International Journal of Advanced Research in Biological Sciences
ISSN: 2348-8069
www.ijarbs.com
(A Peer Reviewed, Referred, Indexed and Open Access Journal)
DOI: 10.22192/ijarbs Coden: IJARQG (USA) Volume 9, Issue 8 -2022

Review Article

DOI: http://dx.doi.org/10.22192/ijarbs.2022.09.08.015

Brucellosis: A review

Yalew Abiyu Senbeto
Ethiopian Institute of Agricultural Research, Pawe Agricultural Research Center,
P.O. Box 25, Pawe, Ethiopia.
E-mail: *yalew6vet@gmail.com*

Abstract

Brucellosis is highly contagious economically important disease caused by gram negative, non-motile intracellular bacteria called *Brucella* which is first discovered by David Bruce in 1887 in Malta Island. It is an occupational neglected zoonotic disease affecting domestic animals such as cattle, sheep, goat, camel and pig, human and wildlife. Brucellosis occurs worldwide and isendemic in Mediterranean countries of Europe, Northern and Eastern Africa, Near East countries, India, Central Asia, Mexico and Central and South America. Prevalence of brucellosis is influenced by factors such as age, sex, species, physiological status, herd size, hygienic status of the farm, poor management, close confinement and climatic conditions. Brucellosis can be transmitted both by horizontal and vertical methods. In animals ingestion of contaminated feed, water and after birth is most important way of transmission where as in human ingestion of raw unpasteurized milk is most important. Clinically, brucellosis is manifested by abortion, retained placenta, orchitis, epididymitis, seminal vesiculitis, sterility and hygroma of joints. Undulant fever, night sweet, weakness, head ache and insomnia are also common in human. Brucellosis can be diagnosed by smear examination, culture, serological and molecular methods. Cultural isolation or detection of *Brucella* organisms is gold standard method. Common control and prevention methods for brucellosis include quarantine of imported stocks, vaccination, and treatment, hygienic disposal of aborted fetuses, fetal membrane and discharges with subsequent disinfection of contaminated areas. Creating awareness about transmission ways of the disease to society is also important. Brucellosis is endemic in Ethiopia and sero prevalence ranging from 0.2% to 38.7% in cattle, 0.4% to 8.5% from small ruminants, 0.53% to 58% from camel and 1.34% to 34.9% from human is reported in different parts of the country.

Keywords: Abortion; Brucellosis; Brucella; occupational disease; Worldwide; Zoonotic.

1. Introduction

Brucellosis is a highly contagious, zoonotic and economically important bacterial disease of animals caused by member of the genus *Brucella*. It stands first in the list of zoonotic bacterial diseases, and 500,000 human cases are reported annually in endemic regions (Khan and Zahoor, 2018). Brucellosis was first discovered by David Bruce in 1887 from spleen of English soldiers killed in war in Malta Island. Therefore, it is called brucellosis disease(Asnake et al., 2017).

It is an occupational disease, occurring most often in veterinarians, farmers, stock inspectors, abattoir workers, laboratory personnel, butchers. The burden that the disease places specifically on low income countries has led the World Health Organization (WHO) to classify it as one of the world's leading 'neglected zoonotic diseases (Franc et al., 2018).

WHO organization classified *Brucellae* as risk group III agents because they can be easily transmitted via aerosols (Yuguda et al.,2019).Brucellosis affects domestic animals such as cattle, sheep, goat, camel and pig, human and wildlife(Tekaet al.,2019).It is also called Malta fever, Cyprus fever, Mediterranean fever, intermittent typhoid, Rock fever, Gibraltar fever, and more commonly, undulant fever in humans (Khan and Zahoor, 2018) and Bang's disease, enzootic abortion, epizootic abortion and contagious abortion in animals (Gebretsadik, 2016).

Brucellosis is essentially a disease of the sexually nature animal, the predilection sites being the reproductive tracts of males and females, especially the pregnant uterus. Allantoic factors stimulate the growth of most *Brucella*. These factors include erythritol, possibly steroid hormones and other substances. Brucellosis results in a serious economic loss in animal production sector and deterioration of public health. It causes economic losses as a result of reproductive wastage through infertility, delayed heat, loss of calves, reduced meat and milk production, culling and international trade bans. Clinical sign of brucellosis is characterized by abortion and retained fetal membrane in cows and orchitis and epididymitis in bulls (Meles and Kibeb, 2018).

Abortion usually occurs during the last stage of pregnancy. Infertility, arthritis, metritis, stillbirths, neonatal mortality and hygroma are also a clinical signs of the disease. The clinical signs of the disease manifested in humans include undulant fever, headache, weakness, profuse sweating, chills, arthralgia, depression, weight loss, hepatomegaly, and splenomegaly and generalized aching (Gebretsadik, 2016)

Both vertical and horizontal transmissions of brucellosis exist in animals. Horizontal transmission occurs through ingestion of contaminated feed, skin penetration, via conjunctiva, inhalation and udder contamination during milking or by licking the discharge of an animal, newborn calf or retained fetal membrane. Fetus can be infected in uterus or suckling of infected dams. Congenital infection that happens during parturition is frequently cleared and only few animals remained infected as adult. In humans the disease is transmitted by ingestion of unpasteurized dairy products, direct contact with infected animals, blood, urine and vaginal discharge of infected animals, aborted fetus or placenta. Transmission through accidental inoculation and occupational aerosol transmission in abattoirs and laboratories has been also reported (Asnake et al. ,2017).

Diagnosis of brucellosis depends on isolation and identification of *Brucella* from aborted materials, udder secretions or from tissues removed at postmortem or patient's serum by detection of specific antibodies using appropriate serological methods. Presumptive diagnosis can be made by assessing specific cell mediated or serological responses to *Brucella* antigens. Brucellosis treatment is mostly not effective because of the intracellular nature of an agent and disease recurrences can occur 3 to 6 months after an early therapy discontinuation (Dubie et al.,2014).

The control and prevention of brucellosis in farm animals depend on animal species involved, *Brucella* Spp. management practices and availability and efficacy of vaccines. The options to control the disease include immunization, testing and removal, and improving management practices and movement control. However, a very important approach to the control of brucellosis that is gaining more and more recognition around the world in recent years is the one health approach to control and prevent human and animal brucellosis (Bedore and Mustefa, 2019).

