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Leptospirosis: Rising Nuisance for Cattle and Threat to Public Health

Amjad Islam Aqib, Muhammad Ijaz, Shahid Hussain Farooqi, Muhammad Shoaib, Muhammad Fakhar-e-Alam Kulyar and Khadija Yasmeen

Abstract

Leptospirosis is a communicable disease at farms that results in abortion and pathological changes in animals and human respectively. Disease is majorly spreading through indirect contact with contaminated urine material. The causative agent belongs to *Leptospira* genus having 21 species, 25 serogroups, and 250 serovars. The prevalence noted at world level is counted to be 41.39% with 30.11% in Asia, 25.62% in Africa, and 46.42% in South Africa. The virulence is attributed to Loa22 protein which is the first protein identified as essential virulence factor. Pathogenesis involves vasculitis following which are direct cytotoxicity and immunological injury resulting in renal failure. Direct examination, PCR, isothermal methods, microscopic agglutination test (MAT) and IgM enzyme-linked immunosorbent assay (ELISA) are diagnostic approaches for leptospirosis. The MAT is a gold standard test for leptospirosis identification. Doxycycline and azithromycin were used as drugs against leptospirosis in mild and severe cases of leptospirosis. Further studies are needed regarding identification, treatment, and effective vaccination.

Keywords: leptospirosis, *Leptospira*, disease outbreaks, leptospirosis vaccine, *Leptospira* tests, epidemiology, prevalence

1. Introduction

Leptospirosis is a worldwide but more neglected zoonotic disease that usually affects humans and animals around the world [1–3] with case records 350,000 annually [4]. Death occurs from 10 to 50% in severe infection cases [5]. Pathogenic *Leptospira* are bacteria that cause the disease through penetration into the mucous membrane or damaged skin of the host [6] and then transfer to the proximal tubule of the kidneys [7]. Infected animals remain asymptomatic and secrete infectious organisms in urine throughout their lifetime [8]. *Leptospira* are excreted in the urine for weeks, months, or longer [9]. It pollutes moist soil, farm land, and rivers. Infection occurs when a person or animal is in intimate contact with a contaminated climate or infected urine of host [6]. The famous *Leptospira* carriers are wild, domestic, and some other mammalian species [10]. Occurrence of leptospirosis in humans is also associated with high temperature, high humidity, and basic hygienic conditions [11, 12]. Human leptospirosis is biphasic, with the general symptoms of pyrogens associated with acute or leptospiremic phase, continuing for about 1 week, and subsequent of

recovery or immunization which is defined by antibody production [13]. In the past few decades, leptospirosis has become an infectious disease of urban environments especially in industrialized and developing countries. Rural areas are also affected with high mortality due to delay in diagnosis and lack of infrastructure with adequate clinical suspicion and other unknown causes like inherent pathogenicity of *Leptospira* strains [8]. Leptospirosis is very common in tropical and subtropical areas where people are very close to animals. Warm and humid environment favors in distribution and survival of pathogen [14]. Sporadic cases are reported throughout the year with incidence ranges from 0.1 to 10 per 100,000 people; and during the epidemic, it can reach over 50 per 10,000 people. Most cases are reported in Sri Lanka, India, Indonesia, Maldives, and Thailand. In the past, Sri Lanka (2008), Jakarta (2003), and Mumbai (2005) have been reported as epidemic areas of Southeast Asia [10]. The molecular classification of *Leptospira* in different species is described on DNA correlation base [3, 15]. The genome of *Leptospira* consists of two round chromosomes whose entire sequence has been established recently [8, 16]. The genome is larger than the genomes of other spirochetes, which shows the viability of *Leptospira* in different harsh environments [17]. Symptoms usually appear suddenly after an incubation period of 2–20 days, with a duration of 14 days at least. About 10% of patients diagnosed with leptospirosis having signs like Weil's disease, which manifests itself as jaundice, kidney failure, and hemorrhagic in pulmonary arteries [18]. Leptospirosis is usually related to headache, fever with muscular pain in both adults and children. Drowsiness, vomiting, abdominal pain, diarrhea, cough, photophobia, arthralgia, and constipation may also occur [19].

