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Review Article **Open Access**

Overview of human and animal brucellosis in Nigeria and its economic impacts on production

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Abstract:

Brucellosis is a wide spread zoonotic bacterial disease of humans and animals**.** In humans the disease is recognized commonly as undulant fever, characterized by headache malaise, and arthritis. Brucellosis can occur in any age group, but mainly found in young men between the ages of 20 and 40 years because of occupational hazards. Domestic animals (cattle, sheep and goat, pigs, dogs etc) are highly susceptible to brucellosis. Generally, brucellosis manifest in female animals as abortion, retained placenta, stillbirth and death of young ones soon after birth. In males, the main features are vesiculitis, orchitis, and epididymitis, which may render infected male infertile for life. The endemicity of brucellosis has remained a threat in low- income countries of sub-Saharan Africa and South Asia and has multiple economic implications across agriculture and public health sectors, and broader implications on economic and social development sectors. Google and Google Scholar were used to retrieve articles used for this review, which included published research articles and local, national and international reports on brucellosis. In this review, we summarised human and animal brucellosis, prevalence of infections in Nigeria, and economic impacts on production. It is believed that this review will guide researchers on the state of brucellosis in developing countries where the disease is still endemic, using Nigeria as a case study.

Keywords: undulant fever; public health; abortion; orchitis; economic impact

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Aperçu de la brucellose humaine et animale au Nigéria et de ses impacts économiques sur la production

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Résumé:

La brucellose est une maladie bactérienne zoonotique largement répandue chez les humains et les animaux. Chez l'homme, la maladie est généralement reconnue comme une fièvre ondulante, caractérisée par des maux de tête et de l'arthrite. La brucellose peut survenir dans n'importe quel groupe d'âge, mais principalement chez les jeunes hommes âgés de 20 à 40 ans en raison des risques professionnels. Les animaux domestiques (bovins, ovins et caprins, porcs, chiens, etc.) sont très sensibles à la brucellose. Généralement, la brucellose se manifeste chez les femelles par l'avortement, la rétention du placenta, la mortinaissance et la mort des jeunes peu après la naissance. Chez les hommes, les principales caractéristiques sont la vésiculite, l'orchite et l'épididymite, qui peuvent rendre l'homme infecté infertile à vie. L'endémicité de la brucellose est restée une menace dans les pays à faible revenu d'Afrique subsaharienne et d'Asie du Sud et a de multiples implications économiques dans les secteurs de l'agriculture et de la santé publique, ainsi que des implications plus larges sur les secteurs du développement économique et social. Google et Google Scholar ont été utilisés pour récupérer les articles utilisés pour cette revue, qui comprenaient des articles de recherche publiés et des rapports locaux, nationaux et internationaux sur la brucellose. Dans cette revue, nous avons résumé la brucellose humaine et animale, la prévalence des infections au Nigeria et les impacts économiques sur la production. On pense que cette revue guidera les chercheurs sur l'état de la brucellose dans les pays en développement où la maladie est encore endémique, en utilisant le Nigeria comme étude de cas.

Mots-clés: fièvre ondulante; santé publique; avortement; orchite; impact économique

Introduction:

Brucellosis is a worldwide bacterial zoonotic disease, caused by several species of Brucella (1,2,3). Brucella is Gram-negative coccobacilli that infect almost all species of domestic animals and man. The domestic animals mainly infected are cattle, swine, goats, sheep and dogs and *Brucella species* known to cause disease in them includes *Brucella abortus, Brucella melitensis, Brucella ovis, Brucella suis, Brucella canis, Brucella microti, Brucella inopinata, Brucella ceti, and Brucella pinnipediali* (4,5,6). In humans, the disease is caused mainly by *B. melitensis* as the most pathogenic species, followed by *B. suis,* whereas *B. abortus* is considered the mildest type of brucellosis (7,8) All ages and sexes, both humans and animals are susceptible to brucellosis, particularly humans with the culture of keeping animals especially the nomads (9,10).

