Public Policy and Administration Research
ISSN 2224-5731(Paper) ISSN 2225-0972(Online)
Vol.5, No.7, 2015

Public Health and Economic Importance of Brucellosis: A Review

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Abstract
Zoonotic diseases are of major concern worldwide. *Brucellosis* is considered to be one of the world's most important causes of illnesses in animals and humans. Brucellosis is an infectious, contagious, double burden and worldwide spread zoonotic disease caused by bacteria of the genus *Brucella* that have a wide host ranges and this facilitates the spread of the disease in different domestic and wild animals including humans. It is a public health problem with adverse health implications both for animals and human beings as well as economic implications for individuals and communities. Management, animal movement, wide ranges of host, herd size, commingling of different animal species are risk factors for animal brucellosis. The possible risk factors for human brucellosis are feeding behavior, occupational exposure, contact with diseased animals or their products and discharges. Brucellosis is characterized by similar clinical signs in different animal species and recognized after the animals are sexually matured. In animals the common clinical signs of brucellosis are abortion, retained placenta, orchitis, epididymitis andarthritis. Infertility is a common sequel of animal brucellosis and this is one of the factors that bring negative impacts on the development of economy of the infected countries. Human brucellosis is characterized by a variable incubation period and clinical signs include symptoms of continued, intermittent or irregular fever of variable duration, with headaches, weakness, profuse sweating, chills, depression and weight loss. In humans undulating fever is the most frequently observed sign. Abortion is also happened during the early trimesters of pregnancy. The disease is known widely distributed in Ethiopia among animals and human. Hence, periodic research should be conducted in the country to evaluate the prevalence of the disease; implementation of well-organized disease control and prevention methods must be undertaken to mitigate its impacts.
Key words: *Brucella, Brucellosis, Economic importance, Public Health Importance*

INTRODUCTION

Brucellosis is an infectious, contagious, and worldwide spread form of an important zoonotic disease caused by bacteria of the genus *Brucella*. *Brucellae* are facultative intracellular parasites of the reticuloendothelial system. The disease primarily affects cattle, sheep, goats, swine, and dogs. Among the members of the Brucella group *Brucella abortus*, *B. melitensis*, and *B. suis* species are not host-specific, and may transmit to other animal species; hence, from epidemiological evidence, the three species (*B. abortus*, *B. melitensis*, and *B. suis)* have distinct host preferences and the organisms are capable to cause an infection in a wide range of host species, including humans. The remaining three members of the species have much greater host specificity. Cross transmission of brucellosis can occur between cattle, swine, sheep and goats and other species including dogs, horses, feral swine, bison, rein deer and camels (Than, 2007 & FAO, 2003).

It is a public health problem in developing countries with adverse health implications both for animals and human beings as well as economic implications for individuals and communities. It is an occupational hazard with those particularly at risk such as laboratory workers, veterinarians, abattoir workers, farmers and animal keepers either living in close proximity with animals or handling aborted fetus and animal products that contaminated by *Brucella* agents. (Radostits *et al*., 2000, FAO *et al*., 2006 & Jim *et al*., 2012).

Millions of individuals are at risk worldwide, especially in countries where infection in animals has not been brought under control, procedures for heat treatment of milk such as pasteurization are not routinely applied, and standards of hygiene in animal husbandry are low. It has a considerable impact on animals and humans health, as well as wide socio-economic impacts especially in countries in which rural income relies largely on livestock breeding and dairy products (Gul & Khan, 2007).

The risk of disease and its severity is determined by the species of *Brucella* to which an individual is exposed. This will be influenced by the species of host animal acting as source of infection. *Brucella melitensis* is the type most frequently reported as a cause of human disease and the most frequently isolated from cases. It is the most virulent type and associated with severe acute disease. Contrary to some traditional views, *B. melitensis* remains fully virulent for man after infecting cattle. The bovine infection presents a particularly serious problem because

of the large volume of infected milk that can be produced by an individual animal and because of the extensive environmental contamination that even single abortions or infected births can produce (Radostist *et al*., 2000).

The major route of infection appears to be through the mucous membranes of the oropharynx and upper respiratory tract or the conjunctiva. Other potential routes of infection are through the mucous membranes of the male or female genital tract and skin penetration. Following exposure, the organisms penetrate intact mucosal surface. After penetration the organisms may be engulfed by phagocytic cells and localized to regional lymph nodes. Then they proliferate, disseminate haemogenously and localize in the reticuloendothelial and reproductive tract (SCAHAW, 2001 & Radostist *et al*., 2007).

Abortion is typically one of the clinical signs of the pregnant females, and orchitis and epididymitis are typical clinical signs of the male. Infertility, and, rarely arthritis, with excretion of the organisms in uterine discharges and in milk are also the signs; headaches, weakness and undulating fever are commonly known signs in humans (Radostits *et al*., 2007).

Naturally infected and vaccinated animals can be serological reactors. After infection, the level of immunoglobulin istotypes IgM, IgG and IgA will significantly increase in serum. IgM antibodies, which appear initially after infection and low levels of IgG, will cause complement-mediated lysis of *Brucella.* Secretary IgA is tend to be abundant in milk where as IgG is high in serum. The O-chain of smooth lypopolysaccharide complex of the cell envelope together with the outer protein epitopes have contributory role as protective immunogens. On the other hands, the immunogenecity of the non-smooth variant is relatively low. The O-chain specific antibodies play a major role in protective immunity, but don't eliminate the organisms as they are protected being intracellular (Radostits *et al*., 2007).

Both in humans and animals, clinically diagnosing of brucellosis is not easily achieved because of the presence of other diseases which have similar clinical signs. Even if clinical history and information about the patient give some clue in humans case, laboratory tests such as screening tests and confirmatory tests are very important tools for a correct identification of the disease in humans and for the detection and confirmation in animals; this enables to take strategic measures for controlling and prevention of brucellosis both in animals and humans accordingly. Even though, it is not generally recommended for animal brucellosis due to its outcome uncertainty, effective antibiotics are essential in human brucellosis for a long period of time (Fernando *et al*., 2010). However, some investigations had been done on prevalence of the brucellosis in some parts of the Ethiopia, it is difficult to note the general prevalence of animal and human brucellosis in the whole country Ethiopia; this may be due to lack of reports on the case throughout the country wide and due to lack of any data or clue about the disease in some animal species like swine, equines and canine hence they are affected by genus *Brucella* (Gebresadik, 2005). Hence, the objectives of this paper are to: -

- Review the public health and economic importance of brucellosis
- Assess the prevalence of brucellosis in different areas of Ethiopia
- Recommend control measures and further study on the current status of brucellosis in the country, Ethiopia

ETIOLOGY

Taxonomy and Classification of *Brucella*

The genus *Brucella* resides within the family *Brucellaceae* order Rhizobiales, class Alphaproteobacteria and phylum Proteobacteria. The Proteobacteria are a major phylum of bacteria, which include a wide variety of pathogens, such as *Escherichia*, *Salmonella*, *Vibrio*, *Helicobactelr*. All proteobacteria are Gram-negative, with an outer membrane mainly composed of lipopolysaccharides (Bergey *et al.,* 1994).

