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# Emerging Infectious Diseases in Water Buffalo - An Economic and Public Health Concern

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## Abstract

Water buffalo is an indispensable livestock in Asia and other countries due to its high meat and milk quality, aside from draft power source. It adapts well to tropical climate and has significant contribution to the livestock industry, provided with improved breeding and good animal husbandry practices. Infectious diseases are hindrance to good reproductive performance of livestock, resulting in huge economic loss. In addition, most of these diseases are zoonotic, posing serious threats on human health. However, its degree of severity varies in each region and is often overlooked. This chapter reviews the common and current updates on emerging bacterial, viral, protozoal, fungal and endoparasitic pathogens that infect water buffaloes worldwide. All of the diseases directly affect the animals' health condition except for schistosomiasis where water buffalo played an important role as shedder of infection to humans. Leptospirosis, brucellosis, Bovine Tb, BVDV and fasciolosis have projected economic impact to water buffalo industry as well as its effect as zoonoses. However, the data seem underquantified since most are neglected diseases and are highly prevalent in developing countries. Further studies are needed particularly in countries where water buffalo is the major livestock than cattle to fully utilize the potential of the animal.

**Keywords:** emerging infectious diseases, economy, public health, water buffalo, zoonosis

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## 1. Introduction

Livestock play an important role in the rural livelihood and economy of developing and several developed countries. They are providers of nourishment for billions of rural and urban households as well as income and employment for producers and others working in simple

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and sometimes complex value chains. Large ruminants, especially domestic water buffalo (*Bubalus bubalis*) are an important livestock species worldwide as it is a source of high quality milk and meat, leather and traction power, in addition to being able to survive on marginal land and subsist on low-quality forages, a good alternative for the breeding livestock especially in tropical countries [1–3]. Water buffalo is known for its rusticity and great adaptability to different topographies, soils and climatic factors. However, they can still be afflicted with various infectious diseases that greatly affect their production performance.

Wild as well as domestic water buffalo population is mainly confined to their breeding sites at 28 countries in Asia, Africa and South America, located in tropical and subtropical areas. A total of 161 million or about 97% of the 166 million water buffalo population are found in Asian countries; while the African region comprises of 2.12%, the South American and European region comprises of 0.84 and 0.15% of the world buffalo population, respectively [4].

The water buffalo were domesticated in Indian subcontinent about 5000 years ago (river buffalo) and in China about 4000 years ago (swamp buffalo) [5]. With around 170 million domestic water buffalo that exists worldwide, more people depend on this gentle beast than on any other domestic animal.

The contact between water buffaloes and cattle or other domestic and wild animals, as well as their access to different ecosystems, has exposed the species to different infectious diseases [2, 6]. These emerging infectious diseases can be caused by bacterial, viral, fungal, protozoal and endoparasites that have a significant economic impact especially in countries or regions where water buffalo served as the major livestock. However, published water buffalo-specific research is limited because it is not an important animal in many countries that have the necessary resources and it is believed that this animals show similar disease manifestation with that of cattle [7].

Several of these water buffalo diseases are endemic in developed and developing countries worldwide. However, epidemiology of these diseases is not fully studied in domesticated water buffalo [81, 82]. Most information on ruminant diseases studied cattle and African wild buffaloes [108]. In addition, livestock importation and exportation is a very important pathway of disease dissemination from one continent to parts of the world [170, 175]. However, still few diseases of water buffaloes are absent in the New World (bovine ephemeral fever) [141] and Australia (trypanosomiasis) [170, 175].

Advancement of the beef and dairy cattle industry has enhanced dispersal of ruminant diseases from endemic parts of Africa, Australia and Southern Asia to the world as observed with bovine ephemeral fever [134, 140], trypanosomiasis [170, 175] and neosporosis [195]. Through these advancements in cattle industry, trypanosomiasis spread out from the tse-tese belt of Africa to the world triggering *Trypanosoma* spp. to have a wider host range that have a varying pathogenicity depending on the immune system and geography of the host [170].

In some cases, spread of ruminant disease is through vectors or reservoir. For example, bovine ephemeral fever is transmitted from one animal to another via mosquitoes [142], and biting flies transmit trypanosomiasis [168]. On the other hand, multi-species bacterial diseases like leptospirosis and brucellosis are known to be transferred via infected urine of rodents, carnivores [8, 9] and other farm animals and infected tissues (placenta, aborted fetuses, etc.) of

aborted animals [2, 56, 57]. In cases of parasitic diseases, snails act as intermediate hosts for fasciolosis [284] and schistosomiasis [298, 299].

The wallowing behavior or submergence to muddy water predisposes the water buffaloes to different diseases like leptospirosis [8, 9], brucellosis [83], fasciolosis [285], and schistosomiasis [295, 298, 299]. In addition, co-mingling with other buffaloes, ruminants and other animals further facilitate the transmission of these diseases. For example, co-mingling of water buffaloes in wallows increases the transfer rate of brucellosis [83] and schistosomiasis [295, 298, 299]. In some cases, water buffaloes acts as the reservoir or “spill-over” host for some diseases like in tuberculosis [94, 95].

Extensive distribution of ruminant diseases have a drastic negative economic impact due to low production output and high animal mortality, threat to public health and international trade and tourism [94]. Deg Nala, an emerging disease of water buffalo often misdiagnosed as foot and mouth disease or mange infection [272], affects milk yield and quality due to infection or necrosis of udder and inguinal canal [271] resulting in lower income to farmers.

Water buffalo also acts as reservoir host for zoonotic diseases like schistosomiasis [295, 298, 299], rotaviral infection [155], leptospirosis [8], brucellosis [84] and tuberculosis [94, 95]. For instance, schistosomiasis, the most prevalent zoonotic parasitic disease globally, infects more than 200 million people in more than 76 countries. With this, \$ 25 million disability-adjusted life years are lost [298, 299].

Control of ruminant diseases is often difficult because the causative agents of certain diseases survive in the environment for months and resistant to most disinfectants like in cases of rotaviral infection [152]. In cases of cryptosporidiosis, high prevalence of the disease is due to contamination of oocyst in the environment from great oocyst shedding in feces and survival of oocyst for few weeks to months [227, 228]. Schistosomiasis and fasciolosis are difficult to control due to non-conformity to habitual good and proper husbandry practices, continuous transmission from shedder animals, quantity of intermediate and final host, malpractices of irrigation systems and poor hygiene management [245, 297, 299].

In this review, the overview of each disease, its distribution, epidemiology, transmission, pathogenesis, diagnosis, treatment and control were discussed in order to fully understand the behavior of such diseases which will be beneficial for veterinarians and other health professionals in the control of diseases.

## 2. Emerging infectious diseases

### 2.1. Bacterial

#### 2.1.1. *Bovine leptospirosis*

Leptospirosis in large ruminants has a worldwide occurrence (**Table 1**). However, majority of the information on this disease is focused on cattle, while it is limited in water buffalo, indicating that both species resemble similar clinical manifestation of the disease [8, 9].

Bovine leptospirosis is caused by pathogenic *Leptospira* spp. which involves the serovar Hardjo maintained by cattle, and has an almost global distribution. *Leptospira borgpetersenii* serovar Hardjo (Hardjobovis, HB) is the common strain of this serovar maintained by cattle, however *L. interrogans* serovar Hardjo (Hardjoprajitno, HP) also occurs in some parts of the world. Chronic infection is more common due to these serovars which can result in important economic losses due to reproductive wastage [8, 10].

Meanwhile, a wide variety of other serovars belonging to the Icterohaemorrhagiae, Canicola, Hebdomadis, Sejroe, Pyrogenes, Autumnalis, Australis, Javanica, Tarassovi and Grippotyphosa serogroups have been reported as causing incidental infections in cattle and water buffalo causing severe disease. Clinical signs include pyrexia, hemolytic anemia, hemoglobinuria, jaundice, occasionally meningitis and death. In lactating cows, incidental infections are often associated with small quantities of blood-tinged milk. The acute phase of clinical disease in serovar Hardjo (both subtypes) infection is usually subclinical, with the exception of lactating cows, where agalactia may occur. Large outbreaks, while very dramatic, are rare and individual cases (even herd outbreaks) can go unobserved unless milk production is recorded [11] (**Table 1**).

In cattle, the most vital economic aspects of chronic leptospirosis are premature birth, still-birth, birth of immuno-compromised calves and abortion. In cases of Hardjo infection, the disease accumulates 6–12 weeks after an acute infection. On the other hand, it only takes 4–6 weeks after an acute disease in some cases [26]. Placental infection may also affect the weight of calves; stillborn or weak calves with Hardjo-infected placentas were significantly lighter than uninfected controls. There has also been an association with retention of fetal membranes [26]. Leptospire have been detected for up to 8 days in post abortion/calving vaginal discharges [27]. Infertility, which responds to antibiotic and/or vaccination, is described in Hardjo infection [28].

Infection most frequently occurs through the mucous membranes of the eye, mouth, nose or genital tract. A period of bacteremia which coincides with acute clinical disease can last for a week from the first day of infection. In this bacteremic phase, the organisms can be isolated from most organs of the body most especially in the blood and cerebrospinal fluid. However, after 10–14 days, this phase ends with the presence of circulating antibodies. Peak titers vary considerably (1000–100,000 in the MAT), and these may be maintained for up to 6 weeks, depending on the species, after which a subsequent gradual decline occurs. A secondary bacteremic period (after 15–26 days) has rarely been reported. Low titers may be detectable for several years in many animals [29]. During leptospiremia, leptospire multiply in the proximal renal tubules and are excreted in the urine [8].

Infection on pregnant females often leads to abortion and other neonatal diseases that can be caused by intrauterine infections during the last trimester of gestation. In the event of immunocompetence development, antibodies against the leptospire can be observed in the fetus [8, 30].

