Review of Heart Water Disease in Domestic Animals

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Abstract: This seminar paper reviews on heart water in domestic animals with respect to its epidemiology, treatment, prevention and control. Heart water or cowdriosis is and peracute, acute, and subacute, noncontagious and tick borne rickettsia disease of ruminants caused by *Rickettsia ruminantium* and transmitted by *Amblyomma* ticks. It occurs in nearly all subSaharan countries of Africa and affects domestic and wild ruminant species. The organism multiplies in vascular endothelial cells throughout the body and in the reticulum cells of the lymph nodes. The disease is characterized by fever, nervous signs, hydro-pericardium, hydrothorax, ascites, edema of the lungs, and high mortality. The diagnosis of the heart water depends on the history, clinical sign, and epidemiological and postmortem examination. Tetracycline antibiotics (especially oxytetracycline) are very effective in the treatment of heart water especially when animals are treated early in the course of the disease. However, in the later stage of the diseases the treatment is not effective so that prevention and tick control is the best way of diseases eradication. This tick borne illness is highly economical significant due to their higher morbidity and mortality as a result of lack of awareness and information about epidemiology, prevention and control of the diseases. Therefore, the veterinarians consider the development of all aspects of heart water research, including vector ecology and control, epidemiology and socioeconomics, as well as vaccine development.

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1. INTRODUCTION

Heart water (cowdriosis) is an per acute, acute, and subacute, noncontiguous infectious disease of ruminants affecting cattle, sheep, goats, and antelope and is caused by the rickettsia organism *Rickettsia ruminantium*, which is transmitted by ticks of the genus *Amblyomma* (Lefevre *et al.*, 2010).

Heart water occurs in all region of sub Saharan Africa, except for desert and rain forest area. The disease is constantly present (endemic) in Africa and the Caribbean island carrier wild life in these locations sustain the disease in nature. To date, heart water has never been reported in Asia despite the presence of many species of *Amblyomma* ticks. The most widely distributed vector in Africa is *A. variegatum*, which occurs throughout western Africa from the Sahel Southwards, in areas of Northeastern Africa including Southern Sudan, most of Ethiopia and North Western Somalia, in most of central and eastern Africa, and in Southern Africa a far south as the Zambezi river system and central Mozambique (OIE, 2007).

Heart water is one of the most important diseases of livestock in Africa. This tick borne illness can significantly decrease productivity in regions where it is endemic. It is particularly serious in non-indigenous livestock that are moved into heart water areas; many of these animals may die. Wild ruminants can also be infected. Most wildlife species appear to carry the organism asymptomatically, but serious illness has been reported in lecher moved into endemic areas, as well as in experimentally infected white-tailed deer (OIE, 2007).

The distribution of the disease and its tick vectors places upper limits on the number of animals currently at risk to heart water. FAO/WHO/OIE (2005) estimates, Africa has a maximum of about 175 million head of cattle that are either in countries where heart water has been confirmed and/or where vectors occur and the disease is likely to be present. The disease is characterized by fever, nervous signs, hydro pericardium, hydrothorax, ascites, edema of the lungs, and high mortality. In some wild ruminants the agent causes subclinical infection. The name heart water is derived from the hydropericardium which commonly seen in this diseases (Quinn *et al.*, 1994).

The diagnosis of the heart water is depending on the history, clinical sign, epidemiological and postmortem examination (Radostits *et al.*, 2007). Heart water can be diagnosed by the identification of *Rickettsia ruminantium* by demonstration of Rickettsia inclusion bodies in the endothelial cell of brain crush smear. Serological test specifically for getting bovine have been applied but are of limited use under field condition owing to cross-reaction with Rickettsia species (Hirsh *et al*., 2004).

Tetracycline antibiotics (especially oxytetracycline) are very effective in the treatment of heart water, especially when animals are treated early in the course of the disease. Tick control has long been advocated as a means of controlling heart water. Even after the infected blood-based vaccine was developed, tick control was still advocated as a supplementary or alternative means of control (Andrew and Norval, 1989).

Therefore the main objective of this seminar paper is:

- ✓ To review the epidemiology heart water diseases.
- ✓ To highlight how to treat, prevent and control heart water.

2. HEART WATER

Heart water (HW) is an acute noncontagious infectious disease of ruminants affecting cattle, sheep, goats, and antelope and is caused by the rickettsial organism *Cowdria ruminantium*, which is transmitted by ticks of the genus Amblyomma. The disease is characterized by fever, nervous signs, hydro-pericardium, hydrothorax, ascites, edema of the lungs, and high mortality. In some wild ruminants the agent causes subclinical infection (Songer, 2005).