Brucellosis has existed for several years, recent evidence from Egyptian ancient skeletons shows that the disease dates back to 750 BC (6). The disease was first reported in 1887 by Dr. David Bruce who isolated the organisms from patients who were living on the island of Malta and was eventually named after him as brucellosis (11). The disease is also known as Malta fever, intermittent fever, Bang's disease, undulant fever, Gibraltar fever, Mediterranean fever, contagious abortion, Maltese fever, Crimean fever, and rocky fever. Thought to have been eradicated in many developed countries, brucellosis is now a re-emerging neglected zoonosis endemic in several zones, especially in the Mediterranean regions, Europe, Africa, Middle East, South and Central Asia and the Central and South America (2,12,13). The impacts of brucellosis are highly devastating in livestock, and in humans especially among African countries, where the documentation of the disease is very poor (14,15,16).

Brucellosis is often a sub-acute or chronic disease in animals. In cattle, sheep, goats, other ruminants and pigs the initial phase following infection is often not apparent (7). In sexually mature animals the infection localizes in the reproductive system and typically produces placentitis followed by abortion in the pregnant female, usually during the last third of pregnancy, and epididymitis and orchitis in the male (3,7) Human brucellosis is a severe acute or chronic systemic disease, often insidious with symptoms similar to a severe influenza known as undulant fever, which persists for several weeks, months or longer and may get progressively worse if untreated (17). The initial symptoms are fatigue and headaches, followed by high fever, chills, drenching sweats, joint pains, backache, and loss of weight and appetite. Long-term effects can include arthritis, swelling of internal organs, depression, chronic fatigue and recurrent fevers (18). The clinical picture of brucellosis is usually not specific in animals or humans and diagnosis needs to be supported by laboratory tests. A history of recent exposure to a known or probable source of *Brucella species,* occupational exposure or residence in high infection prevalence area is a probable case of brucellosis (19).

Brucellosis is invariably transmitted by direct or indirect contact with infected animals or their products. Animals are the natural hosts of the *Brucella* organisms and are reservoirs for human infections. Humans acquire brucellosis mainly through the consumption of raw and unpasteurized milk or dairy products, inhalation, contaminated environment and tissue (2,19). Brucellosis is considered occupational hazard for veterinarians, abattoir workers and livestock keepers (6,7). Infected animal products; blood, placenta or uterine secretions are capable of gaining access to the body through broken skin and mucosa (6,20). Brucellosis has also been reported in terrestrial and marine mammals as in domestic animals (21). Recent studies have shown that increase in travel to endemic countries and have been associated with some outbreaks of brucellosis in the human population (22,23,24). About 500,000 new cases of brucellosis are reported annually in human population (25). Animal-to-animal transmission occurs as a result of the large number of organisms shed in the environment.

Human infections are useful indicator of the presence of disease in animal populations, as animals are reservoir of infection and humans are source of information for the disease surveillance (26). The endemicity of brucellosis in Sub-Saharan Africa (15), is largely due to lack of attention and absence of adequate diagnostic facilities (3,10), lack of public awareness, inadequate public-sector animal health services, and low-income communities (2,27). In this review, we examined the previous outbreaks of brucellosis in human and animal populations in different parts of Nigeria with the view to creating awareness of its public health implications and the huge economic impacts on Nigeria economy.

Methodology and Results:

Online databases were searched for publications relevant to human and animal brucellosis in Nigeria using Google and Google Scholar engine during the month of July 2021. Publications used included research articles and local, national and international reports on brucellosis. Each of the 5 authors screened the retrieved publications for eligibility and relevance to the topic, and for adequate and verifiable referencing. Publications not relevant to the topic or that contained unverifiable information, obsolete references, inadequate referencing and duplicate information were excluded. Of the total of 96 articles obtained from the search, 64 were eligible and used for the review.

Discussion:

Distribution of brucellosis in Nigeria

Brucellosis is widespread and the prevalence of brucellosis varies from country to country and region to region in Africa and in various parts of the world (28). Nigeria is the most populous country in Africa with over 170 million as at 2012 (http://esa.un.org/wpp/ascII-data/disk_navigation_ascII.htm) and has an estimated livestock population of 20.49 million cattle, 23.07 million sheep, 28.07 million goats, 6.54 million pigs (http://www.fao.org/ag/againfo/resources/en/glw/GLW_dens.html), 18,200 – 90,000 camels, and 210,000 horses (http://faostat.fao.org/site/573/default.aspx#ancor) (29). Nigeria, India, Ethiopia, and Bangladesh account for 44% of poor livestock keepers globally, with Nigeria ranking second (14). Livestock production has always been important in Nigeria, and the rapidly emerging livestock sector now ranks second among the 20 poorest countries (14).