The objectives of this paper are

- ✓ To review epidemiology, diagnosis and control and prevention of Brucellosis
- ✓ To review Zoonotic importance of brucellosis
- ✓ To summarize status of brucellosis in Ethiopia

2. History (briefly)

The history of Brucellosis extends back to people's first contact with animals. Studies have demonstrated that the presence of the disease in humans and animals is ancient (Akpınar, 2016). Thus, history of brucellosis does not begin with the isolation and identification of *Brucella melitensis* (*Micrococcus melitensis*) in the 1880s. Many historical accounts of diseases before this time could actually be describing brucellosis including abortion epidemics in animals and fever in humans. The paleo-pathological evidence from the partial skeleton of the late Pliocene *Australopithecus africanus* suggests that brucellosis occasionally affected our direct ancestors 2.3-2.5 million years ago. The pathological, molecular (DNA analysis) and electron microscopy findings from the human skeletal buried cheese remains also suggested the presence of brucellosis long time ago (3000-1200 B.C.) in Bahrain, Persian Gulf, 2100-1550 B.C. in Palestine and Jordan, 79 A.D. in Roman town Pompeii and Herculaneum.1260-1020 A.D. in Butrint, Albania (Gebretsadik, 2016).

In the middle of the 17th century, George Cleghorn (1716-1789) identified cases of recurrent febrile seizures in Minorca while on duty. In 1803, Manuel Rodríguez Caramazana clearly described Malta fever and distributed an eight page brochure about this title in Minorca. Brucellosis was first described by Jeffery Allen Marston in 1860.Marston was the first to define brucellosis; he wrote his findings in detail and defined the disease as "gastric remittent fever (Akpınar, 2016).However, the causative agent of brucellosis, "*Micrococcus melitensis*" (i.e. *Brucella melitensis*), was discovered in 1887 by British surgeon captain David Bruce, his wife Mary Elizabeth Steele and the Maltese microbiologist doctor Giuseppe Caruana-Scicluna from the liver of diseased soldiers in the Mediterranean island of Malta. After this discovery, the Maltese medical doctor Temi Zammit had revealed that the causative agent of Malta fever was transmitted from infected goats to humans through contaminated milk. After ten years of "*Micrococcus melitensis*" discovery, the Danish scientist Bernhard Bang identified "*Bacillus abortus*" (i.e. *Brucella abortus*) in 1897 from bovine aborted fetuses (Rahman, 2015) and the additional name "Bang's disease" was assigned for the disease(Gebretsadik, 2016).

In 1897, Wright and Smith explained that brucellosis was a zoonotic disease after detecting specific antibodies of *Brucella melitensis* in human and animal. Following this, Themistocles Zammit (1864-1935) isolated *B. melitensis* from goat's milk and urine in 1905 and Jacob Traum detected *Brucella suis* from prematurely born piglets' livers, stomachs, and kidneys in the state of Indiana in the United States in 1914.*Brucellaabortus* infections in humans were also reported by Orpen in England in 1924 and *Brucellaovis* in sheep was described by Van Drimmelen in 1953. Subsequently, *Brucella neotoma* was isolated from a wood tick in the state of Utah, in the United States, by Stoenn and Blackman in 1957. In 1968, *Brucella canis* was isolated in beagle dogs by Carmichael and Bruner. Ewalt, Ross, and colleagues isolated *Brucella pinnipediae* and *Brucella ceteace* from whales, dolphins and seals in 1994. Finally, *Brucella microti* was isolated from field mice in Central Europe and the mandibular lymph nodes of a wild red fox by Scholzet al., in 2008 (Rahman, 2015).

Another newly described species, *Brucella microti* was isolated from common voles and red foxes in 2008. Two additional novel strains have recently been isolated from humans in 2010. The first one was isolated from an infected human breast implant and was named *Brucella inopinata* and the second strain showed similarity to *Brucella inopinata* and was isolated from a

patient with chronic lung disease The two most recently described species are *Brucella papionis*, which was isolated from two baboons with retained placenta by Whatmore et al., 2014 and *Brucella vulpis* which was isolated in Austria from the mandibular lymph nodes of two red foxes by Scholzet al., 2016 (Rajala, 2016).

3. Etiology

Brucellosis is caused by species of the bacterial genus *Brucella*. *Brucellae* are Gram- negative coccobacilli or short rods measuring from 0.6 to 1.5 µm long and from 0.5 to 0.7 µm wide, non-motile, non-spore forming, non-capsulated, non-flagelated, aerobic, facultative intracellular bacteria capable of invading, survive and multiply within epithelial cells, placental trophoblasts, dendritic cells and macrophages(Gebretsadik, 2016). To date, twelve different *Brucella* (*B.*) species have been described (Figure 1). The six classical species are *B. melitensis*, *B. abortus*, *B. suis*, *B. ovis*, *B. neotomae* and *B. canis*. *Brucella melitensis*, *B. abortus* and *B. suis* are further classified into biovars (Rajala, 2016). *Brucella melitensis* is the main causative agent of caprine and ovine brucellosis and it is highly pathogenic for humans causing one of the most serious zoonoses in the world (Ferede et al.,2011).

Among thegenus *Brucella*, *B. melitensis*, *B. abortus*, *B. suis*, and *B. ovis* which preferentially infect sheep and goats, cattle, pigs and sheep, respectively are the most important from a socio-economic standpoint. In addition to decreasing productivity in animals, the first three species are the main ones responsible for brucellosis in human beings(Asnake et al., 2017). *Brucellae* produce oxidase, catalase, nitrate reductase, and urease (except *B. ovis*); fail to produce indole; are non hemolytic; do not liquefy gelatin; and have negative methyl red and Voges- Proskauer tests. Most (again except *B. ovis*); utilize glucose as an energy source. *Brucella* spp. have been classified as potential agents of bioterrorism because they may be spread by aerosol and there are no human vaccines(Gemechu, 2017).

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
B. vulpis		Unknown	Unknown	Unknown

Figure 1: *Brucella* Species and biovars affecting different hosts (Rajala 2016)

4. Epidemiology

4.1.Geographic distribution

The geographical distribution of brucellosis is constantly changing, with new foci emerging or re-emerging (Hailu, 2017). The disease occurs worldwide, except in those countries where bovine brucellosis (*B. abortus*) has been eradicated. The disease remains endemic among Mediterranean countries of Europe, Northern and Eastern Africa, Near East countries, India, Central Asia, Mexico and Central and South America. Furthermore, brucellosis is also 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 *B. melitensis* or *B. suis* biovar 1 infection in cattle (Moti et al.,2013).

Central Asia and the Middle East are among the regions with the highest incidence of brucellosis in humans and livestock worldwide and the incidence is rising (Rajala, 2016). Only 17 countries such as Norway, Scotland, Switzerland, United Kingdom, and Sweden and several other countries were formally declared free of Brucellosis. In United State this disease is primarily considered as an occupational hazard (Asnake et al., 2017).