In host-maintained infection, the persistence of leptospire in the oviduct and uterus of non-pregnant females and in the genital tracts of males were observed [31–34]. In vitro studies

Locality	Prevalence (%)	Technique	Authors
New Zealand	5.7 <sup>3</sup>	Serology	Dorjee et al. [12]
Mexico	10.33	MAT	Leon et al. [13]
Sri Lanka	20.3	Serology	Gamage et al. [14]
Thailand	21.5	MAT	Suepaul et al. [15]
Nigeria	3.5	ELISA	Ngbede et al. [16]
Uganda	42.39 <sup>1</sup> and 29.35 <sup>2</sup>	ELISA	Atherstone et al. [17]
Poland	3.2	DAS-ELISA	Rypula et al. [18]
Brazil	32	MAT	de Carvalho et al. [19]
Morocco	9.09	Serology	Lucchese et al. [20]
Thailand	19.80	LAMP	Suwancharoen et al. [21]
Philippines	16.1	nPCR	Villanueva et al. [22]
Nicaragua	30.31 and 15.38	MAT and in vitro culture	Flores et al. [23]
Brazil (Santa Catarina State)	6.44 <sup>2</sup>	MAT	Favero et al. [9]
Northeastern Brazil	42.9 (50.5 <sup>2</sup> , 40.5 <sup>3</sup> , 34.6 <sup>4</sup> )	MAT	Campos et al. [24]
Lao PDR	3.3 <sup>1</sup> 22.2 <sup>2</sup>	ELISA	Olmo et al. [25]

<sup>1</sup>Buffalo.

<sup>2</sup>Cattle.

<sup>3</sup>Sheep.

<sup>4</sup>Goat.

MAT, microscopic agglutination test; ELISA, enzyme-linked immunosorbent assay; LAMP, loop-mediated isothermal amplification.

**Table 1.** Ruminant leptospirosis prevalence studies conducted worldwide.

have also shown that leptospires have the ability to adhere to and penetrate the zona pellucida and enter embryonic cells [30]. Chronic persistence in the mammary gland and its drainage to lymph nodes has also been reported [35]. Symptomless infection is thought to be very common as evidenced by the wide disparity between seroprevalence and apparent disease prevalence.

The primary lesion due to this disease damages the endothelial cells of small blood vessels. The severity of disease varies with the infecting serovar, animal species, age, and the stage of infection [8, 30]. In acute fatal infection, there are no pathognomonic gross changes, but the following can be observed: icterus and the presence of ecchymotic and petechial hemorrhages on the serosal surface of major organs including the lungs, kidney, abomasum and the peritoneum, and pleura and blood in the bladder. Liver may be enlarged with accentuation of the hepatic lobes. Hepatocellular dissociation, intracanalicular cholestasis, hepatocellular necrosis, and Kupffer



cell hypertrophy may be found on histological examination. Acute interstitial nephritis, with tubular and glomerular degeneration, and the infiltration of mononuclear cells, lymphocytes, plasma cells, and macrophages, may be seen on histological examination [8]. Lesions consisting of scattered gray foci which are usually bordered by a ring of hyperemia are concentrated in the kidneys in the case of chronic leptospirosis. [36].

Fetal pathology varies considerably and depends on the species, the stage of gestation at which infection occurred, and the infecting serovar. Pathological examination of fetuses usually reveals only non-specific findings in cattle. In experimental fetal disease, vasculitis with perivascular hemorrhage predominantly in the liver and sometimes in the lungs and meninges with minor tubular necrosis and interstitial nephritis occurs [37]. These were consistent with what is seen in acute leptospirosis in young animals. Placentitis was also a feature [38].

A definitive diagnosis of leptospirosis is required in the confirmation of leptospirosis as a cause of clinical disease, assessment of the infection and/or the immune status of a herd for the purposes of a control or eradication program on either a herd or national basis, epidemiological studies and assessment of the infectivity status of an individual animal to assess its suitability for international trade or for introduction into an uninfected herd [8].

Laboratory diagnostic procedures for leptospirosis fall into two groups: (1) tests for the demonstration of leptospire and (2) tests for antibody detection. Demonstration of leptospire is usually performed in initial bacteremic phase, untreated fatal cases and aborted or stillborn fetuses and the localization phase where leptospire resides at its organ predilection sites of an infected animal. The available methods for the demonstration of leptospire include direct visualization of organisms by dark-field microscopy [39, 40], culture, DNA detection methods [41, 42] and staining (silver and immunochemical) [42–44].

Detection of the organism can be hasten through urine collection upon treatment [45]. Urine samples should be mixed immediately with an equal volume of phosphate buffered saline containing 1% bovine serum albumin on collection [46].

In the tests for antibody detection, serological testing is the mainly used method of diagnosis such as ELISA, while microscopic agglutination test (MAT) is the standard serological test. The MAT is used primarily as a herd test. It is labor and resource demanding and its sensitivity depends on the stage of infection in individual animal [8].

The treatment of acute leptospirosis in individual animals or in herds is dependent on the use of antibiotics plus supportive symptomatic treatment. When treating herd problems, vaccination may be combined with antibiotic treatment to obviate chronic reproductive wastage [8].

A combination of penicillin and streptomycin has been the antibiotic therapy of choice for the treatment of acute leptospirosis, but ampicillin, amoxicillin, tetracyclines, tulathromycin and third generation cephalosporins have also been used [47–50].

Antibiotics are utilized for the medication about incessant renal also genital leptospirosis, a critical part from control projects. Streptomycin at 25 mg/kg has been the most widely

used over vast majority of utilized antimicrobials for the medication of renal carrier animals, although some experiments found to be not powerful [27, 51].

The principles of control are based on the interruption of direct and indirect transmission of infection as well as the reduction of its zoonotic risk. Control strategies must take into consideration the location, number of animals, infecting serovars, maintenance hosts, means of transmission, risk factors and the control options available. Good surveillance information is required. The tools for control include vaccination, antibiotic therapy, assessment of herd/population status (profiling), identification and removal of infected animals, rodent control, reducing risk factors through management systems and permutations of all these methods [8].

Studies have showed that monovalent and bivalent vaccines of serovar Hardjo and Pomona have conferred protection for a year [52]. Multivalent vaccines for cattle compared very unfavorably with monovalent product in a series of experiments [53] but they continue to be sold and the debate about their efficacy continues [48, 54, 55].

### 2.1.2. *Brucellosis*

Brucellosis in water buffalo is acknowledged as a contagious infectious disease caused by *Brucella abortus*, a Gram-negative, non-motile, non-spore forming, aerobic, facultative intracellular coccobacillary bacterium [2, 56, 57]. This bacterium is capable of invading epithelial cells, placental trophoblasts, dendritic cells and macrophages. Reports have found that *B. abortus* biovars 1–6 and 9 were primarily isolated from cattle and buffaloes [57]. In particular, *B. abortus* biovar 1 is the most prevalent biovar in countries where bovine brucellosis is endemic [1].

*Brucella* infections in livestock species represent an enormous economic impact particularly in developing countries due to reproductive problems, reduced milk production and restrictions on animal movements and trade. It is characterized by abortion, predominantly in the last trimester of gestation, premature births followed by retention of placenta, metritis, non-viable calves, infertility, reduction of milk production and lameness as common sequelae to infection in dairy animals while epididymitis and orchitis in bulls [13, 191, 236] (**Table 2**).

This disease of water buffalo has been reported and considered endemic in many developing (**Table 2**). In addition, developed countries in Latin America, Southern Europe, Africa, South and Southeast Asia, and the Middle East, especially in the rural areas, where livestock rearing and production of dairy products and by-products is crucial for family income [2, 7, 56, 75–80].

The epidemiology of *Brucella* infection has not been studied extensively in domestic water buffalo. These animals shed viable brucella in milk, but dam-to-calf transmission has not been evaluated directly. Infected water buffalo expel the bacterium during abortion, and this may serve as a source of infection for herdmates. Experimental studies have



Locality	Prevalence (%)	Technique	Authors
Sudan	2.15 and 3.4	RBPT	Gumaa et al. [58]
Malaysia	0.91 <sup>4</sup>	Serology	Bamaiyi et al. [59]
Turkey	6.86 <sup>a</sup> and 6.25 <sup>f</sup>	RBPT and STAT	Aslan et al. [60]
Argentina	1.8	BPAT	Aznar et al. [61]
Ethiopia	1.9 <sup>2</sup>	RBPT	Sintayehu et al. [62]
Egypt	20	RBPT and CFT	Hegazy et al. [63]
Tajikistan	6.7	Indirect ELISA	Rajala et al. [64]
Argentina	2 <sup>3,4</sup>	BPAT and CFT	Draghi et al. [65]
Morocco	33.48	ELISA	Lucchese et al. [20]
Nigeria	3.9	RBPT	Akinseye et al. [66]
Lao PDR	0.3	ELISA	Douangneun et al. [67]
India	30.40 <sup>a</sup> and 41.55 <sup>b</sup>	RBPT and Indirect ELISA	Pathak et al. [68]
Uganda	14 <sup>2,e</sup> , 29 <sup>2,d</sup> , and 17 <sup>4,e</sup>	IgG and IgM LFA and Milk Ring Test	Miller et al. [69]
Cote d'Ivoire	4.6 <sup>2</sup>	RBPT	Kanoute et al. [70]
Mexico	0.52 <sup>4</sup>	Card Testing and Radial Immunodiffusion	Roman-Ramirez et al. [71]
Pakistan	6.3 <sup>a</sup> , 3.28 <sup>c</sup> , and 6.7 <sup>d</sup>	RBPT, RT-PCR, and Milk Ring Test	Ali et al. [72]
Costa Rica	10.5–11.4 <sup>a</sup> and 4.1–6 <sup>b</sup>	RBPT and ELISA	Hernandez-Mora et al. [73]
Algeria	12	Serology	Kardjadj [74]

<sup>1</sup>Buffalo.

<sup>2</sup>Cattle.

<sup>3</sup>Sheep.

<sup>4</sup>Goat.

<sup>a</sup>RBPT, rose Bengal plate test.

<sup>b</sup>ELISA, enzyme-linked immunosorbent assay.

<sup>c</sup>PCR, polymerase chain reaction (RT-PCR, real-time PCR).

<sup>d</sup>Milk ring test.

<sup>e</sup>LFA, lateral flow assay.

<sup>f</sup>STAT, serum tube agglutination test.

BPAT, buffered plate agglutination test; CFT, complement fixation test.

**Table 2.** Prevalence studies of brucellosis in ruminants.

demonstrated that ingestion of virulent *B. abortus* causes infection in female water buffalo [81, 82]. Co-mingling of many animals in a small area facilitates disease transmission, and congregation of water buffalo in wallows may be an important factor for spread of brucellosis [83].

