Acta Scientific Veterinary Sciences (ISSN: 2582-3183)

Volume 5 Issue 1 January 2023

Review Article

Contagious Bovine Pleuropneumonia: Review

Daba Gudata Chala*

Jimma University College of Agriculture and Veterinary Medicine, Jimma, Ethiopia

***Corresponding Author:** Daba Gudata Chala, Jimma University College of Agriculture and Veterinary Medicine, Jimma, Ethiopia.

Received: July 26, 2022

Published: December 09, 2022

Abstract

Contagious bovine pleuropneumonia is a highly contagious chronic respiratory disease of cattle caused by Mycoplasma mycoides sub-species mycoides small colony. The disease is characterized by a relatively long incubation period and a highly variable clinical course. Recovered animals may harbor the infection in lung sequestra; necrotic areas of lung tissue separated from the surrounding normal tissue by a fibrous capsule. Contagious bovine Pleuropneumonia is current disease of major concern throughout Sub-Saharan Africa. The principal route of infection is by the inhalation of infective droplets from animals active or carrier cases of the disease. Important pathogenicity factors in Mycoplasma mycoides subspecies mycoides small colony are capsular polysaccharide, hydrogen-peroxide and variable surface protein. It is manifested by anorexia, fever and respiratory signs such as dyspnoea, polypnea, cough and nasal discharges. Diagnosis depends on the isolation of an etiological agent. The common methods used for the diagnosis of the disease are complement fixation test and enzyme linked immune sorbent assays. It is considered to be a disease of economic importance. Commonly used antibiotics include tetracycline, tylosin, erythromycin, lincomycin, spectinomycin and tilmicosin. The main problems for control or eradication are the uncontrolled movements of animals and the frequent occurrence of sub-acute or sub-clinical infections and the persistence of chronic carriers after the clinical phase. Therefore, adequate control strategic measures should be implemented for eradication of the disease such as test and slaughter, stamping out, quarantine and vaccination.

Keywords: Cattle; Contagious bovine Pleuropneumonia; Mycoplasma mycoides subspecies mycoides small colony; Sub-Saharan Africa

Introduction

Ethiopia is a leading country in the number of livestock population in the African continent with an estimated 59.5million cattle, 30.7 million sheep, 30.2million goats and 56.53 million poultry [9]. The livestock sector has a significant role in socio-economic activities of the country and contributes much to the national economy particularly with regard to foreign currency earnings through exportation of live animals, meat, skin, and hides [1]. However, the output of this livestock sector in terms of its contributions to the improvement of the livelihood of animal owners and for the growth of national economy is at a lower stage compared to the vast resource on hand (27;28). The major constraints contributing to low productivity include low genetic potential of the animals, poor nutrition and prevailing animal diseases (14;17). Among the health constraints, transboundary animal diseases such as Contagious bovine pleuropneumonia (CBPP) cause the major limitation to the livestock sector development in the country and affect livelihood through their impact on animal health, animal food production, availability and quality [21].

Contagious bovine pleuropneumonia (CBPP) is highly contagious trans-boundary disease of cattle caused by *Mycoplasma mycoides subspecies mycoides* Small Colony (*Mmm*SC). Under natural conditions, it affects only domestic ruminants of the genus *Bos*, mainly *Bos taurus* and *Bos indicus* [2]. It has great potential for rapid spread and causes major impact on cattle production. The disease is manifested by anorexia, fever and respiratory signs such as dyspnea, polypnea, cough and nasal discharges in cattle [40]. The principal route of infection is inhalation of infective droplets of diseased animals [44]. Factors such as age, stress and concurrent infections may predispose to tissue invasion [32] and other risk factors for its spread include high-density confinement in night housings and

mixing of herds at common grass lands and watering places [8]. Due to its high economic impact, OIE declared as one of the most serious contagious animal disease and listed on the group of notifiable animal diseases of high socio-economic impact and regarded as major trans-boundary animal disease (TADs) [21].

Contagious bovine pleuropneumonia (CBPP) has been known to occur in Europe since the 16th century but it gained a world-wide distribution only during the second half of the 19th century because of increased international trade in live cattle. Although CBPP was once found worldwide, it was eradicated from many countries during the mid 20th century `through the application of restrictions to the movement of cattle, as well as test and slaughter policies combined with compensation for livestock owners. Its incidence also began to decline in Africa by the 1970s. However, because of the economic and financial difficulties, the disease came back in the late 1980s and early 1990s. As a result, the disease remains endemic in Africa particularly in tropical and sub-tropical regions (West, central, east and parts of southern Africa) of the continent [3] and it is one of the major constraints to cattle-raising and trade in African countries [4].

Ethiopia is one of east African countries in which CBPP is endemically maintained in various parts of the country. After rinderpest was eradicated, CBPP has become the most important cattle disease that hinders livestock development in the country. This is mainly caused due to the interruption of the consecutive yearly blanket vaccinations with combined rinderpest [33]. According to update and critical analysis of 20years (1996-2016) reports by [1], studies undertaken on CBPP so far in different localities of the country both at production area and the quarantine stations revealed the existence of the disease in different parts of the country with seroprevalence which ranges from 0.4% to 96%. It is now re-emerging as one of the most economically important diseases that impede livestock production and remain a threat to livestock export potential in the country [15]. Therefore, the objective of this review paper is to review on epidemiology, diagnosis, economic importance and control methods of contagious bovine pleuropneumonia.

Literature Review

The Disease

Contagious bovine pleuropneumonia (CBPP) is an acute, subacute or chronic respiratory disease of cattle and occasionally water buffalo and it is one of the most serious cattle diseases in Africa [2]. The most common forms of the disease are the sub-acute and chronic forms and usually cause sub-clinical infections responsible for continuing the spread of the disease. Cattle with acute to subacute disease develop serofibrinous pleuropneumonia and severe pleural effusion. In animal that develop the chronic form of the disease or recover from the acute disease, persistent pulmonary sequestra occur but their ability to transmit the disease is uncertain [32]. On account of its transmissibility and economic impacts, CBPP is now recognized as a priority transboundary animal disease and has thus been categorized in the OIE list"A"diseases. This respiratory disease is characterized by morbidity rates that could be as high as 75% to 90%. The mortality rate seems to vary from 50% to 90% while the case- fatality rate was found to be 50%. The disease is responsible for heavy economic losses due to mortality, loss of weight, reduced working ability and infertility. Additional losses can also be attributed to lost market opportunities due to trade bans [2].