2.1 Etiology

The disease is caused by *Cowdria ruminantium*, a rickettsia agent. It is the only species of the genus *Cowdria*, in the tribe *Ehrlichia*, family *Rickettsiaceae*, and order *Rickettsiales.* The organism multiplies in vascular endothelial cells throughout the body and in the reticulum cells of the lymph nodes (Quinn *et al.*, 1994). It usually occurs in clumps of from less than five to several thousand organisms within the cytoplasm of infected capillary endothelial cells, especially in the brain. The heart water organism is extremely fragile and cannot persist outside of a host for more than a few hours. Because of its fragility, the organisms are stored in dry ice or liquid nitrogen to preserve its infectivity. Heart water strains vary in virulence, and although all are apparently pathogenic for sheep and goats, at least one strain is nonpathogenic for cattle (Radostits *et al.*, 1993).

Morphology and chemical composition

Rickettsia ruminantium is parasitic bacterium of endothelial cell of ruminants and also present in circulating, polynuclear neutrophil leukocytes of animal in the fever stage of the diseases. The individual particles various from 0.2 to 2.5 micro meter in diameter and sounded by gram negative wall, compose of two layers, pleomorphic, coccus and obligate intracellular parasite (Radostits *et al.*, 2007).

The culture characteristics and growth requirement

Establishment of *R. ruminantium* in bovine endothelial cell cultured led to development of in activated vaccine based on the elementary body (EB) stage of the organism, which although safer than the blood vaccine, are less protective and more expensive to produce and still early the risk of inducing immunity to bovine and accidental pathogen transmission. Attempts to grow *R. ruminantium* in tick cell date back over 25 years (Ulinberg *et al*., 1993).

Recently in vitro cultivation of the organism has been achieved. In an Exudes capillaries cell line (IDE8) comprising actively phagocyte like cells, with an ability to support growth in vitro of rickettsia species, not normally transmitted by this ticks. *R. ruminantium* was maintained in Glasgow minimal essential medium 10% of tryptose phosphate broth 10% of new born calf serum in bovine pulmonary artery endothelial cells (BPC). IDE8 cell grow in L-15 (Leibovitz) medium10% tryptose phosphate broth - 5%fetal calf serum 0.1%bovine lipoprotein at 30±2°C.EB and immature morulae in association with dying endothelial cell and cell debris (Kahn *et al*., 2005).

The susceptibility to physical and chemical agent

The heart water organism is fragile and cannot survive outside the cell for more than few hours, so that it needs favorable environmental condition. Temperature: heat liable and loss its viability within 12-38 hours at room temperature (Smith, 2009). Infective stability can be cry preserved in DMSO (Dimethyl Sulfide) or better yet in sucrose potassium phosphate glutamate medium (SPG) Infective halve of thawed stabile kept on ice is only 20 to 30 minutes (Kahn *et al*., 2005).

2.2. Epidemiology

Geographical distribution

Heart water occurs in all region of sub-Saharan Africa, except for desert and rain forest area. The disease is constantly present (endemic) in Africa and the Caribbean island carrier wild life in these locations sustain the disease in nature. To date, heart water has never been reported in Asia despite the presence of many species of *Amblyomma* ticks. The U.S. has two tick species, *A. maculatum* and *A.*

cajennense, that have been shown experimentally to be capable of serving as vectors of heart water (Hirsh *et al.*, 1994). The most widely distributed vector in Africa is *A. variegatum*, which occurs throughout western Africa from the Sahel southwards, in areas of northeastern Africa including southern Sudan, most of Ethiopia and North Western Somalia, in most of central and eastern Africa, and in southern Africa a far south as the Zambezi River system and central Mozambique (OIE, 2007).

Host range

Cowdriosis is mainly diseases of ruminants. All domestic Bovidae are susceptible, that is Cattle, Sheep, Goat and Asian buffalo (*Bubalus bubalis*) which have been introduced into some region of Africa. However heart water causes severe illness in cattle, sheep, goat and water buffalo, it is mild in some indigenous African breed of sheep and goat; and unapparent diseases in several species of antelope indigenous to Africa (Hirsh *et al.*, 2004).

Most observation among these Bovidae was experimental infection and infection was most often subclinical. It is thought indigenous antelopes in endemic areas possess variable resistance to heart water and this may be in addition to age linked resistance. Ruminant from another part of the world are susceptible too (Lefevre *et al.*, 2010).