2. Etiology

Leptospirosis is a prominent communicable disease caused by spirochete bacteria. The bacterial species belong to genus *Leptospira* that have ability to cause a disease in a variety of wild and domestic animal bases [3]. Spirochetes bacteria are motile having hook form or question-mark shape and range in size from 6 to 20 μm in length and 0.1 μm in thickness [4]. Family Leptospiraceae includes genus *Leptospira*, which is further divided into two strains, that is, pathogenic and saprophytic [4, 15]. Pathogenic *Leptospira* have 21 species, 25 serogroups, and 250 serovars [3, 5]. *Leptospira* spp. are obligate aerobes having sluggish growth. Ideal growth temperature for *Leptospira* is 28–30°C [16]. There are different other characteristics of *Leptospira* like size, number of genes and pseudogenes, etc. (**Figure 1**). Serovars “pomona and grippotyphosa” are expectedly found to be the most prevalent candidates [17]. Leptospirosis in cattle is caused by *Leptospira borgpetersenii* and *Leptospira interrogans* serovar Hardjo, strains (well adapted to cattle) Hardjo bovis and Hardjo prajitno [18]. In Brazil as well as in Latin America, *L. borgpetersenii* serovar Hardjo strain Hardjo bovis were isolated from naturally infected cattle. Before this study, only serological studies had shown reactive animals with the serovar Hardjo in various countries [20, 21]. In Brazil, Chile, England, and Columbia, serovar Hardjo was found most prevalent among cattle [22]. Between 1988 and 2007 in France, serovar Serjoe (34%) was most common in cattle [23]. There are different reservoir hosts of *Leptospira* (**Table 1**).

2.1 Prevalence of leptospirosis

Worldwide, the prevalence of animal leptospirosis is reported between 2 and 46% depending upon animal species [12]. More than 15 serogroups of *Leptospira* is observed and isolated from cattle, for example, icterohaemorrhagiae, canicola, pomona and grippotyphosa, etc. (Rocha). Seroprevalence of different serovars

is different in all countries or regions. *L. bratislava* and *L. grippotyphosa* are more in Spain in those cattle which do not have good reproductive health [21]. Latin American countries, like Venezuela, have high prevalence of leptospirosis (80.51%) along with predominance of Sejroe serovar. Lesser incidence (2.6%) of disease has been observed in Peru during desiccated season when there are less chances for bacterial survival and transmission [24]. Similar results have been observed in Colombia and Mexico with the prevalence of 16.4–60.9% and 28.4–52%, respectively [25, 26]. Particularly, in countries like India, the bovine leptospirosis is highly

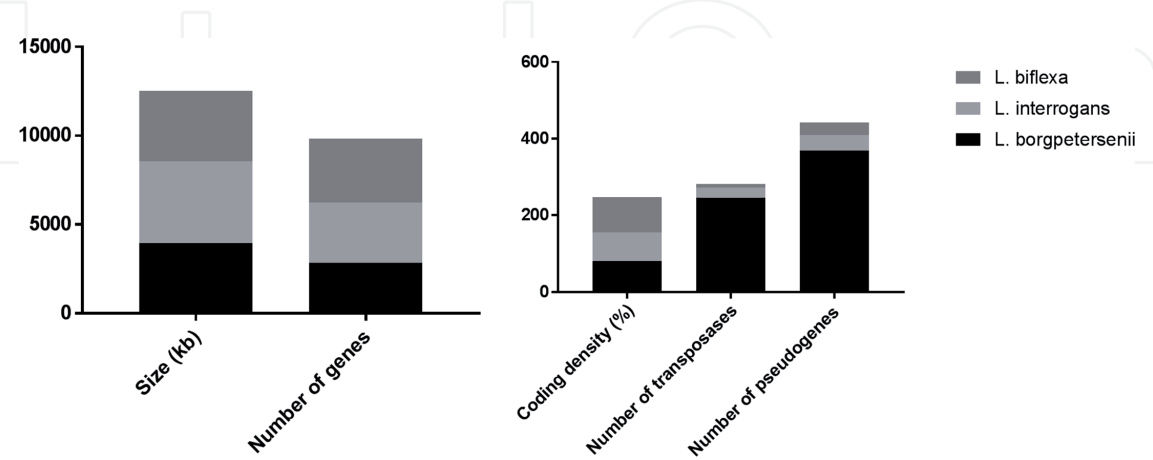


Figure 1.
Main characteristics of pathogenic and trophic genome *Leptospira* spp. [20].