Etiology

The causative agent of contagious bovine pleuropneumonia is *Mycoplasma mycoides sub-species mycoides* small colony which belongs to the class *Mollicutes*, order *Mycoplasmatales*, family *Mycoplasmataceae and* genus *Mycoplasma* [28]. The *Mycoplasmas (Mollicutes)*, formerly called PPLO (Pleuropneumonia-like organisms), arenon-sporulating, Gram-negative, non-motile bacteria, which do not possess a determined shape of the cell. The *Mollicutes* are the smallest of the free-living prokaryotes. *Mollicutes* is the correct term to use when collectively referring to members in this order; however, the trivial name *mycoplasma (s)* is also used for this purpose [5].

There are no internal membrane structures and no cell wall external to the plasma membrane; however, many strains possess surface structures equivalent to a capsule. with the exception of *Acholeplasmas*, *Mycoplasmas* depend on a supply of intact cholesterol, which they incorporate into the membrane, creating sufficient osmotic stability for survival under normal physiological conditions. The *Acholeplasma* synthesize carotenol as a substitute for cholesterol but will incorporate cholesterol if it is provided. Their polymorphism is the consequence of the missing cell wall. *Mycoplasmas* are devoid of not only cell walls but also lack the genetic capacity to produce one, which also renders the

completely resistant to ß-lactam and other cell-wall active drugs (24). Cells sometimes appear as chains and beads, the result of a synchronized genomic replication and cell division. The preferred stains are Giemsa, Castaneda, Dienes and ethylene blue [5]. When observed with dissecting microscope, many species exhibit "f*ried egg*" morphology [44].

Growth of *mycoplasma* is relatively fastidious and requires special media rich in cholesterol with addition of horse serum. The *mollicutes* grow slowly and generally require 3 to 6day incubation before colonies are apparent. Growth is best at 37°c in atmosphere of increased Co_2. The optimum PH for growth of *ureaplasma* is 6, whereas 7.5 for other *mollicutes*. Colony sizes vary from 0.1mm to 1.0mm [39].

In natural conditions, two types of *Mycoplasma mycoides* are recognized: large colony (LC) and small colony (SC). They cannot be differentiated serologically but are different morphologically, culturally and in their pathogenicity and can be distinguished through mouse protection tests. *Mycoplasma mycoides subspeciesm ycoides* Small Colony type (*Mmm*SC) affects only the ruminants of the *Bos* genus (mainly bovine). Large colony types occur almost exclusively in goats, rarely in sheep while SC types cause CBPP in cattle [22]. *Mycoplasma mycoides subspecies mycoides* large colony (LC) type does not result in disease in cattle, but causes septicemia, polyarthritis, mastitis and encephalitis in sheep and goats [2].

Epidemiology

Contagious bovine pleuropneumonia epidemiology is characterized by transmission by direct contact, long incubation period and possibility of early excretion of *Mycoplasma* (up to 20 days before apparition of clinical signs), during the course of the disease and after recovery in "lungers" up to two years). These epidemiological features on one hand and the lack of a reliable screening test to pick up early carriers and lungers on the other hand, make it essential to control cattle movements in order to limit the spread of the disease [39]. The epidemiology of CBPP in Africa is dominated by different factors; these are, cattle is the only species affected, transmission is through the direct contact of susceptible animal with clinical cases or chronic carriers and cattle movement play a very important role in the maintenance and extension of the disease [44].

Host range

Contagious bovine pleuropneumonia is predominantly the disease of cattle and occasionally water buffalo are naturally infected [5]. Clinical cases have also been reported in yak (*Poephagus grunniens/Bos grunniens*) and captive bison (*Bison bison*). Sheep and goats can be infected, although they are not thought to be important in the epidemiology of CBPP (42; 32). There are many reported breed differences with respect to susceptibility. In general, European breeds are tends to be more susceptible than indigenous African breeds [3]. There does seem to be some age resistance, animals less than three years of age are less resistant to experimental challenges. Experimental work in Australia showed that buffaloes could be infected by artificial means but did not spread CBPP to in contact buffaloes [27]. Natural infection has been demonstrated in goats by recovery of the agent from their lungs but experimental inoculation suggested that their susceptibility to the disease is low and the fact that CBPP was eradicated from Botswana by culling only the cattle; although large numbers of goats were present in the affected area, suggests that they do not serve as a reservoir for the disease [29]. *Mycoplasma mycoides subspecies mycoides* Small Colony (*Mmm*SC) had been isolated from milk of sheep with mastitis and goats with pneumonia [16].

Geographical distribution

Contagious bovine pleuropneumonia is still an endemic disease in Africa, Asia, Eastern Europe, and the Iberian Peninsula [48]. With the imminent eradication of rinderpest from Africa, contagious bovine pleuropneumonia (CBPP) has become the disease of prime concern interms of epizootics that affects cattle [15] and it is one of the most serious diseases of cattle in African countries [27] particularly in tropical and subtropical regions (West, Central, East and parts of southern Africa) of the continent. Ethiopia, Kenya, Somalia, Sudan, Tanzania, and Uganda are some of the countries quoted [48].

Source of infection

The primary source of most of the pathogenic *mollicutes* is the host that is infected with the agent [3]. Cattle in the incubatory phase of the disease may harbor *Mmm*SC in their nasal passages for 40days prior to developing clinical signs or antibodies and are

considered to be a potent source of infection [27]. Carrier animals, including sub-clinically infected cattle, can retain viable organisms in encapsulated lung lesions (sequestra) for up to two years. These animals may shed organisms, particularly when stressed. As long as the bacteria remain encapsulated by fibrous tissue in the intact sequestrum the animal will not be infective, but it was thought that condition of stress due to starvation, exhaustions or intercurrent can cause the sequestrum to break down and convert the animal into an active case [4]. Experimental evidence throws some doubt on this explanation, but droplet infection is usually associated with a donar lesion in the lung [44].

Transmission

Closeness of contact, intensity of infection and number of susceptible animals are important factors in the rate of transmission of the disease [2]. Normally, transmissions are by droplet infection from actively infected animals to susceptible animals in close proximity [5]. Outbreaks usually occur as the result of movement of infected animals into a naïve herd. Cattle may be exposed to infections for a period of up to 8months before the disease become established and this necessitates a long period of quarantine before a herd can be declared to be free of the disease. This organism also occurs in saliva, urine, fetal membranes and uterine discharges. Close repeated contact is generally thought to be necessary for transmission; however, *Mmm* SC might be spread over longer distances (upto200meters) if the climatic conditions are favorable [20].

