International Journal of Advanced Research in Biological Sciences
ISSN: 2348-8069
www.ijarbs.com
DOI: 10.22192/ijarbs Coden: IJARQG (USA) Volume 7, Issue 9 -2020

Review Article

DOI: http://dx.doi.org/10.22192/ijarbs.2020.07.09.002

A Review on Zoonotic importance of a Brucellosis.

Wondimu Hailu Enaro

Arbaminch Univeresity, College of Agricultural Science.

Abstract

Brucella is facultative intracellular gram negative, aerobic, catalase-positive, non-motile, non-spore forming and rod shaped (coccobacilli). The Brucella genus is composed of 12 recognized species after isolation and identification of novel species from mandibular lymph nodes of the red fox. Brucellosis is one of the most important zoonotic diseases of public health implications causingsocio-economic impacts on the livelihoods of the poor rural pastoralist communities and the urban population worldwide. It is a bacterial disease, caused by members of the genus Brucella; and in small ruminants Brucellamelitensisis the most common species in developing countries and is associated with clinically apparent disease in humans. Brucellosis also known as “undulant fever”, “Mediterranean fever” or “Malta fever” is a highly contagious zoonosis caused by ingestion of unpasteurized milk or undercooked meat from infected animals, or close contact with their secretions. Brucellosis has been an emerging disease since the discovery of Brucellamelitensis by Bruce in 1887, and it causes a systemic infection with clinical manifestations as fever, sweats, fatigue and joint pain. Because each type has distinctive epidemiologic features, with each new type, the complexity of the interaction with humans has increased. Because new strains may emerge and existing types adapt to changing social and agricultural practices, the picture remains incomplete. Treatment of the disease is difficult because its symptom is complex, it can cause flu and malaria like symptoms. The control of brucellosis requires collaboration of different discipline through one health approach. Especially, in developing country Ethiopia, since the eradication of brucellosis is difficult, its control is very important.

Keywords: Brucellosis, Epidemiology, Zoonotic importance, Transmission.

Introduction

Brucellosis is one of the most common widespread zoonoses throughout the world, mainly caused by *Brucella abortus*, *Brucella melitensis* or *Brucellasuis*, and is transmitted to people from various animal species (WHO,2006). Brucellosis due to *Brucella abortus*, *Brucella melitensis* and *Brucellasuis* were included in the second category (List B) of communicable diseases (Lita*et al.*, 2016). Despite its widespread distribution, it is considered to be a neglected zoonosis because, in many endemic areas, it is not regarded as a priority by national and international health systems (Adone and Pasquali, 2013). It is a major socio-economic importance in domestic animals worldwide; especially so in developing countries where disease controls programs are either non-existent or inadequate. The disease also occurs in wild animals, thus posing a danger of transmission between domestic and wild animals in interface areas.*Brucella* species that cause disease in domestic and wildlife include *Brucella abortus*, *Brucella melitensis*, *Brucella ovis*, *Brucella suis* and *Brucella canis*(Shirima,2005). The disease poses a barrier to trade of animals and animal products, and can causes a public health hazard, and is an impediment to free animal movement (Zinsstag *et al*., 2011).

Brucellosis is an infectious bacterial disease caused by members of the genus *Brucella, and* that characterized by late abortion, retained foetal membranes, and to a lesser extent,orchitis and infection of the accessory sex glands in males and impaired fertility. The disease primarily affects cattle, buffalo, bison, pigs, goats, sheep, dogs, elk, and camels and occasionally horses (Walker,2005; Kahn, 2005;Zinsstag*et al*.,2011). It is essentially a disease of sexually mature animals, the predilection sites being the reproductive tracts of males and female. If the animal is not pregnant, a chronic disease results without symptom and perhaps negative serology. However, if such an animal becomes pregnant the production of simple carbohydrate eryhritol in the fetus and its membranes cases enormous multiplication of bacteria in the uterus and this are likely to end in abortion (Tesfaye *et al*., 2017)

Animals become infected by ingesting contaminated pastures, feedstuffs and water or licking infected placentae, foeti or the genitalia of infected female animals soon after abortion or delivery (Shirima, 2005). The clinical findings are dependent upon the immune status of the herd. Among highly susceptible, non-vaccinated pregnant cattle, abortion after the 5th month of pregnancy is the typical feature of the disease. In subsequent pregnancies the fetus is usually carried to full term although second or even third abortions may occur in the same cow; and retention of the placenta and metritis are common sequelae to abortion (Radostitis *et al*., 2007).

According to Aworh *et al* (2013), Brucellosis is more prevalent in developing countries and considered to be a serious health problem due to lack of effective public health measures, domestic animal health programs, and appropriate diagnostic facilities. Furthermore, the situation is also worsened by the resemblance of the disease with other diseases leading to misdiagnosis and underreporting (Regea, 2017).It was eradicated in several countries through test and slaughter, vaccination and restriction of animal movements (Shirima, 2005).

Brucella abortus, Brucella melitensis, Brucella suis and *Brucella canis* can all cause human brucellosis, whereas *Brucella ovis* and *Brucella neotomae* have not been reported to cause disease in humans (Shirima, 2005). Humans can be infected by consuming contaminated food (mainly raw milk and dairy products) (Sintayehu *et al*., 2015). In addition, it can also infected by contact of the skin, even apparently healthy skin or the digestive, conjunctival or nasopharyngeal mucous membranes with infected animals or matter produced by them (mainly genital secretions, aborted foetuses or placentas, but also infected organs such as the liver, spleen or udder in particular, or contaminated manure or wool) ("FAF, EOHS,"2014).

In human, Brucellosis is an acute or sub-acute febrile illness usually marked by an intermittent or remittent fever accompanied by malaise, anorexia and prostration, and which, in the absence of specific treatment, may persist for weeks or months (WHO, 2006).

The disease is economically important as it is associated with abortion storms in newly infected herds, a high level of retained placenta and hence endometritis or metritis resulting in reduced milk production, infertility. In addition, the zoonotic nature of the disease has a serious impact on public health (Radostitis et al.,2007).According to Mangen et al.(2002) the economic losses due to brucellosis summarized as :1) Losses due to abortion in the affected animal population; 2) Diminished milk production, Brucella mastitis and contamination of milk;3) Cull and condemnation of infected animals due to breeding failure;4) Endangering animal export trade of a nation;5) Human brucellosis causing reduced work capacity through sickness of the affected people;6) Government costs on research and eradication schemes;7) Losses of financial investments.

Despite the advances made in surveillance and control, the prevalence of Brucellosis is increasing in many developing countries due to various sanitary, socio-economic and political factors (Mohammed *et al*., 2016). Many countries have made considerable progress with their eradication programs but in countries like Africa brucellosis is considered to be one of the most serious disease problems facing the veterinary profession (Tesfaye *et al.,* 2017).

In Ethiopia, different study has been conducted in different areas that reported sero prevalence of brucellosis study demonstrated that the overall seroprevalence of small- ruminant brucellosis in and

around Bahir Dar to be 1.2% by the RBPT and 0.4% by CFT. More than half of the sera which tested positive for RBPT, tested negative for CFT. This could be due to cross-reactions between Brucella and other bacteria which share similar epitopes. This prevalence is lower than prevalences recorded in previous studies carried out in different parts of the country; 4.8% in Afar (Ashenafi Feyissa et al., 2007); 9.7% in Afar and Somali (TeshaleSori et al., 2007); 1.5% in sheep and 1.3% in goats in central highlands of Ethiopia (TekeleyeBekele and Kassali, 1990); 16% in Afar Region (Yibeltal, Muhie 2005) and 3.37%, 0.11%, 3.94% and 0.49% from Afar Region, Somali Region, Borena Zone and South Omo Zone, respectively (MelesseBalcha *et al*., 2006). The difference in the prevalence of brucellosis between the current and previous studies might be attributed to the differences in geographical location, sample size and management systems. In Afar and Somali Region, large numbers of different species of animals are raised on communal pastures under limited watering areas, where as the livestock management in the northwestern Ethiopia is characterized by mixed farming, in which fewer animals are raised separately.
Limited financial resources, political instability and lack of commitment by local and regional governments, as well as the presence of other serious livestock diseases (that ispeste des petits ruminants, Rift Valley fever, foot and mouth disease, contagious caprinepleuro pneumonia, lumpy skin disease and African swine fever), in many African countries have diverted attention from important zoonotic diseases such as tuberculosis and brucellosis. There is no strategic control and eradication plan against brucellosis in Ethiopia under implementation (Sintayehu *et al*., 2015). Therefore, the objective this review was;

- To assess the review on the cause of brucellosis both in animals and humans.
- To review the epidemiology of brucellosis both in animals and humans.
- To review the zoonotic importance of brucellosis.
- To review mode of transmission, treatment, control and prevention of brucellosis.

2 Literature review and Discussion

2.1Epidemiology

The epidemiology of the disease in livestock and humans as well as appropriate preventive measures is not well understood, and in particular such information is inadequate in sub-Saharan Africa (McDermott and Arimi, 2002). Despite endemic nature of brucellosis in many developing countries the disease remains under diagnosed and under-reported (Regea, 2017).

The epidemiology of cattle brucellosis is complex and influenced by several factors. These can be broadly classified into factors associated with the transmission of the disease between herds, and factors influencing the maintenance and spread of infection within herds. Routes of transmission from animal to human include: 1- direct contact with infected animals, 2- inhalation of contaminated aerosols, and 3- ingestion of unpasteurized dairy products. The climatic and agro-ecological diversities of Ethiopia may allow a wide range of livestock production systems, and therefore, different management systems, multiple livestock species per holding, stock density and social organizations to handle livestock may account for the widespread risk factors for maintenance and transmission of cattle brucellosis (Megersa*et al*.,2011).

2.1.1 Etoilogy

According to Schelling *et al*(2003), Brucellosis is an economically important and widespread zoonosis in the world caused by bacteria of the genus Brucella, which tend to infect specific animal species; in which cattle is usually infected by *Brucella abortus*, sheep and goats by *Brucella melitensis*, and swine by *Brucella suis* (Awah-Ndukum, 2018).

Brucella is the agent responsible for brucellosis, a contagious infectious animal disease with global distribution that can infect humans ("FAF, EOHS,"2014). Brucella is characterized as small, facultative intracellular, gram negative, aerobic, capnophilic, catalase-positive, non-motile, non-spore forming and rod shaped (coccobacilli) bacteria that can infect many species of animals, including humans. Apart from *Brucella ovis* and *Brucella neotomae*, all brucella species are oxidase positive; as well as all are urease-positive except *Brucella ovis* (Quinn *et al*., 2002).

The Brucella genus is composed of 12 recognized species after isolation and identification of novel species from mandibular lymph nodes of the red fox (Scholz *et al*., 2016).There are six ‘classical’ species*: Brucella abortus*, *Brucella melitensis*, *Brucella suis*, *Brucella ovis*, *Brucella canis* and *Brucella neotomae*, andthe first three of these are subdivided into biovars based on cultural and serological properties (OIE, 2013). They affect many animal species, but especially of those that produce food: sheep (especially milk Producing), goats, cattle and pigs and, on a more localized scale, camels, buffaloes, yaks and reindeer (WHO, 2006).