In Nigeria, brucellosis has been reported in 24.1% of abattoir workers in Abuja, Nigeria with occupational hazard and eating raw meat as risk factors (30). In Bauchi State Nigeria, seroprevalence rate of 33.5% was reported for human brucellosis, with 18.9% of the study population being positive for human IgG, 6.1% for human IgM and 74.15% for both IgG and IgM (19). In the north eastern part of the Nigeria, 5.2% prevalence of brucellosis among 500 occupationally exposed patients was reported (31). In another similar study in north-central part of the country, 43.8% of the 7.8% brucellosis infected hospital patients were reported to be abattoir workers (32). In the southwestern region of Nigeria, over 55% of 7161 people examined for brucellosis in different parts of the region had positive *Brucella abortus* antibodies in their sera, with higher titres found among dairy farmers and slaughter men than the general population (33). In another study in human population, Cadmus et al., (34) reported a high seroprevalence of 66.3% for brucellosis among apparently healthy abattoir workers.

In animals, a prevalence rate of 9.6% was reported in ruminants in Wukari, Taraba State (35). In slaughter cattle, the prevalence rates of 7.8% and 1.9% were reported from Oyo and Lagos (36), 20.0% prevalence in Zamfara State (37), and a herd prevalence of 32.2% in a prison cattle farm in Sokoto State (38). In the three States of Adamawa, Kano, and Kaduna, prevalence rates of 29.2%, 26.7% and 23.3% respectively, were reported (39), while the prevalence of 14.1% was reported in Obudu, Cross River State (40). In Plateau State, the prevalence rates of 37.3%, 2.5% and 3.7% were reported in Bassa, Riyom and Jos South Local Government Areas (LGAs) respectively (40). A more recent study in Kanke Local Government Area, Plateau State, reported a seroprevalence of 38.5% in a herd of cattle (41).

Human brucellosis

Human brucellosis is known by many different names such as Malta fever, Cyprus or Mediterranean fever, intermittent typhoid, Rock fever of Gibraltar, and more commonly, undulant Fever (42). Human brucellosis can occur in any age group, but the majority of cases are found in young men between the ages of 20 and 40 years. This is generally related to occupational hazards in young men (43-47). Brucellosis gained public health importance when the bacteria were transmitted to human via unpasteurized milk, meat, and animal by-products of infected animals (48).

In humans, *Brucella* sp infection results in the formation of granulomas consisting of epithelioid cells, polymorphonuclear leukocytes, lymphocytes, and giant cells. The granulomatous response is characteristic of *B. abortus* infections. In *B. melitensis* infections, the granulomas are very small, but there is often association with toxaemia. *Bordetella suis* infection is often accompanied by chronic abscess formation in joints and the spleen (43,49,50,51)

The human disease usually manifests itself as an acute febrile illness which may progress to a chronically incapacitating disease with severe complications. It is nearly always acquired directly or indirectly from animal sources, of which cattle, sheep, goats and pigs are by far the most important. In these natural hosts, the infection usually establishes itself in the reproductive tract, often resulting in abortion. Excretion in genital discharges and milk is common and is a major source of human infection (7). The onset of symptoms is insidious and according to the length or severity of symptoms of the disease is arbitrarily classified as acute (less than 8 weeks), sub-acute (from 8-52 weeks) or chronic (more than 1 year).

The acute form is a typical brucellosis where almost all patients involved have a history of fever accompanied by weakness, malaise, headache, back-ache, anorexia, weight loss, myalgia, and arthralgia with a temperature of over $38.5^{o}C$ in more than 85% of patients. The sub-acute form, consist of patients who have relapsed due to incomplete or partial antibiotic treatment and patients who have received inappropriate antibiotics because of incorrect diagnosis. The clinical picture is more protean and may be an important cause of fever of unknown origin. The symptoms are generally milder, and localized infection can be seen. Chronic brucellosis is extremely rare in children but more frequent in older people and is similar to chronic fatigue syndrome. Affected patients generally suffer from a psychoneurosis, sweating, and weight loss with ocular manifestations such as episcleritis and uveitis are frequent. Fever is rare and localized infection can be seen (43,49, 51,52).