Host susceptibility

Susceptibility to strain of given virulence varied with the animal species, in general cattle is less susceptible than small ruminants, and sheep are less susceptible than goats (Deem *et al.*, 1996; Lefevre *et al.*, 2010)

At an early stage it was reported that young calves possessed on innate age linked, resistance that was independent of the immune states of the dam, and this was used to immune them, by inoculating the virulent diseases, before the method of infection and treatment was developed (OIE, 2005). However, the resistance of calves is not absolute and 10 to 20% mortality has been reported in animals of less than amount old, 30 to 40% in those aged from 2-3 months. At the age of 9 to 12 months maximal susceptibility is attained in exotic cattle with mortality rate of 50% or more. Nevertheless there are also reports of a rate of 100% mortality in calve aged to 5 months (Hirsh, 1994).Varies factor may be explain, those differences such as the virulence and dose of the inoculated stack (in case of experimental infection), the bovine genotype and more recently, the protective role of colostrum of caw living in endemic areas (Radostits *et al.*, 2007).

Morbidity and mortality

Untreated nonnative cattle, sheep and goats often have sickness rate approaching 100%. Death rate of 80% have been recorded in merino sheep and angora goats, rate of 60%have been recorded in cattle Persians and Afrikaner sheep are more resistant to heart-water, with amorality rate of 6% typically (Quinn *et al*., 2002; Lefevre *et al*., 2010).

Risk factor

The epidemiology of heart water depends upon factors relating to the tick vector, the causative organism, and the vertebrate hosts. Important considerations relating to the tick vector are infection rates in the ticks, seasonal changes influencing tick abundance and activity, and the intensity of tick control. As far as the vertebrate hosts are concerned the availability of wild animal reservoirs and the age and genetic resistance of domestic ruminant populations are of importance (Radostits *et al.*, 1993).

An animal at greatest risk are exotics imported into endemic areas and at times when the vector population is high, usually during the rain, susceptible animals moved to endemic areas, heart water epidemics when vectors spread, in endemically unstable situations, tick control fails, and susceptible animals are raised in endemic areas (Ulinbeg *et al.*, 1993).(

Antigenic and genetic diversity

For a long time it was beloved that there was only one antigenic type of the causal agent of heart water (Uillenberg *et al.*, 1993). Strain originated from very different geographic areas (Nigeria, South Africa, Sudan etc.) can be cross protective. It is now certain that cross protection between may be total, partial or absent. It is essential for vaccine development, that this diversity is characterized (Dupless *et al*., 1981).

Source of infection

Heart water can be reproducing experimentally by inoculating susceptible animal, with blood from infected animal. Blood from such animals is very infective during hyperemic stage of the diseases. It has long been thought that the infectivity of the blood could last from 35 to 105 days after this stage, but it is now known that blood may be infective to ticks, intermittently and for long periods (Andrew and Norval, 1989).

The organism is present in endothelial cell of organs such as brain, kidney, lung node and it injecting emulsion of these organisms from infected animals will reproduce the diseases (Lifevre *et al*., 2010). Vectors are the important source of infection which transmits the disease from sick to health animals. There are more than 13 ticks of *Amblyomma* species (e.g. *A. berbraeum, A. gemma*, etc.) all of which belong to the genes *Ablyomma*, have been shown to be capable of transmitting *E. ruminantium* both in natural condition and experimentally (Kahn *et al.,* 2003, Kifle and Sorri, 2014).

The host were infective to tick only intermittently which suggests that rickettsia are not constantly present (or at least constantly present in sufficient quantities) in the circulation g blood it is currently accepted that latent infection persists in recovered domestic ruminants that constitute a reservoir of the infection for ticks (Andrew andNorval,1989). Wilde animals also have an important role in the transmission of *Rickettsia ruminantium*. It would be particular interest to assess the level of circulation of strain of *R. ruminantium* between wild life and domestic livestock in arrears where they meet, so as to determine the role of wild life in the maintenance of diseases. Certain reptiles, rodents and lagomorphs as well as birds, might also be reservoirs as they can be infected with certain stacks but their importance could well be limited (Radostits *et al.,* 2007).

Endemic stability is state of equilibrium between the infection agent, vectors and the host population. It is characterized by few or even no clinical case. It is necessary that the transmission rate of the pathogen is high and that the host became infected during period of reduced susceptibility to the clinical diseases. So that active protective immunity can acquire successive re-infection maintain protection (Lefevre *et al.,* 2010).

In the cause of heart water colostrums of caw in endemic region has protective role (this is not apparently linked to the presence of antibody which do not appear to play protection role) that may partially explain decreased susceptibility to the diseases of the young calves, but there is also strictly age linked reduced susceptibility to the clinical effect of infection, even in young animal of un infected dam (Kahn *et al.,* 2005). The role of vertical transmission via the colostrums might be important in the maintenance of endemic stability. With calves infected, while they are tolerant to the diseases, despite generally being only lightly infested by *Amblyomma* vectors (Norval, 1996).