Risk factors

CBPP is typical example of multi-factorial diseases, where factors such as intercurrent infections, crowding, inclement climatic conditions, age, genetic constitution, and stress from transportation, handling and experimentation are important determinants of the final out-come of infection [27].

Contagious bovine pleuropneumonia occurs only in cattle; rare natural cases have been observed in buffalo, yak, bison, reindeer and antelopes and the disease has been produced experimentally in captive African buffalo and white tailed deer [44]. There are many reported breed differences with respect to susceptibility. In general, European breeds are tends to be more susceptible than indigenous African breeds. There does seem to be some age resistance, animals less than three years of age are less resistant to experimental challenges [3]. In addition, [31] reported that young animals are more susceptible to acute forms of CBPP infection than adult cattle and thus acutely infected young animals may die of CBPP and may not be available for testing. However, chronic stages of the disease are usually seen in adult cattle as the age progresses [41].

Mycoplasma mycoides subspecies mycoides Small Colony is sensitive to all environment influences; do not ordinarily survive outside the animal body for more than a few hours. Restriction enzyme analysis of strains of the organism found that European strains have different patterns than African strains [44]. The organism can be grouped into two major, epidemiologically distinct, clusters. One cluster contains strains isolated from different European countries since 1980 and second cluster contains African and Australian strains collected over the last 50 years. The current European strain lack a substantial segment of genetic information which may have occurred by deletion events. A variety of potential virulence factors have been identified, including genes of encoding putative variables, surface proteins, enzymes and responsible for the production H_2O_2 and the capsule transport proteins which is thought to have toxic effect on the animal. Molecular epidemiology of CBPP by multilocus sequence analysis of *Mmm* SC strains found a clear distinction between European and African strains. This indicates that the CBPP outbreaks which occurred in European were not introduction from Africa and confirms true re-emergence (39;34).

The occurrence and incidence of CBPP influenced by management system, disease control policies and regulation of the country, knowledge of the disease by farmers, veterinarians and livestock field officers. The diagnosis capabilities of veterinary laboratory, disease surveillance and monitoring system, adequacy of vaccination programs, government budget allocated to control programs, desires of cattle owner and traders to control the disease are critically important management factors, which influence the effectiveness of controlling disease in a country [44]. This affects epidemiology of the disease and crucial factor since CBPP is essentially related to the movement of animals [34].

In parts of Africa where there are dry climatic conditions, nomadism and transhumant pastoral practice are common making it very difficult not only to control livestock movement, but also to conduct disease surveillance because the farmers and their animals move from one place to another in remote areas with few roads and no means of modern communication. Other risk factors that facilitate the spread of the disease include cattle movement for trading and social activities, keeping many livestock in confinement in night housing and communal grazing where livestock share watering points and grassland are responsible for the spread of the contagion [32].

Pathogenesis

Very little is known about the factors and mechanisms that affect the pathogenicity of *Mmm*SC. No secreted toxins have been identified; neither receptor molecules on the bacterial surface that mediate binding to host epithelium or induce other cellular responses in the host tissues. However, certain factors have been associated with the pathogenesis, but the precise modes of action are still elusive [27].

An essential part of the pathogenesis of the disease is thrombosis in the pulmonary vessels, probably prior to the development of pneumonic lesions. The mechanism of development of the thrombosis is not well understood, but is considered, atleast in part, mediated through induction of cytokines [3]. Contagious bovine pleuropneumonia is lobar variety of pneumonia in which the interlobular septa are dilated and prominent due to a great outpouring of plasma and fibrin into them and this dilated septa that give the "*Marbling*" effect to the lung in these areas (2; 21).

Bronchitis, bronchiolitis and alveolitis with predominantly neutrophils and mononuclear cellular response constitute the very early inflammationin *Mycoplasma* pneumonia. Contagious bovine pleuropneumonia is characterized by substantial unilateral pulmonary necrosis, sometimes sequestration and marked serosanguinous fluid accumulation in interstitial and pleura [38]. Vasculitis appears to be an important component of the pathological changes in this disease, explaining the marked exudation and pleurisy. Thrombosis can explain ischemic necrosis and infarcts of the lung. Death results from anoxia and presumably from toxemia). There are various substances produced by the Mollicutes, which are potentially important in disease pathogenesis. Peroxide and super-oxide production may be important in disruption of host cell integrity [27].

Mycoplasma phospholipases are potentially important in pneumonia for they may reduce surface tension of the alveolar surfactant, thus resulting in atelectasis. A galactan polymerin *Mycoplasma mycoides subspecies mycoides* has been shown to modulate the immune response and promote dissemination [3].

Clinical signs

The disease affects the respiratory tract of cattle and characterized by fever, anorexia, dyspnea, polypnea, cough, and nasal discharge. Cattle of all ages are susceptible, but young cattle develop joint swelling rather than lung infections. Many cattle show no disease signs despite being infected and chronically infected animals might act as carriers and sources of infections (45;46).

Depending on the resistance level of the animal and the intensity of exposure, the disease takes an acute, sub-acute to chronic, or the acute course is sometimes followed by a chronic stage which may last for two years (lungers) as a latent phase of the disease [42]. In an affected herd, CBPP can be seen in hyperacute, acute, subacute or chronic forms (31;2). In endemic regions, 13% of cases are of the hyperacute form, 20% of the acute form and 46% of the subacute form. Approximately 21% of animals are resistant to the disease [31].

Hyperacute forms

Contagious Bovine Pleuropneumonia (CBPP) may be rapidly fatal with no clinical signs observed. This form occurs during the on set of an outbreak and death may be all that is seen. In some cases

the animal may die after one to three days with no signs of pneumonia. Death may result from asphyxia, toxaemia or heartfailure (43; 31).

Acute forms

The early stages of CBPP are indistinguishable from any severe pneumonia with pleurisy. Animals show dullness, anorexia, irregular rumination with moderate fever and may show signs of respiratory disease. After a few days, the temperature erises to 40°C or higher, accompanied by a fall in milk yield (in cows), anorexia and cessation of rumination. At this stage, chest pain is evident. Affected animals are reluctant to move and stand with the elbows abducted and the back arched, the head extended and the nostrils dilated. Breathing becomes short and rapid and a moist cough may be present. In the severe form of the disease, the mouth remains wide open and may contain foam. Mucoid discharge from the nostrils may occur. Exercise will aggravate the respiratory distress (31;3).