Reservoir host	Serovar	Reference
Pigs	Pomona, Tarassovi	[8]
Cattle	Hardjo, Pomona	
Horse	Bratislava	
Dog	Canicola	
Sheep	Hardjo	
Rats	Icterohaemorrhagiae, Copenhageni	
Bats	Cynopteri, Wolffi	

Table 1.
Typical reservoir hosts of *Leptospira*.

Country	Year	Diagnostic methods	Specie	Prevalence%	Reference
India	1983	—	Cattle	68	[35]
	2011	MAT	—	87	[36]
Malaysia	1987	MAT	Cattle	40.5	[37]
			Buffalo	31	
Sri Lanka	2011	MAT	Cattle	20.31	[38]
	2014	Nested PCR	Cattle	12.2	[6]
Iran	2011	MAT	Cattle	19.10	[39]
Pakistan	2018	Indirect ELISA	Cattle	25.52	[40]
			Buffalo	20.72	
Bangladesh	2015	ELISA	Cattle	47.27	[41]

Table 2.
Prevalence of bovine leptospirosis in different countries of Asia.

prevalent, that is, up to 87% [27], 89.9% in Poland, and 88.2% in Mexico [28]. In contrary, certain states present lesser incidence, for example, 31.3% in Brazil [29], 27.4% in Australia [30], 30.3% in Tanzania [31], 20.3% in Sri Lanka [32], and 19.1% in Iran [33] (**Table 2**). These variations could be due to altered topographical localities, husbandry and farm management applications, infection immunity among diverse rears, and intensities of normal resistance [29]. In urban areas, leptospirosis is broadly prevalent, as stated by Platts-Mills [34].

3. Pathogenesis

Leptospirosis is termed as “storm of abortion” and is farm economy jeopardizing malaise [42]. *Leptospira* spread in direct and indirect ways, while the latter is a more pronounced method of transfer. Direct transmission involves through infected urine, post abortion uterine discharge, sexual contact, and infected placentae. Indirect involves contact with environment. Bacteria get entry to skin through abraded skin that follows hematogenous spread in the body. Bacteria result vasculitis that in turn results into either direct cytotoxic injury and immunological reactions or massive migration of fluid from intravascular to interstitial compartment. The latter results in renal dysfunction and vascular injury to internal organs. Pathogenic *Leptospira* could not be phagocytosed by macrophages and neutrophils, but if there are specific antibodies present, it can be phagocytosed [22]. It has been suggested that the animals are susceptible to severe or acute leptospirosis caused by increase in production of anti-inflammatory cytokines and chemokines [23]. Although pathogenic *Leptospira* are complementary to bactericidal activity, it has long been known that *Leptospira* has antimicrobial activity [43]. In most studies, leptospiral proteins that bind to one or more components are usually identified in recombinant form. Adhesin LenA (LfhA, Lsa 24) and Len B also bind to complementary regulatory protein factor H [44, 45]. Complement resistance to pathogenic *Leptospira* can also bind to the complement module C4BP, which catalyzes the cleavage of C4b [24]. It leads to decrease in surface deposition of subsequent components of the complement, where decaying species are not available. In subsequent studies, this activity was attributed to the new leptospiral proteins LcpA and Lsa30 [46]. Interestingly, ligand proteins that interact with many host ECM hosts and other proteins also interact with the complement regulators H, FHL-1, FHR1, and C4BP [25]. Surprisingly, the *Leptospira* elongation factor Tu shows a superficial effect and interaction with factor H, as well as binding to many purified host proteins, which leads to its diversity, the so-called “moonlighting protein” [25]. Most of the above studies provide indirect evidence of the role of *Leptospira* protein in the prevention of complement, but recently, it has been shown that the pathogenicity and non-urogenital fecundity of the three complement pathways, including factor B [26]. C2 and C4b are identified in the culture supernatant of the *Leptospira* cleavage component. In fact, inactivation of the above two proteins, Lig B and Len B, does not have a significant effect on pathogenicity [27, 28, 47]. Similarly, functional redundancy must also be considered: LenA and LenB. All proteins have structural and functional similarities to the endostatin of mammals [44].