Mode of transmission

Heart water is transmitted by ticks of the genus *Amblyomma*. Most *Amblyomma* species is three host ticks. Larvae and nymphs become infected when they feed on domestic and wild ruminants and possibly also on certain game birds and reptiles at a time when *E. ruminantium* is circulating in the blood of these hosts. The immature stages of the tick commonly feed on smaller species of domestic and wild ruminants and game birds, while the adults prefer cattle and the larger game animals, such as African buffalo (*Synceruscoffer*) and giraffe (*Giraffecame lopardus*), as hosts (Quinn *et al.,* 1994). Nymphs or adult ticks transmit *E. ruminantium* to susceptible hosts without losing the infection. Intra stadial transmission has been sped ticks under laboratory conditions but it is unlikely that it occurs in the field. Cows may transmit the infection to their calves in colostrums (Smith, 2009).

As ticks remain infective for life, a small number of infected ticks could presumably maintain the infection in a particuraly herd or area. The infection rates of ticks vary according to the season and locality in which they are collected and may be surprisingly low. Experimentally infected carrier sheep can infect ticks for at least seven months. Cattle can infect ticks for a minimum of eight month (OIE, 2007).

The distribution of heart water in Ethiopia

Ethiopia, there are 47 species of ticks which are found on livestock and most of them are important as a vector and diseases agent and also have damaging effect skin and hide production. Number of researcher reported the distribution and abundance of tick species in different part of the country. Amblyomma ticks is one of the most abundant tick genera and has been reported in many part of the country such as Bedele: Etsay Kebede (1985), Nekemte: Belete Mekuria (1987), Harargie Guliat Asrat (1987), Assela: Behailu (2004), Jimma:Ytbarek Getachew (2004), and Awassa Mehare Birhae (2004) with highest prevalence rate. Many of the publication of the diseases are often for short period without detailed follow up which precludes any extensive evaluation of the risk factor which might facilitate better understanding of the diseases it control. The annual fatality rate in Gondar University farm 18.1% of affecting animal (Achenafi *et al*., b 2004). As similarly study conducted in Arsi Ethiopia the mortality rate was 15.71% (Obsa and Zerihun, 1993).

2.3. Pathogenesis

The pathogenesis of heart water is not well understood. Vertebrate hosts are infected with *E. ruminantium* organisms through the saliva of attached ticks and/or by their regurgitated gut content. Initial replication of the organisms seems to take place in cells of the mononuclear phagocyte system in the regional lymph nodes, after which they are disseminated via the blood multiplication, occurs. In domestic ruminants *E. ruminantium* most readily infects endothelial cells of the brain, and this coincides with the onset of the febrile reaction (Stoltsz, 2005).

The electron dense elementary bodies are considered to be the infective forms; they adhere to and penetrate then the endothelial cell where they develop in cytoplasm vacuoles. The entry mechanism in the endothelial cell is unknown, although electron microscope studies suggest phenomena of phagocytosis inside the vacuole of the organism divide by binary fission and for large colony called Morella the organism in such group may be reticular, large in size and of low electron dense elementary bodies. The reticular forms are considered tube non infective vegetative forms that change into intermediate forms of *E. ruminantium.* After development for about 4 to 6 days the host cell rupture and liberates hundreds of elementary bodies (Andrews *et al.*, 2003).

The organism can be found in phagosome of circulating neutrophil, but are more abundant in endothelial cells. Increased vascular permeability with transudation is responsible for effusion into body cavities and tissue edema, and this is particularly noticeable in the lungs, pericardial sac and pleural cavity. Edema of the brain is responsible for the nervous signs; hydropericardium contributes to cardiac dysfunction during the terminal stages of the disease, and progressive pulmonary edema and hydrothorax result in eventual asphyxiation (Hirsh *et al.,* 2004).

It has been demonstrated that antibodies do not control the course of the disease. As *E. ruminantium* is an intracellular parasite it would be expected that both CD8+ cytotoxic T-cells and CD4+ helper T-cells would be important in the development of protective immunity. The antigen of *E. ruminantium* which is currently the best characterized is the immune-dominant MAP1, a protein of about 32 kDa which varies in size from isolate to isolate (Kahn *et al.,* 2003).

2.4. Clinical signs

Infected domestic ruminants may manifest a wide range of clinical signs. The incubation period, course, severity and outcome of artificially-induced disease are influenced by the species, breed and age of animal affected, the route of infection, the virulence of the strain of *E. ruminantium* involved, and the amount and source of infective material administered. Per acute, acute, subacute, and clinically in apparent forms of the disease occur. Death usually follows in animals which show clinical signs if they are not specifically treated for heart-water (Kahn *et al.,* 2005).

The incubation period in naturally infected cattle ranges from nine to 29 days with an average of 18 days. Cows of *Boss Taurus* breeds, especially when in the advanced stages of pregnancy, are particularly prone to develop per acute heart water. Per acutely affected animals are die within a few hours, after the initial development of fever, with or without prodromal signs (Norval *et al*., 1995).