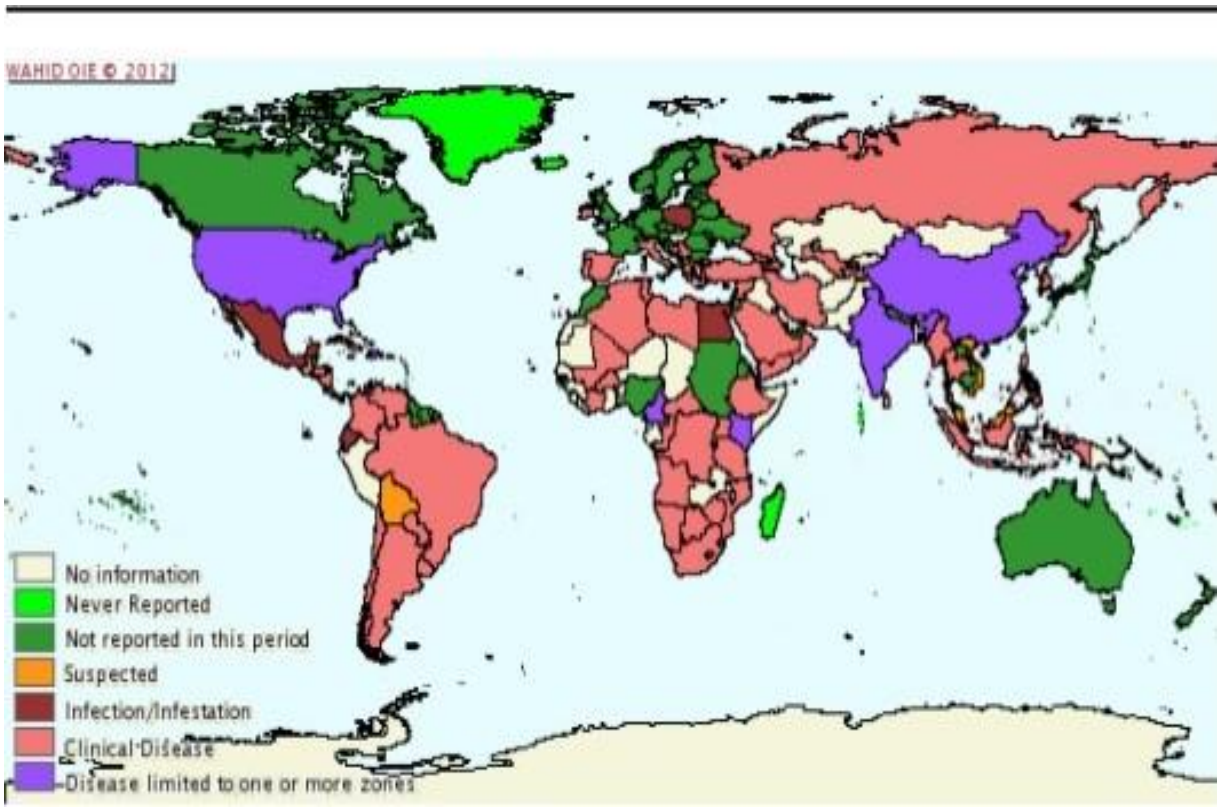

Figure 2: Geographic distribution map of brucellosis(Albornoz, 2013)

4.1. Host range

Brucella infects almost all domestic species except cats, which are naturally resistant to the agent(Khan and Zahoor, 2018). The principle hosts of *Brucella* include; cattle and bison (*B.abortus*), goats and sheep(*B.melitensis*), pigs(*B.suis*), dogs (*B. canis*) and rats(*B. neotomae*)(Mfune, 2015). Most species of *Brucella* are maintained in a limited numberof reservoir hosts.

Maintenance hosts for *B.abortus* include cattle, bison (Bison spp.) water buffalo (*Bubalus bubalus*), African buffalo (*Syncerus caffer*), elk and camels. A feral pig population was recently reported to maintain *B. abortus* in the U.S. Sheep and goats are the reservoir hosts for *B. melitensis*. Sheep are also the maintenance hosts for *B. ovis*. In addition, *B. ovis* occurs in farmed red deer (*Odocoileus virginians*) in New Zealand. *B. canisis* maintained in dogs and *B. neotomae* in rodents. Marine *Brucella* species have been found by culture or serology in many pinniped and cetacean species including seals, sea lions, walruses, porpoises, dolphins, whales and a European otter. Other species including human can become accidental hosts, particularly after close contact. *Brucella abortus*, *B. melitensis* and *B. suis* infections are reported occasionally in many species including horses, cattle, sheep, goats, camels, pigs, moose, chamois, alpine ibex, raccoons, opossums, dogs, coyotes, foxes and wolves(Gemechu, 2017).

4.2. Risk factors

Brucellosis is influenced by a number of risk factors related to production systems, biology of the individual host and environmental factors. These include age, sex, species, reproductive status, herd size and composition, hygienic status of the farm, rate of contact between infected and susceptible animals, farm biosecurity, climatic conditions and geography (Hailu, 2017).Younger animals also tend to be more resistant to infection and frequently clear infections while sexually mature and pregnant animals are more susceptible to infection to the organism than sexually immature animals of either sex. Susceptibility also increases with pregnancy as stage of gestation increases (Fulasa, 2004).A higher sero-prevalence has been reported in animals kept under extensive systems. Large herd sizes and poor housing also increased the risk of exposure to infection(Mfune, 2015).Other risk factors reported include lack of clean water, insufficient manure removal and cleaning, poor management of aborted materials, introduction of new animals from herds that were not free from brucellosis or of unknown status, herds kept in close confinement, and mixed herds (Deka et al., 2018).

4.3. Transmission

The most common route of transmission is ingestion of contaminated pasture, feed, fodder, water, and after birth; aborted fetuses, uterine discharges and new born calves, which contains large doses of infectious organism and constitutes a very important source of infection. However, infection through injured/intact skin, the mucosa at the respiratory system and conjunctiva frequently occurs(Teka et al., 2019). Calves can be infected in uteroor by suckling of infected dams. In animals, brucellosis is highly contagious and cross species transmission of certain *Brucella* spp. can occur(Franc et al., 2018).Venereal infections can also occur and mainly seen with *B. suis* infections. The importance of venereal transmission varies with the species. It is the primary route of transmission for *B. ovis*. *Brucella suis* and *B. canis* are also spread frequently by this route. *Brucella abortus* and *B. melitensis* can be found in semen, but venereal transmission of these organisms is uncommon(Asnake et al., 2017).

Infected semen containing *Brucella* organisms are mostly unlikely to transmit the disease but the chance of spread from the bull is very great if the semen is used for artificial insemination(Kebede et al., 2008). Human-to-human transmission can occur trans-placentally, via breastfeeding, and rarely through sexual intercourse, organ transplantation and blood transfusions. Transmission can also occur through direct contact with infected animals, infected tissues like placenta and aborted tissues, or dairy products. Even though pasteurizing milk is an effective means to kill *Brucella* and prevent infection in humans, it is not routinely practiced in some resource limited communities because of long standing cultural practices and a generalized lack of understanding by the public about the dangers of consuming raw milk(Franc et al., 2018).