*Brucella* spp. taint host units that are skilled of giving those supplement erythritol, henceforth their predilection with carry on with inside units of the genital tracts about animals. Reticuloendothelial cells need a favoring area clinched alongside animals and the primary site in humans, especially human macrophages. [84]. Later confirmation recommends that the host environment must likewise give choline, a fundamental forerunner to the synthesis, toward brucella organisms, of the cell envelope without which those creatures are not virulent [56, 85, 86].

Brucellosis may be diagnosed through direct and indirect methods. The direct methods include isolating and identifying the bacteria in the samples obtained from the suspect animal, such as tissues from aborted fetuses, placenta, vaginal exudates and milk [39, 186]. Isolating the agent is the safest diagnostic method and is considered the gold standard for diagnosis. However, it presents difficulties concerning sample collection and conservation, as well as those concerning the implementation procedures of the technique. Low bacterial loads in collected specimen can lead to false negative result [57]. Polymerase chain reaction (PCR) assays have been created to diagnose *Brucella* at the species level (e.g. the Abortus, Melitensis, Ovis, Suis AMOS PCR). These assays are most useful when applied to DNA extracted from a positive culture [57].

On the other hand, the indirect or serological methods consist in detecting antibodies in serum, milk and seminal plasma [87]. These include milk ring test (MRT), serological tests such as the standard agglutination test (SAT) and buffered agglutination test, which are confirmed by the complement fixation test (CFT) and enzyme-linked immunosorbent assay (ELISA) [57]. According to Molnár et al. [88], the serological methods are one of the main bases used to support brucellosis control programs. The correct diagnosis of brucellosis gives support and assurance to the implementation of eradication programs [2].

The most effective measures for controlling and eradicating bovine brucellosis in high prevalence countries or regions are grounded on vaccination of all susceptible host, serologic tests and slaughter/eradication of positive animals [89]. Vaccination is a critical tool pecker to control or eradicate bovine and buffalo brucellosis, because it prevents abortion miscarriage and consequent pasture ley contamination, recognized as major form to transmission of *B. abortus* to these species. Though RB51 strain has been approved for use in some countries, *B. abortus* strain 19 (S19) is still the most common vaccine suggested against bovine and buffalo brucellosis worldwide. [3].

Natural resistance to bovine brucellosis was also explored in water buffaloes. These include the candidate gene solute carrier family 11A1 (SLC11A1) through monocyte chemotactic/chemoattractant protein 1 (MCP1), Nramp1 (natural resistance-associated macrophage protein 1) gene, particularly the Nramp1BB genotype [90] and the haplotype pair HYA/HYA at the mannose-binding lectin (MBL) [91].

The broad management system, challenges for the achievement of sterile control projects that were done nationally for huge herds and broad regional dimension, and the confusion that water buffaloes are highly resistant to disease are factors that thwart those control from claiming brucellosis clinched alongside water buffaloes [92, 93].

### 2.1.3. Bovine tuberculosis

Bovine tuberculosis (BTb), caused by *Mycobacterium bovis*, is a chronic and zoonotic bacterial disease. *M. bovis* is closely related to *M. tuberculosis* of human, both of which belong to Mycobacterium tuberculosis complex. It remains as an endemic infection in several countries, despite several efforts to control the disease [165, 167, 182, 277]. BTb infects variety of domestic and wildlife hosts, of which is either reservoir or spill-over, wherein buffalo is an example [94, 95].

*M. bovis* is primarily transmitted between animals by inhalation, though can be transmitted through ingestion and skin inoculation, however, these transmission is less commonly observed [94–97]. Pathogenesis of *M. bovis* starts after inhalation of bacilli as it adheres to the alveolar surface of the lung and is phagocytosed by macrophages. Then, macrophages phagocytosed mycobacterial antigens and extant them to T-lymphocytes, an important component of immune response. Classical lesions in buffalo are tuberculosis mass in the lungs and lymph nodes, but can also be established in distal sites [98]. Disease resistance is arbitrated by either the innate or the adaptive immunity and therefore the genes related to either of these processes may be candidate genes for BTB susceptibility loci [97].

The information was skewed on BTb in ruminants, which are most of the studies focus of cattle for domestic livestock and African buffalo in the wildlife. Very few peer-reviewed journals on BTb exist for water buffalo. BTb remains a serious problem for animal and human health in many developing countries [108]. Its extensive distribution has drastic negative economic impact (animal mortality and lower milk production output), affecting public health, international trade and tourism [94].

African buffalos infected with BTb show clinical signs only in late stages of the disease course. The clinical signs of BTb in buffalo at such stage include coughing, debilitation, emaciation and lagging when chased [98, 99]. The incubation period for BTb is 9 months to a year, and infections can be subclinical or dormant for a long period of time and reactivate during periods of stress or in old age [100]. The losses to the cattle industry due to BTb manifests as 10–20% reduced milk and meat production, infertility and carcass contamination [101]. The epidemic of HIV in developing countries in which *M. bovis* is present in animals could make zoonotic tuberculosis a serious public health threat to persons [102–104] (**Table 3**).

Disease prevalence of BTb is 25.3 and 21.6% for cattle and buffaloes, respectively [115] (**Table 3**). Although, prevalence of BTb varies greatly among countries [103]. The results of PCR on suspected samples together confirmed 92.5% cases as Mycobacterium, 86.8% for *M. tuberculosis* complex and 77.4% for *M. bovis* [116]. In Southern Italy, of all domesticated ruminants, water buffalo (*Bubalus bubalis*) plays an important economic role. Raw buffalo milk is very important to an Italian product called “mozzarella di buffala” [117]. It is mandatory that herd from which milk is collected should be free from brucellosis and tuberculosis. Tuberculosis has not yet been eradicated in Southern Italy. It has been reported in 2012 that cattle and buffalo has 0.7% prevalence, and an incidence increase of 0.65% [115]. The animal level prevalence of BTb has been reported to be 13.5 and 14.3% in Ethiopia and India, respectively [118, 119]. In Pakistan, previous study conducted in and around Faisalabad city using tuberculin skin test reported prevalence of 5.1% in cattle and 1.7% in

buffaloes [120]. In Lahore, 6.9% buffaloes showed positive reaction to tuberculin [121]. In Punjab province, 2.45 and 8.48% buffaloes at two farms were found positive to tuberculin test [122]. Another study reported 3% tuberculosis prevalence in buffaloes at Faisalabad and Okara [103].

The “gold standard” diagnosis for TB is still the culture identification [123] or DNA amplification by PCR. Although, some indirect tests are used for screening test, the most frequently employed diagnostic test is intradermal tests (ITT), which is based on the inoculation of an *M. bovis*-purified protein derivative (bovPPD) or concurrent with an *M. avium* PPD (avPPD). However, sensitivity and specificity is the drawback of this test [124]. The gamma-interferon assay, an in vitro test measuring the production of interferon-gamma (IFN) on blood samples, was previously sensitized with a bovine PPD. Although this test has high sensitivity and specificity, it is costly and has limitations of IFN assay in some countries [32, 125].

Locality	Prevalence (%)	Technique	Authors
Uganda	21.6 <sup>1</sup>	Interferon- $\gamma$	Kalema-Zikusoka et al. [105]
Lao PDR	1	ELISA	Vongxay et al. [106]
Brazil	5.63 <sup>1</sup>	Tuberculin Test	Barbosa et al. [107]
El Salvador	18 <sup>3</sup> and 13 <sup>4</sup>	SITT	Linderot de Cardona et al. [108]
Ghana	19 <sup>2</sup>	Anigen Rapid BTB test	Amemor et al. [109]
Eritrea	11.3	SITT	Ghebremariam et al. [110]
Spain <sup>3</sup>	50.44 <sup>a</sup> , 83.23 <sup>b</sup> , 24.92 <sup>c</sup> , 4.86 <sup>d</sup> , 59.42 <sup>e</sup>	Culture, Histopathology, SITT, Interferon- $\gamma$ , ELISA,	Muñoz-Mendoza et al. [111]
Cameroon	41 <sup>f</sup> and 52 <sup>a</sup>	Post mortem Exam and Culture	Egbe et al. [112]
South Africa	48.4 <sup>g</sup> and 43.1 <sup>h</sup>	Ziehl-Neelsen Staining and Multiplex PCR	Bhembe et al. [113]
Democratic Republic of Congo	1.68 <sup>4</sup>	Ziehl-Neelsen Staining	Luboya et al. [114]

<sup>1</sup>Buffalo.

<sup>2</sup>Cattle.

<sup>3</sup>Sheep.

<sup>4</sup>Goat.

<sup>a</sup>Culture.

<sup>b</sup>Histopathology.

<sup>c</sup>SITT, single intradermal tuberculin test.

<sup>d</sup>Interferon- $\gamma$ .

<sup>e</sup>ELISA, enzyme-linked immunosorbent assay.

<sup>f</sup>Post-mortem examination.

<sup>g</sup>Ziehl-Neelsen staining.

<sup>h</sup>PCR, polymerase chain reaction.

**Table 3.** Prevalence studies of bovine tuberculosis in ruminants.

Serological assays (ELISA) have been suggested as an ancillary diagnostic test in screening or to identify immuno-compromised animals in a herd [32, 125]. For this purpose, some antigens have been assessed with variable results [34].

MPB70, a protein secreted by *M. tuberculosis* complex species, is identified as an early B cell target in *M. bovis* infection, and can be robustly identified in infected cattle. A study verified that ELISAs using MPB70 as capture antigen was found to have acceptable specificity and sensitivity [55].

Improving the diagnostic capability is another area for improvement to screen and detect all infected animals especially the subclinical cases. Recently, serologic assays (gamma-interferon assay, the MAPIA and rapid tests) are efforts to provide single point of contact tests, a valuable tool in disease surveillance of free-ranging wildlife [126].

Historically, spread of *M. bovis* is controlled in a domestic cattle herd via whole-herd skin testing, slaughter testing and movement monitoring herds. In addition, the milk pasteurization is important in controlling the zoonosis of tuberculosis. In past years, disease transmission between humans, domestic animals and wildlife has increased. Once a disease becomes endemic in a wildlife population, disease control becomes much more challenging [126].