Brucellosis is an important zoonotic disease caused by infection with bacteria of the Genus Brucella. It was first isolated by Bruce in 1887 from the spleens of soldiers dying of Mediterranean fever on the island of Malta. Bruce called it Micrococcus melitensis. The origin of the disease remained a mystery for nearly 20 years until it was discovered that goats were the source of infection for human populations. Nine Brucella species are currently recognized. Seven of them that affect the terrestrial are, B. abortus, B. melitensis, B. suis, B. ovis, B. canis, B. neotomae, and B. microti, and two that affect marine animals are, B. ceti and B. pinnipedialis. The first three species are called classical Brucella and within these species, seven biovars are recognized for B. abortus, three for B. melitensis and five for B.suis (Schelling*et al.*, 2003).

In general, brucella have a predilection for both female and male reproductive organs in sexually mature animals and each *Brucella* species tends to infect a particular animal species. The target organs and tissues of *Brucella* species are placenta, mammary glands, and epididymis in animal reservoir host (Quinn *et al.*, 2002). Persistent (lifelong) infection is a characteristic of its facultative intracellular organism, with shedding in reproductive and mammary secretions (Radostitis*et al*., 2007).*Brucella* survives in freezing and thawing, and under proper environmental condition, they survive for up to 4 months in milk, urine, water, and damp soil. Most disinfectants active against other gram-negative bacteria kill *Brucella*, and pasteurization also effectively killbrucella in milk(Walker, 1999).

Table 1: The table below summarizes Brucella species, hosts and transmission mode (http://www.ansci.wisc.edu/jjp1/ansci_repro/misc/syllabus, 2002)

Strain Symptoms	Principle Host	Other Hosts	Symptoms	Transmission	Human Disease
Brucellaabortus	Cattle	Sheep, goats, pigs, horses, dogs, humans, wild	Abortion after 5 months	Ingestion, some venereal	undulant fever-control with antibiot
Brucellamelitensis	Sheep, goats. buffalo	cattle, pigs, dogs, humans, camels	Later term abortion, weak young, mastitis (go	Ingestion	Malta fever: can be fatal in human
Brucellaovis	Sheep		most often effects rams, rare abortions		
Brucellasuis	Pig	cattle, horses dogs, humans reindeer, caribou	Abortion and infertility	ingestion and venereal	extremely deadly in humans
Brucellacanis	Dogs	Humans	abortions at 40-60 days	Venereal	mild disease in humans

2.1.2 Mode of disease transmission

Brucellosis occurs in animals of all age groups, but persists commonly in sexually mature animals. Infection is frequently introduced into clean herds or flocks through the introduction of infected animals which are either pregnant, that have recently delivered, or aborted (Shirima, 2005). The risk posed to susceptible animals following parturition of infected cattle depends on three factors: 1) the number of organisms excreted, 2) the survival of these organisms under the existing environmental conditions, and 3) the probability of susceptible animals being exposed to enough organisms to establish infection (World Health Organization, 2006). Brucellas are disseminated by direct or indirect contact with infected animals. Natural transmission occurs by ingestion organisms, most common routes of entry, although exposure through the skin, conjunctiva, genital mucosa, and respiratory routes occurs. The major source for exposure *Brucellaabortus* in cattle and *Brucellamelitensis* in sheep and goats is through aborted fetuses, fetal membranes, and post abortion uterine discharge (Walker, 1999).

Venereal transmission by infected bulls to susceptible cows appears to be rare. Transmission may occur by artificial insemination when Brucella contaminated semen is deposited in the uterus but, reportedly, not when deposited in the midcervix (Kahn, 2005). Intra herd spread occurs by both vertical and horizontal transmission. Horizontal transmission is usually by direct contamination and, although the possibility of introduction of infection by flies, dogs, rats, ticks, infected boots, fodder, and other inanimate objects exists, it is not significant relative to control measures. The organism is ingested by the face fly but is rapidly eliminated and there is no evidence for a role in natural transmission (Radostitis*et al*., 2007).

The reservoirs of Brucella species comprise cattle, goats, sheep and some wildlife (Lita *et al*., 2016). The disease is transmitted to man mainly by direct contact with infected livestock and or through consumption of raw or uncooked animal products (Radostitis *et al*., 2007). Human infections may occur through breaks in the skin when handling infected animal tissues (Regea, 2017). Usually the main source of brucellosis for urban populations is ingestion of fresh milk or dairy products prepared from unheated milk. Cow, sheep, goat or camel milk contaminated with *Brucella melitensis* is particularly hazardous as it is drunk in fairly large volume and may contain large numbers of organisms (WHO, 2006). Common sources for infection are aborted fetuses, fetal membranes, and post abortion uterine discharge, all of which contain large numbers of organisms. *Brucella melitensis*is considered the most virulent species for human followed by *Brucella abortus*, and *Brucella suis*; and *Brucella canis*, *Brucella ovis* and *Brucella neotomae* do no infect humans (Walker, 1999).

People working in direct contact with infected animals: breeders, veterinarians, Artificial insemination technicians, slaughterhouse worker and rendering plant personnel are those most highly exposed to infection; and also one of the agents most often responsible for contamination in laboratories, often through aerosolisation. A few rare cases of infection were observed during handling of vaccine strains (spattering on lips or in the eye, accidental inoculation), and transmission between humans, and sexual transmission in particular has never actually been proven (“French Agency for Food, Environment and occupational Health and Safety,”2014).

Brucellosis is an infection primarily of animals that causes infertility and late-term abortion. Rarely, brucellosis occurs in humans as a zoonosis causing a broad spectrum of symptoms. The ultimate control of human brucellosis will depend on the elimination of the disease in animals; therefore human cases may act as a marker of animal disease.

Brucella bacteria are found in the blood, urine, semen, vaginal discharges, placentas, milk and aborted foetuses of infected animals. It may also be found in the saliva, and nasal, ocular and joint fluids of infected animals.

Humans usually become exposed by contact with bacteria contaminated fluids from infected animals through abraded skin or mucous membranes or by ingestion of infected animal products. In laboratories and during butchering of infected animals, *Brucella* may be transmitted in aerosols. It can also be transmitted on fomites as it withstands drying and can survive in contaminated dust and soil. Survival may be prolonged in conditions of low temperature, high humidity and no sunlight. *Brucella* species are also considered potential bioterrorism agents.

Person-to-person transmission of brucellosis is very rare. Congenital infection may occur through the placenta, during breast feeding or due to contact with the mother's blood, urine or faeces during delivery. There have also been rare reports of transmission after blood transfusions, bone marrow transplant and sexual contact.

Live animal vaccines for brucellosis are known to be pathogenic to humans however they are not currently in use in Australia.

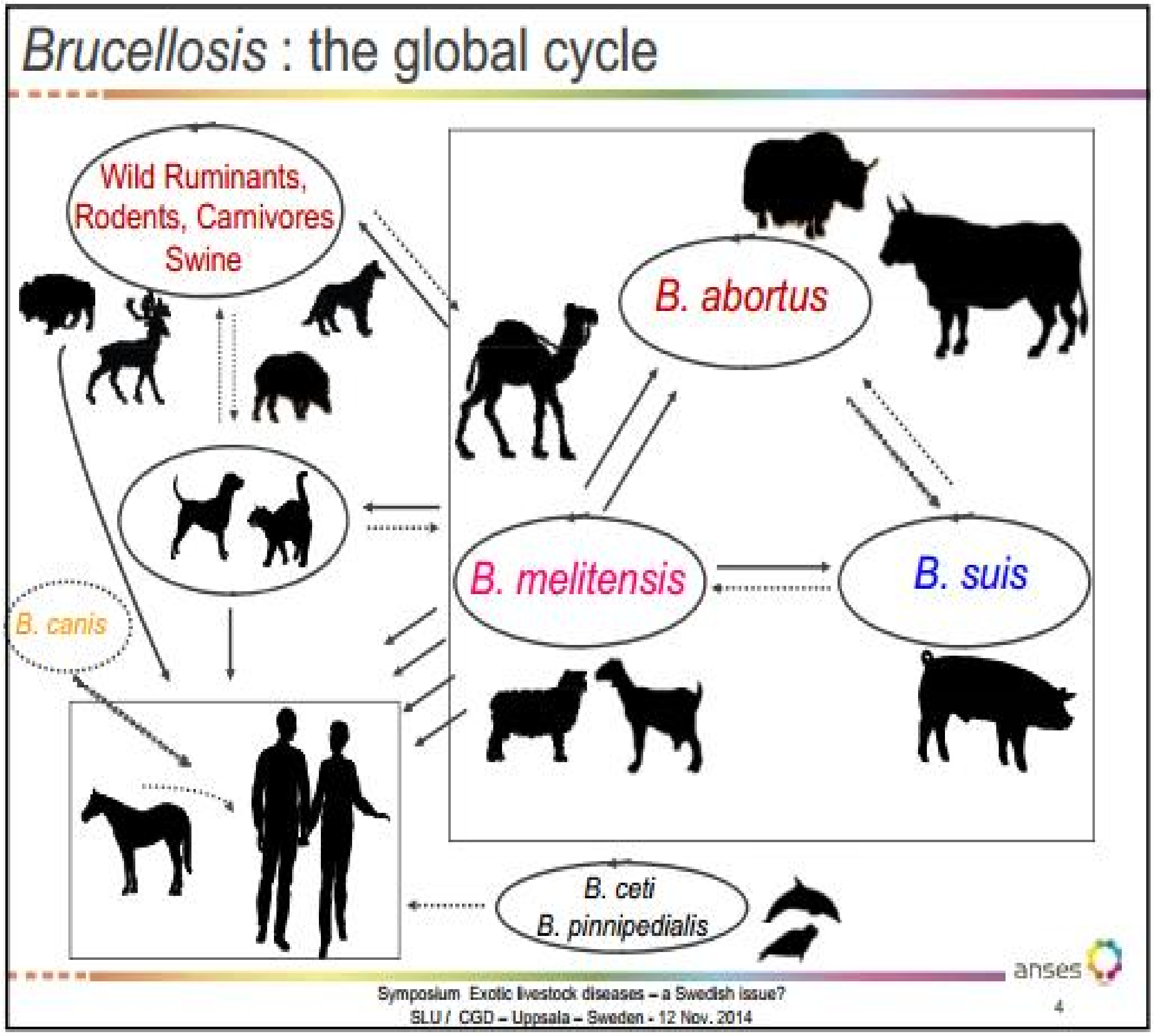


Figure 1: Transmission mode of brucellosis within its host range (Garin-Bastuji, 2014).

2.1.3Host range

According to Seifert (1996), Brucellae can be affects domestic animals such as cattle, sheep, goats, camels and pigs, and creates a serious economic problem for both the intensive and extensive livestock production systems in the tropics, and also affect wild animals, rodents, sea mammals and even fresh water fish (as cited in Degefu *et al*., 2011).

The severity of the disease depends upon many factors such as previous vaccination, age, sex and management such as herd or flock size and density. Abortions are more prevalent in unvaccinated animals and numbers of organisms shed are much greater. The bacteria are found in tissues and fluids associated with pregnancy, the udder and the lymph nodes which drain the relevant areas (World Health Organization, 2006).

Brucellosis in cattle is usually caused by biovars of *Brucella abortus*. In some countries, particularly in southern Europe and western Asia, where cattle are kept in close association with sheep or goats, infection can also be caused by *Brucella melitensis*, and occasionally, *Brucella suis* may cause a chronic infection in the mammary gland of cattle, but it has not been reported to cause abortion or spread to other animals. The disease is usually asymptomatic in non-pregnant females (OIE, 2013). Susceptibility of cattle to *Brucella abortus* infection is influenced by the age, sex, and reproductive status of the individual animal. Sexually mature, pregnant cattle are more susceptible to infection with the organism than sexually immature cattle of either sex. Abortions occur most commonly in outbreaks in unvaccinated heifers after the fifth month of pregnancy, and affected bulls shows orchitis, epididymitis, and seminal vesiculitis (Radostitis *et al*., 2007).