Figure 1: Clinical case of CBPP.
Source: (18).

While classical respiratory signs maybe evident in calves, articular localization of the causative agent with attendant arthritis usually predominates calves less than six month of years (5; 44).

In acute CBPP, there is a severe fibrinous pneumonia with copious pleural exudates. The latter is a striking feature and there may be up to 30 liters' of yellow exudates, containing clots, in the chest cavity. One or both lungs may be partially or completely consolidated, giving a characteristic marbled appearance. Affected areas are swollen, vary from pink to dark red, have a moderately firm consistency and exude clear fluid and sometimes blood from cut surfaces [3].

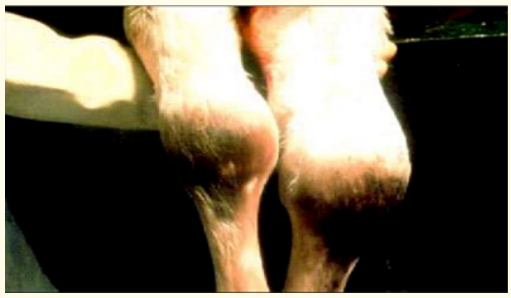

Figure 2: Swollen joints of a calf with acute CBPP.
Source: (18).

Subacute forms

Signs may be limited to as light cough only noticeable when the animal is exercised [2]. Cattle that recover naturally are extremely weak and emaciated. Many infected animals develop chronic or milder forms of the disease, which may be either symptom-less or associated with only a slight temporary rise in body temperature, and some loss of condition. Recovered animals may be clinically normal but in some, an inactive sequestrum forms in the lung, with a necrotic center of sufficient size to produce a toxemia causing unthriftness, a chronic cough, and mild respiratory distress on exercise. The length of the incubation period depends up on the volume of the infective dose, the virulence of the strain, and the immune state of the animal and it can last from a few days up to several months (in occasional instance up to 6months) [3].

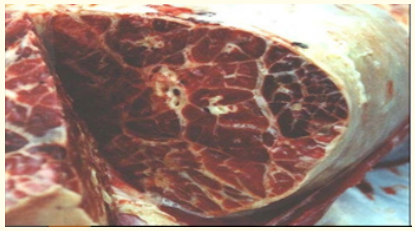

Figure 3: CBPP marbled lung.
Source: (18).

Chronic form

The chronic form is characterized by an apparently healthy state of the animal even though chronic lung lesions are present. These "silent" carriers of CBPP are infectious and thought to be an important factor in spreading the disease among cattle herds. There is considerable variation in the severity of clinical disease from acute, sub-acute to chronic form [44].

Differential Diagnosis

In carrying out a CBPP diagnosis, it is necessary to differentiate this disease from other diseases which may present similar clinical signs or lesions. CBPP is hard to differentiate from other causes of cattle respiratory disease. Pneumonia (particularly unilateral illness) in adults and poly arthritis in calves should be considered warning signs for potential CBPP infection. The way the disease behaves in the herd is as important as the findings in a single animal when carrying out an investigation. Differential diagnosis considered in the diagnosis of CBPP include diseases like Rinderpest, Abscesses, Hemorrhagic septicemia, Foot and mouth disease, Bacterial or viral broncho-pneumonia, Theileriosis, Ephemeral Fever, Tuberculosis, Bovinefarcy, Actinobacillosis, Foreign body reticulum pericarditis (43;2).

Diagnosis

Current state of techniques available for the diagnosis of CBPP clearly demonstrates that recent advances in the study of immunology and molecular biology have and will continue to open avenues for improved CBPP diagnosis. The tools currently available for CBPP diagnosis include history of contact with infected animals, clinical signs, pathologic lesions, (Pleurisy, lung hepatization), identification and isolation of the agent, immune blotting, serology and PCR techniques (39;27). CBPP frequently results in disease in only single lung as compared with other types of pneumonia in which both lungs are affected. In a herd with signs of pneumonia in adults and polyarthritis in calves, CBPP should be considered. Post-mortem lesions may be more useful in the diagnosis [2]. A definitive diagnosis can be made by recovering *M. mycoides Subspecies mycoides* SC from infected animals [38].

Cultural examination

Samples like nasals wabs, broncho alveolar washings, pleural fluid obtained by puncture are collected from live animal. Samples taken to necropsy are lung lesions, lymphnodes, pleural and synovial fluid from animals with arthritis. The causal organisms can be isolated culturally from animals during febrile phase or shortly after post-mortem from blood, pleural exudates (chest fluid) and/or affected lung tissue and lymphnodes. Because of 'fastidious' nature of the agent, samples should be submitted to the laboratory as soon as possible after collection (39;2).

Bio-chemical tests

Mycoplasma mycoides subspecies mycoides small colony type is sensitive to digitonin, does not produce '*film spots*', ferment glucose, reduces tetrazolium salts (aerobically and anaerobically), does not hydrolyze arginine, has no phosphatase activity, and has no or weak proteolytic properties. It is where immunological tests give uncertain results that bio-chemical test is preferred [48].

Serological tests

Serological tests for CBPP are valid at the herd level only because false positive or false negative results may occur in individual animals. Tests on single animals can be misleading, either because the animal is in the early stage of disease, which may last for several months, before specific antibodies are produced, or it may be in the chronic stage of the disease when very few animals are seropositive. False-positive results canoccur (2%), of which an important cause is serological cross-reactions with other *mycoplasmas*, particularly other members of the *M.mycoides*cluster (31;40). The validity of the results has to be confirmed by post-mortem and bacteriological examination, and serological tests on blood taken at the time of slaughter. The CFT and ELISA are recommended for screening and eradication programmes. The highly specific immunoblotting test is useful as a confirmatory test but is not fit for mass screening [40]. The CFT and c-ELISA are the OIE prescribed herd level tests for CBPP and they are said to have specificity of 98% and 99.9%, respectively and sensitivity for both tests is said to be about 70% [36].