3.1 Known virulence factors

The emergence of the mutagenesis system revealed a small number of *Leptospira* genes that encode the components necessary for the manifestation of pathogenicity. The first leptospiral protein, identified as virulence, is Loa 22, and the outer membrane protein containing the C-terminal OmpA domain

appears to mediate the connection between the outer membrane and the peptidoglycan layer (mutant hama loa 22). The presence of a homolog of Loa 22 in *L. biflexa* has an indirect effect on pathogenicity. Since lipopolysaccharide (LPS) is a pathogenic factor for all Gram-negative bacteria, it is not surprising that this hypothesis cannot be obtained until a certain mutant is identified in the *Leptospira*, studies eliminate motility by inactivating flagellated structures or genes involved in biosynthesis. Inactivation of fliY-encoding cholaretic switching protein reduces toxicity in guinea pigs [29]. Mutations in the gene encoding the sensory protein LB139 reduce motility and down-regulation of a number of chemotactic genes and weaken the mutant for hamsters [30]. The lack of similar genes in vegetative bacilli strongly suggests the survival of mammalian species as well as in nutrition intake. Indeed, studies have shown toxicity related activities of *Leptospira* sphingomyelinase such as pore formation and cytotoxicity [31]. However, the key role of leptospiral sphingomyelinase in the pathogenesis is not genetically established. Recently, it has been shown that *Leptospira*-LruA [48] plays an important role in autoimmune response, which is associated with mammalian apolipoprotein A1 [49].

4. Transmission

Transmission of *Leptospira* occurs often with direct contact with infected urine, placenta, or milk. Transmission through venereal or transplacental route is also possible, whereas the most common route is infected urine. If there are leptospiral infected animals present in a dairy farm, the environment is also contaminated. Dairy feeder calves are probably the largest carriers of *Leptospira* in commercial feed yards. Dairy calves have the habit of sucking the scrotum of other calves in the pen, so this would be direct contamination of infected urine from carriers by suckling habit. *Leptospira* survives in the moist, damp, and moderately warm environment and can be easily killed by freezing, dehydration, and direct sunlight (Figure 2).

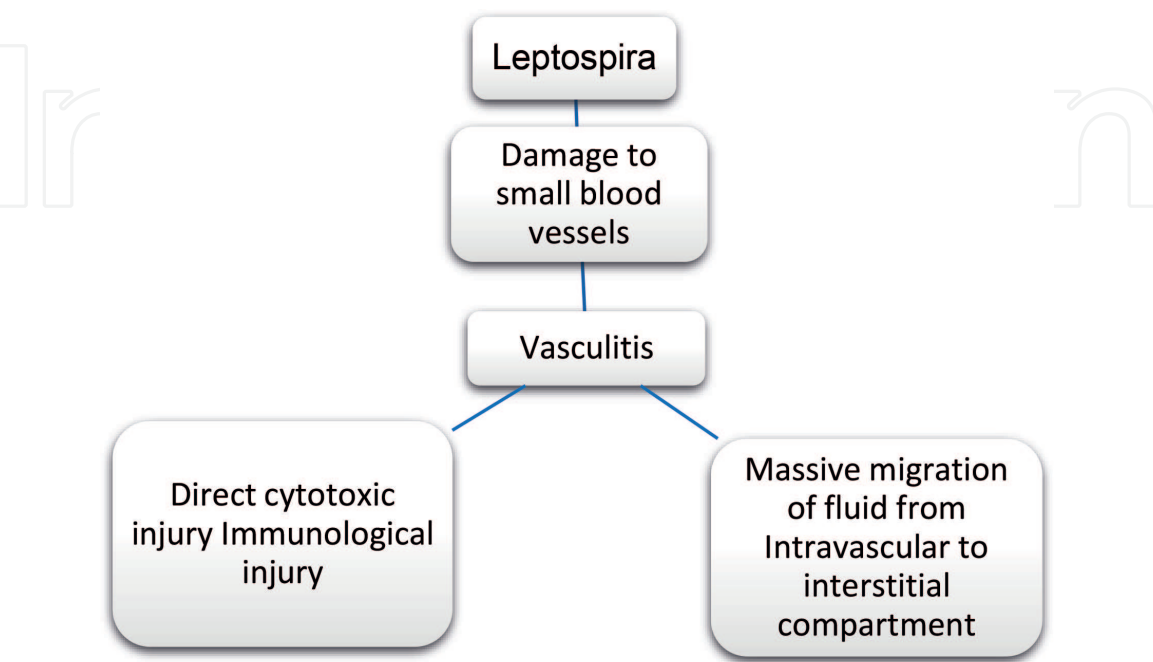


Figure 2.
Mechanism of *Leptospira*.