The genus of *Brucella* are subdivided into six species categorized by antigenic variation and primary preferred host and these include *B. abortus*, *B. melitensis, B. suis, B. ovis, B. canis* and *B. neotomae (*Garry & Christopher, *2010)*. The ability of genus *Brucella* to replicate and persist in host cells is directly associated with its capacity to cause persistent disease and to circumvent innate and adaptive immunity. There are different species of *Brucella* organism that cause disease in different animal species and humans. A single species can cause disease in different animal species and humans, which means it has a range of hosts (FAO, 2003).

Table 1: Hosts affected by *Brucella* species

Hosts	*Brucella* species				
	B. abortus	*B. melitensis*	*B. suis*	*B. ovis*	*B. canis*
Cattle	+	+	(+)	-	-
Sheep	(+)	+	+	+	-
Goats	(+)	+	-	-	-
Swine	(+)	(+)	+	-	-
Dogs	+	+	(+)	-	+
Camels	+	+	-	-	-
Humans	+	+	+	-	+
Horse	+	(+)	(+)	-	-

Source: FAO *et al*. (2006)

Key: +: can be affected, - : can't be affected, (+): rarely affected

The species of *Brucella* and their major hosts are *B. abortus* (cattle), *B. Melitensis* (goats), *B. suis* (pigs), B. canis (dogs), *B. ovis* (sheep) and *B. neotomae (*desert wood rats*)* as indicated in Table 1 above. Some *Brucella* species like *B. abortus*, *B. melitensis*, *B. suis* and *B. canis* can affect a ranges of hosts in addition to their natural hosts resulting hazards on the health of animals including humans; due to this, infected countries are challenged and have been under difficulties to overcome or control brucellosis effectively. In addition to cattle, *B. abortus* can affect other animals like sheep, goats, horses, camels, swine, dogs and humans. *Brucella melitensis* also affects other animals like sheep, horses, swine, camels, dogs and humans. *Brucella suis* also affects different animal species such as cattle, sheep, goats, dogs, camels, horses and humans. *Brucella ovis* affects only ovine while *B. canis* affects dogs and humans (FAO *et al*., 2006).

Morphology and Growth Requirement of Brucella Organisms

Brucellae are coccobacilli or short rods, usually arranged singly but sometimes in pairs or small groups. The organisms are gram negative facultative intracellular parasites. Carbon dioxide is important elements for growth of *Brucella* organism, especially *B. abortus*; such organisms, which require carbon dioxide for their growth, are called capnophilic organisms. At PH < 4, *Brucella* agents do not have potential to survive (Fernando *et al*., 2010).

EPIDEMIOLOGY

Source of Infection and Mode of Transmission

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 (Radostits *et al.*, 2000). 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. Some *Brucella* species have also been detected in other secretions and excretions including urine, feces, hygroma fluids, saliva, and nasal and ocular secretions. In most cases, these sources seem to be relatively unimportant in transmission; however, some could help account for direct non-venereal transmission of *B. ovis* between rams *(*OIE, 2009 & Teferi *et al.,* 2011).

Of the transmission ways of brucellosis to human, ingestion of unpasteurized dairy foods produced from unlicensed family owned flocks whose products are sold door-to-door at low prices is one of the known ways. Dairy products are the main source of infection for people who do not have direct contact with animals. Transmission of infection to humans occurs through breaks in the skin, following direct contact with tissues, blood, urine, vaginal discharges, aborted fetuses or placentas. Occupational aerosol infection in laboratories and abattoirs has also been documented. Accidental inoculation of live vaccines (such as *B. abortus* Strain 19 and *B. melitensis* Rev.1) can also occur, resulting in human infections. There are also case reports of venereal and congenital infection; and it can be transmitted through transplacental transfer and breast feeding even though rarely (FAO, 2003 & Kulkarni *et al*., 2009).

Risk Factors

Environment

The survival of the organism in the environment may play a role in the epidemiology of the disease under unsanitary condition where aborted fetuses are simply left everywhere where livestock, carnivorous animals and humans reach. Bovine infection presents a particularly serious problem because of the large volume of infected milk that can be produced by an individual animal and because of the extensive environmental contamination that even single abortions or infected births can produce. Temperature, humidity and PH influence the organism's ability to survive in the environment. *Brucella* is sensitive to direct sun light, disinfectant and pasteurization. The congregation of a large number of mixed ruminants at water points facilitates disease spread (Radostits *et al.*, 2007).

Reservoirs

Carrier animals facilitate transmission of brucellosis highly by contaminating the environment and also being site of multiplication for the *Brucella* organisms in their body and execrating such agents and again the execrated organisms infect animals and humans then bring hazards on health and economy of the country. The carriers are dogs, cats and wild carnivores, such as foxes and wolves, which may be important as mechanical disseminators of infection by carrying away infected material such as fetuses or fetal membranes enhances the viability of the organisms in the environment, thus increasing the chances of infecting susceptible animals. It should be remembered that wild carnivorous like dogs and cats can acquire infection with *B. abortus, B. melitensis* or *B. suis* from aborted ruminants or swine, usually by ingesting fetal or placental material that left freely in the environment. These animals can then excrete these bacteria and contaminate the environment where other animals and human live and this may present a serious hazard to humans and domestic livestock; hence poor management of wastes disposal and lack of controlling pet animals plays a great role in the spread of brucellosis in animals and humans (Bekele, 2004 & FAO *et al*., 2006).

Host Factors

The host factors, which are associated with spread of the disease brucellosis within a herd, include unvaccinated animals in infected herds, herd size, population density, age, sexual maturity and use of maternity pens. Large herd sizes are often maintained by the purchase of replacement cattle which may be infected. Population density (number of cattle to land area) is attributed to increased contact between susceptible and infected animals. Health status of the animals may also play a great role in acquiring the infection, hence vaccinated and disease free animals are less susceptible than unvaccinated and immune compromised diseased animals (Radostits *et al*., 2007).