Small ruminant brucellosis is most commonly caused by *Brucella meltensi*, and also *Brucella ovis*is an important cause of orchitis and epididymitis in sheep but it is not recognized as a cause of natural infection in goat(Kahn, 2005).

Brucellosis has been reported in the one-humped camel (*Camelus dromedarius*) and in the two-humped camel(*Camelus bactrianus*), and in the South American camelids, llama (*Lama glama*), alpaca (*Lama pacos*), guanaco (*Lamaguinicoe*), and vicuna (*Vicugnevicugne*) related to contact with large and small ruminants infected with *Brucella abortus* or *Brucella melitensis(*OIE,2013).

Porcine brucellosis is an infection caused by biovar 1, 2 or 3 of *Brucella suis*. It occurs in many countries where pigs are raised. Generally, the prevalence is low, but in some areas, such as South America and South-East Asia, the prevalence is much higher. Porcine brucellosis may be a serious, but presently unrecognized, problem in some countries (Pérez-Sancho *et al*., 2015). The most common manifestation of brucellosis in female pigs is abortion, occurring very early or at any time during gestation (OIE,2013).

Brucellosis in horses is caused by *Brucellaabortus* or *Brucellasuis*. Suppurative bursitis, most commonly recognized as fistulous withers or poll evil, is the most common condition associated with brucellosis in horses (Kahn, 2005).

2.1.3.1 Brucellosis in Livestock

Species infecting domestic livestock are *B. abortus* (cattle, bison, and elk), *B. canis* (dogs), *B. melitensis* (goats and sheep), *B. ovis* (sheep), and *B. suis* (caribou and pigs). *Brucella* species have also been isolated from several marine mammal species (cetaceans and pinnipeds).

B. abortus is the principal cause of brucellosis in cattle. The bacteria are shed from an infected animal at or around the time of calving or abortion. Once exposed, the likelihood of an animal becoming infected is variable, depending on age, pregnancy status, and other intrinsic factors of the animal, as well as the number of bacteria to which the animal was exposed (Wyatt, H. Vivian (2014). The most common clinical signs of cattle infected with B. abortus are high incidences of abortions, arthritic joints, and retained placenta.

The two main causes for spontaneous abortion in animals are erythritol, which can promote infections in the fetus and placenta, and the lack of anti-Brucella activity in the amniotic fluid. Males can also harbor the bacteria in their reproductive tracts, namely seminal vesicles, ampullae, testicles, and epididymes

Brucella melitensis in sheep and goats represents, by far, the most important source of brucellosis in humans. This species of *Brucella* is not enzootic in the United States, Canada, northern Europe, Australasia or South East Asia. It is prevalent in Latin America, the Mediterranean area, Central Asia and, especially, in the countries around the Arabian Gulf. Humans are principally infected by the handling of parturient animals and the consumption of raw milk and milk products, especially fresh soft cheeses. In many cases the vehicle of infection is uncertain and bacteria-laden dust is suspected.

2.1.3.2 Brucellosis in Humans

The first recognized human case of brucellosis in the USA was in 1898 in an army officer who contracted the disease in Puerto Rico (Radostitis *et al*., 2007). Brucellosis remains one of the most common zoonotic diseases worldwide, with more than 500,000 human cases reported annually, particularly from developing countries (Gumi *et al*., 2013).

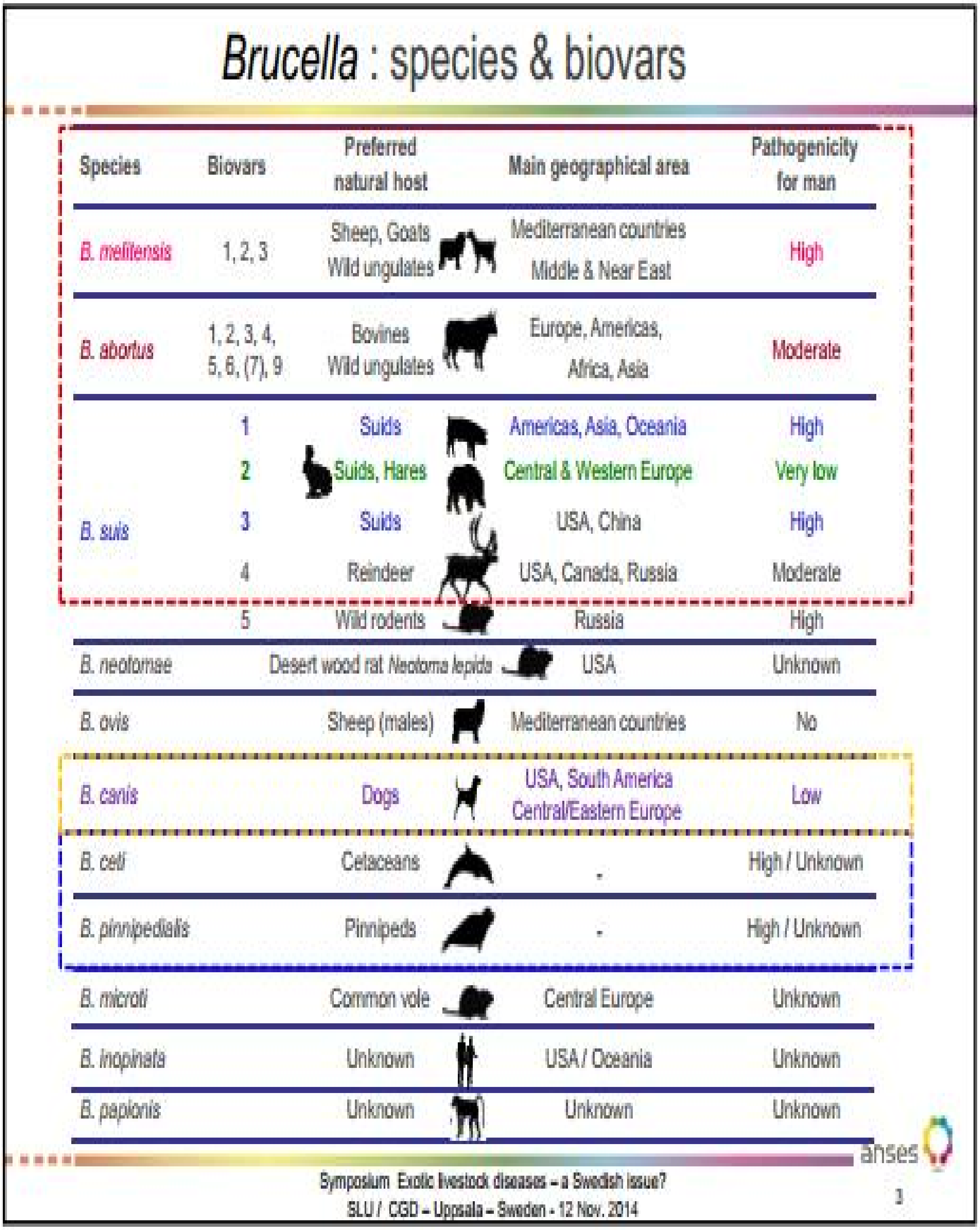
Brucellosis in human also known as “undulant fever”, “Mediterranean fever” or “Malta fever” is a zoonosis and the infection is almost invariably transmitted by direct or indirect contact with infected animals or their products. It affects people of all age groups and of both sexes. Although there has been great progress in controlling the disease in many countries, there still remain regions where the infection persists in domestic animals and, consequently, transmission to the human population frequently occurs. It is an important human disease in many parts of the world especially in the Mediterranean countries of Europe, north and east Africa, the Middle East, south and central Asia and Central and South America and yet it is often unrecognized and frequently goes unreported (WHO, 2006).

Human beings are susceptible to infection with *Brucella abortus, Brucella melitensis, Brucellasuis biovars,* and rarely *Brucella canis;* however, *B. melitensis* causes serious infection and is responsible for the most of worldwide morbidity. It is a systemic disease characterized by acute or insidious onset of continued, intermittent, undulant or irregular fever of variable duration, headache, profuse sweating, chills, weakness, generalized aching, and joint pain (Quinn *et al*., 2002).

Brucellosis is a widespread zoonosis mainly transmitted from cattle, sheep, goats, pigs and camels through direct contact with blood, placenta, fetuses or uterine secretions or through consumption of contaminate draw animal products (especially unpasteurized milk and soft cheese). In endemic areas, human brucellosis has serious public health consequences. Worldwide, Brucellamelitensisis the most prevalent species causing human brucellosis, owing in part to difficulties in immunizing free-ranging goats and sheep. In countries where eradication in animals (through vaccination and/or elimination of infected animals) is not feasible, prevention of human infection is primarily based on raising awareness, food-safety measures, occupational hygiene and laboratory safety. In most countries, brucellosis is a notifiable disease(Gumi *et al.,* 2013).

2.1.4 Geographic distribution

Occurrence of brucellosis is increasing in tropical and subtropical regions because of practices such as nomadism; communities grazing by livestock, and modern changes to wards larger animal populations and increased commerce. Importation of high producing livestock due to demands for additional animal protein and trend toward intensification of animal productionfavors the spread and transmission of the infection (Tesfaye *et al.,* 2017).Brucellosis in livestock and humans is still common in the Middle East, Asia, Africa, South and Central America, the Mediterranean Basin and the Caribbean. *Brucella melitensis* is particularly common in the Mediterranean basin, and it has also been reported from Africa, India and Mexico(CFSPH2009). Only a few world regions are brucellosis-free with regard to domestic animals (except for rare accidental outbreaks in free-range pig farms), and these regions include Northern, Central and Eastern Europe, Australia, Canada, Japan and New Zealand ("French Agency for Food, Environment and occupational Health and Safety,"2014). Also it is considered as a re-emerging problem in many countries such as Israel, Kuwait, Saudi Arabia, Brazil and Colombia, where there is an increasing incidence of *Brucella melitensis* or *Brucella suis* biovar1 infection in cattle. In Ethiopia, brucellosis is endemic and the disease is highly prevalent in cattle, camels and small ruminants in pastoral and agro-pastoral areas (Regea, 2017).



Brucella : species & biovars

Species	Biovars	Preferred natural host	Main geographical area	Pathogenicity for man
B. melitensis	1, 2, 3	Sheep, Goats Wild ungulates	Mediterranean countries Middle & Near East	High
B. abortus	1, 2, 3, 4, 5, 6, (7), 9	Bovines Wild ungulates	Europe, Americas, Africa, Asia	Moderate
B. suis	1	Suids	Americas, Asia, Oceania	High
	2	Suids, Hares	Central & Western Europe	Very low
	3	Suids	USA, China	High
	4	Reindeer	USA, Canada, Russia	Moderate
	5	Wild rodents	Russia	High
B. neotomae		Desert wood rat *Neotoma lepida*	USA	Unknown
B. ovis		Sheep (males)	Mediterranean countries	No
B. canis		Dogs	USA, South America Central/Eastern Europe	Low
B. ceti		Cetaceans	-	High / Unknown
B. pinnipedialis		Pinnipeds	-	High / Unknown
B. microti		Common vole	Central Europe	Unknown
B. inopinata		Unknown	USA / Oceania	Unknown
B. papionis		Unknown	Unknown	Unknown

Figure 2: Geographical distribution of Brucella species (Garin-Bastuji, 2014).