5. Diagnosis

Infection occurred by pathogenic leptospires is divided into two stages, first stage is acute stage or septicaemia (because septicaemia is in this stage), which lasts from 7 to 10 days with headache and myalgia. The second stage is immune stage which is after first week of infection and lasts 4–30 days [34]. During first stage, leptospires are present in blood and can say bacterial count is high in the blood, while when second stage starts, then the level of antibodies IgM and IgG start to increase and this increase in antibodies titer is correlated to elimination of leptospires from blood. *Leptospira* antigens and DNA sometimes may not be detected from the blood; this may be due to late sampling, or sampling in acute stage where proper level of leptospiremia is not developed and due to antibiotic administration, leptospires are eliminated from the blood. False negative results will be there, if we detect antibodies prior to sero-conversion during acute stage. Coagulated blood has serum and clot while non-coagulated blood has plasma, RBCs, WBCs and platelets. That can be collected according to the tests. If you are going to do gene amplification than EDTA, plasma gives the best results [50]. Leptospires can be detected in urine and cerebrospinal fluid samples. Many kits are available in the market for rapid detection of leptospires from blood, urine, and CSF sample; these kits basically detect nucleic acid of leptospires, but for these tests, purification of nucleic acid is required [51].

5.1 Current tools and emerging technologies for diagnosis of *Leptospira*

Different tools are being developed for the study of virulence factors, pathogenicity, and basic cell biology of organisms [52]. These are essential for proper treatment and reduction of the severity of the disease. During acute infection, nonspecific symptoms of leptospires mimic the febrile condition, which are essential for proper treatment and reduce the severity of the disease. Therefore, the diagnosis of leptospirosis is highly dependent on the particular laboratory tests [13]. Serology is the dominant one in diagnosis, while the micro-aggregation test (MAT) is the standard serological reference method. MAT is a sensitive test due to the antigenic heterogeneity of *Leptospira*, which require a large number of serovars as antigens. Furthermore, it is useless at early stage of the disease when antibodies are not present or present in less quantity [18]. Detection of disease in early stage helps the epidemiological investigators. However, antigen detection at this stage is more expensive and complex [13]. Current diagnostic tools for *Leptospira* detections other than MAT are rapid antibody-based tests, direct examination of blood, the rapid nucleic-acid diagnosis, [53], dark field microscopy (DFM), IgM ELISA, and polymerase chain reaction (PCR) [13].

5.1.1 Direct examination

This method is cheap, but for direct examination, dark field microscope is required [54]. Theoretically, leptospires may be diagnosed by direct examination of blood during first week after onset of symptoms. Leptospires are 6–20 μm long and their diameter is 0.15 μm . Because of their size, dark field microscopy is required; 10^{-2} – 10^{-6} leptospires/mL of blood may be observed during the acute stage of leptospirosis [55].

5.1.2 Gene amplification

5.1.2.1 PCR

The use of PCR is increasing in recent years and it has replaced the serological methods in endemic areas, because it is more sensitive and has capacity to give early

diagnosis. Real-time PCR is faster than regular PCR [56]. The threshold level in the urine or blood is 10–100 leptospire/mL (**Figures 3 and 4**) [50, 57].

5.1.2.2 Isothermal methods

In recent years, many isothermal amplification techniques are developed like isothermal technique [59]. This technique can be used as alternative to the PCR. There is no need for constant maintenance of temperature at 60–65°C and no thermal recycler is required; so, these things make it best for developing countries.