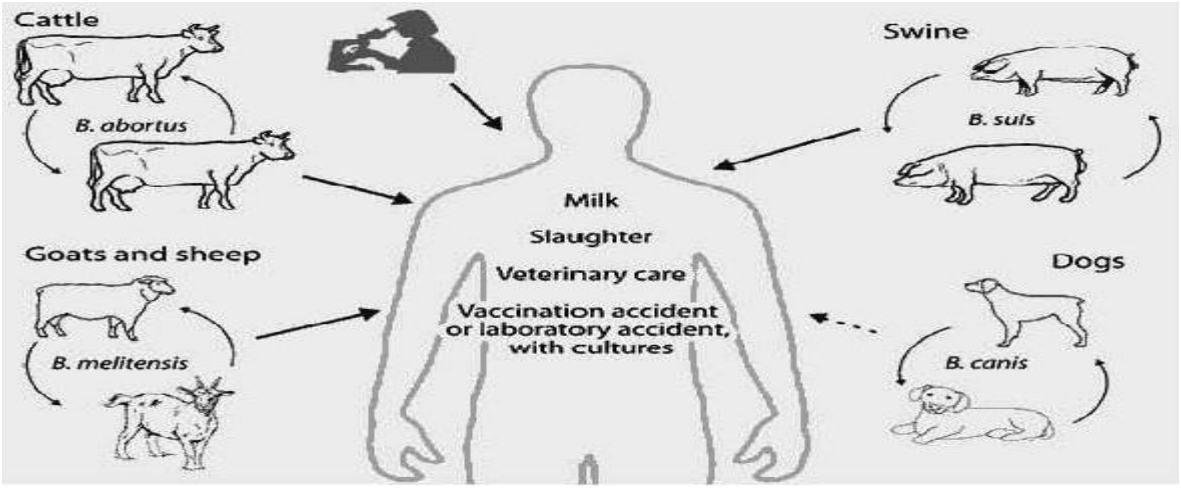

Figure 3: Transmission cycle of *Brucella* to humans(Hailu, 2017)

5. Public health importance

Human brucellosis is widely distributed all over the world. It is considered by the FAO, the WHO and the OIE as one of the widest spread zonooses in the world. Almost all human cases of brucellosis are acquired from animals, in particular goats and sheep(Bayu, 2018). Six *Brucella* species namely; *B. melitensis*, *B. suis*, *B. abortus*, *B. canis*, *B,ceti* and *B. pinnipedialis* can infect humans and the most pathogenic and invasive species for human is *B. melitensis*, followed in descending order by B. suis, *B. abortus* and *B. canis*. *B. melitensis*, *B. suis* and *B. abortus* are also listed as potential bio-weapons by the Centers for Disease Control and Prevention in the USA. This is due to the highly infectious nature of all three species, as they can be readily aerosolized(Asnake et al., 2017). Each year half a million case of brucellosis occurs in humans around the world. The prevalence of infection in animal reservoir provides a key of its occurrence in humans. *B. abortus* and *B. suis* infection usually affect occupational groups. *B. melitensis* infection occurs more frequently than others types in the general population (Dubie et al., 2014).Annual incidence of human brucellosis may range from a few cases to more than 500 cases per 1,000,000 populations in different parts of the world. A global report estimated human cases to be 500,000 each year (Workalemahu et al., 2017).

6. Clinical signs

6.1 Clinical signs in Animals

Infected livestock exhibit clinical signs of great economic significance such as reduced fertility, abortion, and a substantial decline in milk production over an animal's lifespan (Franc et al., 2018). Brucellosis in cattle is characterized primarily by abortion in late pregnancy (from the 5th to the 8th month of gestation), frequently followed by retention of foetal membrane and endometritis which may be the cause of infertility in subsequent pregnancies(Kebede et al., 2008). In sexually mature female cattle, infection localizes in the reproductive system and produces placentitis followed by abortion. Most infected animals abort only once in their lifetime, but may remain infected their entire life. Brucellosis is often asymptomatic in non-pregnant female cattle and after the first abortion(Deka et al., 2018).

In bulls the disease usually causes orchitis, epididymitis, seminal vesiculitis and sterility (Kebede et al., 2008).. Brucellosis may cause infertility in both sexes. Hygromas can also occur in leg joints and are a common manifestation of brucellosis in some tropical countries(Deka et al., 2018).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/fourth months of pregnancy. In case dog and cats, infertility, abortion and still birth/weak puppies are common manifestations (Dubie et al., 2014). When a pregnant animal is infected by *Brucella*, a visible swelling of the mammary gland to the navel region and bleeding from the vagina is not uncommon, even if the cow does not abort. The enlarged udder size (appearance of the 9th month of a pregnant cow) could be used as an indication for the high stage of the disease, where animals shed bacteria in urine, milk, and vaginal discharges(Khan and Zahoor, 2018).

6.3 Clinical Signs in Human

In humans, brucellosis typically manifests as a range of non-specific clinical signs. The acute and chronic symptoms of the disease can result in a significant loss of work days and consequential disparity in the socioeconomic status of infected persons and their families(Franc et al., 2018). The most common symptoms of brucellosis in human include undulant fever (37.8^0c in the morning to 40^0c in the afternoon), night sweets with peculiar odder and weakness. Other common symptoms in human 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* (Dubie et al., 2014).In humans, brucellosis is not confined to the reproductive system, but is also known to cause neurobrucellosis with clinical manifestation of meningitis, encephalitis, stroke, radiculitis, myelitis, peripheral neuropathies, and neuropsychiatric features. Studies have also reported sensorineural deafness, spastic paraparesis, followed by brisk tendon reflexes, bilateral ankle clonus, and extensor plantar responses(Khan and Zahoor, 2018). 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 (Dubie et al., 2014)

7. Diagnosis

The diagnosis of brucellosis can be challenging and is frequently delayed or missed because the clinical picture may mimic other infectious and non-infectious conditions. Thus,It is very difficult to make a diagnosis based on clinical signs despite abortions in the third trimester being indicative of brucellosis; this is because other infectious diseases such as leptospirosis, Rift valley fever and Listeriosis can also cause abortion storms(Mfune, 2015).