Localized brucellosis refers to cases in which organisms are not isolated from blood but are localized in specific tissues such as bone, joints, cerebrospinal fluid, liver, kidneys, spleen, or skin. Localization may be the principal manifestation of systemic infection, or may be the only manifestation of a chronic infection. Localized infection is sometimes referred to as complication when it occurs from systemic infection (49). Brucellosis also increase the risk of spontaneous abortion, premature delivery, miscarriage, and intrauterine infection with fetal death in humans as well, and is usually accompanied with malaise, fatigue, and arthritis (53,54). Human-to-human transmission is unusual. However, rare cases due to blood transfusion, bone marrow transplantation and sexual transmission have been reported (55,56).

Brucellosis in domestic animals

Brucellosis is a disease of many animal species, most especially those of food animals (cattle, sheep, goats and pigs) that produce milk, though other species such as camels, buffaloes, yaks and reindeers are also susceptible (26). Recently brucellosis has also been recognized in marine animals, which may also have the capacity to cause human infection (21). The *Brucella* species are host specific but cross species infections has been reported to occur, especially with *B. melitensis.* Infections in many wildlife species have been reported but those that obviously affect population fecundity to result in human infections are quite rare (27).

In cattle, brucellosis is usually caused by *B. abortus* which has been identified with seven distinct different biovars, namely 1, 2, 3, 4, 5, 6 and 9. The biovar 1 is the most important and widespread *B. abortus* biovar. Natural infection with other *Brucella* species is quite rare. In areas where *B. melitensis* infection is enzootic in small ruminants, it is rarely seen as abortion in cattle even though some infected animals may become carriers and excrete the bacteria in the urine, milk, and vaginal discharges (57,58). The major clinical sign in pregnant females is abortion in bovine and buffalo cows. Abortion usually occurs from the 5^{th} to the 8^{th} month of gestation. The occurrence of abortion is related to some factors such as the stage of pregnancy, the number of infecting organisms and the animal resistance (57,58) Apart from abortion, premature, stillborn or weak calves may occur. Abortion is often followed by placental retention and metritis, which may cause permanent or transient infertility (59).

In bulls, the disease is characterized by fever, vesiculitis, orchitis, and epididymitis. In severe cases, it can also be the reason for testicular abscesses, metritis or orchitis which can lead to lifetime infertility. In cattle, as well as other animals, brucellosis symptoms can be varied from severe acute to subacute or chronic, depending upon the organ of infection and the types of animals (60). Brucellosis in sheep and goats are mainly caused by *B. melitensis* and *B. ovis*, though other *Brucella* species can infect sheep and goats. Biovars 1 and 3 are most frequently isolated in small ruminants in the Mediterranean, the Middle East and Latin America (61). *B. abortus* has been isolated from eight sheep and from their offspring over a period of 40 months (58,62) and *B. suis* was isolated from the semen of a ram (63). The course of *B. melitensis* infection in small ruminants is similar to *B. abortus* infection in cattle, where the main clinical manifestations of brucellosis in ruminants are abortions, stillbirths and the birth of weak offspring which usually occur in the last third of the pregnancy following infection (64). Sheep and goats usually abort only once, but reinvasion of the uterus and shedding of organisms can occur during subsequent pregnancies (65). Milk yield is significantly reduced in animals that abort, as well as in animals whose udder becomes infected after a normal birth, although mastitis is an uncommon clinical finding (62). Acute orchitis and epididymitis usually occur in males, and may result in infertility. Brucellosis may occasionally result in arthritis in both sexes and many non-pregnant sheep and goats may remain asymptomatic (57). The effect of the disease at flock level is characterized by a general decrease in flock fertility, an increase in lamb/kid mortality with a low weaning percentage, a decrease in milk production and an increased culling of males due to chronic lesion on reproductive organs (58, 66,67,68).

In pigs, *B. suis* is the only known species that causes brucellosis leading to systemic infection and reproductive problems. Pigs can also be infected by other *Brucella* species but the infection is invariably self-limiting (69). Clinical signs of *B. suis* infection in pigs vary considerably, depending on the animal age, previous exposure, and the organ involved (70). Manifestations of swine brucellosis are abortion, birth of weak piglets, infertility, orchitis, epididymitis, spondylitis of especially the lumbar and sacral regions, arthritis, paralysis of hindlimbs, and lameness, but many infected herds may have no signs. There is no pyrexia, and death is rare (69). Abscess of different sizes frequently occur in organs and tissues (59).