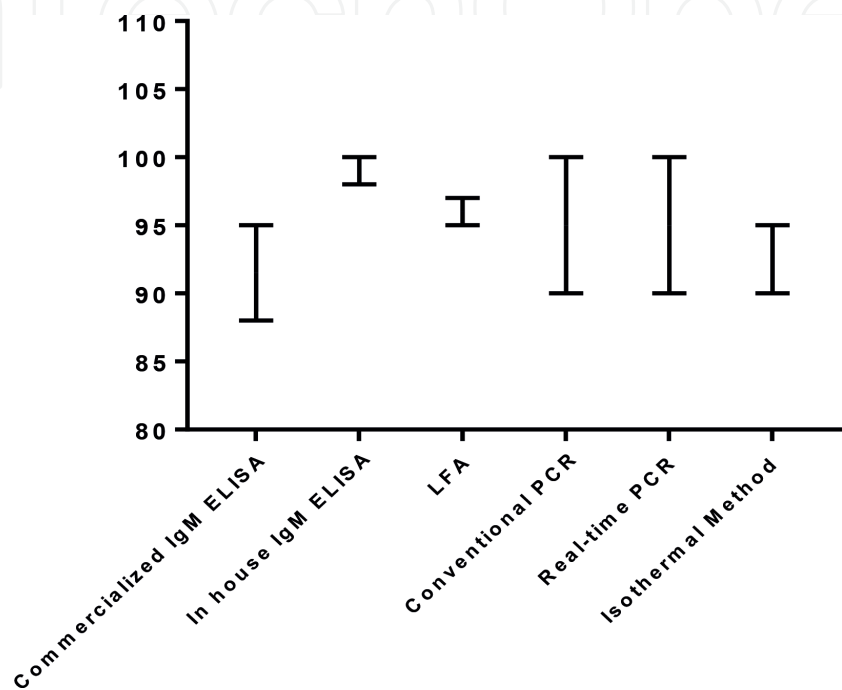


Figure 3.
Specificity of different diagnostic tests during acute phase of leptospirosis [56, 58].

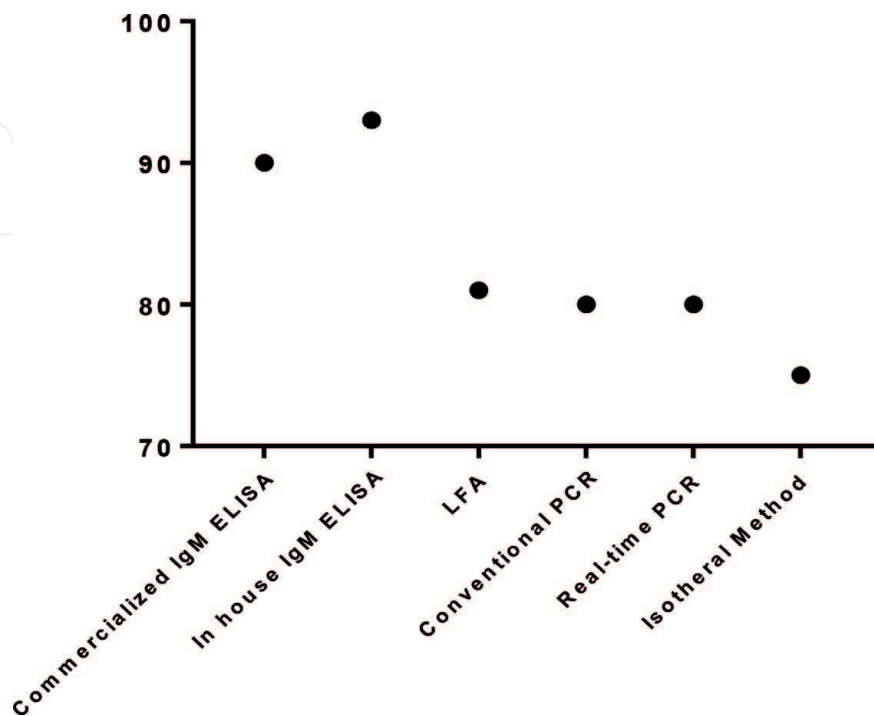


Figure 4.
Sensitivity of different diagnostic tests during acute phase of leptospirosis [58].

For this, an effective and specific amplification is performed by DNA polymerase and six primers in 1 hour under isothermal conditions. Now the amplified DNA can be easily detected by eye observation of fluorescence without using gel electrophoresis [60]. Loop-mediated isothermal amplification (LAMP) methods are recently developed for the quick diagnosis of pathogenic leptospires, and *lipL41* and *rrs* are the genes targeted by LAMP. The specificity of these methods is weak because these can detect the threshold between 2 and 100 leptospires/reactive mixture [61].