- **Complement fixation test:** a test suitable for determining freedom from disease and a prescribed test for international trade. The Camp bell and Turner complement fixation (CF) test remains the recommended procedure (although the current method is slightly different from the original one), and it is widely used in all countries where infection occurs [39]. For antigen titration and harmonization purposes, an international standard positive bovine serum is available from the OIE Reference Laboratory in Teramo, Italy. However, the CFT is still difficult to perform, requiring well trained and experienced personnel [40].

- The limitations of the CF test are well known. With a sensitivity of 63.8% and a specificity of 98% [39], the CFT can detect nearly all sick animals with acute lesions, but rather smaller proportion of animals in the early stages of the disease or of animals with chronic lesions. In addition, therapeutic interventions and improperly conducted prophylactic operations (partial slaughter of the herd) may increase the number of false- negative reactions. However, for groups of animals (herd or epidemiological unit) the CFT is capable of detecting practically 100% of infected groups. The nature of the pathogenesis of the disease is such that the incubation period, during which antibodies are undetectable by the CFT, may last for several months [40].

- **Competitive Enzyme - linked Immuno sorbent Assay (c-ELISA):** c-ELISA developed by the OIE collaborating centre for the diagnosis and control of animal diseases in tropica lcountries [39], has been validated internationally in accordance with OIE standards. Compared with the CFT, the c-ELISA has equal sensitivity and greater specificity. Advice on standard protocols and the availability of reagents can be obtained from the OIE reference laboratories for CBPP or the OIE collaborating centre for ELISA and molecular techniques in animal disease diagnosis [40].

  Validation tests that have been carried out in several African and European countries would indicate: the true specificity of the c-ELISA has been reported to be at least 99.9%; the sensitivity of the c-ELISA and the CFT are similar; and antibodies are detected by the c-ELISA in an infected herd very soon after they can be detected by the CFT, and c-ELISA antibody persists for a longer period of time (37;40). To enhance its repeatability and the robustness, this c-ELISA is now provided as aready- made kit that contains all the necessary reagents, including precoated plates kept in sealed bags. This kit can be obtained commercially and availability can be checked through the OIE reference laboratory in France. Sera are analyzed in single wells. The substrate has been modified and is now TMB (tetramethyl benzidine) in a liquid buffer and the reading is at 450nm. The substrate colourturns from pale green to blue in the first place and becomes yellow once the stopping solution has been added. Mab controls exhibit a darker colour while strong positive serum controls are very pale. The cutoff point has been set at50% and should be valid in every country [40].

- **Immunoblotting test:** A field evaluation indicated an immunoblotting test (IBT) is an immune enzymatic test that is higher sensitivity and specificity than the CF test and has been developed to confirm doubtful CFT or c-ELISA results. A core profile of antigenic bands, present both in experimentally and naturally, infected cattle are immune dominant. The more accurate picture of the immune status of animals given by this tes tis due to the possibility of a more precise analysis of the host's immune response in relation to the electrophoretic profile of *Mmm*SC antigens; thus the test overcomes problems related to non-specific binding. It should be used primarily as a confirmatory test, after other tests and should be used in all cases in which the CF test has given a suspected false result [39].

Nucleic acid recognition methods

Polymerase chain reaction is a rapid and sensitive diagnostic method. It allows detection of *Mmm*SC directly in samples of lungs, bronchial lymphnodes, nasalswabs, pleural fluid and blood. Pre-incubation for 24hr of clinical specimens in growth medium may increase test sensitivity. If used for the identification of new isolates it reduces drastically the time required (24-48hr versus2-3weeks). Detection of the causative agent from bovine samples is one way to confirm a suspect CBPP case. However, isolation and serological or biochemical identification tests are time consuming leading to significantdelays. To overcome this problem, both single and nested PCR systems have been developed for identification of *Mmm*SC [3]. Using samples suchas lung exudates allows the PCR to be performed directly after differential centrifugation store move inflammatory cells and pellet *Mycoplasmas*. For fragments, the PCR is applied after DNA extraction. The PCR can also be performed on urine or blood. The main advantage of the PCR technique is that it can be applied to poorly preserved samples (Contaminated or without any viable *Mycoplasmas* as may occur following antibiotic treatment) [24].

The PCR has become the primary tool for identification of *Mmm*SC. If a sample is PCR positive in a CBPP-free zone, the test confirmed by a second and different PCR; infection can be confirmed by the use of only one immunological test. One of the problems with PCR is the possible occurrence of contamination if the necessary precautions and quality management system are not implemented correctly in the diagnostic laboratory. Great care must be taken to respect the strict separation between those parts of the

laboratory that may contaminated with PCR products such as the electrophores is room and those parts of the laboratory devoted to preparing the reagents [27].

Control and prevention

To make the most efficient use of the increasingly scarce resources, disease control programs must be tailored to the needs of particular communities and to high-priority cattle populations to ensure their efficacy, acceptance and sustainability; therefore, economic evaluation should be generalized [27]. In most continents, control strategies are based on the early detection of outbreaks, control of animal movements, quarantine, vaccination, test and slaughter policies and a stamping-out policy [44]. However, stamping out, test and slaughter policies may not be economically feasible in endemic African countries. This was demonstrated by a stamping-out eradication of CBPP in Botswana during 1996, which led to negative effects on short-term economics and increased malnutrition in children. Thus, these methods may not prove realistic and vaccination is the most frequently used control strategy in combination with animal movement control (19;19). Extensive vaccination programs and chemotherapy are the remaining options for CBPP control in Africa and of these, vaccination which is major control method practiced in Ethiopia [3].

CBPP vaccination was initially (1920‟stoearly1970‟s) based on broth T1 vaccine which was later replaced by freeze-dried live attenuated *Mmm*SC vaccine T1/44 vaccine [39]. A streptomycin resistant variant (T1SR) was developed and used in combination with rinderpest vaccine (26;36). The only commercially available vaccines are live attenuated vaccines using the T1/44 and T1sr strains. The former is more widely used, as it provides coverage for a year, while the duration of immunity of the T1sr vaccine is shorter. The latter has the advantage of inducing fewer adverse reactions and being unlikely to cause clinical disease, as sometimes occurs with T1/44, w here especially first time vaccination may induce a Williams reaction that is sufficiently severe to require treatment [2]. To be effective, vaccination must be repeated initially at short intervals and there after annually over 3-5years [18].