Brucellosis seroprevalence increased with age and sexual maturity. The antibody titer against *Brucella* appears to be associated with age, as low prevalence in young stock has been reported than the adults. This low prevalence in young animals may be explained on the basis that the animal may harbor the organism without expressing any detectable antibodies until their first parturition or abortion. It may be possible that after entry, the organism localizes itself in the regional lymph nodes and enjoy there without provoking antibody production until the animal is conceived and start secreting erythritol, which stimulates and supports the growth of *Brucella* organisms. This is related to the fact that sex hormones and meso-erythritol (in male testicles and seminal vesicles) and erythritol in female, allantoic fluid stimulate the growth and multiplication of *Brucella* organisms and tend to increase in concentration with age and sexual maturity (Wadood *et al*., 2009, Radostits *et al.,* 2007 & Jergefa *et al.,* 2009).

In dairy farm, a higher seroprevalence of bovine brucellosis in females than males was reported as the result of that males are kept for relatively shorter time duration in breeding herd than females and thus the chance of exposure is lower for males and the spread of disease under natural condition is also not important. Moreover, females experience comparatively greater physiological stress during pregnancy and lactation due to which they are more susceptible to infection (Wadood *et al*., 2009). In animals, a higher prevalence was encountered on farms that used artificial insemination due to poor hygiene practices before and after insemination and inappropriate techniques of using equipments and inseminating (Radostits *et al*., 2000 & Jergefa *et al.,* 2009).

Management

The spread of the disease from one herd to another and from one area to another is almost always due to the movement of infected animals from an infected herd into a non infected susceptible herd. Hence, lack of strict movement control of animal from one area to another, lack of proper hygienic practices and good husbandry management play a great role in increament of the prevalence of brucellosis The source of replacement stock was found to affect the prevalence of brucellosis as a matter of a fact that the reproductive and health status of

these replacement animals may be under the risk of Brucellosis. The main risk for introducing the disease into a previously non-infected area is by purchase of infected animals (Tigist *et al*., 2011).

There are many risk factors for occurrence of brucellosis in human beings and from these factors some of them are food consumption behavior, hygienic practices (sanitation), occupational exposure, seasons, health status of the veterinary professionals and lack of practicing bio security level III. Feeding behavior such as Consumption of unpasteurized milk and milk products from cows, small ruminants or camels is considered to be the risk factor of infection in human brucellosis. Occupational exposure is one of the risk factors that affect risk groups like veterinarians, laboratory workers, food processors and farmers who handle infected animals and aborted fetuses or placenta (OIE, 2009).

PATHEGENESIS

Brucella may enter the host via ingestion or inhalation, or through conjunctiva or skin abrasions. After infecting the host, the pathogen becomes sequestered within cells of the reticuloendothelial system. The smooth lipopolysaccharides that cover the bacterium and proteins involved in signaling, gene regulation, and transmembrane transportation are among the factors suspected to be involved in the virulence of Brucella. The smooth, non endotoxic lipopolysaccharides help to block the development of innate and specific immunity during the early stage of infection; it protects the pathogen from the microbicidal activities of the immune system and has a role in cell entry and immune evasion of the infected cell (Porte *et al*., 2003 & Lapaque *et al*., 2005). The lipopolysaccharides are thought to alter the capacity of the infected cell to present foreign antigens to the Major Histocompatibility Complex (MHC class II) antigen presentation system, hence preventing attack and killing of the infected cell by the immune system. Additionally, smooth lipopolysaccharide in Brucella may be involved in the inhibition of apoptosis of infected cells, since resistance to apoptosis of infected cells has been observed in patients with acute and chronic disease (Lapaque *et al*., 2005 & Maria *et al*., 2007).

The two-component BvrR/BvrS gene sensing system that acts through a cascade of protein phosphorylation to modulate bacterial gene expression is thought to be one of the key factors involved in the modulation of cell binding and penetration. The BvrR/BvrS system of *Brucella* has a profound effect on the expression of various cell-surface proteins including Omp25 (also known as Omp3a) and Omp22 (Omp3b) (Guzman *et al*., 2002, Lopez *et al*., 2002 & Maria *et al*., 2007). In *Brucella*, VirB is thought to be essential for intracellular survival; however, the transported effector substrate in *Brucella* has not yet been identified and it is very unlikely that the transported molecule is a classic virulence factor. The VirB pumping system is built from a series of proteins encoded by the VirB operon (Celli *et al*., 2005 & Maria *et al*., 2007).

VirB seems to have a role in adherence of the bacterium to the host cell, cell entry, and it modulates the intracellular trafficking and replication of the bacterium (Boschiroli *et al*., 2002). After binding to macrophages, *Brucella* is taken up by internalization vesicles that would normally fuse with endosomes. After acidification, these endosomes lyse, destroying their contents. Acidification is thought to induce VirB expression (Arenas *et al*., 2000).

The VirB system is suspected to interact with components of the endoplasmic reticulum, neutralizing the pH and allowing the *Brucellae* to undergo regulated cell division within the endoplasmic reticulum's safe environment (Boschiroli *et al*., 2002). Heat shock protein 60 (Hsp60), a member of the GroEl family of chaperonins, is expressed on the cell surface of wild-type *Brucella* species but not on VirB mutants. Hsp60 seems to play a part in cell adherence by binding to a cellular prion molecule called PrPr. Since the exportation of Hsp60 is VirB-dependent, it has been postulated that Hsp60 could in fact be a virulence factor (Watarai, 2004)**.**

Rough strains (strains with lipopolysaccharide lacking the O-side chain) are less virulent because of their inability to overcome the host defence system; these rough strains do not confer host cells resistance to apoptosis. From genus *Brucella*, *B .ovis* and *B. canis* are classified under rough strains group while *B. abortus, B. melitensis* and *B. suis* are categorized under smooth strains group (high virulent and have O-side chain) (Porte *et al*., 2003).

CLINICAL FEATURES OF BRUCELLOSIS

Disease in Animals

Clinically, the disease is characterized by one or more of the following signs in animal species and these are abortion, retained placenta, orchitis, epididymitis and, rarely, arthritis, with excretion of the organisms in uterine discharges and in milk (Radostits *et al*., 2007). Infertility is a common sequel of animal brucellosis and this is one of the factors that bring negative impacts on the development of economy of the infected countries. In

horses, *B. abortus* and occasionally *B. suis* can cause inflammation of the supraspinous or supraatlantal bursa; these syndromes are known, respectively, as fistulous withers or poll evil. The bursal sac becomes distended by clear, viscous, straw colored exudates and develops a thickened wall. Fistulous withers are most common clinical sign of equine brucellosis and some horses appear to suffer a generalized infection with clinical signs including, general stiffness, lameness, fluctuating temperature and lethargy (Radostits *et al*., 2000 & Musa, 2004).