BTb is traditionally controlled using quarantine of infected or suspected herds, slaughter testing and milk pasteurization [94, 127]. Although traditional control programs have eradicated or almost eradicated the disease from farm animals and pets in some developed countries [128, 129], BTb is still prevalent in Great Britain, Ireland, New Zealand, Africa and many more developing countries [98, 130]. In fact, tuberculosis has a great negative impact on economy and public health [95, 130].

Poor husbandry and biosecurity, like co-mingling of infected livestock with wild animals, increases the spread of disease and the number of reservoir host. With this, the disease cannot be eradicated since the bacteria are circulating within the herd and reservoir hosts [126]. Controlling population densities of wildlife reservoirs and successfully implementing proper biosecurity to minimize interaction between wild and domestic animals can help to control and prevent the horizontal transmission of the disease. However, these methods may be insufficient in eradicate the disease. In addition, focal depopulation of wildlife reservoir is another control measure that can be employed successfully. Unfortunately, due to biodiversity and animal welfare issues, this extreme eradication measure should not be patronized [126]. Regardless of the methods employed, the control of bovine tuberculosis once establishes itself in a wildlife maintenance host population is generally a long-term commitment. It appears that BTb in its many forms remains an important disease in both domestic and wild animals and that its eventual control will remain an on-going concern for many decades into the foreseeable future [126]. Prevalence of tuberculosis is high in developing countries because the control strategies are lacking or poorly executed [128, 129].

Development of vaccines for wildlife is the articulated theme by researchers worldwide for control to eradication of tuberculosis. The vaccine should reduce the shedding of *M. bovis* or prevent the development of the disease in reservoir hosts. Development of an oral-bait vaccine is objective of researchers to immunized wide range of free-range wildlife species.



In addition, researchers are also thinking of developing a vaccine that can differentiate its immunization against wild-type *M. bovis* infection following animal death. This may mean that researchers are thinking of a genetically engineered vaccine is more than the conventional BCG-based vaccine [126].

## 2.2. Viral

### 2.2.1. Bovine ephemeral fever

Bovine ephemeral fever (BEF) is an economically important disease affecting cattle, yak and water buffalo among other ruminants. This disease is caused by the arthropod-borne bovine ephemeral fever virus (BEFV) belonging to the family Rhabdoviridae under the genus Ephemerovirus [131]. Although it is not contagious among vertebrates, its epizootiology is consistent with insect-borne transmission. Infected animals are characterized by high fever, spontaneous abortion, lameness or paralysis [132–134] and its distribution among bovines covers Africa, Middle East, Australia and Asia [135].

Although its origin is quite unclear, the first report of BEF was documented in China in 1955, while the first strain of BEFV, the JB76H strain, was isolated from an infected dairy cattle during an epidemic in the country in 1976 [136, 137]. Subsequently, the disease was also reported in some countries in the East Africa, Rhodesia, Kenya, South Africa, Indonesia, India, Egypt, Palestine, Australia and Japan [138, 139]. Though bovine ephemeral fever has been endemic in several areas in Africa, Australia and Southern Asia, the advancement of cattle industry has enhanced its dispersal into a larger area [134, 140]. On the other hand, the disease has never been reported in the Western Hemisphere, North and South America. Serological evidences also showed that New Zealand and Pacific Islands are not affected by the disease. Presently, bovine ephemeral fever is enzootic in South Africa, India, Japan and some areas in Australia [141].

Many factors propose that mosquitoes are the main vectors of the disease. Commonly observed clinical signs are abrupt fever of about 41°C high, lasting for 1–3 days with severe decrease in milk production, lethargy, ocular and nasal discharge, stiffness, dyspnea, depression, salivation, anorexia, lameness and ruminal stasis, [142] though in some reports, prolonged paralysis and ataxia were observed in some animals following the acute stage of infection. Severe cases can lead to mortality which might be caused by exposure, starvation or even pneumonia [39].

BEF is usually diagnosed through serological assays. If the animal was exposed previously to another ephemerovirus, anamnestic responses to BEFV during the first infection can happen. The most frequently used diagnostic assays are the ELISA and viral neutralization [143]. In some countries, molecular methods such as reverse transcription polymerase reaction and real-time loop-mediated isothermal amplification are also being done for faster and more sensitive detection of the disease [141].

Under the electron microscope, the BEF virus has a bullet shape with fringe of fine surface projections measuring about  $80 \times 120 \pm 140$  nm. However, South African strains are mostly conical in shape resembling the bullet-shaped Asian and Australian strains serologically. The



citrated blood from affected cattle remains infectious at 48°C. However, there is a decrease of infectivity of the virus at extreme pH conditions (2.5 or 12) within 10 min. Consequently, the virus is inactivated within 10 min at 568°C and 18 h at 378°C [144].

Isolation of the virus is done by inoculating leucocyte from an infected cow into suckling mice (1 ± 3 days old) intracerebrally or suckling hamster and rats. The virus grows very well in BHK-21 cells inoculated from mouse brain or bovine leucocyte suspension. It also grows in bovine kidney, hamster lung, Vero and *Aedes albopictus* cell lines and hamster lung tissue culture [145].

Handling of the disease includes the usage of non-steroidal anti-inflammatory drugs and administration of calcium borogluconate to hypocalcemic animals in order to reduce the clinical signs. Vaccination is also considered as the most effective approach to control the disease. Previous studies have applied live attenuated, inactivated, subunit and recombinant vaccines experimentally and commercially. However, live vaccines generally induce more prolonged immunity [146].

### 2.2.2. Rotavirus infection

Rotavirus belongs to the family Reoviridae under the genus Rotavirus. The virion has a triple layer capsid that covers a genome of double-stranded RNA. Its envelope is lipid-free and has three concentric layers of protein made up of 3 of the 13 proteins that the rotavirus genome encodes [147]. The most common rotaviruses isolated from human and animals have a common group antigen present on the major inner capsid protein VP6 and are now categorized into group A [148] which are commonly isolated from rotaviral diarrhea cases. Other rotaviruses that lack the said antigen are characterized as non-group A rotaviruses and are classified into groups B, C, D, E, F and G. Furthermore, group A rotaviruses are subdivided into subgroups I and II, based on their antigenicity of a separate domain present in the VP6 [148, 149]. The two outer capsid proteins, VP7 and VP4, independently produce neutralizing antibodies, induce protective immunity, and are used to classify rotaviruses into G (for glycoprotein) and P (for protease-sensitive) types, respectively [150]. Neonatal diarrhea caused by RVA boRV projects significant economic loss in the dairy and beef industry due to increased morbidity and mortality, treatment costs and reduced growth rates [150].

The virus attacks the villi upon its entrance in the small intestine suppressing effectively absorption of nutrients into the animal's body that leads to dehydration. The incubation period of the virus lasts for about 12–24 hours and the infected calves are usually feverless [147]. Clinical signs include runny diarrhea, dehydration and loss of appetite and if severity increases, it leads to mortality [151]. No specific treatment is being used for this disease. Hence, replacing lost fluids and restoring the balance of the body's important electrolytes are most applicable. Usage of antibiotics is not recommended, however, it can be administered if there is a presence of secondary infection caused by bacteria [152]. Animals that have recovered often return to their normal bodyweight in around 10–28 days after the infection [147].

Transmission of the disease to other animals usually occurs upon contact with infected feces [153]. Infected calves excrete the virus in their feces up to the age of 6–8 weeks [154]. It is quite

hard to eradicate for it survives for several months and can resist several disinfectants [152]. Also, the disease is considered as zoonotic [155]. Thus, vaccines are used for the prevention of the disease [156]. Also, passive immunity plays a vital role in the prevention of rotavirus infection. The transfer of colostral antibodies provides early immunity in new born animals and serves as the most important form of protection for a newly born calf. However, this type of protection lasts for only 3–4 days, thus it only reduces the rotaviral diarrhea rather than eliminating it. In this regard, continuous colostrum feeding is advised [157].

Diagnosis for the disease is also being carried out using antigen-antibody assays along with PCR and electron microscopy [188]. Also, the disease can be detected through agglutination and polyacrylamide gel electrophoresis. Detection techniques dealing on the viral RNA such as RT-PCR, nested RT-PCR and real-time qPCR are even becoming a more widely used way of diagnosis [147].

### 2.2.3. *Bovine viral diarrhea*

Bovine viral diarrhea virus (BVDV) is another significant pathogen causing respiratory and reproductive illnesses infecting ruminants that leads to various clinical problems including abortion. BVDV belongs to family Flaviviridae under the genus Pestivirus, subdivided into four well-known species: bovine viral diarrhea virus 1 (BVDV-1), bovine viral diarrhea virus 2 (BVDV-2), border disease virus (BDV) and classical swine fever virus (CSFV), previously known as hog cholera virus. BVDV has a worldwide distribution and its natural hosts include a wide range of domestic and wildlife animal populations, ruminants in particular [158, 159]. Previously, another type of BVDV was identified: the HoBi-like pestiviruses, also known as the bovine viral diarrhea virus 3 [160]. This type of BVDV has been occasionally reported from naturally infected cattle in Brazil, Asia and Europe [161].

Clinical symptoms of the disease include diarrhea, mucosal disease and reproduction dysfunctions such as abortion, teratogenesis, embryo resorption, fetal mummification and still-birth [45]. Also, birth of an immunotolerant calf with persistent infection (PI) is also possible if the mother has been infected by the disease from 50 to 125 days of gestation [162]. The most birth defect among calves caused by this disease is cerebral hypoplasia characterized by ataxia, tremors, wide stance, stumbling and failure to nurse. Severe cases can lead to death [160].

The disease is more frequently transmitted vertically leading to births of persistently infected calves. On the other hand, it can also be transmitted horizontally through direct contact among infected animals [163, 164]. There is no known treatment for this disease and only supportive therapy is being applied. However, upon detection, the infected animal should be culled [151].