Antibiotic treatment against CBPP is widely used. It is not part of any official control strategy due to suspicion that its use could facilitate developments of sequestra, increase the number of carrier animals, increase development of resistant strains, and mask the occurrence of clinical disease [21]. Masking of clinical disease will make diagnosis difficult, which may contribute to unrecognized infections and CBPP transmission. Nevertheless, antibiotics are widely used in pastoralist communities [30]. [6] Carried out an invitro trial of the effects of five commonly used antibiotics on a number of strains of *Mmm*SC and concluded that tilmicosin and danofloxacin were effective both interms of mycoplasmastatic and mycoplasmacidal activity; florfenicol and a tetracycline provide intermediate effectiveness while spectinomycin was ineffective against some strains. Commonly used antibiotics include tetracycline, Tylosin, erythromycin, lincomycin, spectinomycin and tilmicosin. Tylosin and spiramycin are effective in the control of excessive vaccination reactions and should be of value in the treatment of clinical cases resistance to some of these antimicrobials has been noted. Animals that do not respond to treatment often become carriers [27].

Economic importance of CBPP

Contagious Bovine Pleuropneumonia is considered to be a disease of great economic importance because of its high mortality rate, production loss, increased production cost due to cost of disease control, loss of weight and working ability, delaying marketing, reduced fertility, trade bans and reduced investment in livestock production [44]. The presence of CBPP in a herd results indirect losses due to its impact on cattle production, through increased mortalities, reduced milk yield, reduced weight gain and reduced fertility rate and therefore it compromises both household and national food security due to loss of protein and draught power. CBPP also causes indirect losses through additional cost of treatment, preventive vaccination, field diagnostic testing and slaughter of clinical cases, surveillance activities, disruption of trade and the limitation of investment opportunities due to reluctance in adoption of improved breeds [12]. In addition to these, it leads to imposition of rigorous limitations to international trade soon CBPP affected countries in accordance with world organization of Animal Health (OIE) regulations [7].

Contagious Bovine Pleuropneumonia is considered as one of the main stumbling blocks to the growth of the livestock industry in the African continent causing losses estimated to be around two billion US dollars per years [50] and the disease has been causing significant economic losses on the livestock sector and the national economy. It accounts for a loss of over 8.96million US dollars per year [1]. Thus, over the last decades, the country has lost a substan-

tial market share and foreign exchange earnings due to frequent bans by the Middle East countries [23].

Status of CBPP in Ethiopia

Regarding the situation in east Africa in general and Ethiopiain particular, there is a suggestion that CBPP was introduced into East Africa from India by the army of field Marshal Napier when he invaded Ethiopiain 1867-1868 (31; 1). Countries in East Africa reported 66% of the total outbreaks (58% in Ethiopia and Tanzania and 8% in other countries in the region). Ethiopia is one of east African countries in which CBPP is endemically maintained in various parts of the country with 25% morbidity and more than 10% mortality [31]. A total of 583 outbreaks of CBPP were reported between 1995 and 2002 in Ethiopia in which highest outbreaks (187) were reported in 1998 [1].

Vaccination was the main control strategy practiced in Ethiopia for the last 30years in combination with Rinderpest vaccine which has rendered protection and restrained the disease to relatively low level until 1992/93. After Rinderpest has been brought under control, CBPP is considered to be among the most important cattle diseases and impediments to livestock development in the country [34]. CBPP is one of the great plagues, which continue to devastate cattle herds on which so many people are dependent in the lowlands. In the highlands, the consecutive yearly blanket vaccinations with combined Rinderpest and CBPP have certainly contained the disease to a relatively low level during the past years. But with the adoption of a strategy to wards Rinderpest eradication, the vaccinations in the highlands have ceased since 1992/93. Currently, CBPP vaccination in the country is based on targeted and ring vaccination in the face of outbreaks [48]. The usual blanket coverage was around 50% and never reached the desired 80-100% level. Generally, the irregularity and low rate of vaccinations since 1993 seems to contribute to the increased incidence of the disease and its further spread and now the disease is one of the major threats in the country hindering and challenging the livestock production [11].

According to reports of various outbreaks, national Sero-surveillance and research results from 1997 to 2010, CBPP was found to be present in almost all regional states [12]. Studies conducted in Western Ethiopia [10], Northern Ethiopia [49], Southern Ethiopia [15], South west Ethiopi a (Mamo*etal*.,2018) and different regions of the country revealed that CBPP is posing a major threat to cattle in many parts of the country there by causing considerable economic losses through morbidity and mortality. Furthermore, CBPP has been reported from different export quarantine centers in the country (25; 11) signifying that CBPP remain a threat to livestock export market and may reduce the investment in livestock production.

In general at the country level, CBPP sero-prevalence studies have been conducted in different localities of the country. However, there is a great variation of reports from different areas (11; 10). The sero-prevalence in different parts of Ethiopia are summarized in table below.

CBPP diagnostic approaches like clinical examination, post-mortem examination to observe the characteristic lesions in organs of dead and or slaughtered animals and laboratory examination to confirm the presence of infection, an outbreak investigations to isolate and identify the causative agent of *Mycoplasma* species through post-mortem examination and sample collection, sero-prevalence studies, sick animals for autopsy and bacteriological specimen collection, and the clinical and pathological findings as well as the biochemical tests performed so far were the major method that used CBPP diagnosis in Ethiopia [34,47].

Conclusion and Recommendations

Contagious bovine pleuropneumonia (CBPP) is an acute, subacute or chronic respiratory disease of cattle caused by Mycoplasma mycoides subspecies mycoides small colony (MmmSC). Transmission of the disease occurs through direct contact between an infected and a susceptible animal which becomes infected by inhaling droplets disseminated by coughing. The epidemiology of CBPP is dominated by different factors. These are; cattle are the only species affected, transmission is through the direct contact of susceptible animal with clinical cases or chronic carriers and cattle movements play a very important role in the maintenance and extension of the disease. The tools currently available for CBPP diagnosis include clinical signs, identification and isolation of the agent, immunoblotting, serology and PCR techniques. Commonly used antibiotics include tetracyclines, tylosin, erythromycin, lincomycin, spectinomycin, and tilmicosin. Control strategies are based on the early detection of outbreaks, control of animal movements, quarantine, vaccination, test and slaughter policies and a stamping-out policy. The disease has serious implications for food security and peoples 'livelihoods in affected countries. The disease is posing a major threat to cattle in many parts of the country there by caus-

Parts of the country	Study area	Sample size	Overall sero-prevalence	Reference
Central Ethiopia	Export quarantine centers in and a round Adama	3,111	4%	[25]
Southern Ethiopia	Amaro special district	400	31.8%.	[15]
Northern Ethiopia	Southern zone of Tigray (Alamata, Raya Azebo, Ofla,and Endamehoni)	384	11.9%	[49]
Western part of Ethiopia	Western Oromia Zones (Western Shoa, Horro Guduru Wollega, and Eastern Wollega)	386	28.5%	[10]
Southwest Ethiopia	Gimbo district of Keffazone	384	8.1%	[28]

Table 1: Recently reported sero-prevalence of CBPP in different parts of Ethiopia.

ing considerable economic losses through morbidity and mortality. The occurrence of such disease may cause restriction on the trade of animals and animal products internationally, affecting the export earnings of the country, there by threatening the livelihood of the farmers and national agricultural economy.