7.1 Bacteriological diagnosis

7.1.1 Stained smear Examination

Brucella organisms can be demonstrated through stained smears prepared from fetal membranes, fetal stomach contents, vaginal swabs, semen, etc. The most common staining methods are the modified Ziehl-Neelsen and the modified Köster methods. *Brucellae* are coccobacilli or short rods, usually arranged singly but sometimes in pairs or small groups. They are not truly acid fast. However, they are resistant to decolorisation by weak acids, and stain red against a blue background.Thus, the Stamp's modified Ziehl Nelsen staining is used to identify *Brucella* organisms as they stain red against a blue background when examined under a light microscope. However, other organisms that cause abortions like *Chlamydia*, *Coxiella* and *Norcardia* spp are also acid-fast and stain the same color. Therefore, careful examination and identification of *Brucella* from these organisms is important(Mfune, 2015)

7.1.2 Culture

The only 'gold standard' method for the diagnosis of brucellosis is the cultural isolation or detection of *Brucella* organisms from the infected host (Gebretsadik, 2016). Valid clinical samples for culture include blood, bone marrow, joint fluid, semen, and cerebral spinal fluid in humans and aborted fetuses, fetal membranes, vaginal secretions, sperm, milk, blood, and hygroma fluid in animals. Farrell's medium is most commonly used for culture of potential *Brucella* species from tissue samples. These media contain several antibiotics capable of inhibiting the growth of other bacteria present in clinical samples(Higgins, 2015).Growth is seen after 2-3 days and only considered negative after 2-3 weeks of incubation. Culture method is time consuming and has limitation as *Brucellae* are fastidious slow growers and hence they can be easily overgrown by other bacteria which often lead to misdiagnosis. In chronic cases, cultures may fail to grow due to low levels of bacteria (Mfune, 2015).

7.2 Serological diagnosis

Serological tests are crucial for laboratory diagnosis of brucellosis since most of control and eradication programs rely on these methods. Inactivated whole bacteria or purified fractions (i.e. lipopolysaccharide or membrane proteins) are used as antigens for detecting antibodies generated by the host during the infection. Antibodies against smooth *Brucella* spp. (e.g. *B. abortus*, *B. melitensis*, and *B. suis*) cross react with antigen preparations from *B. abortus*, whereas antibodies against rough *Brucella* spp. (e.g. *B. ovis* and *B. canis*) cross react with antigen preparations from *B. ovis*(Beruktayet and Mersha, 2016). The most common serological tests used both in livestock and humans are the serum agglutination test, the complement fixation test, Rose Bengal test, Enzyme Linked Immune Sorbent Assay and the fluorescence polarization assay (Higgins, 2015).

7.2.1 Serum Agglutination Test

A suspension of *Brucella* possessing active antigen will agglutinate when exposed to homologous *Brucella* antibody. This agglutination forms clumps of bacteria which become macroscopically visible. Serum agglutination test (SAT) isused to detect brucellosis by measuring agglutinating antibodies of theIgM, IgG 1, IgG 2, and IgA types. The SAT can be used to detect acute infections, as antibodies of the IgM type usually appear first after infection and are more reactive in the SAT than antibodies of the IgG 1and IgG 2types. However, because the SAT may yield both false negative or false positive results it effectively detects brucellosis only on a herd basis(Bayu, 2018).

7.2.2 Fluorescent Polarization Assay

The basis for the fluorescence polarization assay (FPA) is simple. The rate of rotation of a molecule in solution is inversely proportional to its size. A small molecule will rotate rapidly while larger molecules rotate more slowly. By attaching a fluorescing molecule to an antigen molecule, the rate of rotation can be measured using polarized light. The result is a measurement of the time it takes the molecule to rotate through a given angle. In the case of brucellosis serology, small molecular weight subunit of O-polysacharide (OPS) is labeled with fluoresce in isothiocyanate and used as the antigen. When testing serum, blood or milk, if antibody to the OPS is present in the samples tested, the rate of rotation of the labeled antigen will be reduced. The rate of reduction is proportional to the amount of antibody present (Poester et al., 2010).

7.2.3 Rose Bengal Plate Test

Rose Bengal test (RBPT) was developed by Rose and Roekpe (1957) for the diagnosis of bovine brucellosis to differentiate specific *Brucella* agglutinins from non-specific factors. When the antigen was buffered at pH 4.0 they observed that agglutination of *B. abortus* cells by non-specific agglutinins of bovine serum was inhibited whereas the activity of specific *Brucella*

antibodies was not affected. Despite the scanty and sometimes conflicting information available, this test is internationally acknowledged as the test of choice for the screening of brucellosis in cattle as well as in small ruminants (Gebretsadik, 2016).

The RBPT is one of a group of tests known as the buffered *Brucella* antigen tests which rely on theprinciple that the ability of IgM antibodies to bind to antigen is markedly reduced at a low pH. It is a simple spot agglutination test where drops of stained antigen and serum are mixed on a plate and any resulting agglutination signifies a positive reaction. The test is an excellent screening test but may be oversensitive for diagnosis in individual animals, particularly vaccinated ones(Asnake et al., 2017).

7.2.4 Enzyme Linked Immune Sorbent Assay

Enzyme Linked Immune Sorbent assay (ELISA) is an excellent method for screening large populations for *Brucella* antibodies and for differentiation between acute and chronic phases of the disease. It is the test of choice for complicated, local or chronic cases particularly when other tests are negative while the case is under high clinical suspicion. ELISA can reveal total and individual specific immunoglobulins (IgG, IgA and IgM) within 4-6 hours with high sensitivity and specificity. In addition to the detection of immunoglobulin classes, ELISA can also detect *Brucella* specific IgG subclasses and other *Brucella* immunoglobulins such as IgE(Hailu, 2017).

7.2.5 Complement Fixation Test

Complement fixation test (CFT) is the most widely used confirmatory test and recommended by OIE. The CFT is based on the detection of specific antibodies of the IgM and IgG1 that fix complement. It is highly specific but laborious and requires highly trained personnel as well as suitable laboratory facilities. Its specificity is very important for the control and eradication of brucellosis but may test negative when antibodies of the IgG2 type hinder complement fixation(Gebretsadik, 2016).

7.3 Molecular Diagnosis

Polymerase chain reaction (PCR) based techniques have been developed in recent years and are in use as alternative diagnostic tests for brucellosis. They are based on the detection of specific sequences of *Brucella*spp. DNA in clinical samples. PCR techniques have lower diagnostic sensitivity and higher specificity than culture methods hence best results are obtained when the two are combined(Mfune, 2015). Molecular techniques are important tools for diagnosis and epidemiologic studies, providing relevant information for identification of species and biotypes of *Brucella* spp. allowing differentiation between virulent and vaccine strains. Molecular detection of *Brucella* spp. can be done directly on clinical samples without previous isolation of the organism. In addition, these techniques can be used to complement results obtained from phenotypic tests. Despite the high degree of DNA homology within the genus *Brucella*, several molecular methods, including PCR, PCR restriction fragment length polymorphism (RFLP) and Southern blot, have been developed that allow, to a certain extent, differentiation between *Brucella* species and some of their biovars (Hailu, 2017).