Detection methods for the disease include virus isolation, immunohistochemistry, polymerase chain reaction and serology depending on the setting of the disease. Immunohistochemistry is more applicable for herd surveillance and screening since samples may be collected from cattle of any age. Thus, allowing simpler sampling, stable samples for transport and results are not affected by passive antibodies. On the other hand, polymerase chain reaction is

advantageous for pooled blood or milk samples since trace amount of virus can be identified using this technique [45]. Both virus isolation and polymerase chain reaction methods require subsequent testing within 3 weeks of the first testing to discriminate transient infection from persistent infection [165].

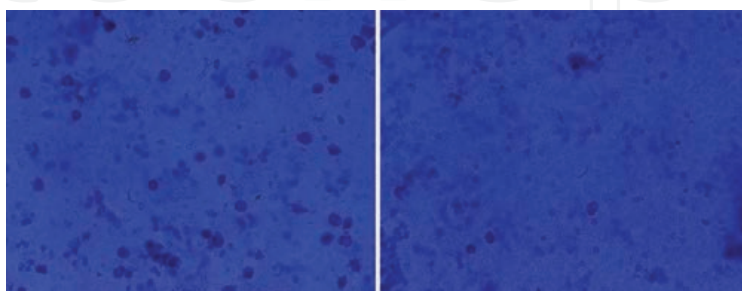
The presently known control measure for BVDV is through vaccination [166]. Two types of vaccine for BVDV are being used: the modified live virus (MLV) vaccines and the killed virus (KV) vaccines. MLV vaccines have few antigens and only require one dose during the initial immunization step since the viral antigen replicates in the vaccinated animal thus, boosting the immunogenic mass. However, this vaccine is not stable in varying temperature and can be easily deactivated by some chemicals. Also, it is not recommended to administer this vaccine to pregnant cattle. On the other hand, the KV vaccines are more expensive since it requires more antigens per dose and more than one dose of vaccine is usually given during initial immunization, but this type of vaccine remains stable in varying temperature and are not easily deactivated by chemicals [167].

### 2.3. Protozoal

#### 2.3.1. Trypanosomiasis (*Trypanosoma evansi*)

*Trypanosoma evansi*, the causative agent of Surra, is a blood and occasional tissue parasite to variety of animals transmitted by biting flies [168] (**Figure 1**). *T. evansi*-infected animal exhibits fever, anemia, weakness and nervous signs that are responsible for low production yield of meat, milk, draught power, fertility and even manure. In the absence of proper treatment, chronic wasting is observed leading to abortion and death [169].

Among salivarian trypanosomes, *T. evansi* has the widest host range, however, susceptibility is dependent on host immune system and can vary geographically [170]. In theory, the wide range of hosts of *T. evansi* is attributed to the deletion of maxicircle kinetoplast DNA [171–173]. This is also the reason why *T. evansi* can no longer be transmitted by Glossina flies [174]. Thus, the transmission of the parasite is through biting flies. Through the new vector, *T. evansi* spread from tsetse belt of Africa toward the rest of the world through livestock exportation. However, it is still absent in Australia [170, 175].



**Figure 1.** Presence of adult *T. evansi* upon blood parasite examination (BPE) of an infected water buffalo (Photo from Philippine Carabao Center).

Originally, the principal host of *T. evansi* is the camel, however, it is also present in equids and other mammals, like the water buffalo. In Asia, *T. evansi* is one of the major blood parasites of water buffaloes; and considered as economically important disease in the Philippines [169]. In the Americas, it is found in water buffaloes with prevalence of 40% in some cases. However, clinical signs of trypanosomiasis are reportedly due to *T. vivax* than *T. evansi* [176].

Trypanosomiasis caused by *T. evansi* has been categorized as mild, chronic or subclinical disease of Bovinae, mainly in Latin America and Africa [177] (Table 4). One-third of a century in Asia, numerous reports displayed Surra still as major disease of cattle and water buffaloes, especially in Southeast Asian countries. Infection results in anemia, great loss in the production of meat, milk, draught, leading to total wasting and death of the animal [175]. In Indonesia, clinical signs disrupt the heifer's estrus cycle [178]. In Thailand, novel clinical signs are observed with the addition of edema of the legs, conjunctivitis and dyspnea [179]. Meningoencephalitis is the most observed nervous signs [180]. Imported buffaloes from Australia are very susceptible to the infection due to absence of the parasite in the source

Locality	Prevalence (%)	Technique	Authors
Jordan	8.2 <sup>1</sup>	BPE and MIT	Abo-Shehada et al. [183]
	9.6 <sup>2</sup>		
Tanzania	30.4 <sup>a</sup>	PRF-LAMP	Laohasinnarong et al. [184]
	0.6–2 <sup>b</sup>	PCR	
Spain (Canary Islands)	5	ELISA	Rodriguez Diego et al., [185]
North Vietnam	22.4	CAT	Nguyen et al., [186]
South Africa	23.7 <sup>c</sup>	ELISA	Nguyen et al., [187]
	29 <sup>d</sup>	TeGMG-4r ELISA	
	19.9 <sup>e</sup>	ICT	
Thailand	12.2	Indirect ELISA	Kocher et al., [188]
Zambia	6.1	Microscopy	Laohasinnarong et al. [189]
	7.5 <sup>b</sup>	PCR	
	18.6 <sup>a</sup>	PRF-LAMP	
Zambia	19.8 <sup>3</sup>	PCR	Musinguzi et al. [190]

<sup>1</sup>Camel.

<sup>2</sup>Horses.

<sup>3</sup>*T. vivax*.

<sup>a</sup>PRF-LAMP, loop-mediated isothermal amplification.

<sup>b</sup>PCR, polymerase chain reaction.

<sup>c</sup>ELISA, enzyme-linked immunosorbent assay.

<sup>d</sup>TeGMG-4r ELISA.

<sup>e</sup>ICT, immunochromatograph test.

BPE, blood parasite examination; CAT, card agglutination test.

**Table 4.** Prevalence studies of ruminant trypanosomiasis worldwide.

country. A study in Vietnam in 1971–1981 concluded that 10% of buffalo deaths in Vietnam following massive importation of buffalo from Thailand and Cambodia; serological studies confirmed 10–40% are positive. Similarly, 15–54% of cattle and buffaloes are seropositive in Thailand [181]. In the Philippines, two patterns demonstrated are acute disease and chronic wasting disease. Similar Vietnam study, 10% of buffalo deaths within months in the Philippines are attributed to trypanosomiasis [70]. In addition, an alarming rate of 47% of abortion is attributed to trypanosomiasis [170, 182] (**Table 4**).

Anemia is one of the most consistent clinical sign of trypanosomiasis. In water buffaloes, trypanosomiasis infection causes a significant drop in hemoglobin concentration, packed cell volume and red blood cell count, creatinine and urea and liver alkaline phosphatase, in contradiction, total leucocyte count increases together with lactate dehydrogenase enzymes (LDH) activity, globulin, total bilirubin and indirect bilirubin, highlighting a link between immune and metabolic disorders [169, 191, 192].

The most common therapeutic drug used against surra is diminazene aceturate, though isometamidium chloride, cymelarsan, suramin and quinapyramine can also be used [193]. A dose of 7 mg/kg bw intramuscularly of diminazene aceturate (DA) is used to treat animals infected with *T. evansi*. In cases of high parasitemia, 3.5 mg/kg bw dose of DA is used to reduce the parasitemia and a second injection of the 7 mg/kg bw is used to ensure that all parasites are killed. If the treatment failed, isometamidium chloride and cymelarsan can be used separately at 0.5 mg/kg bw by deep intramuscular injection in cattle and water buffaloes [170, 194].

In the past, *T. evansi* could only be eradicated from areas where it can be detected and controlled at a very early stage. During quarantine, infected animals should be euthanized and later dispose the carcass carefully. On the other hand, if the infection is enzootic, eradication is impossible due to existence of wide variety of domestic and wild host, transmission by non-specific vectors and due to subclinical carriers. Under these conditions, reduction of infected areas is highly improbable, however, its spread can be easily predicted. Thus, *T. evansi* has an unobvious spreading pattern [169].

### 2.3.2. Neosporosis

*Neospora caninum* is an intracellular, obligate protozoan parasite of phylum Apicomplexa. It causes abortion in cattle and water buffaloes worldwide impacting dairy and beef industries [195]. Aside from cattle, literatures cite that water buffaloes of Asia are also infected by the parasite [216]. In the same environment and potential exposure, water buffalo shows a higher seroprevalence than cattle (48.3 versus 28.3%) [195, 196].

In a recent worldwide review, seroprevalence of dairy and beef cattle is at 16.1 and 11.5%, respectively, and in water buffalo is at least higher than cattle [195]. Vertical transmission is the most persistent way the parasite stays in the herd [89]. Viable *N. caninum* can be isolated from tissues of naturally infected water buffaloes and this indicates that it is an intermediate host for the parasite [197]. In Brazil, four out of seven dogs that have ingested infected buffalo brain have shed oocysts and gamma-interferon knockout mice have develop clinical neosporosis after oral inoculation of oocysts [198].



The initial claim on seroprevalence of *N. caninum* in buffalo is reported in 1995 from blood collected at a slaughterhouse in Vietnam [199]. Since then, various countries have reported prevalence of *N. caninum*. Despite the clear association of *N. caninum* and abortion in cattle [32, 33], it is less commonly seen in water buffalo [195, 200]. In addition, experimental infection that would normally cause abortion in cattle is not observed in water buffalo. However, studies of Chryssafidis et al. [201] and Konrad et al. [200] demonstrated that experimental infection of pregnant water buffalo in early gestation with *N. caninum* will result in abortion and lesions in placentomes and fetuses. In addition, experimental infections results in seroconversion (measured via IFAT) at 7–11 days post-infection, peaking at 3 months and persisting up to a year [185, 197]. However, a 20% increase in seroprevalence is reported in aborting than non-aborting cases in water buffaloes. Despite several researchers reporting the high seroprevalence in buffalo herd, a gap still exists in *N. caninum* abortion cases (Table 5) [202]. *N. caninum* stimulates an immune response from T helper (Th) 1 immune response that limits its multiplication [120], however, this same scenario leads to placental damage and, ultimately in abortion [203, 204].