Acute heart water, the most common form of the disease, mainly affects cattle between the ages of three and 18 months. It is characterized by a fever of 40 °C or higher, which usually persists for three to six days. Certain breeds develop diarrhea most commonly. A profuse, often hemorrhagic, diarrhea may be the most prominent clinical sign during the later stages of acute heart water, nervous signs occur which range from mild in coordination to pronounced convulsions. The acute form of the disease, by far the most commonly observed syndrome, is seen in nonnative and indigenous domestic ruminants (Jongejan *et al*., 1992). A sudden fever is followed by in appetence, depression, listlessness, and rapid breathing. Nervous signs then develop, the most prominent being chewing movements, twitching of the eyelids, protrusion of the tongue and circling, often with high stepping gait (Cowdry *et al*., 1991).

The animals are hypersensitive when handled or exposed to sudden noise or bright light. Slight tapping with a finger on the fore head of the animal often evokes an exaggerated in some cases of heart-water blinking reflex. They frequently show a peculiar high-stepping gait that is usually more pronounced in the front limbs. Calves may wander around aimlessly and walk into fences, and some, previously unaccustomed to handling by humans, may be approached with ease. Animals may stand with their heads held low, make constant chewing movements, and push against (Kahn *et al.,* 2003). In the later stages they often fall down suddenly, assume a position of lateral recumbence, and show opisthotonos and either have frequent bouts of leg-pedaling movements or the legs may be extended and stiff. In most cases the animals weaken rapidly and death usually follows soon after the commencement of a convulsive attack (Radostits *et al*., 1993).

Severe hydropericardium and hydrothorax, and in some cases a degree of ascites, are striking changes in most fatal cases of the disease. However, hydro pericardium is usually more pronounced in sheep and goats than in cattle. The transudate is a transparent to slightly turbid, light yellow fluid which may coagulate on exposure to air. Several litters of transudate may be present in the thorax in cattle, while in sheep up to 500 ml and in goats rarely more than 20 ml may be present (Quinn *et al.,* 2002).

A moderate to severe edema of the lungs occurs in most animals that die of the disease, but it is particularly severe in animals which have suffered from the per-acute or acute form. Frothy edematous fluid oozes from the cut surface of the lungs. The trachea and bronchi are often filled with frothy serous foam occasionally accompanied by a fibrous coagulum, and their mucous membranes are often congested and contain petechial and ecchymosed. Edema of the brain commonly occurs in animals suffering from the per-acute and acute forms of heart-water (Dupleess *et al.,* 1991).

Rarely, the disease may run a sub-acute course characterized by prolonged fever, coughing (a result of lung edema), and mild in coordination; recovery or death occurs in 1 to 2 weeks. A mild or subclinical form of the disease, known as "heart water fever," is seen in partially immune cattle or sheep, in calves less 3 weeks old, in antelope, and in some indigenous breeds of sheep and cattle with high natural resistance to the disease. The only clinical sign in this form of the disease is a transient febrile response (Stoltsz, 2005).

2.5. **Post mortem finding**

Macroscopic lesion

The gross lesions in cattle, sheep, and goats are very similar. Heart water derives its name from one of the prominent lesions observed in the disease, namely pronounced hydropericardium the accumulation of straw colored to reddish fluid in the pericardium is more consistently observed in sheep and goats than in cattle (Hirsh and Zee, 1994). Ascites, hydro thorax, mediastinal edema, and edema of the lungs all resulting from increased vascular permeability with consequent transudation, are frequently encountered. Sub endocardial, petechial hemorrhages are usually seen, and sub mucosal and subserosal hemorrhages may occur elsewhere in the body. Degeneration of the myocardium and liver parenchyma, splenomegaly, edema of lymph nodes, nephritis, and catarrhal and hemorrhagic mastitis and enteritis are all commonly encountered. Meningeal congestion and edema are often present. Brain congestion may occur, but brain lesions can be remarkably few when one considers the severity of the nervous signs observed in this disease (Lefevre *et al.,* 2010).

Microscopic lesion

These are not pathognomonic for heart water apart from observation of *E. ruminantium* in endothelial cell of the blood vessels. The only important histo- pathological changes are lung edema and interstial pneumonia, the lesion are the result of increased vascular permeability with infiltration by numerous macrophage (Quinn *et al*., 2002). In general there is no correlation between the severity of the diseases and that of the lesion and the number of the rickettsia present in the tissue. The slight pathological changes in the infected endothelial cell strongly suggested that *E. ruminanntium* is not directly responsible for vascular hyper permeablity (nottoxin has been found) but the latter is more probably asso0ciated with the activation of the secretion of pro-inflammatory cytokines, as reaction to the infection (Lefevre *et al.,* 2010).