8. Prevention, control and treatment

Prevention and control of brucellosis can be adopted realistically through understanding of local and regional variations in animal husbandry practices, social-customs, infrastructures and epidemiological patterns of the disease. The common approaches used to control brucellosis include quarantine of imported stocks, hygienic disposal of aborted fetuses, fetal membrane and discharges with subsequent disinfection of contaminated area. Animals which are in advanced pregnancy should be isolated until parturition and replacement stock should be purchased from herd free of brucellosis and decide for or against immunization of negative animals. Eradication by test and slaughter of

positive reactor is also possible. To prevent the disease in control and eradication of the infection in animal reservoirs, educating the farmers to take care in handling and disposing of aborted fetus, fetal membrane and discharges as well as not to drink unpasteurized milk and educating abattoir workers in transmission of infection via skin abrasion is important (Beruktayet and Mersha, 2016).

Hygienic methods to the control of brucellosis are also applied, to reduce exposure of susceptible animals to those that are infected. Owners should be informed about disease transmission and recommendations, such as separation of parturient animals, pasteurization of milk for consumption, avoidance of handling of parturient materials. Unauthorized sale or movement of animals from an infected area to other areas should be forbidden. Similarly, importations into clean areas must be restricted to animals that originate from brucellosis-free areas, that have a herd/flock history of freedom from the disease and that have given negative reactions to recently performed diagnostic tests. In practice, it is much more difficult to control the movement of livestock kept under pastoral and agro pastoral conditions than that of beef or dairy cattle kept under intensive conditions because the owners of herds and flocks may be accustomed to seasonal migrations which may cross national boundaries(Hailu, 2017).

One of the most successful methods for prevention and control of livestock brucellosis is through vaccination. In different parts of the world both live vaccines and killed vaccines are available. However, currently no vaccine has been approved for the prevention of human brucellosis. Vaccination is generally recommended for sero-prevalence rates between 2 and 10%. Whether a strategy of test and segregation alone for high seroprevalence rates is sufficient may depend on the farming conditions. This might be appropriate for farms in conjunction with appropriate hygienic measures, but supplementation with vaccination may be required to control the disease in extensive livestock conditions(Moti et al., 2013).

Treatment in animals is neither effective nor practical since *Brucella* spp. are facultative intracellular bacteria that can survive and multiply within macrophages. Following exposure to antibiotics such as penicillin and oxytetracycline, *Brucella* undergoes L-transformation which hinders serological detection and results in carrier state animals. Unsuccessful treatments have been reported because the drugs are unable to penetrate the cell membrane barrier due to the intracellular sequestration of the organisms in the lymph nodes, mammary glands and reproductive organs(Mfune, 2015). Though the complex nature of brucellosis makes it harder to treat, long term treatment with an antibiotic is thought to be beneficial. Several conventional antibiotics including tetracycline, trimethoprim-sulfamethoxazole, aminoglycosides, rifampicin, quinolones, chloramphenicol, doxycycline, and streptomycin are commonly used in clinics (Khan and Zahoor, 2018).

However, the optimal treatment for brucellosis is a combination regimen using two antibiotics since mono therapies with single antibiotics have been associated with high relapse rates. Combination of doxycycline with streptomycin is currently the best therapeutic option with less side effects and less relapses, especially in cases of acute and localized forms of brucellosis(Hailu, 2017). For human, the drug of choice recommended is rifampicin at dosage of 600-900 mg daily combined with doxycycline at 200 mg daily. Both drugs are given in the morning as a single dose and relapse is unusual after a course of treatment continued for at least 5 weeks (Beruktayet and Mersha, 2016).

9. Status of brucellosis in Ethiopia

Brucellosis is endemic in Ethiopia and it is highly prevalent in cattle, camels and small ruminants in pastoral and agro-pastoral areas of the country(Gemechu, 2017). In Ethiopia,brucellosis was first reported in 1970 by Veterinary section of the US Navy Medical Research unit. Since then, several serological surveys have been reported and found the prevalence of bovine brucellosis to range from 0.2% in south western

Ethiopiato 38.7% in western Ethiopia(Meles and Kibeb, 2018). Bovine brucellosis sero prevalence of 2.77% in Addis Ababa dairy cattle (Edao et al., 2018), animal level prevalence of 2.4% and herd level prevalence of 37.84% in and around Alage district (Asgedom et al., 2016), 1.9% individual animal level and 10.6% herd level prevalence in exotic and cross breed dairy cattle of Ethiopia(Asmare et al., 2013), 3.3% in extensive cattle production system of Tigray region (Berhe et al., 2007), 6.52% (3/46) isolation rate from dairy cattle of Ethiopia(Geresu et al., 2016), 2.28% (Minda et al., 2016), 2% in Eastern Showa (Alemu et al., 2014) and 1.04% from Chencha District of GamoGofa zone (Meles and Kibeb, 2018) was reported.

Small ruminant sero prevalence of 5.2% RBPT and 2.2% CFT in selected pastoral and agro pastoral low lands of Ethiopia (Sintayehu et al., 2015), 2.34% RBPT and 1.56% CFT from Yabello district (Dabassa et al., 2013), 1.99% RBPT and 1.76% CFT from Bishoftu and Modjo export abattoirs (Tsegay et al., 2015), 1.72% RBPT and 1.37% CFT in Somali Region (Mohammed et al., 2017), 1.56% RBPT in East Shewa (Lemu et al., 2015), 8.1% in Yabello district of Borena Zone(Wakene et al., 2017), 8.5% RBPT and 3.6% CFT from pastoral areas of Oromia and Somali regional states (Tsehay et al., 2014), 1.2% RBPT and 0.4 % CFT from Bahardar(Ferede et al., 2011) was also previously reported in Ethiopia.

An overall sero-prevalence of 1.76% was reported Tselemti district, Northern Ethiopia(Zenebe Kelkay et al., 2017). From a total of 53 clinical samples cultured in *Brucella* selective growth media, Zaba 2016 recorded an isolation rate of 11.32 % from Arbamich Zuria and Mirab Abaya small ruminants. A prevalence of 14.4 % *B. melitensis* infection in North Gonder from small ruminant was also reported (Wolde, 2017). Four isolates of *B. melitensis* were also isolated from goats in Afar region (Tekle et al., 2019).

Camel brucellosis prevalence of 2-58% from Afar, 82% from Somali, Afar and Oromia0,9% from Southern Ethiopia, 6.5% from Akaki, 2.43% from Jijiga and Babile, 2.2% from Borena, 3.6% from Yabello and 0.53% from Bale and Borena are reported by different studies(Gutema and Tesfaye, 2019).From camel, brucellosis sero prevalence of 6.33% (19/300) by RBPT and 3.67% (11/300) using CFT reported in Tigray(Tassew and Kassahun, 2014).