Disease in Humans

Human brucellosis is characterized by a variable incubation period (from several days up to several months), and clinical signs includes symptoms of continued, intermittent or irregular fever of variable duration, with headaches, weakness, profuse sweating, chills, depression and weight loss. Localized suppurative infections may also occur. Abortion is also happened during the early trimesters of pregnancy (FAO, 2003 & Than, 2007).

DIAGNOSIS

Clinical Signs

Clinically diagnosing of brucellosis in both humans and animals is not easily achieved because of the presence of other diseases which have similar clinical signs. Physicians dealing with a febrile patient living in an endemic area or recently travelled to a country where brucellosis is endemic must be aware of the possibility that the patient could be infected with *Brucella.* For this reason, correct clinical history taking is essential to orientate the diagnosis, and the need for some very basic questions (profession, food ingested, contact with animals and travel to endemic areas) must be emphasized (Fernando *et al*., 2010).

Bacteriology

In Bacteriological test**,** appropriate facilities are needed to isolate and identify all suspect *Brucella* species from abortion materials (fetal stomach contents and cotyledons), blood, milk and vaginal discharges, as well as tissues from slaughtered reactor animals, such as supra mammary lymph nodes. The use of highly selective culture media and the development of equipments for maceration of tissues have made isolation of *Brucella* a more rewarding task. Specimens for culturing must be carefully collected and appropriately handled during transportation (FAO, 2003 & Fernando *et al*., 2010).

There are a range of commercially available culture media for growing *Brucella*; the most common basal media in use are triptcase soy, bacto tryptose, triptic soy and tryptone soya. Frequently, field samples are contaminated with other bacteria, thus, selective media should be used to avoid overgrowth by fast growing agents. The use of selective culture media is needed to increase the probability of success of bacterial culture, and it is compulsory for the adequate bacteriological diagnosis of brucellosis. Any basal media mentioned above with agar may be used to prepare selective media. The most widely selective media used are the kuzdas, morse and farrell´s mediums. The kuzdas and morse use the following antibiotics and quantities per liter of basal medium, 100 mg of cycloheximide (fungistat), 25,000 units of bacitracin (active against gram-positive bacteria) and 6,000 units of polymyxin B (active against gram-negative bacteria). The farrell´s medium is prepared by the addition of the followings antibiotics and quantities per liter of basal medium, bacitracin (25mg), polymyxin B sulphate (5mg), nalidixic acid (5mg), nystatin (100,000 units), vancomycin (20mg), natamycin (50mg). As Farrell´s medium is rather inhibitory for some strains of *B. abortus*, *B. melitensis*, and *B. ovis*, a modified Thayer-Martin medium may be used together with Farrell's. This medium can be prepared with GC medium as basal medium supplemented with 1% hemoglobin and the following antibiotics per liter of medium, colistin methanesulphonate (7.5mg) vancomycin (3mg), nitrofurantoin (10mg), nystatin (100,000 units) and amphotericin B (2.5mg) (Fernando *et al*., 2010 & Miguel *et al*., 2011).

Classical identification and typing of *Brucella* species in to their respective species and biovars are the work should be undertaken after culturing any suspected specimen in appropriate media. After 48-72h of incubation at 37°C, *Brucella* colonies are 0.5 to 1.0 mm in diameter with a convex and circular outline. Smooth strains (*B. abortus, B. melitensis* and *B. suis*) are transparent and pale yellow, resembling droplets of honey with a shiny surface when observed in transmitted light. Rough colonies (*B. ovis* and *B. canis*) are more opaque with a granular surface when compared with the smooth strains of *Brucella* organisms. Dissociation of *Brucella* can be detected by the emulsification of a colony in 0.1% w/v aqueous acriflavine. Smooth colonies, *B. abortus, B. melitensis* and *B. suis* produce a yellow uniform suspension whereas rough colonies *B. ovis* and *B. canis* produce granular agglutinates. Colonial variation can be detected also by examining the plates under oblique light after staining the colonies with crystal violet. Smooth colonies appear translucent and pale yellow and rough colonies are stained with red, purple or blue with opaque and granular appearance (Fernando *et al*., 2010).

Colonial morphology, staining, slide agglutination with anti-*Brucella* serum (smooth or rough), urease, catalase and oxidase tests are the basis for a culture to be identified as belonging to the genus *Brucella*. Once a culture has been identified as *Brucella*, it is important to classify the species and the biovars. This further classification of such agents should be done in well specialized or reference laboratories that have full necessary facilities and requirements for classification and identification purposes without any confusing and challenging accordingly. These tests are cumbersome and include carbon dioxide requirement (CO_2), production of hydrogen sulphide (H2S), dye sensitivity (thionin and basic fuchsin), phage lysis, agglutination with specific antisera and in some cases it is necessary to use the oxidative metabolic method. This latter test is time consuming and hazardous to laboratory personnel. For these reasons it should be performed only by international reference laboratories (Fernando *et al*., 2010 & Miguel *et al*., 2011).

Serology

Serological tests can be divided broadly into two groups and these are screening tests and confirmatory tests. Some screening tests used in the field clinics or in regional laboratories, such as the Rose Bengal, Buffered Plate Agglutination Test (BPAT). The Rose Bengal Plate Test (RBPT) has a very high sensitivity to ensure that infected animals are not missed. The milk ring test is also an excellent screening test for dairy cattle. Indirect ELISA tests are also being used to screen milk and serum. Confirmatory tests include Complement Fixation Tests (CFT), competitive ELISA, Fluorescence Polarization Assay (FPA) are very useful in distinguishing vaccinal antibody responses from those induced by field infections (FAO, 2003).

In RBPT, *B abortus* s99 or s1119.3 cells are stained with Rose Bengal or Brilliant Green while in BPAT the cells are stained with Crystal Violet and suspended in a buffer which when mixed with the appropriate volume of serum results in a final PH of 3.65.This PH discourages agglutination by IgM but encourages agglutination by IgG1, reducing cross reaction. Antibody resulting from *B. abortus* s19 vaccination will react in these tests. These testes are considered as a suitable screening test for brucellosis followed by confirmatory tests like CFT (Fernando *et al*., 2010 & Miguel *et al*., 2011).