Abortions have been observed as early as 17 days following natural insemination by boars disseminating *B. suis* in the semen. Early abortions are usually unnoticed by the owner, and the only evidence of infection is that the sow displays signs of oestrus 30 to 45 days after mating. Little or no vaginal discharge is observed in early abortions. Abortions that occur during mid or late stages of gestation are usually associated with females that acquire infection after 35 to 40 days of pregnancy (58,70). The rate of abortion is higher in sows or gilts exposed to *B. suis* via the genital tract at the time of breeding. Abortions may occur at any time and are influenced more by the time of exposure to the *B. suis* rather than by the stage of gestation (69). Infected boars are unlikely to develop localized genital infection. However, boars that do develop genital infection hardly recover from it. Infertility and lack of sexual activity may occur in infected boars and is frequently associated with testicular abnormality. Most often, boars have infections in their accessory genital glands. Infection of the genital organs lasts for a shorter period of time in the female than in the male (58).

In dogs, *Brucella canis* infection is one of the major causes of reproductive disorders in wild and domestic dogs. The highest prevalence occurs among breeding dogs in commercial kennels (71), where significant reproductive losses can be seen. Up to 75% fewer puppies may be weaned from affected kennels according the hygienic and sanitary conditions (71,72). Clinical signs vary from asymptomatic to mild, despite an ongoing systemic infection. Morbidity is high but mortality is low. Bacteraemia develops within two to three weeks after infection but the incubation period to clinical reproductive signs is variable (73).

The major cardinal sign of canine brucellosis is late abortion, which can occur between 30-57 days of gestation, being more common from 45 to 55 days of gestation in about 75% of the cases. Abortions are followed by mucoid, serosanguineous, brownish or grey vaginal discharge that persists for up to six weeks (73,74). The infected female can produce consecutive abortions and present litters of sick born pups that die a few hours to more than one month after delivery and apparently normal offspring can also develop the disease later in life (58,75). Abortions, premature litters and conception failures are frequently observed in infected kennels. Resorption or early embryonic death within 2 to 3 weeks after breeding can also occur, which usually mistaken for failure to conceive (73,74). Pups are lost as early as 20 days or are carried nearly to term. Infected bitches may deliver a normal litter the next pregnancy or give birth to living, partly autolyzed, stillborn and normal pups that die within hours. The surviving pups are bacteraemic for a minimum of several months (74). Other congenitally infected pups can be born normal and later develop brucellosis in life (58).

In male dogs, clinical manifestations are severe epididymitis, orchitis and prostatitis. Epididymitis usually begins 5 weeks after infection. Acute inflammation, with pain and swelling, enables physical examination and detection of orchitis and epididymitis. During the acute phase, epididymal swelling increases in size, accompanied by pain and presence of serosanguineous fluids in the tunica. Scrotal dermatitis develops from the constant licking by the male dogs, leading to infective dermatitis from secondary contamination by non-haemolytic staphylococci (74,75).

Economic impacts of brucellosis on production

Brucellosis is consistently ranked among the most economically important zoonoses globally (13,14,76). The economic impact of brucellosis varies by geography and livestock system and could be rightly referred to as multiple burdens with significant economic implications on humans, livestock and wildlife (2). Brucellosis has been successfully controlled or eliminated in livestock populations in many high-income countries persisting only in wildlife populations as sources of reservoirs infection (e. g. Bison and Elk in North America). In emerging middle-income countries, the brucellosis picture is much more variable as they tend to report the greatest number of outbreaks and animal losses with its attendant economic cost whereas, in low-income countries, the disease is endemic and neglected, with large disease and livelihood burdens in animals and people, and almost no effective control (76,77). Not surprisingly, most of these countries have less public investment in veterinary and health services, weaker surveillance and operational capacity. Endemicity of brucellosis in low-income countries of sub-Saharan Africa and South Asia has multiple economic implications across agriculture and public health, and broader implications on economic and social development sectors.