Based on the above conclusion the following recommendations are forwarded:

- Research should be done on the epidemiological situation of the disease.
- Research in the improvements of vaccine should continue and include the possibility of differentiation between vaccinated and non-vaccinated animals.
- Controlling and prevention strategy of this economically devastating disease of cattle should be applied.

Bibliography

1. Abdela N and Yune N. "Sero-prevalence and Distribution of Contagious Bovine Pleuro-pneumonia in Ethiopia: Update and Critical Analysis of 20Years (1996-2016) Reports". *Frontiers in Veterinary Science* 4 (2017): 100.

2. Abera Z., *et al.* "Review on Contagious Bovine Pleuropneumonia and its Economic Impacts". *Academic Journal of Animal Diseases* 5.1 (2016): 01-15.

3. Admassu B., *et al.* "Contagious Bovine Pleuropneumonia in Ethiopia". *Academic Journal of Animal Diseases* 4.2 (2015): 87-103.

4. Alemayehu G., *et al.* "Lowsero-prevalence of Contagious Bovine Pleuropneumonia (CBPP) in bulls originated from Borena pastoral area of Southern Ethiopia". *Tropical Animal Health and Production* 47.5 (2014): 983-987.

5. Andrews AH., *et al.* "Bovine medicine: diseases and husbandry of cattle". John Wiley and Sons (2008).

6. Ayling RD., *et al.* "Comparison of *in vitro* activity of danofloxacin, florfenicol, oxytetracycline, spectinomycin and tilmicosin against Mycoplasma mycoides subspecies mycoides small colony type". *Veterinary Record-English Edition* 146.9 (2000): 243-245.

7. Bonnet P and Lesnoff M. "Decision making, scales and quality of economic evaluations for the control of contagious bovine pleuropneumonia (CBPP): The use of economic analysis methods incombination with epidemiological and geographical models to help decision making for CBPP control in Ethiopia" (2009).

8. Bonnet P., *et al.* "Seroprevalence of contagious bovine pleuropneumonia in Ethiopian highlands (West Wollega zone, Boji District)". *Ethiopian Veterinary Journal* 9.2 (2005): 85-93.

9. CSA. "Agricultural Sample Survey, VolumeII, Report on livestock and livestock characteristics (private peasant holdings)". Statistical Bulletin585, Central Statistical Agency (CSA) Federal Democratic Republic of Ethiopia Addis Ababa, Ethiopia (2017).

10. Daniel G., *et al.* "Contagious bovine pleuropneumonia: Seroprevalence and risk factors in Western Oromia, Ethiopia". *Onderstepoort Journal of Veterinary Research* 83.1 (2016): 1-5.

11. Dele E., *et al.* "Seroprevalence of trade hampering livestock diseases in animals originated from Borena at export quarantine Centers in Adama, Central Ethiopia". *African Journal of Basic and Applied Science* 6 (2014): 30-36.

12. Demil E. "Review on Economic Impact of Contagious Bovine Pleuropneumonia (CBPP)". *Academic Journal of Animal Diseases* 6.2 (2017): 51-56.

13. Dereje K., *et al.* "Isolation, Identification and Antimicrobial Susceptibility Test of Mastitis Causing Bacteria at Holeta Agricultural Research Center Dairy Farms". *International Journal of Animal Science and Technology* 2.1 (2018): 6-13.

14. Duguma B., *et al.* "Survey of major diseases affecting dairy cattle in Jimma town, Oromia, Ethiopia". *Global Veterinaria* 8.1 (2012): 62-66.

15. Ebisa T., *et al.* "Study on Seroprevalence and Risk Factors Contagious Bovine Pleuropneumonia in Southern Nation and Nationality People of Ethiopia Regional State in Amaro Special District". *Science, Technology and Arts Research Journal* 4.4 (2012): 106-112.

16. Egwu GO., *et al.* "Isolates of Mycoplasma mycoides subspecies mycoides (SC) in small ruminants in Sahel zone of Nigeria and its implications on disease control". *African Journal of Biotechnology* 11.23 (2012): 6396-6401.

17. Eshetu E and Abraham Z. "Review on live animal and meat export marketing system in Ethiopia: challenges and opportunities". *Journal of Scientific and Innovative Research* 5.2 (2016): 59-64.

18. FAO. Food and Agriculture Organization of the United Nations (FAO). "Recognizing contagious bovine pleuropneumonia". FAO Animal Mannual Health Manual, FAO, Rome (2002): 3-17.

19. FAO. "Cancontagious bovine pleuropneumonia (CBPP) be eradicated? Proceeding of the FAO-OIE-AU/IBAR-IAEA Consultative group on CBPP-Fifthmeeting, Rome, 14-16 October 2015.FAO Animal Production and Health Proceedings.No.19. Rome, Italy (2016).

20. Francis MI., *et al.* "Prevalence of contagious bovine pleuropneumonia based on gross lesions in cattle at slaughter in Adamawa State, Nigeria". *Sokoto Journal of Veterinary Sciences* 16.1 (2018): 31-37.

21. Geresu MA., *et al.* "Sero-epidemiological investigation and risk factors for contagious bovine pleuropneumonia infection of cattle in Dello Mena and Sawena Districts of Bale Zone, Southeastern Ethiopia". *Journal of Public Health and Epidemiology* 9.5 (2017): 122-132.

22. Gorton TS., *et al.* "Development of real-time diagnostic assays specific for Mycoplasma mycoides subspecies mycoides Small Colony". *Veterinary Microbiology* 111.1-2 (2005): 51-58.