In Milk Ring Test, the agglutination test has been adapted to test milk for antibody to *Brucella* species. The format of this test is a little different in that hematoxylin stained *Brucella* cells are added to whole milk. The reaction is allowed to take place. Immunoglobulins present in the milk will in part be attached to fat globules *via* the Fc portion of the molecule. If antibody to *Brucella* species is present, agglutination will take place resulting in a purple band at the top of the milk. If no antibody is present, the fat layer will remain a buff colour and the purple antigen will be distributed throughout the milk. 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 derived from mastitis, colostrums and milk from late in the lactation cycle. Still, in spite of its problems, it may be used as an inexpensive screening test in conjunction with other tests (Fernando *et al*., 2010 & Huber *et al.,* 1986).

In spite of the number of reagents required for the complement fixation test and its technical complications, it is a widely used confirmatory test for brucellosis. The basic test consists of *B. abortus* antigen, usually whole cells, incubated with dilutions of heat inactivated (to destroy indigenous complement) serum and a titrated source of complement, usually guinea pig serum. After a suitable time a pre-titrated amount of sheep erythrocytes coated with rabbit antibody is added. If a primary immune complex (*B. abortus* cells and test serum) is formed due to the presence of certain antibody isotypes in the serum, complement was activated and therefore not available to react with the secondary immune complex of sheep erythrocytes and rabbit antibody, resulting in no or only slight lysis of the erythrocytes. Alternately, if no primary immune complex was formed, complement would cause all the sensitized sheep erythrocytes to lyse. The complement fixation test is technically challenging because a large number of reagents must be titrated daily and a large number of controls of all the reagents is required. It is also an expensive test again because of the large number of reagents needed and because it is labor intensive. However, since only IgG1 isotype of antibody fixes complement well, the test specificity is high. Unfortunately the test does not allow for discrimination of *B. abortus* S19 derived antibody. Other problems include the subjectivity of the interpretation of results, occasional direct activation of complement by serum (anticomplementary activity) and the inability of the test for use with haemolysed serum samples. In spite of the shortcomings, the complement fixation test has been and is a valuable asset as a confirmatory test in control/eradication programs (Fernando *et al*., 2010).

Competitive ELISA were developed in order to overcome some of the problems arising from residual *B. abortus* S19 vaccinal antibody and from cross reacting antibody. By selecting a monoclonal antibody with slightly higher

affinity for the antigen than most of the vaccinal/cross reacting antibody but with lower affinity than antibody arising from infection, reactivity by vaccinal antibody could be eliminated in the majority of cases. The specificity of the competitive ELISA is very high; however, it is slightly less sensitive than the indirect ELISA. This assay is an excellent confirmatory assay for the diagnosis of brucellosis in most mammalian species. The indirect ELISA generally have very high sensitivity but because they are largely unable to distinguish *B. abortus* S19 vaccinal antibody and cross reacting antibody, the specificity can be slightly lower than the assay specificity in areas where vaccination is not practiced (Fernando *et al*., 2010).

Fluorescence Polarization Assay (FPA) is one of the diagnostic methods that used for detecting antibodies. It is very accurate and the sensitivity specificity can be manipulated by altering the cutoff value between positive and negative reactions to provide a very sensitive screening test as well as a highly specific confirmatory test. The FPA is capable of distinguishing vaccinal antibody in most vaccinated animals and it can eliminate some cross reactions as well. 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 OPS is labeled with fluoroescein isothiocyanate and used as the antigen. When testing serum, blood and milk or other specimens, if antibody to the OPS is present, the rate of rotation of the labelled antigen will be reduced. The rate of reduction is proportional to the amount of antibody present (Fernando *et al*., 2010).

Table 2: Sensitivity and Specificity Index of the Serological Tests for Brucellosis

Tests	% Sensitivity	% Specificity	Performance Index (Min-Max)
RBPT	21.0 - 98.3	68.8 – 100	89.8 - 198.3
BPAT	75.4 - 99.	9 90.6 – 100	166.0 - 199.9
CFT	23.0 - 97.0	30.6 – 100	53.6 - 197.0
IELISA	92.0 – 100	90.6 – 100	182.6 - 199.8
CELISA	97.5 – 100	99.7 - 99.8	197.3 - 199.8
FPA	99.0 - 99.3	96.9 – 100	195.9 - 199.3

Source: Fernando *et al*. (2010)

Sensitivity and specificity ranges for the commonly used serological tests for brucellosis are tabulated in the (Table-6) above and the Performance Index provides an overall estimate of the accuracy of the test by adding the sensitivity and specificity values; the minimum and maximum values represent the lowest and highest indexes (Fernando *et al*., 2010).

Molecular Technique

Molecular biology as a diagnostic tool is advancing and will soon be at the point of replacing actual bacterial isolation. The use of the Polymerase Chain Reaction (PCR) to identify *Brucella* DNA at genus, species and even biovar levels has becoming extended to improve diagnostic tests and a diversity of methods have been developed. Applications for PCR methods range from the diagnosis of the disease to characterization of field isolates for epidemiological purposes including taxonomic studies. PCR-based assays are also useful in chronically infected patients where the yield of bacteria from blood cultures is usually low. It is rapid, safe and cost effective, the only real problems being some uncertainties regarding specificity (Fernando *et al*., 2010). In addition to the commonly used PCR assays, a new Multiplex-PCR assay was developed that specifically identified *B. neotomae*, *B. pinnipedialis*, *B. ceti*, and *B. microti*. Furthermore, it differentiated *B. abortus* biovars 1, 2, 4 from biovars 3, 5, 6, 9, as well as between *B. suis* biovar 1, biovars 3, 4, and biovars 2 and 5 (Huber *et al*., 2009).

MANAGEMENT STRATEGIES

Treatment, Prevention and Control of Brucellosis in Animals

Antibiotic treatment of known infected animals, or of those which are potentially exposed to *Brucellae* agents, has not been commonly used and it should be ruled out as an option in the control of brucellosis. A limited number of studies have shown rapid reductions in the incidence of brucellosis when the herd of flock was treated but this procedure is considered to be restricted in practice. Treatment has been used in animals of special breeding value, but because of the uncertain outcome it is not generally recommended (Radostits *et al*., 2000 & FAO, 2003).

It is nearly always more economical and practical to prevent diseases than to attempt to control or eliminate them. For brucellosis, the measures of prevention include Careful selection of replacement animals. Replacement

animals, 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. In addition, a serological test prior to commingling different animal species is necessary; preventing contacts and commingling with herds of 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, non-viable fetuses and disinfection of contaminated areas should be performed thoroughly (Radostits *et al.,* 2000 & FAO *et al*., 2006).