High prevalence of brucellosis associated with increasing intensification of small and medium-sized livestock enterprises and relatively uncontrolled livestock movement in traditional pasture-based systems also reflect in the economic cost. In livestock several studies have shown positive associations between greater productivity losses and higher prevalence as seropositive animals have higher rates of abortion, stillbirth, infertility and calf mortality, as well as reduced growth and longer calving intervals (2,78). Often, infected females will abort only once, although they may remain infected their entire life. Long-standing infections can result in arthritis and hygromas which is a useful marker for brucellosis at herd level.

Production losses are not just limited to pregnancy outcomes but might as well include milk especially in high income countries where it has been documented that aborting cows kept for milking produced 20% to 25% less milk for that season, while seropositive non-aborting cows produced 10% below potential (2). Animal brucellosis caused by *B. melitensis* usually occurs in outbreaks rather than in a more regular endemic pattern and the resulting productivity losses are less well documented in tropical Asia and Africa. The reverse is however the case in some other countries where sheep and goat husbandry substantially contribute to gross domestic product (GDP). For instance, a study in India estimated the annual economic loss at Rs.1180 and Rs.2121.82 (current exchange rate of $1=Rs.56 during this study) per infected sheep and goat respectively (79). Studies on the economic production losses of bovine brucellosis are reasonably consistent across a range of production systems in Africa, with losses estimated at 6% to 10% of the income per animal (77,80,81). In Nigeria, losses were estimated at US $575,605 per year or US $3.16 per bovine (prevalence 7% to 12%) (82), while that of Argentina were estimated at US $60 million per year or US $1.20 per bovine when the prevalence was around 5% (83).

In humans, the main risks for people are occupational (contact with livestock) and consumption of dairy products. Several studies in vulnerable populations reported high seroprevalences an average of 11% among livestock keepers/abattoir workers and 7% among suspect hospital patients. Economic losses caused by the disease in humans are a consequence of the cost of hospital treatment, cost of drugs, patient out of pocket treatment expenses, and loss of work or income due to illness. In Spain, losses from hospital costs and lost pay were estimated at 787.92 pesetas per patient (84), while estimated costs per case in New Zealand were NZ $3,181 (85). Broader human disability adjusted life year (DALY) burdens for brucellosis are yet to be estimated globally or across low-income countries (86). This reflects the fact that human brucellosis is even more under reported than animal brucellosis. It usually presents as an acute febrile illness often mistaken for malaria or typhoid (7,87). There is therefore a great need to introduce earlier differential diagnosis for brucellosis in high-risk populations (88).

On a general note, estimating the economic impact of brucellosis requires holistic and all-encompassing approach which will put together several of the factors enumerated above. Some of these factors includes but are not limited to; (i) cost of illness in livestock (medication treatment cost, loss of production); (ii) cost of prevention (vaccination, livestock sector treatment, herd slaughter, market loss due to risk of infected meat and milk, mortality, morbidity, lower production, loss of exports increased biosecurity); (iii) opportunity costs (loss of animal genetic resources, loss of opportunities occasioned by spending on disease prevention and cure); and (iv) cost of illness in human (cost of drugs, patient out of pocket treatment expenses, and loss of work or income due to illness). It should however be noted that some possible outcome, for instance, feeling of unwell, emotional cost of infertility following abortion, sterility, still birth etc, and risk of loss of life in humans, may not be accurately quantified although these costs exist

Diagnosis of brucellosis

Human brucellosis has a wide clinical spectrum and presents various diagnostic difficulties because it mimics many other diseases. The diagnosis of brucellosis requires the isolation of *Brucella* from blood or body tissues or the combination of suggestive clinical presentation and positive serology. Proper diagnosis is one of the key obstacles for the complete eradication of brucellosis. Amplification of *Brucella* DNA by polymerase chain reaction (PCR) assay is currently used in the diagnosis of brucellosis. For PCR, peripheral blood or non-blood samples can be used. It was reported that the sensitivity of PCR was 100% and the specificity 98.3% in patients with brucellosis of bacteraemic, non-bacteraemic and focal complications (89,90)

Several serologic tests have been developed to measure antibodies against *Brucella* which includes; tube agglutination test (TAT), Rose Bengal test (RBT), anti-Brucella Coombs test, and enzyme-linked immunosorbent assay (ELISA). The TAT is widely used, and a single titer of $\geq$160 or a fourfold rise in titer is considered significant (91-93). Serology for laboratory workers exposed to *Brucella* is usually performed at 0, 6, 12, 18, and 24 weeks, post exposure. The immune response to *Brucella* is characterized by an initial production of IgM antibodies followed by IgG antibodies. The major antigens that are useful for diagnosis of brucellosis are the smooth (S) lipopolysaccharide (LPS) of *Brucella* outer membrane and internal proteins.