2.6. Diagnosis

The diagnosis of the heart-water is depending on the history, clinical sign, and epidemiological and post- mortem examination. The presence of *Amblyomma* ticks plus the rather characteristic signs and lesions of heart water allows tentative field diagnosis of the disease, which must then be confirmed by demonstration of the causative organism, its antigens, or its DNA (Andrew and Norval, 1989, Quinn *et al.,* 2002).

Laboratory diagnosis

Specimens for the laboratory

From live animals, collect 10 ml of blood using heparin as an anticoagulant and add sufficient DSMO to make a 10 percent concentration; freeze on dry ice. Collect an additional 50 ml of heparinized blood and 10 ml of serum. From a dead animal, submit smears of cerebral cortex or half of the brain unpreserved and a set of tissues in 10 percent buffered formalin (Hirsh *et al*., 1994; Quinn *et al*., 2002).

Isolation and identification of the pathogen

The isolation of *E .ruminantiumin* cell culture is not easy and takes more time and therefore sensitive molecular method have been developed. That makes it possible to detect it more rapidly and examine more numerous samples (Andrew and Norval, 1989). But isolation in animal is possible to demonstrate the occurrence of *E. ruminantium* in an area or in adhered by feeding suspected ticks on susceptible ruminants or by inoculating intravenously with emulsified ticks (Lefevre *et al.,* 2010). Such ground up ticks kept in liquid nitrogen until animals can be inoculated. The clinical reaction of the animal is monitored and the diagnosis is confirmed after death by examine the brain smear. This method of isolation in vivo is still extensively used for isolation of new strain from field (Uilenbeg *et al.,* 1993)

Heart water is also diagnosed by observing *R. ruminantium* colonies in the brain or intima of blood vessels. Brain smears are air dried, fixed with methanol and stained with Giemsa. *R. ruminantiu*m occurs as clumps or reddish purple to blue, coccoid to pleomorphic organisms inside capillary endothelial cells. These organisms are often found close to the nucleus, and may be in a ring or horseshow. *R. ruminantium* can also be detected in formalin fixed brain sections using immune peroxidase techniques. Colonies can be difficult or impossible to find in some animals that have been treated with antibiotics. Only a few colonies may be found in animals with per-acute disease (Radostits *et al.,* 2007; Kahn *et al.,* 2005).

Serological diagnosis

The first serological method to be real use was developed by Dupleess, using the particular tropism of the Kumm isolate of *E. ruminantium* for Maurine cells. In fact serological studies only started with the development of immune enzymatic, IFA and immune blotting (Dupless, 1981). But there is some limitation: false positive reaction has been encountered during epidemiological survey .The reaction due to existence of homologues of the protein MAP-1 in the presence and persistence-of circulating antibody (OIE, 2008).

Immune fluorescence antibody test

The immune fluorescence antibody (IFA) test is carried out an antigen consisting of peritoneal macrophages of infected mice .later the specificity of the IFA test has been improved by using primary culture of poly nuclear neutrophil leucocytes of the existence of serotype using neutrophil of goats infected by different stocks of *E. ruminantum* (Dupless, 1981; Lefevre *et al.*, 2010).

Enzyme–linked immune sorbent assay (ELISA)

All ELISA using crude antigen of *E. ruminantium* have now been replaced by two ELISA based on recombinant antigen, developed to counter the problem of cross reaction. The first an indirect ELISA using as the antigen fragment of the MAP1 protein between amino acid 47 and 152 named MAP-P (OIE, 2005).The second is competitive ELISA (C-ELISA) with entire MAP1protein produced in baculo virus reacting with monoclonal antibodies. The antigen MAP1-B and the monoclonal antibody in the C-ELISA have been selected because of their low cross-reactivity with another species of Ehrlichia (Radostits *et al.*, 1993).

Molecular diagnosis

This method is most accurate and confirmatory diagnosis especially in the case of carrier state of heart-water. It is carried out by using polymerase chain reaction (PCR) tests and other specialist technique. PCR can find this organism in the blood from just before the onset of the fever to a few days after recovery, but detection in carrier animals is inconsistent. Positive PCR reactions are sometimes seen in areas where neither heart-water nor its tick vectors are known to exist, possibly due to cross-reactions with other rickettsia species (OIE, 2007).

2.7. Differential diagnosis

The per-acute form of HW can be confused with anthrax. The acute nervous form of HW can be confused with rabies, tetanus, chlamydiosis, bacterial meningitis or encephalitis, cerebral trypanosomiasis, piroplasmosis or theileriosis, and various intoxications such as with strychnine, lead, organophosphates, or chlorinated-hydrocarbons (Uilenberg *et al.*, 1992). Heavy helminthes infestations may produce accumulations of fluid similar to those seen in HW. Arsenical poisoning may resemble the enteric form of the disease, and certain poisonous plants (e.g., Cestrum laevigatum, Pachystigma spp., Patvetta spp.) may produce signs and lesions similar to those seen in heart-water. Most diseases can be eliminated by the history nutritional aspects whether the infection is contagious or not presence of the vectored in combination with the examination of blood smears, organism smears and brain smear (Radostits *et al*., 2007).