The aim of animal brucellosis 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. In many countries, methods for the control of brucellosis are backed by governmental regulation/legislation (FAO, 2003 & FAO *et al*., 2006).

Vaccination of animals usually results in elimination of clinical disease and the reduction in numbers of organisms excreted by animals which become infected. In many countries, vaccination is the only practical and economical means of control of animal brucellosis. The most successful method for prevention and control of brucellosis in animals is through vaccination. While the ideal vaccine does not exist, the attenuated strains of *B. melitensis* strain Rev.1 for sheep and goats and *B. abortus* strain 19 have proven to be superior to all others. It is often recommended that vaccination with strains 19 and Rev.1 should be limited to sexually immature female animals. This is to minimize stimulation of post vaccinal antibodies which may confuse the interpretation of diagnostic tests and also to prevent possible abortions induced by the vaccines. Positive serological reactors and secretors must be removed from the herd on detection (Radostits *et al*., 2000 & FAO *et al*., 2006).

Treatment, Prevention and Control of Brucellosis in Human

The essential element in the treatment 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. A variety of antimicrobial drugs have activity in vitro against *Brucella* species; however, the results of routine susceptibility tests do not always correlate with clinical efficacy. Consequently, beta-lactam antibiotics, such as penicillins and cephalosporins, and macrolide antibiotics, such as erythromycin, are associated with unacceptably high rates of relapse when used to treat patients with brucellosis. Although newer macrolides, such as azithromycin and clarithromycin are more active in vitro than erythromycin, they have not shown superiority over current regimens for treatment of patients with brucellosis, and their role in therapy remains to be determined. Doxycycline with gentamicine or repampin used for treating patient more than eight years of old (FAO *et al*., 2006).

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. 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. The lack of safe, effective, widely available vaccines approved for human use means that prophylaxis currently plays little part in the prevention of human disease (FAO, 2003).

Food safety is one of the principal pillars on which protection of human health resides; hence humans are infected by *Brucella* mainly through inappropriately prepared and/or preserved food of animal origin. Laws, regulations and veterinary policy measures alone will not bring the desired results. The whole community needs to be involved through health education in schools, in the workplace and in the population at large. Firstly, the higher the level of self-reliance and social awareness, the more individuals and families will accept responsibility for protecting their animals and themselves from disease hazards transmitted directly, through food of animal origin, or fomites (FAO, 2003).

All persons carrying out high-risk procedures, which includes contact with animals suffering from or suspected of having brucellosis, should wear adequate protective clothing. This includes an overall or coat, rubber or plastic apron, rubber gloves and boots and eye protection (face shield, goggles). The risk of infection is greatest

when dealing with aborting animals or those undergoing parturition but hazardous activities also include contacts with infected animals in other circumstances like shearing, dipping, clinical examination, vaccination and treatment, and the disinfection and cleaning of contaminated premises. The work clothes should be reserved for this purpose and retained on the premises. They should be disinfected after use either by heat treatment (boiling or steaming), by fumigation with formaldehyde or by soaking in a disinfectant solution of appropriate concentration (iodophor, phenolic soap, chloramine or hypochlorite). Particular attention should be given to the disinfection of footwear to ensure that infection is not transferred outside the premises or into the house or tent (FAO *et al*., 2006)**.**

ECONOMIC IMPORTANCE OF BRUCELLOSIS

Brucellosis is a major veterinary and human health importance in economy of affected countries. Among the genus *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 socioeconomic standpoint. In addition to decreasing productivity in animals, the first three species are the main ones responsible for brucellosis in human beings (Miguel *et al*., 2011).

Costs include production loss associated with infection in animals, preventive program, and in human disease cost of treatment and absenteeism from work brings many economical impacts. Losses in animal production due to brucellosis disease can be of major important, primarily because of the decreased milk production by aborting dairy animals; the common sequel of infertility increases the period between lactation, and in an infected herd the average inter calving period may be prolonged by several months. This is of greatest importance in beef herds where the calves represent the sole source of income. A high incidence of temporary and permanent infertility results in heavy culling of valuable and some deaths occur as the result of acute metritis following retention of the placenta. The effect of the disease on ram's fertility can influence the number of rams that are required in a flock; the required ram to ewe ratio is significantly reduced in *B. ovis*-free flocks. The percentage of lambs born early and within the first three weeks of the lambing period is also markedly increased (Radostits *et al*., 2000).

ZOONOTIC IMPORTANCE OF BRUCELLOSIS

Expansion of animal industries, the lack of hygienic measures in animal husbandry and poor food handling partly account for brucellosis to remain a public health hazard. International travel and the importation of different dairy products into *Brucella* free regions contribute to the ever-increasing concern over human brucellosis. Brucellosis is a zoonotic disease occurring in humans and various species of domesticated and feral animals. Human brucellosis can be a very debilitating disease, although the case fatality rate is generally low; it often becomes sub-clinical or chronic, especially if not recognized early and treated promptly. All ages of human beings are susceptible, and even congenital cases have been recorded (FAO *et al.,* 2006). High risk groups include those exposed through occupation in contexts where animal infection occurs, such as slaughterhouse workers, hunters, farmers and veterinarians (FAO, 2003).

The three species of *Brucella* of major concern here are *B. abortus* (biovars 1–6), affecting primarily cattle and other bovidae, *B. suis* (biovars 1-5), affecting primarily swine; and *B. melitensis* (biovars 1–3), affecting primarily sheep and goats. The persistent infection of the mammary glands and supramammary lymph nodes leads to a constant or intermittent shedding of the organisms in the milk in succeeding lactations. It provides an important source of infection for man and young animals. Of the three species, *B. melitensis* is highly pathogenic for human beings (FAO, 2003 & SCAHAW, 2001). In addition to the above three *Brucella* species, *B. canis* also has zoonotic importance and its infections in humans resemble brucellosis caused by other *Brucella* species (CFSPH, 2012).

Risk Factors for Humans Brucellosis

Occupational exposure

Brucellosis is an occupational hazard with those particularly at risk either living in close proximity with animals or handling them. These include people who work with farm animals, especially cattle, sheep, goats and pigs; farmers, farm labourers, animal attendants, stockmen, shepherds, sheep shearers, goatherds, pig keepers, veterinarians and inseminators are at risk through direct contact with infected animals or through exposure to a heavily contaminated environment. Infection may occur by inhalation, conjunctiva contamination, accidental ingestion, skin contamination especially via cuts or abrasions, and accidental self-inoculation with live vaccines. Also humans get infected by direct contact with infected animal products, ingestion of contaminated food, and inhalation of contaminated aerosols during laboratory works (FAO, 2003 & Ngenzi, 2011). It is important to

note that *B. canis* in culture, like all *Brucellae*, poses a significant occupational risk of infection to laboratory staff (FAO *et al*., 2006 & Jim, 2012).