Locality	Positive (%)	Technique	Authors
Egypt	68.0	DAT	Dubey et al. [32]
Vietnam	1.5	IFAT and ELISA	Huong et al. [205]
Brazil	36.5	IFAT	Gondim et al. [206]
Italy	34.6	IFAT	Guarino et al. [207]
Brazil	56	IFAT	Souza et al. [208]
Brazil	63.9	IFAT	Fujii et al. [209]
Brazil	70.9	IFAT	Gennari et al. [210]
Brazil	14.6	ELISA	Vogel et al. [211]
China	0	ELISA	Yu et al. [212]
Argentina	64.0	IFAT	Campero et al. [213]
Iran	37.0	ELISA	Hajikolaei et al. [214]
Philippines	3.8	ELISA	Konnai et al. [215]
Philippines	27.3	ELISA	Abes and Divina [216]
Brazil	40.9	IFAT	Silva et al. [217]
Pakistan	54.7	ELISA	Nasir et al. [218]
Argentina	42.2	IFAT	Konrad et al. [200]
Italy	51.0	ELISA	Auriemma et al. [219]
Brazil	55.6 <sup>a</sup> and 48.9 <sup>b</sup>	IFAT and ELISA	Silva et al. [79]
Argentina	43.3	IFAT	Moore et al. [196]
Morocco	8.52	ELISA	Lucchese et al. [20]
Lao PDR	68.9 <sup>a</sup> and 7.8 <sup>b</sup>	ELISA	Olmo et al. [25]

<sup>a</sup>DAT, direct agglutination test; IFAT, indirect fluorescent antibody test.

<sup>b</sup>ELISA, enzyme-linked immunosorbent assay.

**Table 5.** *N. caninum* serological studies conducted on water buffalo worldwide.



In a Pakistani study, seroprevalence of *N. caninum* is high (54.7%) and corroborated that aborted cases have a higher seroprevalence than non-aborted cases (78.9 versus 55%) [125]. In Italy, *N. caninum* DNA has been detected in aborted fetuses [219]. Underreporting might be the reason for a lower seroprevalence in water buffaloes than cattle, because water buffaloes are typically used in less economically stable areas [197]. In general, water buffalo reproductive system is less efficient than cattle and reproductive losses are sometimes unnoticeable. In addition, reproductive physiology of water buffaloes is different from cattle because they are seasonal breeders [49, 197].

Serology, molecular assays and histological analysis are some diagnostic examinations done for neosporosis [32]. Lesions caused by *N. caninum* in water buffaloes are uncommon, due to few studies showing direct association between the parasite and abortions [197, 218, 219]. The lesions seen naturally aborted buffalo caused by *N. caninum* consists of non-suppurative inflammation in placenta, brain, heart and other organs [33]. In a study in Italy, a herd with 34.6% *N. caninum* seropositive, four aborted fetuses' organs were examined histopathologically. Non-suppurative encephalitis and myocarditis were observed in two fetuses and the other two were observed to have protozoan-like cysts, however, identity was not confirmed [207]. In another study in Italy, lesions of aborted fetuses were confined to the brain and heart [219]. Polymerase chain reaction (PCR) testing detected *N. caninum* DNA in all fetuses. The samples were also tested for other abortifacients and samples were only positive for *N. caninum* DNA [219].

Several serological assays (NAT and IFAT) have been used to measure seroprevalence and describe the epidemiology of *N. caninum* in water buffalo [197]. Overall, researchers have used developed and validated assays for cattle to water buffaloes. However, majority of research studies conducted on water buffaloes used a high cut-off value of 1:100 or above that mostly missed animal with lower titers. Limited support has been carried out, except from recent studies. First, subunit ELISA is compared to standard indirect cattle-specific IDEXX ELISA resulting in high values in kappa statistics, signifying respectable agreement. Another study compared the pan-ruminant indirect ELISA by IDEXX to IFAT, cutting-off threshold substantially downward and arriving at a high diagnostic test performance [220].

Calves positive for the disease can be treated with toltrazuril to prevent vertical transmission in small scale farming, however, this method is not recommended in large scale farming [221]. There is an available vaccine against *N. caninum* (Neoguard<sup>®</sup>—irradiated tachyzoites), however, efficacy is at mostly 50%. In addition, there is an available attenuated live vaccine (NC-Nowra<sup>®</sup>) that demonstrate higher efficacy, but at a higher cost and limited stocks and shelf life [55, 221].

As stated earlier, the parasite is transmitted vertically in the herd. Consequently, it is best to prevent and control transmission of the parasite. In addition, Dubey et al. [31] reported that another way of controlling neosporosis is through proper biosecurity measures: (1) quarantine of new animals, (2) preventing the entry of wild carnivores and rodent control in the farm, (3) feed, water and semen safety test and (4) reduce stress to the suspected animals [221].

### 2.3.3. Cryptosporidiosis

*Cryptosporidium* spp., a parasite under phylum Apicomplexa, has a wide range of hosts including humans and domesticated and wild animals [222]. It causes diarrhea in humans and

animals, however is self-limiting to immunocompetent hosts. In addition, young and immunocompetent host may die of life-threatening diarrhea [223, 224]. Livestock are susceptible to *Cryptosporidium* spp., causing significant production losses of diminished weight gain, stunted growth, neonatal deaths, decreased milk production [84, 137] and additional cost in veterinary drugs [137].

Cryptosporidiosis in cattle is commonly caused by four major *Cryptosporidium* spp. namely: *C. parvum*, *C. bovis*, *C. ryanae* and *C. andersoni* [225]. The major contributor to cryptosporidiosis zoonosis transmission is *C. parvum*, and dairy calves are its most common reservoir host [35, 226]. Dairy calves play as the source of infection and contaminate to the environment due to high prevalence and great oocysts shedding (millions to billions oocysts per animal) [227]. *Cryptosporidium* oocysts can persist in the feces and environment from few weeks to months [228].

The members of the genus *Cryptosporidium* have indistinguishable morphologic characteristics [226]. With this, molecular assays are used to differentiate *Cryptosporidium* spp. of animals in species and subtype levels. These studies further improve the understanding of public health importance and interspecies transmission of *Cryptosporidium* spp. The variances of infection rate in animals are attributed to variances in age, breed, season, environmental conditions and husbandry practices [229]. As the animals became older, infection rate decreases up to 0.48%. These results corroborated to reports of Abou-Eisha [230] and Amer et al. [231] for adult water buffaloes of Egypt and Rodriguez Diego et al. [185] in buffalo of Cuba, stating that no oocyst may be found in adult buffalo due to resistance of buffalo as specie as they grow older or immunity due to previous infections. On contrary, it might also be attributed to sensitivity of microscopic tests [229]. **Table 6** shows studies related to prevalence of *Cryptosporidium* in water buffaloes.

*Cryptosporidium* and *Giardia* commonly cause protozoal enteritis of human and animals [245–248]. Oocysts or cysts of both genera spread through feco-oral route via direct contact of infected feces to food and water [249–251]. Clinical manifestation may vary from self-limiting [252, 253] to life-threatening diarrhea [254–256] depending on the immunity of the affected individual [238]. Humans are infected with a variety of species and genotypes of *Cryptosporidium* [257] and *Giardia* [258]. However, previous molecular-based studies suggest that *C. hominis*, *C. parvum* and *G. duodenalis* assemblages A and B are most common cause for human disease cases [87, 238, 259, 260]. *C. hominis* is transmitted only through human to human [261], while, *C. parvum* and *G. duodenalis* are transmitted through human to human or animal to human [238, 260, 261].

Studies have shown that livestock is a main source of giardiasis and cryptosporidiosis in humans from claims of different molecular-based studies [199, 238, 262]. Many studies proved that cattle are carriers of various zoonotic species of *Giardia* and *Cryptosporidium* [263–265]. Santin et al. [264] reported that *C. parvum* is predominantly found in sucklings, *C. bovis* and *C. ryanae* in weaned cattle and *C. andersoni* in adults. In contrast, little is known about the variety of species and genotypes found in water buffaloes (*Bubalus bubalis*) [238]. In developing countries, water buffalo plays a role in agricultural economics from draft power and transportation to meat and milk production, and into some extent hide and leather industries [245]. Large ruminants, cattle and buffalo, excrete bulk fecal waste daily, thus, environmental contamination and potential outbreak of Cryptosporidiosis is imminent [199, 238, 266].

Locality	Prevalence (%)	Technique	Authors
Italy	14.7	ELISA	Saralli et al. [232]
Spain	—	PCR-RFLP	Gomez-Couso et al. [233]
Italy	34.9	ELISA	Rinaldi et al. [234]
Egypt	14.19	Fecal Examination	El-Khodery and Osman [33]
Egypt	22.5	Sheathers sugar Flootation and Modified ZN	Shoukry et al. [235]
Pakistan	24.0	ZN	Nasir et al. [236]
Philippines	5–50	Kinyoun Acid Fast Test	Villanueva et al. [22]
India	38.3	Fecal Examination	Bhat et al. [237]
Nepal	—	PCR-RFLP	Feng et al. [227]
Australia	12.2	PCR	Abeywardena et al. [238]
South Africa	2.8	PCR-RFLP	Abu Sarma et al. [239]
Egypt	32.2	PCR	Helmy et al. [240]
Italy	14.2	ELISA	Galiero et al. [241]
Egypt	1.29	ZN	Mahfouz et al. [229]
China	43.0	PCR	Ma et al. [242]
Brazil	48.2	nPCR	Aquino et al. [243]
Australia	30 <sup>1</sup> and 12 <sup>2</sup>	qPCR	Zahedi et al. [244]

<sup>1</sup>Domesticated/farmed buffalo.

<sup>2</sup>Wild buffalo.

PCR, polymerase chain reaction (qPCR, real-time PCR; nPCR, nested PCR; PCR-RFLP, PCR restriction fragment length polymorphism); ELISA, enzyme-linked immunosorbent assay; ZN, Ziehl-Neelsen acid fast.

**Table 6.** Prevalence of cryptosporidiosis in different countries.

*Cryptosporidium* spp. invades the epithelial lining cells of the jejunum and to some extent, in immuno-compromised individuals, the ileum [267]. Parasite invasion destroys the epithelial lining of the small intestine leading to villous atrophy, preventing nutrient absorption and causing diarrhea [225, 238, 245].