5.1.3 Serological tests

5.1.3.1 The microscopic agglutination test (MAT)

This microscopic agglutination test is developed in Pasteur Institute. Dark field microscopy is required to see agglutination of live leptospires cultures with patient's serum. This is the gold standard test for leptospirosis. It determines the anti-*Leptospira* immunoglobulin titers in human and animal serum at the serogroup level, so it is used for clinical and epidemiological investigations [62]. MAT is performed on micro titration plates, dilutions of serum which is collected from the patient is made and then equal volume of leptospiral culture is added to form agglutinations of distinctive patterns that consist of highly dense packs of partly intact leptospires. The test is read by DFM.

5.1.3.2 IgM enzyme-linked immunosorbent assay (ELISA)

Normal ELISA is commonly used to diagnose leptospirosis. Enzyme immunoassay of leptospirosis can be performed using a commercially available kit or antigen obtained internally. Which is commonly used to detect IgM, and sometimes to detect IgG antibodies against leptospiral antigens. The presence of IgM antibodies indicates current or recent leptospirosis. The commercially available *Leptospira* IgM ELISA is used for the serological detection of acute leptospirosis infection in a patient's serum sample. This ELISA is based on the principle that any *Leptospira* IgM antibody present in the patient's serum binds to the *Leptospira* antigen that adheres to the microporous surface of the microwell. Residual serum was removed from these wells by washing with 1% buffer (included in the kit). Peroxidase-conjugated anti-human IgM is presented after adding to the wells, and the plate is reincubated so that the bound antigen-antibody complex binds to the conjugate. The wells are washed again and a colorless substrate system, tetramethylbenzidine hydroperoxide, is added. The substrate is hydrolyzed, and the chromogen is blue. When the reaction is stopped with phosphoric acid, TMB turns yellow. The development of color indicates the presence of visual acuity IgM antibody against *Leptospira* in serum samples [63].

6. Necropsy findings

Cows with acute leptospirosis are characterized by anemia, jaundice, hemoglobinuria, and lower lobe hemorrhage. An ulcer and bleeding may be present on the mucous membrane of the peritoneum. Pulmonary edema and emphysema are also common in cattle. Histologically, there is a progressive and diffuse interstitial nephritis and liver necrosis in the centre of the lobules. Sometimes the vascular lesions of the meninges are transferred to chronic infections. *Leptospira* can be seen in the silvery spots of a part of tortuous tubules proximal to the kidneys. In acute infection, there is minimal inflammation, and in the middle of the leaflet, there are only tubes filled with hemoglobin and visible liver necrosis. At a later

stage, progressive interstitial nephritis is characterized by a small white cortical lesion, which initially slightly increases or decreases with increasing age of the lesion. The fruit of a broken cow is usually automated by the fact that there is no damage or bacteria. Even fresh fruit, positive identification of leptospirosis in lesions is not easy. Although the use of fluorescent antibody technology facilitates the identification of organisms, false positive results are common unless experienced diagnosticians interpret the test. Although dark field microscopy can be attempted, it is not suitable for tissue collected at dissection. Although PCR technology is important, in some cases, several primer sequences may be required.

Samples for confirmation of diagnosis are kidney, liver and placenta. Histology of kidney, liver, brain, heart, lungs and placenta can be performed. While for serological analysis heart blood serum or pericardial fluid from foetus can also be obtained.

The zoonotic potential of this organism should keep in mind during handling of carcasses and submitting specimens.

7. Treatment

Treatment is based on severity of illness being presented by animal which in most of the cases is mild and self-limiting requiring no care. Other considerations, while treatment is considered, include differential diagnosis, cost, and availability of drugs. Treatment obtained based on in-vitro studies presented doxycycline, ampicillin, azithromycin or amoxicillin [64]. The double-blind randomized trials conducted on 29 patients produced promising results by reducing symptoms of malaise in 2 days preventing leptospiremia. The treatment, however, was not conclusive prevention from progression to severity [65]. Doxycycline or azithromycin is the drug of choice in endemic areas while contraindicated in pregnancy [64]. Sever cases are responsive to penicillin G sodium in studies conducted before 90s. The emerging resistance has narrowed spectrum of antibiotic use against infections [66]. Open randomized trial conducted with experiment involving 256 patients proved nonsignificant difference among penicillin G, cefotaxime, and doxycycline antibiotics [67]. Some of meta-analysis studies have reported nonsignificant difference between penicillin G and placebo on mortality [68]. Mortality is reported to increase up to 70% with pulmonary involvement which is due to immune-mediated inflammatory response. The therapeutic indicated for this complication is steroidal drugs. Early steroid administration was found responsive but methodologically flawed in various studies. Desmopressin was evaluated in various randomized studies as adjunct therapy with nonsignificant mortality benefits [69]. Therapy is considered beneficial with doxycycline or azithromycin along with steroid administration in mild and severe cases. Variations in studies are reported with nonsignificant benefits to mortality reduction.