Persons involved in the processing of animal products may be at high risk of exposure to brucellosis. These include slaughtermen, butchers, meat packers, collectors of fetal calf serum, processors of hides, skins and wool, renderers and dairy workers. The abattoir workers have high chance to be under risk of Brucellosis case and this may be due to high proximity they have to the *Brucella* microorganisms from that of infected animals organs and parts especially uterus and udder, which come to the abattoir to be slaughtered (Ngenzi, 2011).

Under absence of strict safety precautions in laboratory, the workers become infected seriously by *Brucella* agents that found in the infected sample like discharge from the reproductive organs, sample from aborted fetus, milk sample taken from infected dairy animal and any potentially contaminated materials. Inoculation of live vaccines (such as *B. abortus* Strain 19 and *B. melitensis* Rev.1) accidentally can also occur, resulting in human infections (FAO, 2003).

Feeding behavior

The majority of human brucellosis cases in many countries are caused by the ingestion of unpasteurized dairy foods produced from unlicensed family owned flocks whose products are sold door-to-door at low prices. Dairy products are the main source of infection for people who do not have direct contact with animals. Camel milk is a known source of infection for humans those who consume unpasteurized raw camel milk. Much of the milk which is consumed is now rendered safe by pasteurization or boiling, but cheese made from sheep and goat milk is preferably prepared from untreated milk and by the use of rennet from lambs and kids that may have come from *Brucella* infected animals. During the course of cheese manufacture, any *Brucella* present in the milk become trapped in the clot and thus concentrated in the cheese, although bacteria may subsequently be inactivated by manufacturing or ripening processes. (SCAHAW, 2001).

In contrast to dairy products, the survival time of *Brucella* in meat seems extremely short, except in frozen carcasses where the organism can survive for years. The number of organisms per gram of muscle is small and rapidly decreases with the pH drop of the meat. Direct contamination of abattoir workers is prevented by a proper and hygienic removal and disposal of mammary glands, reproductive organs and lymph nodes which are the most heavily contaminated. These precautions also prevent the contamination of the carcass by utero-vaginal secretions (SCAHAW, 2001). Muscle tissue usually contains low concentrations of *Brucella* organisms but liver, kidney, spleen, udder and testis may contain much higher concentrations. In some countries, dishes prepared from these organs may be eaten raw or undercooked (FAO *et al*., 2006).

Age and sex

In industrialized countries and in those others in which food hygiene prevents food-borne brucellosis, the disease is very largely occupational and the majority of cases are males between the ages of 20 and 45 years. In these situations, the disease is usually caused by *B. abortus* or *B. suis*. In countries or areas where *B. melitensis* is prevalent, the practices followed in marketing and distributing sheep and goat milk products in particular make the enforcement of hygienic measures very difficult. In this situation the whole population is at risk and many cases occur in women and children. In nomadic societies, the adults have often been exposed to infection at an early age and do not manifest acute disease, although many may have sequelae from chronic infection. Under such conditions children account for a high proportion of acute cases and brucellosis is largely a pediatric problem (FAO *et al*., 2006).

Pregnancy and breastfeeding

At the time of pregnancy, females are not potent to defense disease causing agents and they become susceptible to infectious agents easily and this may increase the chance of disease transmission from mother to the infants before and after birth. From such diseases, brucellosis is one of the diseases which poses health hazards during the course of pregnancy; and carries the risk of spontaneous abortion or intrauterine transmission to the infant. Abortion is a frequent complication of brucellosis in animals, where placental localization is believed to be associated with erythritol, a growth stimulant for *Brucella* organisms. Although erythritol is not present in human placental tissue, *Brucella* bacteremia can result in abortion, especially during the early trimesters. Whether the rate of abortions from brucellosis exceeds rates associated with bacteremia from other bacterial causes is unclear. In any event, prompt diagnosis and treatment of brucellosis during pregnancy can be lifesaving for the fetus. Very rare human-to-human transmission from lactating mothers to their breastfed infants has been reported (FAO *et al*., 2006).

Seasons
In humans, prevalence of the disease is high in summer season. Notifications of human brucellosis, which are mandatory in Italy, reach a peak between April and June. However, considering the standard incubation period of 2-4 weeks, and the fact that lamb slaughter is traditionally at a peak during the Easter period, it might be expected that occupational exposure would result in a peak of human cases between March and May. The observed peak between April and June could be related to the production and consumption of fresh cheese, starting just after lamb slaughter (Gul & Khan, 2007).

Bioterrorism
Brucella could be used to attack human and/or animal populations. The organism can be obtained from natural sources in many parts of the world. *Brucella melitensis* and *B.suis* have been developed experimentally as biological weapons by state sponsored programmes. Their relative stability in aerosol form combined with low infectious dose make them suitable agents for this purpose (FAO *et al*., 2006).

CURRENT STATUS OF BRUCELLOSIS IN ETHIOPIA

In Domestic Animals

In Ethiopia, there is no documented information on how and when brucellosis was introduced and established. However, in the last two decades several serological surveys have showed that bovine brucellosis is an endemic and wide spread disease in the country (Gebresadik, 2005). The overall seroprevalence of animal and human brucellosis is reported in different areas of Ethiopia in different times by different authorities and these noted in the Table-2. 3, 4, and 5 found on the next pages accordingly.

Seroprevalence of bovine brucellosis were reported in areas like Tigray Region, East Showa Zone, Central Oromia, Jimma Zone, Jijjiga, Arsi Zone, Agro-Pastoral Areas of and Southern, Eastern Ethiopia & Guto Gida District East Wollega Zone as (3.19), (11.2%), (2.9%), (3.1%), (1.38%), (0.05%), (3.5%) & (1.97 %), by Gebretsadik *et al*. (2007), Hunduma & Regassa (2009), Jegerfa *et al*. (2009), Nuraddis *et al*. (2010), Hailu *et al.* (2011), Teferi *et al. (*2011)*,* & Bekele *et al*. (2011) & Moti *et al.* (2012), respectively.

Result (11.2%) reported by Hunduma & Regassa (2009) is high when compared with the results that reported by the other authorities (Table-3) below and this may be due to the test used during the study, which is RBPT that used only for screening test and may reason for giving high prevalence. If confirmatory test like Complement Fixation Test is used, the prevalence of the case at the site might be reduced or lowered from the reported result (11.9%) by some present; only using the screening test for brucellosis affects the result of the study to be reported. Other factors like time difference, place of study, animal management, laboratory facilities, sampling and sample handling qualities may also contribute for the high or less prevalence of the disease when different studies undertaken on brucellosis case by various authorities at different time and study areas when compared.

