

Anaplasmosis in Ruminants of Iran: An Overview

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Abstract

Ruminant infections by *Anaplasma* species are increasingly identified as significant and potentially fatal arthropod-transmitted diseases.

Molecular diagnostic methods and epidemiological studies indicate that "anaplasma" infections are distributed in the whole world. Depending on the host and the bacterial species and bacterial strains symptoms vary from severe in sensitive animal to no sign in persistent infected animals. In Iran, five species including *Anaplasma marginale*, *A. centrale*, *A. bovis*, *A. phagocytophilum* and *A. ovis* are recognized in ruminants.

Various factors have contributed to *Anaplasma* spp. detection in Iran including better consciousness by veterinarians; upgrade diagnostic tools and advanced techniques in molecular biology.

The information about pathogen prevalence and genotypes and their vectors in different hosts and environments helps the foundation of surveillance and control programs for these pathogens. These findings may be used to create models to predict the risks of anaplasmosis and control, prevention, and treatment of disease.

Keywords: Iran; Anaplasmosis; *Anaplasma* species; Ruminant

Introduction

One of the most important tick-borne diseases in ruminants is anaplasmosis. The disease is caused by species of the genus *Anaplasma* (Rickettsiales: Anaplasmataceae) [1]. Five species including *Anaplasma marginale*, *A. centrale*, *A. bovis*, *A. phagocytophilum* and *A. ovis* are recognized in ruminants [2].

A. marginale, *A. centrale* and *A. ovis* live in red blood cell. These three species have similarity in structure, life cycle and transmission by ticks and flies; however, they carry special capacity for their host's infection [3-5].

A. marginale can cause severe disease with important economic loss in the cattle of the tropical and subtropical regions throughout the world. The clinical signs of the disease are advanced hemolytic anemia connect to fever, got thinner, abortion, declined milk production and in some cases death of the affected animal. Recovered cattle from anaplasmosis act as risk of the other cattle and they can carry the organism lifelong [3,6].

In contrast, *A. ovis* unable to cause acute disease in usual situation; anyway, under some conditions such as tensions like long-distance transfer and animal relocation, lack of rain, very warm weather, deficient pasture, vaccination, deworming and heavy tick infestation or other predisposing factors can cause anaplasmosis [6,7]. Co-infection of *A. ovis* with other pathogens in sheep (*Anaplasma* spp., *Theileria* spp. and *Babesia* spp.) reported in some researches. The weakened immune system in sheep infected with *A. ovis* increase chance to getting other infection and in the end death. Additionally, public health is another importance aspect of infection with *A. ovis* [6,7].

A. centrale can infect cattle red blood cells, the organism causes mild anaplasmosis. Infection with *A. centrale* supplies an effective and persistent immunity against fatal field strains of *A. marginale*. *A. centrale* live vaccines have been most widely used for vaccination against acute anaplasmosis by *A. marginale* [8].

Among *Anaplasma* species, *A. bovis* and *A. phagocytophilum* are leukocytic *Anaplasma* which infect monocytes and granulocytes, respectively [9].

A. bovis was first identified in 1936 while infected *Hyalomma* sp. ticks from Iran were fed to French cattle for experimental transmission of *Theileria* sp. *A. bovis* tends to infect monocyte cells and causes mild clinical signs same as weight loss, anemia, fever and rarely abortion and death in cattle of tropical and subtropical regions of the world. Survivors are lifelong carriers [10].

A. phagocytophilum is an agent that can infect both humans and animals. The organism tends to infect neutrophils. This organism has long been recognized as a veterinary agent, but in 1994, first human infection was reported. *A. phagocytophilum* has been considered as an emerging pathogen of public health importance. *A. phagocytophilum* in cattle causes tick borne fever (TBF). Clinical signs of the disease include inclusions neutrophils,

leukopenia, high fever, reduced milk yield, reduced fertility and abortions. In most cases *A. phagocytophilum* infections do not cause acute disease except when associated with secondary which rarely cause death [11].

A. phagocytophilum is trans-stadially transmitted by the tick vectors. *Ixodes ricinus* is the most vector of *A. phagocytophilum* in Europe. In addition, *Ixodes ricinus* has been identified as *A. phagocytophilum* vector in Iran [9]. Other ticks have been involved in the transmission of *A. phagocytophilum*, too [11].

A. marginale and *A. ovis* are diagnosed in red blood cells based on the position of inclusion bodies in the margin of erythrocytes. In acute anaplasmosis, Giemsa-stained blood smears is an appropriate method to discover inclusion bodies of the Anaplasma agents in erythrocytes, but in pre-symptomatic and carrier animals due to the small number of infected red blood cells this method is not suitable [12].

Immunofluorescent antibody (IFA) and competitive enzyme-linked immunosorbent assay (cELISA) based on the major surface protein 5 (MSP5) have been used in epidemiological studies but because of antigenic similarity, they do not discriminate between different Anaplasma species [13].

Molecular tests for the detection of bacteria that cannot be cultured are suitable. Polymerase chain reaction (PCR) test based on the 16S rRNA gene is very valuable method for the detection of rickettsia and Anaplasma/Ehrlichia genera. *A. marginale*, *A. centrale* and *A. ovis* have similar sequence in 16S rRNA gene. PCR-restriction fragment length polymorphism (RFLP) test planned by Noaman could discriminate *A. ovis*, *A. centrale* and *A. marginale* based on 16S rRNA gene in hosts [5]. For the first time they showed that analysis of the 16S rRNA gene helps to identify genera as well as to identify species. However, the detection of the Anaplasma species by PCR-RFLP requires a lot of time and troublesome for use in large sample size and epidemiological studies [13].

From six *A. marginale* identified major surface proteins (MSPs), MSP5, MSP4 and MSP1a were encoded by single genes and MSP3, MSP2 and MSP1b were encoded by several genes. MSP4 and MSP1a were used to describe the Anaplasma spp. diversity. The results approved that MSP4 provides useful phylogeographic knowledge while MSP1a is not a benefit marker for the description of geographic isolates of *A. marginale* [6].

In North America, Europe and Africa, *A. phagocytophilum* have been detected in human and confirmed by serological and molecular methods. In Asia serological evidence of human infection with *A. phagocytophilum* was reported in Korea and the first molecular detection of *A. phagocytophilum* in the wild deer and cattle was reported from Japan [9,11]. Nucleotide sequence of hyper variable region of 16S rRNA gene in Anaplasma spp. has been used for the discrimination of *Anaplasma* spp. from each other. Previously, *A. bovis* and *A. phagocytophilum* were found in cattle of Iran by molecular methods, [10,11].

Many species of hard ticks are extended throughout Iran and they are the most important external parasites of cattle and small ruminants of Iran. Although more is known about ticks as

responsible for the transmission of several rickettsia pathogens to cattle but there is little research on the anaplasmosis and its vectors in Iran [14].

Despite identification of Anaplasma species in Iranian ruminants based on the molecular assays, but there is many unbeknownst about the reservoirs and vectors of the disease. Due to the extent, there are different climates in Iran and in each climate exist different vectors. In addition, the migration of small ruminants and ruminant facilitate transfer from one region to another leads to the emergence of new diseases in the different regions. This situation makes the difference in the epidemiology of the pathogens in different regions and therefore in each area epidemiological study of the disease is necessary.

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