2.1.5 Risk Factors

Animal risk factors: Susceptibility of cattle to B. abortus infection is influenced by the age, sex and reproductive status of the individual animal. Sexually mature pregnant cattle are more susceptible to infection with the organism than sexually immature cattle of either sex. Susceptibility increases as stage of gestation increases(Radostits*et al*,2006).

Pathogen risk factor: B. abortus is a facultative intracellular organism capable of multiplication and survival within the host phagosome. The organisms are phagocytised by poly morphonuclar leucocytes in which some survive and multiply. The organism is able to survive within macrophages because; it has the ability to survive phagolysosome. The bacterium possesses an unconvenential non-endotoxin lipopolysaccaride, which confers resistance to antimicrobial attacks and modulates the host immune response. These properties make lipopolysaccharide an important virulence factor for Brucella survival and replication in the host(Radostits*et al*, 2006).

Occupational risk factors: Laboratory workers handling Brucella cultures are at high risk of acquiring brucellosis trough accidents, aresolization and/or inadequate laboratory procedures. In addition to this, abattoir workers, farmers and veterinarians are at high risk of acquiring the infection(Colibaliy&Yamego, 2000).

Managemental risk factors: The spread of the disease from one herd to the other and from one area to another is almost always due to the movement of an infected animal from infected herd in to a non-infected susceptible herd. A case-control study of brucellosis in Canada indicates that, herds located close to other infected herds and those herds whose owners made frequent purchase of cattle had an increased risk of acquiring brucellosis. Once infected, the time required to become free of brucellosis was increased by large herd size, active abortion and by loss housing(Radostits*et al*, 2006).

2.1.6Pathogenesis

Invading Brucella usually localize in the lymph nodes, draining the invasion site, resulting in hyperplasia of lymphoid and reticulo-endothelial tissue and the infiltration of inflammatory cells. Survival of the first line of defense by the bacteria results in local infection and the escape of Brucella from the lymph nodes in to the blood. During bacteraemic phase, bones, joints, eyes and brain can be infected, but the bacteria are most frequently isolated from supra-mammary lymph nodes, milk, iliac lymph nodes, spleen and uterus. In bulls, the predilection sites for infection are also the reproductive organs and the associated lymph nodes. During the acute phase of infection, the semen contains large number of Brucella but as the infection becomes chronic, the number of Brucella excreted decreases. However, it may also continue to be excreted for years or just become intermittent (Acha&Szyfres, 2001).After the Brucella organisms spread through the hematogenous route in females then also reach the placenta and finally to the fetus. The preferential localization to the reproductive tract of the pregnant animal is due to the presence of the allantoic fluid factors that would stimulate the growth of Brucella. Erythritol (four-carbon alcohol) is considered to be one of the factors, which are elevated in the placenta and fetal fluid from about the fifth month of gestation. An initial localization within erythrophagostictrophoblsates of the placentome adjacent to chorio-allntoic membrane results in rupture of the cells and ulceration of the membrane. The damage to placental tissue together with foetal infection and foetal stress inducing maternal hormonal changes may cause abortion (Radostits*et al*., 2000).

B. abortus has predilection in the pregnant uterus, udder, testicle and accessory male sex glands, lymphnodes, joint capsule and bursa. After initial invasion of the body, localization occurs initially in the lymph nodes. B. abortus is phogocytized by macrophages and neutrophils in an effort by the host to eliminate the organism. However, once inside phagocyte, B. abortus is able to survive and replicate. The phagocyte migrates via the lymphatic system to the draining lymph node where Brucella infection causes cell lysis and eventual lymph node hemorrhage 2-3 weeks following exposure. Because of vascular injury some of the bacteria inter to the blood streams and subsequent bacteremia occurs, which disseminates the pathogen throughout the body. If the infected animals are pregnant, B. abortus will colonize and replicate in high number in the chronic trophoblasts ofthe developing fetus. The resulting tissue necrosis of the fetal membrane follows transmission of bacteria to the fetus. The net effect of chorionic and fetal colonization is abortion during the last trimester of pregnancy. In fetus, naturally and experimentally infected with B. abortus, the tissue changes include lymphoid hyperplasia in multiple lymph nodes, lymphoid depletion in thymic cortex, adrenal cortical hyperplasia and disseminated inflammatory foci composed mainly of large mononuclear leukocytes. In cattle abortion occurs principally in the last three months of pregnancy, while in dogs occur around 50 days of gestation. Abortion in swine can occur at any time in gestation(Radostits *et al.,* 2006).

2.1.7 Clinical Sign

Clinical findings of brucellosis such as fever, headache, back pain, sweats, malaise, and anorexia are usually non-specific. The onset of clinical manifestations can be insidious or acute, beginning within 2 to 4 weeks following infection. Compared with the symptoms, there are often few signs in the physical examination (Jundishapur J Microbiol. 2011). Mild lymph-adenopathy and splenomegaly or hepatomegaly may be seen in a portion of patients (BMC Infect Dis. 2003). Recurrence of symptoms after therapy may or may not be associated with relapse of the disease. Bacteriologic relapse usually appears within 3 to 6 months after discontinuing drug treatment and is not usually caused by antibiotic resistance (Antimicrob Agents Chemother. 1986). In chronic brucellosis, symptoms can recur after a long period of time and are associated with fever which is one of the most objective signs of infection. An important laboratory finding is the persistence of high titers of IgG antibodies (BMC Infect Dis. 2003). In some patients persistent nonspecific symptoms may be seen without elevated titers of IgG. The reason for this condition is not clear, but some investigators believe that it may be due to exacerbation of pre-existing psychoneurosis by the infection(Rev Infect Dis. 1991).

2.1.7.1 Clinical Sign in Animals

In some cases patients with brucellosis present with a range of complications. The most important complications of brucellosis (Wiley; 2005) are as follows; gastrointestinal symptoms - anorexia, nausea, vomiting, pain, diarrhea, and constipation, which are observed in 70% of brucellosis cases. Hepatobiliary system; hepatic involvement is common in brucellosis. Skeletal complications; osteoarticular complications are the most common focal forms of the disease and have been reported in 10% to 80% of cases depending on the series, the ages of the patients, and the infecting Brucella spp. Nervous system; depression and lack of concentration are common symptoms in brucellosis, however direct invasion of the central nervous system occurs in less than 5% of cases. Neurological syndromes in brucellosis include; meningitis, encephalitis, myelitis-radiculoneuronitis, brain abscess, epidural abscess, granuloma, and demyelization and meningo-vascular syndromes (Wiley,2005).

Cardiovascular involvement; endocarditis occurs in less than 2% of cases, but it accounts for the majority of brucellosis-related deaths. Genitourinary complications; interstitial nephritis, pyelonephritis, glomerulonephritis, and immunoglobulin nephropathy have been reported.

Epididymo-orchitis occurs in up to 10% of men with brucellosis (Harrison’s principles of internal medicine 16th ed. 2005). Hematological complications; hematologic manifestations of brucellosis include anemia, leukope-nia, thrombocytopenia, and clotting disorders. Ocular complications; uveitis is generally a late complication, consisting variably of chronic iridocyclitis, nummular keratitis, multi focal choroiditis, and optic neuritis (PLoS Med. 2007).

In highly susceptible non vaccinated pregnant cow, abortion occurs after the 5thmonths of pregnancy; in bull, orchitis and epididmytis are cardinal signs. In case of horse, it is usually associated B.abortus with chronic bursal enlargement of the neck and withers, and abortion in mares. Brucellosis in swine has acute symptoms like abortion, infertility and birth of weak piglets, orchitis, epididymitis and arthritis. Sheep and goats have similar to that observed in other species of animals. Abortion in goats occurs most frequently in the third or fourth months of pregnancy. In case of dog and cats, infertility either in male or female, abortion and still birth or weak puppies are common manifestations (Radostits et al., 2006).

2.1.7.2 Clinical Signs in Humans

The most common symptoms of brucellosis include undulant fever in which the temperature can vary from 37.8^0c in the morning to 40^0c in the afternoon; night sweets with peculiar odder and weakness. Common symptoms also include insomnia, anorexia, headache, constipation, sexual impotence, nervousness, encephalitis, spondilitis, arthritis, endocarditis, orchitis and depression. Spontaneous abortion mostly in the first and second trimesters of pregnancy, are seen in pregnant women infected with Brucella. Lack of appropriate therapy during the acute phases may result in localization of Brucella in various tissues and organs and lead to sub -acute or chronic disease which is very hard to treat(Mantur&Mangalgi2007).

2.2Diagnosis

Diagnosis of brucellosis is based on clinical findings (nonspecific), history (including occupation, travel to an endemic area and ingestion of unpasteurized dairy products) and laboratory tests such as serology or bacterial isolation. Although modern diagnostic techniques such as nucleic acid amplification have been introduced, they are not yet widely available especially in areas with restricted resources. Blood and tissue based polymerase chain reactions (PCR) can detect brucellosis, although PCR is more sensitive and quicker than blood culture (Harrisons principles of internal medicine 16th ed. 2005).

Diagnosis of brucellosis is the corner stone of any control and eradication programmes of the disease. Especially in humans due to its heterogeneous and poorly specific clinical symptoms, the diagnosis of brucellosis always requires laboratory conformation. It is made possible by direct demonstration of the causal organism using staining, immunoflorecent antibody, culture, and directly demonstration of antibodies using serological techniques (Walker, 1999).

For the diagnosis of brucellosis, the organism may be recovered from a variety of materials which usually depends on the presenting clinical signs (OIE, 2009). In animals, the placenta is the most infective and contains the greatest concentration of bacteria; this is followed by the lymph nodes and milk; and from blood in humans (Poiester et al., 2010). Furthermore, other materials rich in the organism include: Stomach contents, spleen and lungs from aborted foetuses, vaginal swabs, semen, and arthritis or hygroma fluids from adult animals. From animal carcasses, the preferred tissues for culture are the mammary gland, supramammary, medial and internal iliac, retropharyngeal, parotid and prescapular lymph nodes and spleen (OIE, 2009; Ahmed *et al*., 2010). All specimens must be packed separately, cooled and transported immediately to the laboratory in leak proof containers. For humans, blood for culture is the material of choice, but specimens need to be obtained early in the disease. The samples should be frozen until required for culture (OIE, 2009). There is no ideal tissue for the isolation of Brucella from marine mammals, unlessgrosslesions are found in the tissues. However, the recommended tissues for the recovery of Brucella in marine mammals are the spleen, the mammary gland, the mandibular, gastric, external and internal iliac and colorectal lymph nodes, the testes and blood (Foster *et al*., 2002).

A definite diagnosis requires the isolation of brucellae from the blood, bone marrow or other tissues (Wiley; 2005). How-ever, cultural examinations are time consuming, hazardous and not sensitive. Thus, clinicians often rely on indirect proof of infection.
A variety of serological tests have been developed, but at least two serological tests should be combined to con-firm an active infection. Usually, the standard tube agglutination (STA) test (Wright) is used first and the 2mercap-toetanole (2ME) test will confirm its results (with 97.1% sensitivity and 100% specificity) (Jundishapur, 2011). In the absence of a bacteriologic examination an initial diagnosis is made by showing high titers of IgG- antibodies against Brucella in the serum. (Jundishapur,2011). According to the National Program against Brucellosis (NPB) diagnosis is based on serological tests (Wright > 1/80 and 2 ME > 1/20) in the presence of clinical findings suggestive of brucellosis (Ghasemi, 2008). Other techniques such as polymerase chain reaction (PCR) have been used to diagnose brucellosis (Wiley, 2005). Khosravi*et al*, (2006). reported that the high degree of sensitivity of a PCR assay, together with its speed, versatility in sample handling, and risk reduction for laboratory personnel, make this technique a very useful tool for the diagnosis of brucellosis, compared with conventional culture method (Pak, 2006).

