agents including the administration of the drug at sub lethal blood levels to animals, can produce the development of drug resistant parasites, a problem that will require the development of new drugs (Vial and Gorenflot 2006).

### 13- Economic importance

Recently *Babesia* becomes the most widespread parasite due to exposure of 400 million cattle to infection through the world (Osman and Gaadee 2013). Bovine babesiosis

impairs cattle improvement programs due to their imposing significant economic burden on meat and milk production beside to costs of treatment and tick control. It is currently considered as the most important endemic parasitic disease affecting cattle in Egypt (Adham et al., 2009). Babesiosis, especially in cattle has great economic importance, because unlike many other parasitic diseases, it affects adults more severely than young cattle, leading to direct losses through death and the restriction of movement of animals by quarantine laws (Onoja et al., 2013). The consequence is that the quality of cattle in endemic areas remains low, therefore impeding the development of the cattle industry and the wellbeing of producers and their families (Mosqueda et al., 2012).

### 14- Status of bovine babesiosis in Egypt

Bovine piroplasmids are endemic in Egypt and widespread in other regions of the world including the Mediterranean Basin (Ibrahim et al., 2009). The variable infection rates of babesiosis among cattle in Egypt have been reported by numbers of studies such as: Ezzat (1960) found that *B. bigemina* was the most common blood parasite in cattle in Assuite governorate. Mohan (1968) found that 15% of the buffaloes and 20% of cattle infected with *B. bigemina* in Egypt. El- Allawy (1973) stated that the incidence of *B. bigemina* in cattle was from 7.05 to 10.66% by using blood films examinations in Assuit governorate.

Sakla (1975) reported that 8.6 of buffaloes and 8.7 of cattle infected with *B. bigemina* on examination stained blood samples, in Assuit governorate, Egypt. Ahmed (1980) recorded that the rate of infection of *B. bigemina* was 8.5 in cattle in Sharkia governorate.

Gattase (1983) found that the rate of cattle infection with *B. bigemina* were 25.5% and 27.77% in Port Said and Ismailia respectively. While El- Bahy (1986) stated that 38% of cattle

were infected with *B. bigemina*, in Fayoum governorate. **Chafick (1987)** reported that the incidence of *Babesia spp.*, in calves over one year old was 4.97% and calves over two years old was 10.89% in Assuit governorate. **El-Sawalhy (1987)** recorded that 4.5% of native cattle breed and 8.6% of foreign cattle breed were positive for *B. bigemina* in Qalyobia governorate. **Abo El-Kheir (1989)** observed a wide variation in the incidence of *B. bigemina* in cattle as 2.89, 4.46, 5 and 10.17% in Giza, Beni Suef, El- Minyia and Fayoum governorates, respectively. **Gattase (1990)** recorded that the incidence of *Babesia spp.*, was 7.62 % in cattle using ELISA in Suez Canal Zone. **Abd El-Gawad (1993)** observed that the incidence of *B. bigemina* and *B. bovis* in cattle was 8.62 and 1.65% respectively in Beni Suef governorate. **El-Ghaysh (1993)** found that the incidence of *B. bigemina* in Cairo, Delta and Upper Egypt was 12.5, 4 and 5.7% in cattle respectively. While the incidence of *B. bovis* was 13.5, 8 and 8.6% in cattle in the same region respectively. **Ashmawy et al., (1998)** investigated *B. bigemina* infection in a local breed of cattle with Giemsa-stained blood films. Prevalence was higher in Hoosh-Easa (67.8%) and Shubrakheit (25%) followed by Damanhour (37%) and Itay Elbaroud (17.8%) in Behaira Province. **Salem (1999)** recorded that the incidence of *Babesia bigemina* in cattle was 40.9%, while the incidence of *B. bovis* was 30% as measured by PCR technique. While by microscopic examination only 1.8% was detected in Giza governorate. **Adham et al., (2009)** found that the prevalence of *B. bovis* and *B. bigemina* in *Boophilus annulatus* ticks were 55 and 66%, respectively. Also, presence of 12% dual infection with *B. bovis* and *B. bigemina* was observed in Egypt. **Ibrahim et al., (2009)** examined cattle for the presence of piroplasm, the results discovered the majority of *Babesia spp.*, infection (26%), most of them

infected by *B. bigemina* (17%) in Egypt. **Mervat et al., (2010)** detected *B. bigemina* in cattle in 38% by Giemsa stained blood smears in Qalyobia Governorate. **Fadly (2012)** showed that the incidence of *Babesia spp.* in cattle by blood film examination were 19.33 % at Behaira province. **Nayel et al., (2012)** found that the prevalence of *Babesia spp.* was 8.15% by direct microscopy using Giemsa-stained thin blood smears in Menofia. Moreover, **Ibrahim et al., (2013)** recorded the prevalence of *B. bigemina* and *B. bovis* from cattle by nPCR were 5.30 and 3.97% respectively in Behaira and Fayoum provinces. **El Moghazy et al., (2014)** revealed that the infection rate with blood films examination was 22.47% in Qalyobia Governorate. **Elsify et al., (2015)** found cattle infection with *B. bovis* and *B. bigemina*, 3.18 and 9.97% using PCR assays in Egypt. The seroprevalence of protozoan infections in cattle in Qena and Sohag governorate, Upper Egypt was determined with enzyme-linked immunosorbent assays using species-specific diagnostic antigens as reported by **Fereig et al. (2017)** in his study, they found that 33.2% and 42.2% of examined cattle were found to be positive for specific antibodies against *B. bovis* and *B. bigemina*, respectively. **El-Bahy et al., (2018)** found the infection with *Babesia spp.* was 9.42% in Behaira. Cattle management, climatic condition, immune status, tick distribution, breeds, and the sampling condition might explain the variation in prevalence rates between previous studies in Egypt.

### 15- Methods of control of bovine babesiosis in Egypt

Control of babesiosis is mainly based on the chemotherapy and tick eradication in Egypt. Imidocarb dipropionate salt (Imizol) is effective for babesiosis. Diminazene aceturate (Berenil) is widely used. Supportive therapy such as vitamins, electrolytes and hematinic drugs and blood transfusion may be essential if the animal is to survive (**Mohammed and Elshahawy 2017**). The

most effective procedure for the control of babesiosis is to eradicate its vector, the *Boophilus* tick by dipping all cattle once a week (El Sawalhy 2012). It has to be taken into consideration that cattle management, the proper use of acaricides and frequency of application of acaricides as more than six applications per year will create a risk for the development of resistant ticks (Aboelhadid et al., 2018).

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