In human, brucellosis sero-prevalence of 4.8% from Addis Ababa, 3.6% from Jimma University hospital(Tolosa et al., 2007), 2.6% from North western Ethiopia, 34.9% from Borana, 29.4% from Hamer, 3.% from Metema and16.5% from Afar are reported (Hailu, 2017). Zewolda and Wereta (2012) also reported an overall sero prevalence of 11.9% by RBPT and 7.6% by CFT from camel, and a prevalence of 16% and 15% human brucellosis in Afra RBPT and CFT respectively. A sero prevalence of 4.7% (RBPT) and 1.34% (CFT) human brucellosis is also reported in abattoir workers at DebreZeit and Modjo export abattoir, Central Ethiopia(Tsegay et al., 2017).

10. References

Akpınar, O., 2016. Historical perspective of brucellosis: A microbiological and epidemiological overview. *Infezioni in Medicina*, 24 (1), 77-86.

Albornoz, A., 2013. *Brucellosis ppt* [online]. Slid e share. Available from: https://es.slidesha re.net/achestroker/infecto-cahn4c [Accessed 23 Jan, 2020].

Alemu, F., Admasu, P., Feyera, T., and Niguse, A ., 2014. Seroprevalence of bovine brucello sis in eastern Showa, Ethiopia. *Academic Journal of Animal Diseases*, 3 (3), 27-32.

Asgedom, H., Damena, D., and Duguma, R., 2016. Seroprevalence of bovine brucellosis and associated risk factors in and around Alage district, Ethiopia. *Springer Plus*, 5 (1), 851.

Asmare, K., Sibhat, B., Molla, W., Ayelet, G., Shiferaw, J., Martin, A. D., Skjerve, E., and Godfroid, J., 2013. The status of bovine brucellosis in Ethiopia with special emphasis on exotic and cross bred cattle in dairy and breeding farms. *Acta Tropica* [online], 126 (3), 186-192. Available from: http://dx.doi.org/10.1016/j.actatropica.2013.02.015.

Asnake, Y., Abrhaley, A., and Abuna, F., 2017. Brucellosis: Zoonotic Importance, Prevention And Control. *Nature and Science*, 15 (6), 18-30.

Bayu, M. D., 2018. Overview on CommonPathological Changes and Diagnostic Methods of Caprine and Ovine Brucellosis. *Journal of Veterinary Science & Medicine*, 6 (2), 01-12.

Bedore, B. and Mustefa, M., 2019. Review on Epidemiolgy and Economic Impact of Small Ruminant Brucellosis in Ethiopian Perspective. *Veterinary Medicine*, 4 (2), 77-86.

Berhe, G., Belihu, K., and Asfaw, Y., 2007. Seroepidemiological investigation of bovine brucellosis in the extensive cattle production system of Tigray region of Ethiopia. *International Journal of Applied Research in Veterinary Medicine*, 5 (2), 65.

Beruktayet, W. and Mersha, C., 2016. Review of Cattle Brucellosis in Ethiopia. *Academic Journal of Animal Diseases*, 5 (2), 28-39.

Dabassa, G., Tefera, M., and Addis, M., 2013. Small ruminant brucellosis:seroprevalence survey in Yabello district , Ethiopia. *Asian Journal of Animal Science*.

Deka, R. P., Magnusson, U., Grace, D., and Lindahl, J., 2018. Bovine brucellosis: prevalence, risk factors, economic cost and control options with particular reference to India- a review. *Infection Ecology and Epidemiology*, 9, 1-7. https://doi.org/10.1080/20008686.2018.1556548.

Dubie, T., Adugna, M., Sisay, T., and Mukitar, Y., 2014. The economic and public health significance of brucellosis. *Global Research Journal of Public Health and Epidemiology*, 1 (7), 2360-7920.

Edao, B. M., Hailegebreal, G., Berg, S., Zewude, A., Zeleke, Y., Sori, T., Almaw, G., Whatmore, A. M., Ameni, G., and Wood, J. L. N., 2018. Brucellosis in the Addis Ababa dairy cattle: the myths and the realities. *BMC Veterinary Research*, 14 (1), 396.

FAO, 2020. *Animal Health* [online]. Food and Agriculture Organization of the United Nations. Available from: http://www.fao.org/animal-health/en/ [Accessed 23 Jan 2020].

Ferede, Y., Mengesha, D., Mekonen, G., and H/melekot, M., 2011. Study on the seroprevalence of small ruminant brucellosis in and around Bahir Dar, North West Ethiopia. *Ethiopian Veterinary Journal*, 15 (2), 35-44.

Franc, K. A., Krecek, R. C., Häsler, B. N., and Arenas-Gamboa, A. M., 2018. Brucellosis remains a neglected disease in the developing world: A call for interdisciplinary action. *BMC Public Health*, 18 (1), 1-9.

Fulasa, T. T., 2004. Seroprevalence study of bovine brucellosis and its public health significance in selected sites of Jimma Zone, Western Ethiopia. [online]. available from: http://eprints.uanl.mx/5481/1/1020149995.pdf.

Gebretsadik, M. T., 2016. Seroprevalence of brucellosis and isolation of brucella from small ruminants that had history of recent abortion in selected Kebeles of Amibara district, Afar region, Ethiopia. Addis Ababa University.

Gemechu, R., 2017. Brucellosis and Its Control through One Health Approaches in Ethiopia. *Journal of Veterinary Medicine and Research Review*, 4 (3), 1080.

Geresu, M. A., Ameni, G., Wubete, A., Arenas-Gamboa, A. M., and Kassa, G. M., 2016. Isolation and Identification of Brucella Species from Dairy Cattle by Biochemical Tests: The First Report from Ethiopia. *World s Veterinary Journal*, 6 (2), 80-88.

Gutema, F. and Tesfaye, J., 2019. Review on Camel Brucellosis : Public health importance and status in Ethiopia . *Journal of Agricultural Science and Research*, 7 (7), 513–529.

Hailu, Y. G., 2017. Seroprevalence and isolation of brucella species from camel and cattle with history of recent abortion in Amibara district, Afar Regional State.. http://www.tandfonline.com/doi/abs/10.1080/14639947.2011.564813%0Ahttp://dx.doi.org/10.1080/15426432.2015.1080605%0Ahttps://doi.org/10.1080/15426432.2015.1080605%0Ahttp://heinonline.org/HOL/Page?handle=hein.journals/abaj102&div=144&start_page=26&collection.

Higgins, J., 2015. Characterization of Brucella infection in ruminant hosts: Disease pathogenesis, immunology, and epidemiology. [online]. Colorado State University. Available from: https://search.proquest.com/docview/1755925232?accountid=27931.

Kebede, T., Ejeta, G., and Ameni, G., 2008. Seroprevalence of bovine brucellosis in smallholder farms in central Ethiopia (Wuchale-Jida district). *Revue de Medecine Veterinaire*, 159 (1), 3-9.

Khan, M. Z. and Zahoor, M., 2018. An Overview of Brucellosis in Cattle and Humans , and its Serological and Molecular Diagnosis in Control Strategies. *Tropical Medicine and Infectious Disease*, 3 (65), 1-14.