23. Hurrissa B and Eshetu J. "Challenges and opportunities of livestock marketing in Ethiopia". In Proceedings of the 10th annual conference of the Ethiopian Society of Animal Production (ESAP). *Addis Ababa, Ethiopia* (2002): 1-13.

24. Kasper D and Harrison TR. "Harrison's principles of internal medicine vol 1". McGraw-Hill, Medical Publishing Division (2005).

25. Kassaye D and Molla W. "Seroprevalence of contagious bovine pleuropneumonia at export quarantine centers in and around Adama, Ethiopia". *Tropical Animal Health and Production* 45.1 (2013): 275-279.

26. Litamoi JK. "Overview of contagious bovine pleuropneumonia vaccine production and quality in Africa". In Report of second meeting of the FAO/OIE/OAU/IAEA consultative group on contagious bovine pleuropneumonia (CBPP). Rome, Italy (2000).

27. Mamo Y and Beshah A. "Review on Contagious Bovine Pleuropneumonia". *Biomedicine and Nursing* 3.1 (2017): 1-18.

28. Mamo Y., *et al.* "Contagious Bovine Pleuropneumonia: Seroprevalence and Risk Factors in Gimbo District, South west Ethiopia". *Veterinary Medicine International* 18 (2018): 1-7.

29. March JB., *et al.* "Rapid Detection of Contagious Caprine Pleuropneumonia Usinga *Mycoplasma apricolum* subsp. Capripneumoniae CapsularP olysaccharide-Specific Antigen Detection Latex Agglutination Test". *Journal of Clinical Microbiology* 38.11 (2000): 152-159.

30. Mariner JC., *et al.* "A model of contagious bovine pleuropneumonia transmission dynamics in East Africa". *Preventive Veterinary Medicine* 73.1 (2006): 55-74.

31. Masiga WN., *et al.* "Manifestation and epidemiology of contagious bovine pleuropneumonia in Africa". *Revue Scientifiqueet Technique-Office International des Epizooties* 15.4 (1996): 1283-1308.

32. Mbiri P. "A retrospective analysis of the epidemiology and control measures of contagious bovine pleuropneumonia in the northern communal areas of Namibia from 2001 to 2013". (Doctor a dissertation, University of Pretoria) (2017).

33. Mersha T. "Epidemiological Study on Contagious Bovine Pleuropneumonia and Farmers Knowledge, Attitude and Practice Towards The Disease In Selected District of East Wollega And West Showa Zones, Western Ethiopia". (MVSc. Thesis), Bishoftu, Ethiopia (2017).

34. Mersha T. "Sero-prevalence of contagious bovine pleuropneumonia and its potential risk factors in selected sites of Western Oromia, Ethiopia". *Ethiopian Veterinary Journal* 20.2 (2016): 31-41.

35. Mitchell SE. "Organic agriculture in Oklahoma: Catalysts and Roadblocks for Producers (Doctoral dissertation, Oklahoma State University) (2007).

36. Mtui-Malamsha NJ. "Contagious Bovine Pleuropneumonia (CBPP) in the Maasai ecosystem of south-western Kenya: Evaluation of seroprevalence, risk factors and vaccine safety and efficacy". *The Journal of General Microbiology* 14 (2009): 97-207.

37. Niang M., *et al.* "Pulmonary and serum antibody responses elicited in zebu cattle experimentally infected with Mycoplasma mycoides subsp. Mycoides SC by contacte xposure". *Veterinary Research* 37.5 (2006): 733-744.

38. Nicholas RAJ., *et al.* "Vaccines for Mycoplasma diseases in animals and man". *Journal of Comparative Pathology* 140.2-3 (2009): 85-96.

39. Office International Des Epizooties (OIE). "Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (Mammals, birds and bees), 6th edition". Office International Des Epizooties, Paris (2008): 712-724.

40. OIE. "Manual of Diagnostic Tests and Vaccines for Terrestrial Animals". in Chapter2.4.9. Contagious bovine Pleuropneumonia, OIE, Paris (2014).

41. Olabode HOK., *et al.* "Serological Evidence of Contagious Bovine Pleuro-Pneumonia antibodies in trade cattle (*Bos indicus*) sold in Kwara state-Nigeria". *Online International Journal of Microbiology Research* 1.1 (2013): 14-19.

42. Pilo P., *et al.* "Molecular mechanisms of pathogenicity of Mycoplasma mycoides subsp. Mycoides SC". *The Veterinary Journal* 174.3 (2007): 513-521.

43. Radiostits OM., *et al.* "Veterinary Medicine: A textbook of the diseases of cattle, sheep, pigs, goats and horses. 8th edition". BaillièreTindall (1994): 910-913.

44. Radostits OM., *et al.* "Veterinary medicine, a text book of the diseases of cattle, sheep, pig, goat, and horse, 10th edition., Saunders Elsevier (2007): 1131-1135.

45. Schnee C., *et al.* "Assessment of a novel multiplex real time PCR assay for the detection of the CBPP agent *Mycoplasma mycoides subsp.* Mycoides SC through experimental infection in cattle". *BMC Veterinary Research* 7.1 (2011): 47.

46. Schubert E., *et al*. "Serological testing of cattle experimentally infected with Mycoplasma mycoides subsp. Mycoides Small Colony using four different tests reveals a variety of seroconversion patterns". *BMC Veterinary Research* 7.1 (2011): 72.

47. Sori T., *et al*. "Isolation and identification of Mycoplasma mycoides subspecies mycoides Small Colony bovine biotype in Eastern Ethiopia". *The International Journal of Applied Research in Veterinary Medicine* 3 (2005): 30-34.

48. Tegegn A. "Contagious Bovine Pleuropneumonia (CBPP): Literature Review on Distribution, Seroprevalence, and Associated Risk Factors which Plays Major Role in an Economic Loss of this Sector". *Austin Journal of Veterinary Science and Animal Husbandry* 4.2 (2017): 10-36.

49. Teklue T., *et al.* "Epidemiological status of contagious bovine pleuropneumonia in Southern Zone of Tigray Regions, Northern Ethiopia". *Animal and Veterinary Sciences* 3.1 (2010): 32-36.

50. Vilei EM and Frey J. "Detection of Mycoplasma mycoides subsp. Mycoides SC in bronchialveolar lavage fluids of cows based on a TaqMan real-time PCR discriminating wild types trains from an lppQ-mutant vaccines train used for DIVA-strategies". *Journal of Microbiological Methods* 81.3 (2010): 211-218.