2.2.1 Culture Technique and Microscopic Examination

Specimen of fetal stomach, lung, liver, placenta, cotyledon and vaginal discharges are stained with Gram stain and modified ZiehlNeelsen stains. Brucella appears as small red-colored, coccobacili in clumps. Blood or bone marrow samples can be taken cultured in 5-10% blood agar is used .To check up bacterial and fungal contamination; Brucella selective media are often used. The selective media are nutritive media, blood agar based with 5% seronegative equine or bovine serum. On primary isolation it usually requires the addition of 5 -10% carbon dioxide and takes 3-5 days incubation at 37c^{o}for visible colonies to appear(Maquire, 2002).

Marin et al. (1996) reported that a presumptive bacteriological diagnosis of Brucellacan be made by means of the microscopic examination of smears from vaginal swabs, placentas or aborted foetuses, stained with the Stamp modification of the Ziehl-Neelsen staining method. However, morphologically-related micro-orga-nisms, such as Chlamydophilaabortus, Chlamydia psittaci and Coxiellaburnettican mislead the diagnosis because of their superficial similarity (Marin et al., 1996; Poiester*et al*., 2010). Accordingly, the isolation of B. melitensis on appropriate culture media such as Farrell's selective media is recommended for an accurate diagnosis (Farrell, 1974). Vaginal swabs and milk samples are the best samples to use in isoating B. melitensis from sheep and goats (Marin *et al.*, 1996).

Guinea pigs are the most sensitive laboratory animals. Two guinea pigs are intramuscularly inoculated 0.5-1ml of suspected tissue homogenate and sacrificed at three and six weeks post inoculation and serum is taken along with spleen and other abnormal tissue for serology and bacteriological examination, respectively (Maquire, 2002).

2.2.2 Serological Examination

Body fluids such as serum, uterine discharge, vaginal mucus, milk, or semen plasma from a suspected animal may contain different quantities of antibodies of the M, G1, G2, and A isotypes directed against Brucella(Beh, 1974). Infected animals may not always produce all antibody isotypes in detectable quantities; therefore, results from several serological tests should be used as a presumptive evidence of infection (FAO, 2005). In addition, depending on the sensitivity and specificity, serological tests can be used to screen for, or confirm brucellosis.

Traditionally, screening tests are inexpensive, fast and highly sensitive, but most of the time, lack specificity. However, confirmatory tests are required to be both sensitive and specific, thereby eliminating some false positive reactions. Most confirmatory tests are more complicated and more expensive to perform than the screening tests (Diaz et al., 2011). The commonly used serological tests include milk ring test (MRT), serum agglutination test (SAT), standard plate agglutination test (SPAT), complement fixation test (CFT), 2-mercapto-ethanol test (2-MET), buffered antigen test (BPAT), and rose Bengal plate test (RBPT). Others include the card test (CARD), Rivanol test, Coombs test, indirect immune-flourescent test (IFAT), heat inactivation test (HIT), skin test, immune-assay and molecular biology technique(Beh, 1974).

Milk Ring Test (Mrt)

The MRT is basically a rapid agglutination test carried out on whole milk or cream. Haematoxylin stained Brucella cells are added to whole milk and incubated for reaction to take place (McCaughey, 1972; Hubber and Nicoletti, 1986). Immunoglobulins present in the milk will, in part, be attached to fat globules via the Fc portion of the fat molecule (Poiesteret al., 2010). The immunoglobulinsdetected by MRT areIgM and IgA. This test may be applied to individual animals or to pooled milk samples using a larger volume of milk, relative to the pool size (MacMillan et al., 1990). The milk ring test is prone to false reactions caused by abnormal milk due to mastitis, presence of colostrum and milk from the late lactation (Al-Maririand Haj-Mahmoud, 2010). False negatives may also occur in milk with a low concentration of lacteal antibodies or lacking fat-clustering factors (Bercovich, 1998). In spite of these problems, the MRT has been found to be extremely effective, and is usually the method of choice in dairy herds, and may be used as an inexpensive screening test in conjunction with other tests (Corbel, 2006).

Serum Agglutination Test

This test is based on the reactivity of antibodies against the smooth lipopolysaccharide of Brucella. Excess of antibodies resulting in false negative reaction due to prozone effect can be overcome by applying a serial dilution of 1:2 through 1:64 of the serum samples thus increasing the test specificity (Afify et al., 2013). The test is performed at a near neutral pH, which makes it more efficient in detecting IgM antibody. Hence, it is best used to detect acute infections. It is less effective for IgG, resulting in low assay specificity (Corbel, 1972; Nielsen et al., 1984). Due to this fact, the SAT, despite being sensitive, is generally not used as a single test, but rather it is used in combination with other tests. Other short comings of the test include false positive and false negative results (Poiester et al., 2010). For this reason, the test is only suitable for herd testing, rather than for testing individual animals.

Rose Bengal Plate Test (RBPT)

The RBPT is a spot agglutination technique which is also known as the card test or buffered Brucella antigen test (Stemshorn et al., 1985). It uses a suspension of B. abortus smooth cells stained with the Rose Bengal dye, buffered to pH 3.65. At neutral pH, this test can measure the presence of IgM, IgG1 and IgG2. However, IgM appears to be the most active. At the buffered pH of 3.65, RBPT, prevents agglutination with IgM, and apparently, measures only IgG1 (Corbel, 1972). It was considered that while the test gave few false negative results, it gave many false positives, possibly due, in significant part, to reaction with IgM in animals with previous vaccination. In situations where vaccination is not routinely conducted, the use of this test can give a good record of exposure of animals to Brucella organisms.

It is an internationally recommended test for the screening of brucellosis in small ruminants, but lacks standardization of the antigen. Low pH of the antigen enhances the specificity of the test, while the temperature of the antigen and the ambient temperature at which the reaction takes place may influence the sensitivity and specificity of the test (Alton, 1981; Macmillan *et al*., 1990). Corbel (1972) observed that the sensitivity of the test was associated with fractions containing immuno-globulinIgG, especially the IgG1.

Complement Fixation Test (CFT)

The CFT detects mainly the IgG1isotype antibody, as the IgMisotypes are partially destroyed during the inactivation process. Since antibodies of the IgG1 type usually appear after antibodies of the IgM type, control and surveillance of this disease is best done with SAT and CFT (WHO/MZCP, 1998). The test shows good correlations with the recovery of Brucella organisms from artificial recovery or naturally-infected animals (Madsen, 1994).Although the test is fast and accurate, it does not allow for discrimination between antibodies due to infection from vaccinal antibodies (Nielsen, 2002; Poiester*et al*., 2010). Other problems include large number of reagents and controls needed to carry out the test. Furthermore, each time the assay is set up, a large number of titrations are needed, and interpretation of the results is subjective due to differences in techniques (Madsen, 1994). Occasionally, there is direct activation of complement by serum (anti-complementary activity) and the inability of the test to be amenable for use with haemolysed serum samples. The laborious nature of this test and the requirement of highly- trained personnel and suitable laboratory facilities make the CFT less suitable for use in developing countries (FAO, 2005). The CFT may also test false negative, when antibodies of the IgG2 type hinder complement fixation (Nielsen et al., 1988; MacMillan et al., 1990). Despite these inherent problems, the CFT is a widely used test, and has been regarded as the most specific and accepted serological test for diagnosis of brucellosis. Thus, it is a recommended test for international trade (OIE, 2009).

Enzyme-Linked Immune Sorbent Assay (ELISA)

The ELISA tests offer excellent sensitivity and specificity whilst being robust, fairly simple to perform with a minimum of equipment and readily available from a number of commercial sources in kit form. They are more suitable than the CFT for use in smaller laboratories and ELISA technology is now used for diagnosis of a wide range of animal and human diseases. Although in principle ELISAs can be used for the tests of serum from all species of animal and man, results may vary between laboratories depending on the exact methodology used. Not all standardization issues have yet been fully addressed. For screening, the test is generally carried out at a single dilution. It should be noted, however, that although the ELISAs are more sensitive than the RBPT, sometimes they do not detect infected animals which are RBPT positive. It is also important to note that ELISAs are only marginally more specific than RBPT or CFT (WHO, 1997). There are also other serological diagnostic tests that use for diagnosis of brucellosis such as SAT, PCR, and so on (Epameinondas, 2005).

2.2.3 Differential Diagnosis

The diagnosis of the cause of abortion in a single animal or in a group of cattle is difficult because of the multiplicity of causes that may be involved. When an abortion problem is under investigation, a systemic approach should be used. This includes a complete laboratory evaluation and follow-up inquiries into each herd. The following procedure is recommended:

- Ascertain the age of the fetus by inspection and from the breeding records
- Take blood samples for serological tests for brucellosis and leptospirosis
- Examine uterine fluids and the contents of the fetal abomasum at the earliest opportunity for trichomonads, and subsequently by cultural methods for B. abortus, Campylobacter fetus, trichomonads, Listeria spp., and fungi
- Supplement these tests by examination of urine for leptospires, and of the placenta or uterine fluid for bacteria and fungi, especially if the fetus is not available
- Examine placenta fixed in formalin for evidence of placentitis.

In the early stages of the investigation, the herd history may be of value in suggesting the possible etiological agent. For example, in brucellosis, abortion at 6 months or later is the major complaint, whereas in trichomoniasis and vibriosis, failure to conceive and prolongation of the diestrual period is the usualhistory(Microbiol, 2005).

The protean character of this disease makes it difficult to differentiate. Syndromes that need differentiation include:

- Abortion and infertility in sows
- Posterior paresis diseases of spinal cord
- Mortality in young pigs is also caused by many agents and the important entities are listed under disease of the newborn. ETEC is the most common cause of PWD in pigs. This pathotype is characterized by the production of enterotoxins and adhesins, both essential for disease development. Enterotoxins produced by ETEC may be heat stable [STa, STb, or enteroaggregative E. coli heat stable enterotoxin 1 (EAST1)] or heat labile (LT). Enterotoxin genes are on plasmids of ETEC bacteria and act on the intestinal epithelium of pigs.Thecritically ill neonates depends on many factors, including the nature and severity of the disease, facilities available for care and the expertise of the personnel caring for the neonate(Amezcua,*etal*2002).

Many rams with abnormalities of intrascrotal tissues do not have brucellosis(Genetzky, 1995). Most are cases of epididymitis and need to be differentiatedwithBorder disease, Salmonellosis, Toxoplasmosis, etc.Abortion in ewes may be associated with a number of infectious diseases. Some of the diseases that need to be differentiated with animal brucellosis are summarized as;

- Leptospirosis
- Infectious bovine rhino-tracheitis
- Mycoses
- Trichomonosis
- Neosporosis
- Vibriosis
- Epizootic bovine abortion
- Bovine virus diarrhea
- Enzootic abortion of ewes
- Salmonellosis
- Toxoplasmosis
- Rift Valley fever
- Tick borne fever2

The signs and symptoms of brucellosis can be nonspecific and can mimic those of many other diseases; therefore, meticulous attention is needed in making the diagnosis and in treating patients. The primary diagnostic pitfall is failu re to consider possible *Brucella* infection in a patient with history that suggests a possible source of infection (eg, a farmer, a traveler to an endemic region, or a veterinarian).