Lemu, D., Mamo, H., Deressa, A., and Pal, M., 2015. A study on seroprevalence of brucellosis in goats and sheep in East Shewa, Ethiopia. *Ethiopian International Journal of Multidisciplinary Research* 1 (4), 14-18.

Meles, Y. and Kibeb, L., 2018. Sero-Prevalence of Bovine Brucellosis in and Around Chencha District, Gomogofa Zone, South Eastern Ethiopia. *World Journal of Pharmaceutical Research*, 7 (1), 1448-1460.

Mfune, R. L., 2015. Epidemiological study of bovine brucellosis in smallholder dairy cattle in Lushoto and Rungwe districts, Tanzania. Sokoine university.

Minda, A. G., Gobena, A., Tesfu, kassa, Getachew, T., Angella, A., and Gezahegne, M. K., 2016. Seropositivity and risk factors for Brucella in dairy cows in Asella and Bishoftu towns, Oromia Regional State, Ethiopia. *African Journal of Microbiology Research*, 10 (7), 203-213.

Mohammed, M., Mindaye, S., Hailemariam, Z., Tamerat, N., and Muktar, Y., 2017. Sero-Prevalence of Small Ruminant Brucellosis in Three Selected Districts of Somali Region, Eastern Ethiopia. *Journal of Veterinary Science and Animal Husbandry*, 5 (1), 1-6.

Moti, Y., Hailu, D., Tadele, T., Kelay, B., Ronald, C., and Sally, C., 2013. Brucellosis in Ethiopia. *African Journal of Microbiology Research*, 7 (14), 1150-1157.

Poester, F. P., Nielsen, K., Samartino, L. E., and Yu, W. L., 2010. Diagnosis of Brucellosis. *The Open Veterinary Science Journal*, 4, 46-60.

Ragan, V., Vroegindewey, G., and Babcock, S., 2013. International standards for brucellosis prevention and management. *Rev. sci. tech. Off. int. Epiz.*, 32 (1), 189-198.

Rahman, A. A., 2015. Epidemiology of brucellosis in humans and domestic ruminants in Bangladesh. University of Liege-Faculty of Veterinary Medicine.

Rajala, E. L., 2016. Brucella in Tajikistan - zoonotic risks of urbanized livestock in a low-income country. Swedish University of Agricultural Sciences.

Sintayehu, G., Melesse, B., Abayneh, D., Sintayehu, A., Melaku, S., Alehegne, W., Mesfin, S., De Blas, I., Casal, J., Allepuz, A., Martin-Valls, G., Africa, T., and Abera, K., 2015. Epidemiological survey of brucellosis in sheep and goats in selected pastoral and agro-pastoral lowlands of Ethiopia. *OIE Revue Scientifique et Technique*, 34 (3), 881-883.

Tassew, H. and Kassahun, F., 2014. Sero-Epidemiological Study of Camel Brucellosis in Mehoni District, South Eastern Tigray, Ethiopia. *Journal of Microbiology Research*, 4 (1), 18-23.

Teka, D., Tadesse, B., Kinfe, G., and Denberga, Y., 2019. Sero-Prevalence of Bovine Brucellosis and its Associated Risk Factors in Becho District, South West Shewa, Oromia Regional State, Ethiopia. *ARC Journal of Animal and Veterinary Sciences*, 5 (2), 35-45.

Tolosa, T., Regassa, F., Belihu, K., and Tizazu, G., 2007. Brief Communication: Brucellosis among patients with fever of unknown origin in Jimma University Hospital South Western Ethipiopia. *Ethiopia Journal of Health and Science*, 17 (1), 1-6.

Tsegay, A., Tuli, G., Kassa, T., and Kebede, N., 2015. Seroprevalence and risk factors of Brucellosis in small ruminants slaughtered at Debre Ziet and Modjo export abattoirs, Ethiopia. *Journal of Infection in Developing Countries*, 9 (4), 373-380.

Tsegay, A., Tuli, G., Kassa, T., and Kebede, N., 2017. Seroprevalence and risk factors of brucellosis in abattoir workers at Debre Zeit and Modjo export abattoir, Central Ethiopia. *BMC Infectious Diseases* 17 (1), 1-8. http://dx.doi.org/10.1186/s12879-017-2208-0.

Tsehay, H., Getachew, G., Morka, A., Tadesse, B., and Eyob, B., 2014. Seroprevalence of brucellosis in small ruminants in pastoral areas of Oromia and Somali regional states, Ethiopia. *Journal of Veterinary Medicine and Animal Health*, 6 (11), 289-294.

Wakene, W. Z., Kasim, S., Ahmed, A., Bulbula, A., Liban, H., Bulcha, A., Belete, M., Abichu, G., and Kinfe, G., 2017. Small ruminant brucellosis and awareness of pastoralist community about zoonotic importance of the disease in yabello districts of Borena zone Oromiya regional state, Southeren Ethiopia. *International Journal of Infectious Diseases*, 2 (2), 27-36.

WHO, 2020. *Brucellosis*. World Health Organizat ion. https://www.who.int/zoonoses/diseases/brucellosis/en/ [Accessed 23 Jan 2020].

Workalemahu, B., Sewunet, T., and Astatkie, A., 2017. Seroepidemiology of Human Brucellosis among Blood Donors in Southern Ethiopia : Calling Attention to a Neglected Zoonotic Disease, 96 (1), 88-92.

Yuguda, M. U., Sundaram, S., Lakshmanan, G., Ayyasamy, E., Purushothaman, S., Kannan, P., and Sanjeevi, T., 2019. Serosurveillance of Bovine Brucellosis Using RBPT and c-ELISA and Comparative Evaluation of Test Performance. *International Journal of Current Microbiology and Applied Sciences*, 8 (08), 559-568.

Zenebe Kelkay, M., Gugsa, G., Hagos, Y., and Taddelle, H., 2017. Journal of Veterinary Medicine and Animal Health Sero-prevalence and associated risk factors for Brucella sero-positivity among small ruminants in Tselemti districts, Northern Ethiopia. *Journal of Veterinary Medicine and Animal Health* 9 (11), 320-326.

Zewolda, S. and Wereta, M., 2012. Seroprevalence of Brucella Infection in Camel and Its Public Health Significance in Selected Districts of Afar Region, Ethiopia. *Journal of Environmental and Occupational Science*, 1 (2), 91-98.

Access this Article in Online	
Quick Response Code	Website: www.ijarbs.com Subject: Veterinary Sciences
DOI:10.22192/ijarbs.2022.09.08.015	

How to cite this article:
Yalew Abiyu Senbeto. (2022). Brucellosis: A review. Int. J. Adv. Res. Biol. Sci. 9(8): 146-161.
DOI: http://dx.doi.org/10.22192/ijarbs.2022.09.08.015