Still, cryptosporidiosis is self-limiting, but treatment can help manage the disease especially for the immuno-compromised animals. In ruminants, halofuginone, synthetic drug from quinazolinone, has therapeutic effect against cryptosporidiosis [268]. A study on the efficacy of halofuginone against cryptosporidiosis has promising results due to its capacity to reduce oocysts excretion and diarrhea, and delay the onset of infection in calves infected with *C. parvum* [269].

Though there are plenty of treatment regimen, prevention is still the best option in protecting animals and humans against *Cryptosporidium* spp. Identifying critical control points in husbandry and health management is the key requirement in preventing and controlling these parasites [238].

## 2.4. Fungal

### 2.4.1. Deg Nala disease

Deg Nala is a disease of water buffalo characterized by lameness, edema of the extremities, gangrenous ulceration or necrosis of mouth, ears, hooves and tail (sloughing of epidermis) (**Figure 2**), general wasting, recumbency and eventual death [270]. The condition is usually afebrile and limits the movements of the affected animals due to painful condition of the legs [271]. It affects the milk yield of dairy animals due to involvement of udder and inguinal canal. This leads to significant loss of milk yield which has not been quantified so far [271].

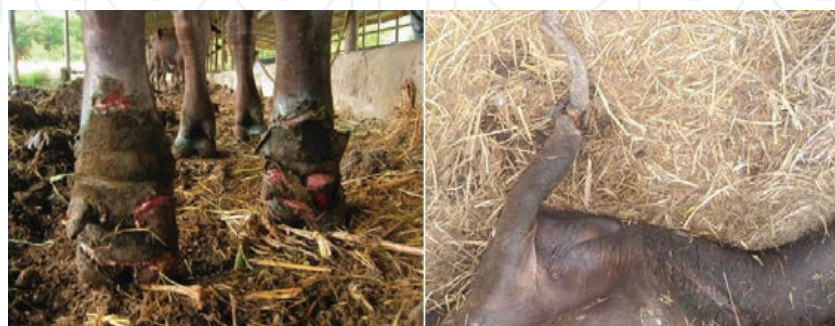
The disease is named due to its first occurrence around Muridke (District Sheipura), an area bordering the course of Nala Deg (a monsoon rain water stream) in the Indo-Pakistan region, which was first reported in the 1930s [271].

Deg Nala causes serious concern to the farmers and shows a severe impact on rural economy. It is often overlooked and misdiagnosed as foot and mouth disease and/or mange infection [272].

The disease is considered to be caused by mycotoxin produced mainly by *Fusarium* spp. Different species of fungi such as *Aspergillus* spp. and *Penicillium* spp. are also reported cause this disease [273]. Meanwhile, Indian researchers reported the Deg Nala is due to excess ingestion of toxic amount of selenium (Se) in rice straw grown on selenium-rich soil [272–274].

Several *Fusarium* spp. were isolated, including *F. oxysporum*, *F. equiseti* and *F. moniliforme* in experimental infection. However, only *F. oxysporum* showed clinical signs of Deg Nala disease 20–23 days post-infection in one study. However, it should be noted that the number of affected animals may be due to either variation in the susceptibility of the water buffaloes or variability of pathogenesis of strains of *Fusarium* spp. [274].

The mycotoxin produced by the metabolism of *Fusarium* fungus grown on paddy/rice straw dissolves the collagen and elastin into collagenase and elastinase, respectively [275]. As a result, the dependent parts of the ear, tail and foot blood supply is obstructed due to action of mycotoxins performing cutaneous vasoconstriction, and ultimately tissue die of anoxia [276].



**Figure 2.** Typical signs of water buffaloes with Deg Nala disease, including gangrenous ulceration or necrosis of the hoof (left) and tail (right) (photo from Philippine Carabao Center).



The animals fed with *Fusarium* spp. mycotoxin-infected rice straw experienced loss in body weight due to anorexia and increased tissue catabolism. The progressive posterior weakness may be due to degenerative changes of adjoining musculature. In Deg Nala endemic regions, the disease develop upon release of fungi toxin compounds fostered under promotive environmental settings such as temperature, humidity and water content of rice straw. The unique characteristic of Deg Nala is its confinement to a particular endemic region which may be explained by the need of optimal temperature for fungal growth. Improper storage practices of rice straw as feedstock for water buffaloes is of utmost importance followed by the rural farmers which make it more likely to spoil with fungal contamination [272].

In the case of chronic selenium toxicosis, the disease is more prevalent in peak winter season along with feeding of lush green fodder with high moisture content and mostly those in the rice growing parts of some countries such as India [271–274]. Feeding of green fodders and cereal straws containing 1.1–24 times the upper toxic limits of 5 ppm cause Se toxicity in animals [277]. For indicators of SE condition of an animal, blood SE plus erythrocyte glutathione peroxidase activity are valuable. Blood SE levels can be classified as impending toxicity, toxic and highly fatal for 1.5–1.75 ppm, above 2 ppm and exceeding 3.4 ppm, respectively [278].

Buffalo are more frequently affected than cattle and younger animals appeared to be more susceptible. Arora et al. [279] reported chronic selenium toxicity, as a result of Deg Nala disease in buffaloes. Arora et al. [279] reported that 80% of Deg Nala was cured by feeding pentasulfate mixture [273].

The administration of oxytetracycline is effective at early stage of Deg Nala disease in buffaloes [280]. Also, cases of Deg Nala disease have been successfully treated using proprietary pentasulfate mixture based on sulfur and Se antagonism [279]. Antagonism between arsenic (As) and Se, whereby each reduces the toxicity of the other, has been reported in animal models [281, 282]. Proper management of the wound is recommended for complete recovery of the animal.

It is advisable to stop feeding mold-smelling straw to the animal and to prevent contamination of lesion of animal to dust and dirt. Inadequate postharvest drying of rice plants before stacking and stacking at low-lying places or near water channels were the factors identified with occurrence of the disease [283].

## 2.5. Endoparasites

### 2.5.1. Fasciolosis

Fasciolosis is an endoparasitic disease caused by a trematode known as *Fasciola* species (*F. gigantica* and *F. hepatica*). This disease occurs in almost every tropical and subtropical countries with *F. gigantica* as most common in Africa and Indian subcontinent, Hawaii and the Philippines (Table 7). Fasciolosis epidemic in tropical regions of Southern and South East Asia and Africa is caused by *F. gigantica*. *F. gigantica* and *F. hepatica* share a geographical distribution in most African and Asian counties and occasionally in the same country, however, the environmental requirements of the snail intermediate hosts and the harbored flukes are distinguishable [284].

One of the leading causes of morbidity and mortality in ruminants worldwide is Fasciolosis. Small ruminants are less exposed to fasciolosis than buffaloes and cattle which provide major draft power in rice field farming activities. Both buffaloes and cattle have a wallowing nature that predisposes them to infection (**Figure 3**). Higher prevalence of fasciolosis was observed in animals more than 3 months old compared to other age groups simply because they are more often to eat or graze on farm grasses resulting to greater exposure to infection.

Infection with *Fasciola* spp. occurs when metacercariae are accidentally ingested on raw freshwater vegetation. The metacercariae migrates through the intestinal wall and peritoneal cavity to the liver where adults mature in the biliary ducts. Eggs pass through the bile ducts into the intestine where it then passes into the feces [284]. In humans, maturation from metacercariae into adult flukes takes approximately 3–4 months [285] (**Figure 3**).

Fasciolosis ranges in severity from a fatal disease in sheep to an asymptomatic infection in cattle [286, 287]. The course of infection is usually determined by the number of ingested metacercariae. Fasciolosis can be classified into two such as (a) subacute and (b) chronic fasciolosis. Subacute fasciolosis cases have survival of 7–10 weeks with tremendous liver damage, however, the animal dies from hemorrhage and anemia, while chronic fasciolosis clinical manifestations includes anemia, wasting, submandibular edema, and decreased milk production, yet heavily infected cattle displays no clinical signs [286] (**Table 7**).

Most of *F. gigantica* and *F. hepatica* early studies assumed that infection and diseases caused by both fluke are similar. However, new studies on difference of *F. hepatica* and *F. gigantica* based on fluke biomass and average size, extent of liver damage, plasma glutamate dehydrogenase (GLDH) levels and gamma-glutamyl transpeptidases (GGT) response for the first 10 weeks of infection recognized *F. hepatica* develops more quickly than *F. gigantica* that results in an increase GLDH levels in plasma pointing out a greater damage to liver parenchyma [167] and an increased in the GGT levels at 10 weeks post-infection, indicating epithelial damage in the bile duct [77, 294].

The diagnosis of fasciolosis is imperative for planning treatment and the eradication program in an endemic area. Different diagnostic techniques are developed since then. Coproscopic detection through sedimentation technique is useful; however, there is concern in terms of sensitivity. Hence, immunodiagnostic techniques are recommended like enzyme-linked



**Figure 3.** Presence of adult *F. gigantica* upon incision of the liver (left); a gall bladder of severely infected water buffalo filled with adult liver flukes (right) (photo from Philippine Carabao Center).



Locality	Prevalence (%)	Technique	Authors
Nigeria	9.1 <sup>1</sup> , 12 <sup>3</sup> , 54.3 <sup>2</sup>	Sedimentation technique	Adediran et al. [288]
Pakistan	5.68	PCR	Ayaz et al. [289]
Philippines <sup>1</sup>	95.33 <sup>a</sup> and 96.00 <sup>b</sup>	Quantitative PCR and FEA-SD	Gordon et al. [290]
Botswana	0.09	Post mortem examination	Mochankana and Robertson [291]
Vietnam	23.4	Microscopy examination	Nguyen et al. [292]
Egypt	30.88	Post mortem examination	Elshraway and Mahmoud [293]

<sup>1</sup>Buffalo.

<sup>2</sup>Cattle.

<sup>3</sup>Sheep.

<sup>4</sup>Goat.

<sup>a</sup>PCR, polymerase chain reaction.

<sup>b</sup>FEA-SD, formalin-ethyl acetate sedimentation.

**Table 7.** Prevalence studies of Fasciolosis in different countries.

immunosorbent assay (ELISA). A recently developed technology is FgCL-3 ELISA which showed 100 and 97% sensitivity under experimental and field situations [269]. Another platform is through molecular technique which is more specific than coproscopic and immunodiagnostic techniques. In Samar, Philippines, Gordon et al. [295] used quantitative real-time polymerase chain reaction in the detection of *F. gigantica* and it showed high prevalence of the disease.