2.2.4 Necropsy Finding

In the acute stage, there is inflammatory edema in the loose scrotal fascia, exudate in the tunica vaginalis and early granulation tissue formation. In the chronic stage, the tunics of the testes become thickened and fibrous and develop adhesions. There are circumscribed indurations in the epididymis and these granulomata may also be present in the testicle. In advanced stages they undergo caseation necrosis. As the epididymis enlarges the testicle becomes atrophied. B. avis can usually be isolated from the genital organs, especially the tail of the epididymis, and rarely from internal organs and lymph nodes.

The abortus is characterized by thickening and edema, sometimes restricted to only a part of the placenta, with firm, elevated yellow-white plaques in the inter cotyledonary areas and varying degrees of cotyledonary necrosis. Microscopically, organisms are visible within the cytoplasm of trophoblasts of the inflamed placenta. A vasculitis is often present. The organism can be isolated from the placenta and the stomach and lungs of the lamb

Samples for confirmation of diagnosis

Bacteriology -epididymal granuloma, seminal vesicle, inguinal lymph node/fetal lung, stomach content, placenta (CULT -has special growth requirements, CYTO -Stamp's Or Kosters'stain on placental smear)
Histology -formalin-fixed epididymis, testicle, inguinal lymph node/placenta, fetal lung, liver, spleen, kidney, heart, brain

Necrotizing placentitis and disseminated inflammatory reactions in aborted fetal tissues are the characteristic changes. Adult animals are seldom necropsied. Findings in bovine fetuses infected with B. abortus usually include serohemorrhagic fluid in the body cavities and subcutis, and apneumonia. Often granulomatous lesions and focal necrosis are noted in several fetal organs and a granulomatous leptomeningitis may also occur. Pneumonia is not a consistent finding and its character may vary. The placenta is usually edematous. There may be leathery plaques on the external surface of the chorion and there is necrosis of the cotyledons. The key microscopi c feature of this inflamedchorioallantois is the presenc e of intra cytoplasmic coccobacilli within chorionic tro phoblasts (Searson1986).

2.3Treatment

Brucellosis is treated with antibiotics, although the most effectiveantibiotic regimens and treatment durations are unclear (Cisneros1990; Karabay 2004). There are some limitations in choosingthe best regimen: there is a limited choice of antibiotics that actintracellularly (eg doxycycline and streptomycin) (Agalar 1999); and the prolonged treatment needed to prevent relapse may increase the occurrence of adverse events (including gastric discomfort, hepatotoxicity (liver toxicity), nephrotoxicity (kidney toxic-ity), and allergic reactions) and reduce adherence to the treatment. Regimens that combine two or more antibiotics are now recommended by most experts due to high relapse rates with treatmentwith one type of antibiotic (monotherapy) (Agalar 1999; Pappas2005b). 'In 1971, the World Health Organization (WHO) suggested a 21-day regimen of tetracycline this regimen was successful in reducing the early symptoms, it failed totreat the disease completely, and immediate relapses were seen insome patients (Ariza 1985; Cisneros 1990). Accordingly, in 1986the Joint Food and Agriculture Organization of the United Nations (FAO)/World Health Organization (WHO) Expert Committee on Brucellosis proposed two new regimens: rifampicin (600to 900 mg/day orally) plus doxycycline (200 mg/day orally) forsix weeks; and doxycycline (100 mg/day orally) for 45 days plusstreptomycin (1 g/day intramuscularly) for two to three weeks(WHO 1986). The rifampicin−doxycycline regimen is the mostpopular treatment, possibly because it is cheap and easily available(Pappas 2005b), while streptomycin requires parenteral administration in a hospital setting or in an appropriately set-up primarycare network, both of which are restricted in lower income countries (Pappas 2005a). The above-mentioned combinations werereplicated in the 2006 WHO recommendations (WHO 2006).Other antibiotic formulations, including quinolones (e.g. ciprofloxacin and ofloxacin) and trimethoprim/sulfamethoxazole (co-trimoxazole), have been used (Pappas 2005b; WHO 2006). However, questions remain about their effectiveness (Pappas 2006;WHO 2006).

Treatment protocols may differ in children less than eight yearsand pregnant women because of adverse effects of some medications including inhibition of bone growth due to tetracycline treatment in children and teratogenic potential of some drugs, such asStreptomycin (WHO 2006).

Treatment is unsuccessful because of the intracellular sequestration of the organisms in lymph nodes, the mammary gland, and reproductive organs and the bacteria are facultative intracellular bacteria that can survive and multiply within the cells of the macrophage system. Treatment failures are considered to be due not to the development of antimicrobial resistance but rather to the inability of the drug to penetrate the cell membrane barrier (Radostitis*et al*.,2007). Though the complex nature of brucellosis makes it harder to treat, long-term treatment with an antibiotic is thought to be beneficial. In most cases, antibiotics in combination are found to be more effective against the infection; however, the state of the disease still does not lose its importance. Several conventional antibiotics including tetracycline, trimeth oprim sulfamethoxazole, aminoglycosides, rifampicin, quinolones, chloramphenicol, doxycycline, and strept omycin are commonly used in clinics. In several cases, the application of antibiotics in a specific order has given best results. Likewise, a case reported that treatment with doxycycline for six months, followed by streptomycin for three weeks was found very effective against brucellosis in human.

Due to the intracellular localization of Brucella and its ability to adapt to the environmental conditions encountered in its replicative niche e.g. macrophage (Seleem et al., 2008), treatment of domestic animals with antibiotics is not usually successful. Even though, treatment failure and relapse rates are also high in humans, treatment depend on the drug combination of doxycycline with streptomycin which is currently the best therapeutic option with less side effects and less relapses, especially in cases of acute and localized forms of brucellosis (Seleem*et al*., 2009). Neither streptomycin nor doxycycline alone can prevent multiplication of intracellular Brucella (Shasha*et al*., 1994). Although the doxycycline streptomycine regimen is considered as the golden standard treatment, it is less practical because the streptomycin must be administered parentrally for 3 weeks. A combination of doxycycline treatment (6 weeks duration) with parentrally administered gentamicin (5 mg/kg) for 7 days is also considered an acceptable alternate regimen (Glynn & Lynn, 2008).

Measures to prevent and control brucellosis rely upon direct approaches, aimed at minimizing the risk of spreading infection among animals. Collectively, these measures reduce the exposure of animals to *Brucella*species, and increase resistance to infection in susceptible animals(Adone and Pasquali, 2013).

Approaches at Control and Prevention of brucellosis depend on the animal species involved, Brucella species, management practices, and availability and efficacy of vaccines. Approaches used to brucellosis includes 1) immunization alone 2) testing and removing of infected animals in conjunction with an immunization program, and 3) testing and removing of infected animals without immunization(Walker,1999).

2.4Prevention and Control Strategies

As the ultimate source infected animals or their products, prevention must be based on elimination of human brucellosis is direct or indirect exposure to of such contact (WHO, 2006). In addition, prevention of human brucellosis depends mainly on programmes to control and eradicate the disease in farm animals in order to reduce the prevalence of infection in herds through implementation of health control and/or medical measures (animal vaccination), and when possible to attain eradication of the disease, initially farm by farm, and then on a regional and national level ("FAF, EOHS"2014). Every case of human brucellosis is directly or indirectly linked with infected animals or their products. So, the control of human brucellosis depends on minimizing/ controlling disease burden in animals and reducing animal to human transmission (Zinsstag et al., 2011).

Methods of prevention include health education to reduce occupational and food-borne risks, including pasteurization of all dairy products. However, education campaigns have never resulted in fully eliminating the risks of infection, and the ultimate prevention of human infection remains elimination of the infection among animals (Regea, 2017).

The control of the disease in humans is impaired by the lack of available vaccines, thus leaving the control of animal brucellosis as the most effective strategy to prevent human infection (Pérez-Sancho et al., 2015). In many situations there is little alternative but to attempt to minimize impact of the disease and to reduce the risk of infection by personal hygiene, adoption of safe working practices, protection of the environment and food hygiene (World Health Organization, 2006). To lower your risk of getting brucellosis from a natural source: Avoid eating or drinking unpasteurized milk, cheese, or ice cream (including queso fresco), uncooked meat thoroughly, and use disinfects in the area where the animals are aborted (Regea, 2017).

Application of vaccines in the control and eradication of brucellosis in humans has shown unsatisfactory results. The use of live vaccines has often provoked unacceptable reactions in individuals. The recent attempt of developing analogue mutants of another Brucella species and the use of Brucella nucleic acid in the production of animal and human vaccines offers hope in the control of the disease (Shirima, 2005).

Vaccination of young heifers, a strategic measure during the early years of eradication schemes, is discontinued when the prevalence of brucellosis reaches low levels that result to predominantly cell-mediated immunity. Three types of vaccines are used in cattle attenuated strain 19(S19) vaccine, adjuvanted 45/20 vaccine and the more recent RB51 vaccine:

1. S19 vaccine is administered to female calves up to 5 months of age, and vaccination of mature animals leads to persistent antibody titres.
2. 45/20 bacterin, although less effective, has been is some national eradication schemes, and even when administered to adult animal, the vaccine does not induce persistent antibody titres
3. RB51 strain is stable, rough mutants who induce good protection against abortion and does not result persistent antibody titres (Quinn *et al*., 2002).

For brucellosis prevention, the following measures can be used as alternatives, it includes:

- Careful selection of replacement animals. These, whether purchased or produced from existing stock, should originate from *Brucella*-free herds or flocks. Pre-purchase tests are necessary unless the replacements are from populations in geographically circumscribed areas that are known to be free of the disease.
- Isolation of purchased replacements for at least 30 days and in addition a serological test prior to commingling is necessary.
- Prevention of contacts and commingling with herds or flocks of unknown status or those with brucellosis.
- If possible, laboratory assistance should be utilized to diagnose causation of abortions, premature births, or other clinical signs. Suspect animals should be isolated until a diagnosis can be made.

- Herds and flocks should be included in surveillance measures such as periodic milk ring tests in cattle (at least four times per year), and testing of slaughtered animals with simple screening serological procedures such as the RBT.
- Proper disposal (burial or burning) of placentas and non-viable fetuses, and disinfection of contaminated areas should be performed thoroughly(WHO,2006).

3 Conclusion and Recommendation

Brucellosis is one of the most widespread zoonoses, mainly caused by *Brucellaabortus*, *Brucella melitensis* or *Brucella suis*, and is transmitted to people from various animal species that mainly by direct contact with infected livestock or through consumption of raw or uncooked animal products. In human, Brucellosis is always caused by *B. melitensis*(cause Undulant or Malta fever) followed by *B. suis*, *B. abortus* and *B. canis*, and it causes a systemic infection with clinical manifestations as fever, sweats, fatigue and joint pain .

The disease primarily affect cattle, buffalo, bison, pigs, goats, sheep ,dogs, elk, camels and occasional horses, and it can be late abortion, retained foetal membranes, and to a lesser extent, orchitis and infection of the accessory sex glands in males and impaired fertility. Aborted fetuses, placental membranes or fluids, and other vaginal discharges present after an infected animal has aborted or calved are all highly contaminated with infectious *Brucella* organisms. It causes considerable economic losses in livestock production due to abortion, infertility and reduction in milk production, and in addition, the zoonotic nature of the disease has a serious impact on public health.