Table 3: Prevalence of Bovine Brucellosis in some parts of Ethiopia

Study Area	Prevalence	References
Tigray Region	3.19%	Gebretsadik *et al*. (2007)
East Showa Zone, Oromia	11.2%	Hunduma & Regassa (2009)
Central Oromia	2.9%	Jegerfa *et al*. (2009)
Jimma Zone	3.1%	Nuraddis *et al*. (2010)
Southern And Eastern Ethiopia	3.5%	Bekele *et al*. (2011)
Arsi zone	0.05%	Teferi *et at.* (2011)
Jijiga Zone	1.38%	Hailu *et al. (*2011)
East Wollega Zone	1.9%	Moti *et al.* (2012)

Different authorities had reported prevalence of small ruminant in different parts of Ethiopia in various time and there is similarity between results documented (1.5%), (4.2%), (0.4%), (1.5%), by Mohamed *et al*. (2010), Tigist *et al*. (2011), Yeshiwas *et al*. (2011), and Mihreteab *et al*. (2011) in South Wollo, South Omo Zone, Bahir Dari and Jijiga Zone respectively and this indicated in Table-4 below. Hence, it was almost similar results were documented on small ruminant brucellosis in some areas of Ethiopia.

Table 4: Prevalence of Small ruminant Brucellosis in some parts of Ethiopia

Study area	Prevalence	References
South Wollo	1.5%	Mohamed *et al.*(2010)
South Omo Zone	4.2%	Tigist *et al.* (2011)
Bahir Dari	0.4%	Yeshiwas *et al.*(2011)
Jijiga	1.5%	Mihreteab *et al.*(2011)

As noted in the Table-5 below, some researches had been done on Camel brucellosis in different areas of Ethiopia where Camels are reared. Its prevalence was reported as (9.5%) Bekele (2004), (4.2%) Teshome *et al.* (2003), (1.6%) Omer *et al.* (2011), (1.5%) Ismail *et al.* (2012) in Borana Low Land, some camel rearing areas of Ethiopia, and Dire Dawa respectively. Prevalence of cattle and small ruminant brucellosis at the area, nature of management, commingling of different animal species and herd size are the key factors for occurrence of camel brucellosis.

Table 5: Prevalence of Camel Brucellosis in some parts of Ethiopia

Study area	Prevalence	References
Camel rearing regions of Ethiopia	4.2%	Teshome *et al.* (2003)
Borana Low Land	9.5%	Bekele (2004)
Dire Dawa	1.6%	Omer *et al.* (2011)
Dire Dawa	1.5%	Ismail *et al.*(2012)

In Ethiopia, there is no research done on Swine, Canine, Equine and wild animal brucellosis. This may be due to lack of due attention to this animals in concern of the disease, availability of the animals as the other animal (in case of swine), lack of well organized agency that take care for them (in case of wild animals). The lack of available laboratory diagnostic tests poses another impediment to the understanding of the epidemiology of these agents in the country. Even though these animals may serve as a source for infection for animals such as cattle, sheep, goats and also for humans directly or indirectly and play a great role on economy of the country multi-directionally, no any documents and due attention taken to investigate research, which concerns brucellosis case in such animal species in Ethiopia up to the present time.

In Humans

High prevalence of human brucellosis was reported from two study areas, in Borana and Hamer by Genene *et al.* (2009) when compared to the other reports (Table-6) and this may be due to the type of test that the researchers used (anti body test: IgM), which has high cross reaction with antibody titer which is due to infection with other microorganisms in comparison to other confirmatory tests as reported by Fernando *et al.* (2010). Because of the early onset of IgM antibody production, theoretically it would be best to measure this isotype as an indicator of exposure, however, a number of other microorganisms contain antigens with epitopes similar to those of OPS and the main antibody response to these cross reacting antigens is IgM. Therefore, measurement of IgM antibody sometimes gives false positive reactions in serological tests leading to low assay specificity (Corbel, 1985 & Fernando *et al.*, 2010).

The Brucella smooth lipopolysaccharide antigen tends to show cross reactivity with other Gram-negative bacteria such as *Yersinia enterocolitica, Vibrio cholerae, Escherichia coli* O:157, and *Francisella tularensis*, increasing the possibility of false-positive results. To exclude the possibility of cross-reactive IgM antibodies, the 2-mercaptoethanol test for measuring specific agglutinating IgG antibodies is sometimes used; results are compared with the serum agglutination test titer and reactivity in the 2-mercaptoethanol test is taken as evidence for the presence of specific IgG antibodies. However, many patients have low levels of agglutinating IgG antibodies and results can easily be misinterpreted (Maria *et al.*, 2007).

Table 6: Prevalence of Human Brucellosis in some areas of Ethiopia

Study Area	Prevalence	References
Addis Ababa	4.8%	Jiksa, 2003
Jimma University Hospital	3.6%	Tadele *et al.*, 2007
North Western Ethiopia	2.6%	Abebe *et al.*, 2009
Borana	34.9%	Genene *et al.*, 2009
Hamer	29.4%	Genene *et al.*, 2009
Metema	3.0%	Genene *et al.*, 2009

CONCLUSION AND RECOMMENDATIONS

Of the infectious contagious zoonotic diseases, brucellosis is one of the most important bacterial diseases distributed throughout the world and it is the challenging case in developing countries. Being a double burden disease, it affects the economy of developing countries in reducing production of livestock multi-directionally and putting humans under economic crises due to cost of treatment both in animals and humans. Even though, some researches had been done on prevalence of the disease in some areas of the Ethiopia, it is difficult to note the general prevalence of animal and human brucellosis in the whole country Ethiopia; this may be due to lack of reports on the disease throughout the country wide and due to lack of any data or clue about the disease in some animal species that affected by genus *Brucella*. Based on the above conclusion, the following recommendations are forwarded as:

- Researches should have to be done uniformly in the whole areas of the country Ethiopia on all animal species that affected by *Brucella* agents including equine, swine and canine to overcome the spread of the disease in between animal species and humans.
- The studies should be supported by diagnostic methods that enable us to now the most widely distributed strains of *Brucella* agents both in animal species and humans.
- Implementation of well-organized disease control and prevention methods must be undertaken to mitigate the economic losses and public health hazard caused by the disease.

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