The Centre for Disease Control (CDC) recommends that *Brucella* serology testing only be performed using tests approved by the Food and Drug Administration (FDA) or validated under the Clinical Laboratory Improvement Amendments (CLIA) and shown to reliably detect the presence of *Brucella* antibodies. Results from these tests should be considered supportive evidence for recent infection only and interpreted in the context of a clinically compatible illness and exposure history. Detection of antibodies to *Brucella* cytoplasmic proteins by ELISA and Western blot in cerebrospinal fluid (CSF) is another diagnostic approach in neuro-brucellosis (94). Among the serological methods currently in practice, the serum agglutination test (SAT) is commonly used for the diagnosis of *Brucella* infection in humans (95).

Prevention and control of brucellosis

Despite the huge efforts invested on the control of animal brucellosis, results have not always matched the expectations, particularly in ovine and caprine brucellosis, in which control has proven to be more challenging than that of bovine brucellosis (96, 97). This situation may be the consequence of the combination of several factors, including but not limited to those inherent to the infected host, the aetiological agent, epidemiological situations and environmental factors bordering on human cultural practice (98,99). Many stakeholders have employed various strategies, either in isolation or in combination, which were not without their peculiar differences and challenges.

Prevention of brucellosis is based on surveillance and the prevention of risk factors. The most effective prevention strategy is the elimination of infection in animals. Vaccination of cattle, goats and sheep is recommended in enzootic areas with high prevalence rates. Serological or other testing and culling can also be effective in areas with low prevalence. In countries where eradication in animals through vaccination or elimination of infected animals is not feasible, prevention of human infection is primarily based on raising awareness, food safety measures, occupational hygiene and laboratory safety. Moreover, pasteurization of milk for direct consumption and for creating derivatives such as cheese is an important step to preventing transmission from animals to humans. Education campaigns about avoiding unpasteurized milk products can be effective, as well as government policies on their sale (90). In agricultural work and meat processing, protective barriers and correct handling and disposal of afterbirths, animal carcasses and internal organs are an important prevention strategy. Surveillance using serological tests, as well as tests on milk such as the milk ring test, can be used for screening and could play an important role in campaigns to eliminate the disease. As well, individual animal testing both for trade and for disease control purposes, is practiced (7,100).

In endemic areas, vaccination is often used to reduce the incidence of infection. Several vaccines are available that use modified live viruses as detailed in the OIE Manual of Diagnostic Test and Vaccines for Terrestrial Animals, and as the disease becomes closer to being eliminated, a test and stamping-out program is required to completely eliminate it. Human brucellosis is best prevented by controlling the infection in animal population.

Pasteurization of milk from infected animals was an important way to reduce infection in humans (101).

Summarily, despite the nature of this disease and the perceived challenges of its control in animals (the primary host), three major strategies including strict bio-security at the farm level, test and slaughter programs, and immunization of susceptible population, have been demonstrated as effective tools to control brucellosis in domestic animals especially when used in combination. In addition to these strategies, other complementary tools such as epidemiological situation in a given setting, availability of resources, animal identification, animal movement control, economic compensations, and others, should be considered to ensure the success of each instituted program per time (96,102).

Conclusion:

In conclusion, brucellosis can be considered a paradigm of the need for a "One World, One Health" strategy given that the only approach to achieve the control and subsequent eradication of this zoonotic disease is the cooperation between the industry, producers, and public and animal health authorities (103). It is therefore necessary that all hands should be on deck and all necessary arsenals be employed to combat this silent and often neglected zoonosis whose negative impact cannot be denied in several parts of the world, especially in developing countries.

Contribution of authors:

UCS conceptualized the study and contributed to the introduction and distribution of brucellosis in Nigeria; KE contributed to human brucellosis and diagnosis; OEO contributed to economic impacts of brucellosis, prevention and control; IE contributed to brucellosis in domestic animals; and LPD revised the entire manuscript and provided conclusion for the review.

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