Since people working in direct contact with infected animals: breeders, veterinarians, artificial insemination technicians, slaughterhouse worker, laboratories worker and rendering plant personnel are those most highly exposed to infection; these people must be awareness on transmission of disease. Education of people in order to avoid consuming unpasteurized milk and milk derivatives, and careful handling and disposal of afterbirths, especially in cases of abortion is important.

Small discussion groups and lectures are extremely useful means of communication and could be followed immediately by such actions as formation of action committees or even by collection of diagnostic samples or immunization. Several audiovisual aids are available which could be used in conjunction with lectures or group discussion with great advantage. Others, such as posters and wall pictures, can be used on work premises to remind workers of various dangers or of precautions they have to take in handling potentially infected animals or products. It is important to enlist the aid of community leaders in the education campaign.

The development of delayed hypersensitivity to intradermally administered Brucella-specific antigens is an indication of past exposure to infection but does not indicate its current significance. Although used in the past in some countries, the intradermal test is not recommended for diagnosis. The use of undefined and unstandardized antigen preparations may also provoke antibodies which interfere with subsequent serological tests.With increasing use of live Brucella vaccines to immunize cattle (B. abortus strain 19 and RB 51) and sheep and goats (B. melitensis strain Rev 1), the problem of accidental self-inoculation by veterinarians is widespread.

The essential element in the treatment of all forms of human brucellosis is the administration of effective antibiotics for an adequate length of time. Antibiotic treatment should be implemented at as early a stage as possible, even in patients who appear to be showing a spontaneous improvement. In those patients with complications, additional treatment, including in some cases surgical intervention, will be necessary.

As the ultimate source of human brucellosis is direct or indirect exposure to infected animals or their products, prevention must be based on elimination of such contact. The obvious way to do this elimination of the disease from animals is often beyond the financial and human resources of many developing countries. The technical and social difficulties involved in eradicating B. melitensis from small ruminants have even taxed the resources of some developed countries.

Vaccination is an extremely important and effective facet of most control strategies but has the disadvantage that its use may confuse diagnosis by stimulating the production of hypersensitivity or antibodies detectable by serological tests. Antibody titres may persist for a prolonged period in a small proportion of vaccinated animals and this proportion increases with age at vaccination.

Farm workers and animal attendants in particular, should wear adequate protective clothing when contact with infected animals is probable or if the environment is likely to have been contaminated by excreta, abortions or parturition products from animals with brucellosis.Farm implements used for handling contaminated material should be disinfected after use by immersion in a suitable disinfectant (iodophor, phenolic soap or dilute caustic soda).

Brucellosis is a zoonosis with a strong correlation between animal and human diseases. While public health measures such as pasteurisation and education have varying degrees of success, it remains primarily a veterinary responsibility to control brucellosis, including application of principles of epidemiology and animal husbandry.Careful selection of replacement animals. These, whether purchased or produced from existing stock, should originate from Brucella-free herds or flocks. Pre-purchase tests are necessary unless the replacements are from populations in geographically circumscribed areas that are known to be free of the disease.

The aim of an animal control programme is to reduce the impact of a disease on human health and the economic consequences. The elimination of the disease from the population is not the objective of a control programme, and it is implicit that some "acceptable level" of infection will remain in the population. Control programmes have an indefinite duration and will need to be maintained even after the "acceptable level" of infection has been reached, so that the disease does not re-emerge.

There are no pathognomonic signs of brucellosis in animals at individual level; the occurrence of abortion storms in naive herds/flocks is usually a strong indicator of infection. Therefore, serological (and sometimes allergic) tests are the usual method of identifying possible infected animals.The decision about slaughter of test-positive animals is made after regulatory, economic and prevalence factors are considered. In most cases, test and slaughter of positive animals is only successful in reducing the incidence if the herd or flock prevalence is very low (e.g. 2%).The immediate slaughter of test-positive animals is expensive and requires animal owner cooperation. Compensation is usually necessary. Furthermore, the application of test and slaughter policies is unlikely to be successful with brucellosis of sheep and goats where the diagnostic tests are less reliable than in cattle. Test and slaughter is also unlikely to be successful in cattle if the remainder of the herd is unvaccinated, especially in large populations.

The goal in the application of hygiene methods to the control of brucellosis is reduction of exposure of susceptible animals to those that are infected, or to their discharges and tissues. This is a classical procedure in disease control. Factors such as the methods of animal husbandry (e.g. commingling of herds or flocks), patterns of commerce, prevalence of clinical signs, type of facilities, and degree of dedication of the owners of animals, will also determine success. Owners are often poorly informed about disease transmission and recommendations, such as separation of parturient animals, can be difficult or impossible to implement.

Brucellosis may be avoided by using proper sanitation methods. Proper herd management strategies can also aid in the avoidance of the disease. These include: Maintaining closed herds, recording individual animal identification and maintaining accurate records, isolating and testing purchased additions as well as cattle re-entering the herd and arranging diagnostic workups and necropsies for potentially or suspected brucellosis infected cattle.

References

Acha,N., Szyfers, B. (2001):Zonoosis and communicable disease common to man and animals.VolI. Bacteriosis and Mycosis.3rdedition. Scientific and Technical Pulication.No.580.Washngton,D.C,U.S.A.,Pp.40-62.

Adone, R. and Pasquali, P. (2013): Epidemiosurveillance of brucellosis.*Rev. sci. tech. Off. int. Epiz.* 32 (1), 199-205.

Afify, M. Al-Zahrani SH, El-Koumi, M.A. (2013). Brucellosis-Induced Pancytopenia in Children: A Prospective Study. Life Sci. J.10:1.

Alavi, S.M.,Alavi SMR, Alavi, L. Relapsed human brucellosis and re-lated risk factors. Pak, J. Med Sci. (2009);25 (1):46-50.

Alavi, S.M.,Alavi, L. Comparative study of current diagnostic method with clinical based method for brucellosis: presentation of diagnostic clinical criteria in limited resource area. Jundishapur J Microbiol. (2011);3 (3):121-4.

Al-Mariri, A., Haj-Mahmoud, N. (2010): Detection of Brucellaabortus in bovine milk by polymerase chain reaction. Acta Vet. Brno. 79:277-280.

Amezcua, R., Friendship, R.M,, Dewey, C.E., Gyles, C., and Fairbrother, J.M. (2002): Presentation of post weaning *Escherichia coli* diarrhea in souther n Ontario, prevalence of hemolytic *E. coli* sero gr oups involved, and their antimicrobial resistance patterns. Can J Vet Res. 66:73–78

Ariza J, Bosch J, Gudiol F, Linares J, Viladrich PF, Martin R. Rel-evance of in vitro antimicrobial susceptibility of Brucellameli-tensis to relapse rate in human brucellosis. AntimicrobAgents Chemother. (1986);30(6):958-60.

Ariza J, Bosilkovski M, Cascio A, Colmenero JD, Corbel MJ, Fala-gas ME, et al. Perspectives for the treatment of brucellosis in the 21st century: the Ioannina recommendations. PLoS Med. (2007);4(12):e317.

Awah-Ndukum, J., Mouiche, M.M., Bayang, H.N., NguNgwa,V., Assana, E., Feussom, K.J.M., Manchang,T.K., Zoli, P.A.(2018): Seroprevalence and Associated Risk Factors of Brucellosis among Indigenous Cattle in the Adamawa and North Regions of Cameroon. *Veter. Medic. Intern*. Volume 2018, 10 pages

Aworh, (*2013***)** andGoncalves, (2006); Introduction *Brucellosis,* a neglected debilitating zoonosis, in the slaughtering area

Balcha, M., Sintayehu, G., and Wubetie, A., 2006.Epidemiological surveillance of brucellosis in small ruminants of the pastoral areas of Ethiopia. In: Proceedings of Research Projects Completion Workshop, 1-2 February 2007, Ethiopian Institute of Agricultural Research, Addis Ababa, Ethiopia, pp. 220-221, 233.

Beh, K.J. (1974): Quantitative distribution of Brucella antibody among immunoglobulin classes in vaccinated and infected cattle. Res. Vet. Sci. 17:1-4.

Bekele,T., and Kasali, O.B. 1990. Brucellosis in sheep and goats in central Ethiopia. Bull. Anim. Hlth. Prod. Afr. 38, 23-25.

Bercovich, Z. (1998): Maintenance of Brucellaabortus free herds: A review with emphasis on epidemiology and the problems of diagnosing brucellosis in areas of low prevalence. Vet. Quart. 20(3):81-88.

Center for Food Security and Public Health (2009): Brucellosis. Retrieved from www.cfsph.iastate.edu/Factsheets/pdfs/brucellosi s.pdf (accessed on 30 may 2018).

Cisneros, J.M.,Viciana, P.,Colmenero, J., Pachón, J., Martinez, C. and Alarcón, A. Multicenter prospective study of treatment of Brucellamelitensis brucellosis with doxycycline for 6 weeks plus streptomycin for 2 weeks. Antimicrobial Agents and Chemotherapy (1990);34 (5):881–3.

Cluff, L.E. Medical aspects of delayed convalescence. Rev Infect Dis. 1991;13(Suppl 1):S138-40.

Colibaliy, N.D. and Yamego, K.R. (2000): Prevalence and control of zoonotic disease: Collaboration between public health workers and veterinarians in Burkina faso. ACTA Trop., 76:53-57.

Corbel M.J. (2006): Brucellosis in humans and animals. World Health Organization in collaboration with the Food and Agriculture Organization of the United Nations and World Organization for Animal Health.

Corbel, M.J. (1972): Characterization of Antibodies Active in the Rose Bengel Plate Test. Vet. Rec. 9:484-485.

Corbel, M.J. (2006): Brucellosis in humans and animals. Gene va. World Health Organization, 2006:36–41.

Degefu, H., Mohamud, M., Hailemelekot, M. and Yohannes, M. (2011): Seroprevalence of bovine brucellosis in agro pastoralareas of Jijjiga zone of Somali National RegionalState, Eastern Ethiopia.*Ethiop. Vet. J., 15 (1), 37-47.*

Díaz, R., Casanova, A.,Ariza, J., and Moriyón, I. (2011): The Rose Bengal Test in Human Brucellosis: A Neglected Test for the Diagnosis of a Neglected Disease. PLoSNegl. Trop. Dis. 5(4):e950.

Epameinondas, T., Georgiou's, P., Nicholas, A., and Mile, B., (*2005)*: The sensitivity of RBPT (Erganis et al., *2005*):*brucellosis* in large animal herds.

FAO (Food and Agriculture Organization of the United Nations),(2005); Bovine Brucellosis. Retrieved February13, 2012

Feyissa, A., Sori, T., Getahun, E., Fikru, Regasa, F., and Yigezu, L., (2007): Distribution of brucellosis among Small ruminants in the pastoral region of Afar. Rev Sie. Tech. Off. Int. Epiz, 26(3), 731-739.

Foster, G., MacMillan, A.P. and Godfroid J (2002): A review of Brucella sp. infection of sea mammals with particular emphasis on isolates from Scotland. Vet. Microbiol. 90:563-80.

French Agency for Food, Environment and occupational Health and Safety (2014):

Brucella species. Retrieved from http://www.anses.fr/en/system/files/BIORISK2013sa0188EN. Pdf (accessed on 31 may 2018).

Garin-Bastuji, B. (2014): Brucellosis: An emerging disease with public health implications?.Httpt: //www. Slues.org.centrb.cgd (accessed on 31 may 2018).

Genetzky, R.M. (1995): CompendContinEducPract Vet 17:447. 6

Georgios, P.,Nikolaos. A., Mile, B., andEpameinondas, T. (2005): Brucellosis. N Engl. J. Med. 352: 25-36.