Infected ruminants are usually treated with anthelmintic drugs like albendazole, triclabendazole and bromofenofos. But latest study showed that with the frequent usage of these common anthelmintic drugs, anthelmintic resistance may have developed in water buffaloes [296]. Other endeavor is the use of medicinal plant-like betel nut as dewormer in water buffaloes.

Fasciolosis control is a difficult and habitual task comprising of good and proper husbandry practices, good hygiene management (for animal excrements, waste waters, etc.) and effective integrated treatment and control for infected host and intermediate host, respectively. The use of predators (ducks and frogs) and molluscicides for control and possible elimination of the snail intermediate host is impossible as it is labor extensive, costly and may disturb the ecological balance in the area [297]. Vaccine development was vigorously pursued, however, despite persistent efforts, a vaccine with adequate protection against fasciolosis has not yet been developed to the point of commercialization [297].

### 2.5.2. Schistosomiasis

Schistosomiasis or bilharzia is one of the most prevalent parasitic diseases worldwide that currently infects over 200 million people in more than 76 countries, resulting in approximately

25 million disability-adjusted life years lost [298, 299]. The disease is caused by blood fluke species of the genus *Schistosoma*, namely *S. mansoni*, *S. mekongi*, *S. haematobium*, *S. intercalatum* and *S. japonicum*. Of particular importance is *S. japonicum* which is a zoonosis with a wide spectrum of definitive hosts (aside from humans), making control measures more complicated [298, 299].

Schistosomiasis japonica (term used for the disease caused by *S. japonicum*) is recognized as an important zoonotic disease in China, the Philippines and isolated pockets of Indonesia. Aside from established infection in human, *S. japonicum* can infect a variety of wild and domestic animals which have varying effects in transmission of infection to human. It is generally accepted that bovines, particularly water buffalo is considered the major reservoir of this human infection in China and the Philippines (**Table 8**) since they are naturally infected with schistosomes due to their wallowing behavior in marshes and deposit more eggs into the environment through their feces [295, 298, 299].

Although human infection caused by *Schistosoma* spp. can be reduced by treatment of praziquantel, control of schistosomiasis japonica still remains to be difficult, because of continuous transmission from shedder animals [245]. Variable factors like the amount and quantity of host species, nonuniformity in irrigation management and practices and the possibility of genetic restrictions of infectivity to humans influenced and may cause complexity to the absolute importance of specific host species to human transmission by *S. japonicum* [299] (**Table 8**).

Animal schistosomiasis is traditionally diagnosed using direct coprological parasitologic techniques, for example, Kato-Katz technique and miracidia hatching. These simple and economical diagnostic techniques are very helpful in areas and cases with medium to very high infection intensity but has a drawback for low-level infections. Lately, polymerase chain reaction (PCR) platforms (e.g. convention and qualitative PCR) had been developed to amplify and detect the parasite DNA for the three zoonotic species of schistosoma [299].

Effective control measures of schistosomiasis japonica can be learned from China. Over the last 5 decades, China has remarkable schistosomiasis program achievements that drastically reduce the disease prevalence and morbidity, and the Chinese government is aiming to eradicate the disease in the country by 2020. The successful Chinese control action plan targets the importance on involvement on bovine considering efficacy of praziquantel, biosecurity measures on common grazing areas, mechanization as farm equipments and development of effective vaccine [301].

Schistosomiasis japonica has been eliminated in Japan and the coastal plains of China by a combination of medical treatment, health education, improved water quality and sanitation and snail control through environmental modification, molluscicide and new farming methods. In addition, several measures can be initiated such as mapping of the transmission patterns in humans and animals which can lead to a better understanding of transmission of schistosomiasis between different host species [302].

Locality	Prevalence (%)	Technique	Authors
Philippines	3.7 <sup>c</sup> , 3.7 <sup>d</sup> , 0 <sup>e</sup> and 51.5 <sup>a</sup>	Danish Bilharziasis Laboratory Technique, Kato-Katz technique, Miracidia hatching and RT-PCR	Wu et al. [300]
Philippines	51	RT-PCR	Gordon et al. [295]
Philippines	87.50 <sup>2,a</sup> and 77.08 <sup>2,b</sup> 80.00 <sup>1,a</sup> and 55.24 <sup>1,b</sup>	RT-PCR and FEA-SD	Gordon et al. [295]

<sup>1</sup>Buffalo.  
<sup>2</sup>Cattle.  
<sup>a</sup>PCR, polymerase chain reaction.  
<sup>b</sup>FEA-SD, formalin-ethyl acetate sedimentation.  
<sup>c</sup>Danish Bilharziasis laboratory technique.  
<sup>d</sup>Kato-Katz technique.  
<sup>e</sup>Miracidia hatching.

**Table 8.** Prevalence studies of *Schistosoma* in the Philippines.

### 3. Economic and public health impact

From the diseases affecting water buffalo that were discussed, those that are zoonotic include leptospirosis, bovine tuberculosis, brucellosis, trypanosomiasis, cryptosporidiosis, fasciolosis and schistosomiasis. Also, the economic impact of these diseases in the water buffalo industry is alarming, particularly whose effects are unquantifiable since it is a neglected disease and highly prevalent in developing countries.

Bovine leptospirosis is an example of a zoonotic disease wherein the real economic hazard is quite difficult to be determined. In Argentina, for example, the reported losses from an outbreak is approximately US\$ 150,000 in regards of 100 calf deaths due to abortion, vaccination and treatment of the 1300 survivors along 1 year [65]. In France, the annual cost of leptospirosis in dairy cattle herds was estimated from US\$ 97 to 2611/aborted cow [303].

Another disease with limited information on its impact among livestock in endemic regions/countries, particularly on its host population dynamics and demographics, economic losses and social impact on animal owners is Surra (*T. evansi* infection).

In the case of brucellosis, official estimates report annual losses of about \$600 million in Latin America due to bovine brucellosis [124]. The national program for the eradication of brucellosis in the US costs \$3.5 billion between 1934 and 1997. The losses due to reduced milk production and increased occurrence of miscarriages in 1952 were \$400 million [92]. Meanwhile, brucellosis as a zoonosis accounts for an annual occurrence of more than 500,000 cases [178, 238], which is considered the most common zoonosis worldwide. On the other hand, a national survey in India in bovines found a brucellosis prevalence of 5% in cattle and 3% in water buffaloes. The occurrence of the disease is usually high in organized farms (50%) compared to the marginal herds (10%) and this primarily associated with intensive farming practices in large organized animal farms [40].

The economic loss in Argentina due to BTb is at US\$ 63 million [304]. In the United States, cost/benefit analysis of eradication showed an actual cost of US\$ 538 million between 1917 and 1992 (current programs cost approximately US\$ 3.5–4.0 million per year [94, 305]. Although cattle are the main reservoir of the bacterium, buffaloes are also infected by *M. bovis*, developing same clinical characteristics [34, 306, 307]. Buffalo embodies a significant economic activity in many countries such as Brazil where its herd of water buffalo (approximately 3 million animals) is the largest one of the Americas. They are mostly raised in rural areas and are great in adapting to various environmental conditions [87]. They also represent a potential zoonotic threat because they can be a source of infection to other animal species and to human beings [34, 130, 307].

BVDV infection presents an economic concern since it affects both health and productivity of the herd. During outbreaks of acute BVD, losses were estimated to be \$50–\$100 per cow in the herd. In Canada, where in severe acute BVD was reported around 1998, the estimated losses was \$40,000–\$100,000 per herd, or \$400 per cow in the each herd [164].

*Fasciola* spp. infection can also infect human and is classified as a neglected tropical disease. It was recorded that global losses incidental to fasciolosis were estimated over US \$3200 million per year [4]. Species-wise prevalence of fasciolosis varies in different regions, globally. In India, goats were more infected than buffaloes [308]. Also, overall caprine fasciolosis was observed to be 20.75% in Bangladesh [309]. Recently, in Corrientes, Argentina, appearance of fasciolosis was observed in different buffalo populations showing 28.5% prevalence rate [310]. In the provinces of Punjab (30.5%) and Sidh (42.06%), Pakistan, there was a remarkably high prevalence of fasciolosis in buffalo [286, 311]. Likewise, in Nepal, there was above 50% prevalence rate in large ruminants. Meanwhile, in South East Asia, China and Poland, had a prevalence rate of 27.7% [312], 34.8% and 32% [301]. A coproscopy examination in Iringa district, Tanzania, reported that overall prevalence of fasciolosis in traditional, large scale dairy and small scale dairy cattle was 63.8, 46.2 and 28.4%, respectively.

In the case of schistosomiasis, three recent interventional studies strongly support the contribution of water buffaloes to human transmission along the lake and marshlands region of China. In two studies, *S. japonicum* reinfection of humans were 48–49% lower than praziquantel medicated farm animals and individuals. A result from an operational research suggests that improvement in hygiene and removal of bovine from an infected area will likely decrease the human infection by 88% than the control areas. An analytical modeling of intra-species transmission dynamics from different ecological settings in China indicates that 39–99% of zoonosis of *Schistosomiasis japonicum* infection came from buffaloes [299].

#### 4. Conclusion

In conclusion, this review demonstrated the importance of water buffalo as a progressive livestock industry in several countries worldwide, harnessing its adaptability in tropical and subtropical climate without affecting its reproductive performance. Also, several infectious diseases affecting this animal were discussed that have an enormous negative economic impact in the industry as well as its threat to human health. Knowledge on these common diseases in water buffaloes and its management will be beneficial to veterinarians and farmers

in preventing the occurrence of those infectious diseases. In addition, limited studies and published articles on infectious diseases in water buffalo were available, since it is believed that diseases in cattle are similar to that of water buffalo. This should be changed because both species behave differently in such diseases. Aside from the conventional control and prevention methods against the discussed infectious diseases, development of a simpler and practical farm management practices are needed. Lastly, more studies should be conducted, especially in areas where water buffalo is the main livestock animal in order to utilize the full potential of the animal and uplift the water buffalo industry.

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