2.8. Treatment

Tetracycline antibiotics (especially oxy tetracycline) are very effective in the treatment of heart water, especially when animals are treated early in the course of the disease. Tetracycline antibiotics administered before signs appear will suppress the disease entirely, but will allow immunity to develop. Doxy cyclone and rifamycine are both very effective, and a wide variety of sulfonamides have successfully been used in heart-water treatment. Treatment for ruminal atony, a commonly observed sequel to this disease, may be indicated, and diuretics may be useful to control fluid accumulations in body cavities (Andrew and Norval, 1989).

Short-acting formulations of oxytetracycline are most commonly used at a dosage rate of 10 to 20 mg/kg body weight, either administered intramuscularly as a single dose, or half the calculated dose is given intravenously and the other half intramuscularly (Deems *et al*.,1996). This treatment is usually repeated 24 hours later. A longacting oxytetracycline preparation has been shown to be equally effective. Doxycycline has been used successfully at a dose rate of 2 mg/kg body weight in the treatment of experimentally induced heart water in sheep (Hirsh *et al*., 2004).

2.9. **Prevention and control**

Tick control

Tick control has long been advocated as a means of controlling heart water. Even after the infected blood based vaccine was developed, tick control was still advocated as a supplementary or alternative means of control (Andrew and Norval, 1989).

Tick control can be either intensive or strategic, but intensive tick control has largely fallen into disuse. The main disadvantage is that animals may lose all immunity to tick borne diseases because of the lack of a natural challenge. Strategic tick control implies the control of tick numbers so that natural infection of livestock occurs and high levels of immunity are maintained (Andrew and Norval, 1989).

Preventative measures for heart water include implementation of an effective tick control program using acaricides which are products aimed at killing ticks, as well as regular inspection of animals and pastures for ticks (Quinn *et al*., 2002). It is fraught with difficulties and does not provide a long-term solution to heart-water problems. There are some major problems associated with the control of heart-water by vector control. The costs of acaricides (particularly the foreign exchange component) and their application are becoming too high to be met in several affected countries. National tick control programs suffer organizational problems and are vulnerable to political or economic instability (Radostits *et al.,* 2007).

Acquired resistance to acaricides in one or more tick species can adversely affect control programs. Intensive tick control can create endemic instability for heart water. Control of heart-water by intensive tick control may adversely affect endemic stability for other tick-borne diseases such as babesiosis (this is potentially a problem associated with *Amblyomma* eradication in the Caribbean (Dupless, 1981). Tick control has little effect on *Amblyomma* abundance where alternate hosts for the adult stage are present; this is because the aggregation-attachment pheromone emitted by attached males' causes unfed nymphs and adults to attach in preference to the untreated hosts.

Dipping or spraying using acaricides pollutes the environment and may result in residues in meat and milk. A significant advance in the control of *A. hebraeum* and *A. variegatum* has been the utilization of the aggregation-attachment phermone, naturally emitted by the attached males, to attract unfed nymphs and adults to a source of pesticide (Norval *et al.,* 1989). Synthetic pheromone components and an acaricides can be incorporated into slow-releasing Plastic tick decoys', which can be attached to the hosts (Andrew *et al*., 2005). This slow-release tick decoy system has the following advantages over traditional dipping or spraying. It uses less acaricides per head treated and should therefore be less costly and less of an environmental hazard. It is long lasting and removes the need for frequent mustering of animals for dipping or spraying. Control is directed specifically at *Amblyomma* ticks and so should not affect the epidemiology of tick-borne diseases other than heart water (Kifle and Sori, 2014).

Chemotherapy

The first chemotherapeutic agent found to be effective against heart water was the sulfonamide drug `Uleron' (Uilenberg *et al.*, 1993). Subsequently other drugs, in particular tetracycline, have been found to be effective (Weiss *et al.,* 1952; van Amstel and Oberem, 1987). Two major problems appear to be preventing the widespread adoption of chemotherapy as a control strategy. First, there often are difficulties in the early diagnosis of the disease when chemotherapy is most likely to be effective (OIE, 2OO7). The second problem is the relatively high cost of drugs such as the tetracycline's, in both local and foreign currency terms.

Chemoprophylaxis

(Andrew *et al.,* 1989) reported that susceptible cattle introduced to an endemic heart water area and given three injections of long-acting ox tetracycline on days 7, 14 and 21 after introduction did not develop clinical disease. Again, major constraint to the widespread adoption of this methodology is the cost.