Geresu, M.A., Ameni, G., Kassa, T., Tuli G, Arenas, A., and Gezahegne, M.K. (2016): Serositivity and risk factors for Brucella in dairy cows in Asella a nd Bishoftu towns, Oromia regional state, Ethiopi a. Afr J Microbiol Res.10(7):203 13. https://doi.org/10.5897/AJMR2015.7707.

Ghasemi, R. The most important control activities in Iran. [cit-ed]; Available from: http://www. elib. ir/persian/public_health_ebook/09_16. htm.

Glynn, M. K., Lynn, T.V. (2008): Brucellosis. J. Am. Vet. Med. Assoc., 233: 900–908.

Gumi, B., Firdessa, R., Yamuah, L., Sori, T.,Tolosa, T., Aseffa, A., Zinsstag, J.,and Schelling, E.(2013): Seroprevalence of Brucellosis and Q-Fever in SoutheastEthiopian Pastoral Livestock.*J.Vet. Sci. Med. Diagn*. 2(1).

Hubber, J., and Nicoletti, P. (1986): Comparison of the results of card, rivanol, complement fixation and milk ring test with the isolation rate of Brucellaabortus from cattle. Am. J. Vet. Res. 47:1529-31.

Kahn, C.M. (2005): The Merck Veterinary Manual.Brucellosis in large animal. 9th edition. Merck and co. inc, white house station, N.J., U.S.A. pp 1110-1112.

Khosravi, A,D., Abassi, E., andAlavi, S.M. (2006): Isolation of Brucellamelitensis and Brucellaabortus from brucellosis patients by conventional culture method and polymerase chain reaction technique. Pak J Med Sci. 22(4):396-400.

King, D.P.,*etal*., J C1in Microbiol 2005; 43:604

Lita, E.P., Erume, J., Nasinyama, G.W. and Ochi, E.B. (2016): A Review on Epidemiology and Public Health Importance ofBrucellosis with Special Reference to Sudd Wetland Region SouthSudan. *Intern.Jour. of Rese. Stud. inBioscie.*Volume 4, Issue 12, PP 7-13

MacMillan, A.P, GreiserWilke, I., Moennig, V., and Mathias, L.A. (1990): A competition enzyme immunoassay for brucellosis diagnosis. Dtsch.Tierarztl. wochensch. 97(2):83-85.

Madsen, M. (1994): Evaluation of a rapid enzyme immunoassay test kits for the serological diagnosis of brucellosis. BAHPA. 42:93-97.

Maguire, M. E., Kehres, D.G., A. Janakiraman, and Slauch, J. M. (2002):Brucella MntH in Mn^{2+} transport and virulence 42.

Mangen, M. J., Otte, J., Pfeiffer, D., and Chilonda, P. (2002):Bovine brucellosis in Sub-Saharan Africa: Estimation of sero-prevalence and impacton meat and milk off take potential.*Livestock Policy Discussion Paper*.No. 8.

Mantur, B.G. and Mangalgi, S.S. (2007): Evaluation o f conventional castanedaandlysis centrifugation blood culture techniques for diagnosis of human brucellosis. J. Clin. Microbiol. 42: 4327–4328.

Marín, C.M., Jimenez de Bagüés, M.P., Barberán, M., and Blasco, J.M.(1996): Comparison of two selective media for the isolation of Brucellamelitensis from naturally infected sheep and goats. Vet. Rec. 138: 409-411.

McCaughey, W.J. (1972):Brucella milk ring tests on churn samples: a three year study. Vet. Rec. 90:6-10.

McDermott, J.J.and Arimi, S.M. (2002): Brucellosis in Sub-Saharan Africa: epidemiology, control and impact. *Veterinary Microbiology*, 20:111-134.

Megersa, B., Biffa,D., Niguse, F., Rufael,T., Asmare,K., andSkjerv, E. (2011): Cattle brucellosis in traditional livestock husbandry practice in Southern and Eastern Ethiopia, and its zoonotic implication. *ActaVeterinariaScandinavica*2012, 53:24

Mohammed, M., Mindaye, S., Hailemariam,Z. , Tamerat, N., and Muktar, Y.(2016): Sero-Prevalence of Small Ruminant Brucellosis in Three Selected Districts of Somali Region, Eastern Ethiopia.*Jour. of Veter. Science & Animal Husbandry* 2019.5.

Muhie, Y. (200: A Sero-prevalence Study of Small Ruminant Brucellosis in Selected Sites of the Afar and Somali Regions, Ethiopia. DVM Thesis, Factuality of Veterinary Medicine, Addis Ababa University, DebreZeit, Ethiopia.

Nielsen, K. (2002): Diagnosis of brucellosis by serology. Vet. Microbiol. 90:447-59.

Nielsen, K.H., Wright, P.F.and Cherwonogrodzky, J.H . (1988): A Review of Enzyme Immunoassay for Detection of Antibody to Brucellaabortus in Cattle. Vet ImmunolImmunop. (18):331-347.

Nimri, L.F. (2003): Diagnosis of recent and relapsed cases of human brucellosis by PCR assay. BMC Infect Dis.;3:5.

Office International des Epizooties (2013): Bovine brucellosis: Manual of diagnostic tests and vaccines for terrestrial animals OIE, Paris; 2013, 409-435.

OIE Terrestrial Manual, (2009): Bovine brucellosis. R etrieved February 02, 2012 fromhttp://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.04.03_BOVI NE_BRUCELL.

Pappas, M.D., NikolaosAkritidis, M.D., Mile Bosilkovski, M.D. and N Engl J Med (*2005)*: The *B.* Melitensis Genome.352:2325-2336.

Pérez-Sancho, M., García-Seco, T., Domínguez, L. and Álvare, J.(2015): Control of Animal Brucellosis:The Most Effective Toolto Prevent Human Brucellosis. http://dx. doi. org/ 10. 5772/61222

Poiester, F.P., Nielsen, K.,Samartino, L.E. and Yu, W.L. (2010): Diagnosis of Brucellosis. Open Vet.Sci. J. 4:46.

Quinn, P.J., Markey, B.K, Carter ME, Donnely, W.J.C ,, Lonard, F.C, andMaquire, D. (2002). Brucellaspecies in Veterinary Microbiology and Microbial Disease, Londen, Black Well science Ltd., Pp. 999-1000.

Quinn, P.J., Markey, B.K, Carter, M.E., Donnely, W.J. C., Lonard, F.C, and Maquire, D. (200): Brucellaspecies in Veterinary Microbiology and Microbial Disease, Londen, Black Well

Quinn, P.J., Markey,B.K., Carter,M.E., Donnelly, W.J. C., Leonard,F.C. (2002): Veterinary Microbiology and Microbial diseases. Great Britain. Blackwell.pp 162-166.

Radostitis, E.D., Gay, C.C. and I nchcliff, K.W. (2006):Veterinary MedicineTextbook of the disease of cattle, sheep, pigs, goats, and horses, 9th ed., Ne wyork: W. B. Sounders Company ltd. Pp. 867 - 882.

Radostitis, O.M., Gay, C.C., Hinchcliff, K.W. and Constable, P.D.(2007): A Textbook of the Diseases of Cattle, Horses, Sheep, Pigs and Goats .10th edition. Spain: Saunders Elseier. pp 963-993

Regea, G. (2017): Brucellosis and Its Control through One Health Approaches in Ethiopia.*Jou. Vet. Med. Res. 4(3): 108.*

Schelling, E., Diguimbaye, C., Daoud, S., Nicolet, J., Boerlin, P., Tanner M., and Zinsstag., J.,(2003): Author information Prev Vet Med. Dec 12;61(**4**):279-93.

Scholz, H.C., Revilla-Fernández, S., Al Dahouk, S., Hammerl, J.A. and Zygmunt. M.S. (2016) :Brucellavulpes sp. nov., isolated from mandibular lymph nodes of red foxes (Vulpesvulpes). *Int. J. Syst. Evol. Microbiol* 66: 2090-8. .

Searson, E. (1986):AustVet 63:30

Shirima, G. (2005): The epidemiology of brucellosis inanimals and humans in Arusha and Manyara regions in Tanzania. Faculty of Veterinary Medicine,University of Glasgow, Tanzania, PhD thesis.

Sintayehu, G., Melesse , B., Abayneh , D., Sintayehu , A., Melaku, S., Alehegne, W., Mesfin ,S., De Blas, I., Casal, J., Allepuz, A., Martin-Valls, G.T. and Africa, T.Abera, K.(2015): Epidemiological survey of brucellosis in sheepand goats in selected pastoral and agro-pastorallowlands of Ethiopia. *Rev. Sci. Tech. Off. Int. Epiz.*, 34 **(3**)

Sori, T., Muchie, Y., Dagne, A., and Kidanemariam, A. (2007):Sero-prevalence of small ruminant brucellosis in selected districts of Afar and Somalia pastoral areas of Eastern Ethiopia; The impact of husbandry practices. Rev. Vet. Med.,pp. 157, 557-563

Tabatabaei, S., Zahraei, M., Ahmadnia, H., Ghotbi, M., and Rahimi, F. (2008):.Principles of disease prevention and Surveillance. Center for diseases control, Vice-chancellor for health, ministry of health and medi-cal education, 1st ed.

Tesfaye, G., Wondimu, A., Asebe, G., Regasa, G. andMamo, G. (2017): Sero-prevalence of Bovine Brucellosis in and Around Kombolcha, Amhara Regional State, Ethiopia. *Mycobact. Dis.* 7: 242.

Walke, R.L. (*2005):Vet* Med B Infect Dis *Vet* Public Health. Weller, P.F and Guerrant, D.H, (ed) Pathogens and Practice, pp 52:444...

Walker, L.R. (1999): BrucellainVeterinary Microbiology. Dwight, C., Hirsh, D.c. and Zee, Y.C. (ed). BlackGG science. Pp. 196-202.

Walker,R.L.(1999): Brucella. Veterinary Microbiology. United State of America. Blackwell science.pp 200-2007

WHO /MZCP (1998): Human and Animal Brucellosis. Report of a WHO/MZCP Wokshop, Damascus, Syria, 4th-5thMay.

Wiley, and Young, E.J. (2005): Brucella species. In: Mandell GL, Douglas RG, Ben-nett JE, editors. Principles and practice of infectious diseases. Churchill Livingstone: p. 2669-74.

World Health Organization (2005): Brucellosis in humans and animals, Geneva WHO guidance.

World Health Organization, (2006): Brucellosis in Hu mans and Animals. Geneva, Switzerlad: WHO Press.

Wyatt, H., and Vivian, (2014):"How did Sir David Bruce forget Zammit and his goats ?"(PDF). Journal of Maltese History. Malta: Department of History, University of Malta. **4** (1): 41.ISSN 2077-4338. Archived from the original (PDF) on 2016-07-21.Journal archive

Zinsstag, J., Schelling, E., Solera, X., Blasco, J., and Moriyon, I., (2011): Brucellosis: Oxford Textbook of Zoonoses. pp. 54-64.

Access this Article in Online	
	Website: www.ijarbs.com
Quick Response Code	Subject: Veterinary Medicine
DOI:10.22192/ijarbs.2020.07.09.002	

How to cite this article:
Wondimu Hailu Enaro. (2020). A Review on Zoonotic importance of a Brucellosis. Int. J. Adv. Res. Biol. Sci. 7(9): 9-31.
DOI: http://dx.doi.org/10.22192/ijarbs.2020.07.09.002