Infection and treatment method of immunization

Infections are produced by intravenous inoculation of whole blood from reacting animals (sheep) or stabilate made from ticks fed on reacting animals (Hirsh, 1981). After inoculation the temperatures of individual animals must be monitored so that treatment can be initiated at or soon after the start of the febrile reaction. Treatment prior to the febrile reaction may prevent the development of immunity and treatment too late in the reaction can result in death. For best results this method of immunization obviously needs to be carried out under strict veterinary supervision (Quinn and Markey, 2003).

The disadvantage of this method is infected blood or stabilate must be stored on dry is infection must be administered intravenously. The need to monitor febrile reactions in individual animals limits the number that can be immunized at any one time. Deaths frequently occur if procedures are not adhered to strictly. Use of whole blood introduces a risk of transmitting other pathogens. The procedure, which includes the use of tetracycline's, is costly some problems exist with cross-immunity between immunizing and field stocks of *C. ruminantium* (Du Plessis *et al.*, 1989).

Attenuated cell culture vaccine

The development of an attenuated vaccine for heart-water, to replace the infection and Treatment method of immunization, would represent a significant advance in practical terms (Quinn *et al.*, 2005).

Molecular vaccine

Recombinant and DNA vaccines are still future prospect for the control of cowdriosis. DNA vaccine based on the MAP1gene has been reported to protect 38% of mice against lethal challenges. More promising results more promising result against homologous and even heterologous challenges (4 strain) were later obtained with plasmid DNA immunization in sheep using cocktail 4CDS from the 1H12 locus in the laboratory but further evaluation is required also against heterologous and particularly field challenges (Quinn et al.,2003).

2.10. Economic importance

The distribution of the disease and its tick vectors places upper limits on the number of animals currently at risk to heart-water. Using FAO/WHO/OIE (2005) estimates, Africa has a maximum of about 175 million head of cattle that are either in countries where heart-water has been confirmed and/or where vectors occur and the disease is likely to be present. But the economic impact of heart-water is difficult to quantify, both because of the under reporting and because the actual occurrence of the disease may be partially suppressed by a range of factors. These include the use of acaricides, antimicrobial prophylaxis, immunization by infection and treatment, the resistance of certain animal breeds to the disease, and endemic stability (Stoltsz, 2005).

The economic impact of the disease on these animals at risk can be separated into two categories these are disease-related mortality and non-lethal losses. Losses in each category include mortality of susceptible animals moved to endemic areas, caused by heart-water epidemics when vectors spread, in endemically unstable situations, when tick control fails, and when susceptible animals are raised in endemic areas (Radostits *et al*., 1993).

Nonlethal losses, this includes production losses caused by sub-clinical (carrier state) infections, losses due to the costs of control of heart water and its vectors and the treatment of clinical cases, lost production potential caused by the inability to upgrade local livestock by cross-breeding with exotic breeds imported into a heart-water endemic area, and production losses caused by infestations of vectors (Kahn *et al.,* 2005). The circumstances in which heart-water causes mortality in domestic livestock are now well defined. Cattle, sheep and goats are moved from heart-water free to endemic areas. This has occurred when high-yielding exotic breeds have been introduced to upgrade or replace local stock (OIE, 2007).

CONCLUSION AND RECOMMENDATION

Generally heart water (HW) is an acute noncontiguous infectious disease of ruminants affecting cattle, sheep, goats, and antelope and is caused by the rickettsia organism *Rickettsia ruminantium*, which is transmitted by ticks of the genus *Amblyomma.* Heart water occurs only where its *Amblyomma* tick vectors are present. Epidemiology depends on interaction of tick vector, causative agent, and vertebrate hosts. The disease is characterized by fever, nervous signs, hydro pericardium, hydrothorax, as cites, edema of the lungs, and high mortality. Heart-water is very economically important due to their higher sickness and death rate especially exotic breeds because of exotic breeds are highly sensitive to the diseases and they need highly proper management than local breeds.

Antibiotic treatment of the diseases is effective in the early stage of the diseases but in the later stage antibiotic treatment is not effective due to the immunity is suppress and the cell is rupture. so that the effective way of eradication of the diseases is prevention and control that means vaccination of the animal at exact time and exact type of vaccination, proper management of animal husbandry, tick control and increase the awareness of veterinarians and owners about prevention and control.

Therefore based on the above conclusion the following recommendations are forwarded.

- ❖ The veterinarian should be aware of the epidemiology and risk factor of heart-water,
- ❖ Increase the awareness of the farmers about prevention and control of heart-water diseases,
- ❖ Concerned veterinarians should be give attention to prevent and control strategies,
- ❖ The veterinarians consider the development of all aspects of heart-water research, including vector ecology and control, epidemiology and socioeconomics, as well as vaccine development, to be essential.

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