7.1 Blood transfusion

Leptospirosis is a zoonosis with worldwide distribution. It is more prevalent in the developing countries. Hemorrhagic manifestations constitute the common clinical feature in leptospirosis [70]. In cattle, acute hemolytic syndrome of leptospirosis has been reported characterized by fever, icterus, anemia, and hemoglobinuria [71]. Without effective treatment, hemolytic syndrome in cattle may result in death. A high mortality rate of severe disease was determined to be associated with certain serotypes of *Leptospira* [72]. The disease, for instance, causes a decrease in erythrocyte and platelet counts, leading to anemia and hemorrhagic diathesis, respectively.

Elevated bilirubin levels result from hemolysis and hepatorenal failure, indicating the characteristic nature of clinical signs [73]. Blood transfusion was reported to be quite effective in cases of life-threatening anemia in cattle. Previous reports suggest that timely transfusion of whole fresh blood be administered to overcome severe hemolytic leptospirosis. Indeed, transfusion providing the vital components such as erythrocytes, platelets, and plasma contributes to repair the present collapses, that is, anemia, hemorrhagic diathesis, septicemia, and hepatorenal failure, in affected cattle [71]. A PCV value of 15% or less developing acutely may require transfusion, while chronic anemia can be tolerated in cattle without any transfusion [74].

7.2 Vaccination

The optimal control regime for leptospirosis is to prevent clinical disease and exfoliation in the urine in animals exposed to different serotypes of *Leptospira*. The most common method of controlling leptospirosis in cattle is vaccination and selective treatment. In addition, proper quarantine procedures should be implemented to prevent the introduction of hajo in the herd by buying infected animals. However, leptospirosis and wild animals gave rise as a carrier of the prevalence of serotypes of hardjo infections in cattle, mainly to prevent the overall impact of leptospirosis in most dairy products and Rieben beef failure. This is impossible. Thus, vaccination depends on an increase in the resistance of an animal to leptospiral serotype infection in this area. In all cases, the effort (buildings, under the control of rodents around swamps and creeks, for example, surround) must be made in order to limit direct and indirect contact between the cattle and *Leptospira*. In addition, proper quarantine procedures should be implemented to prevent the introduction of hajo in the herd by buying infected animals. However, leptospirosis and wild animals gave rise as a carrier of the prevalence of serotypes of hardjo infections in cattle, mainly to prevent the overall impact of leptospirosis in most dairy products and Rieben beef failure. This is impossible. Thus, vaccination depends on an increase in the resistance of an animal to leptospiral serotype infection in this area. The leptoral vaccine currently available for cattle in the United States is a 5-fold bacterial whole cell vaccine, including Pomona, Canicola, Icterohaemorrhagiae, Grippotyphosa, and Hardjo serotypes. These antigens can also be used in various combinations of other viral and bacterial vaccines. In the United States, a series of experimental studies and field data are available from the United States. Typical leptospirosis vaccines are Hajo kidney serotype infection, urinary tract infection or fetus (ha-ha type). This does not exclude the fact that the state indicates that the country is isolated from the United States. Many of the available Hardjo vaccines were approved many years ago in rigorous efficacy studies that mimic the natural route of exposure, and the last method to determine whether the Hardjo serotypes are infected with cattle is Hardjo stocks which did not use the serotype. However, recently two Hardjo vaccine serotypes have been widely studied using appropriate strains and methods. Compared to many other Hardjo serotype vaccines, these two products have shown excellent protection against infection and Hardjo hemoglobin isolation [75].

8. Conclusion

Leptospirosis is a major zoonotic disease resulting in high mortality in humans and animals. The disease is diagnosed clinically by fever, headache, vomiting, abdominal pain, and arthralgia. Leptospirosis is caused by more than 250 serovars, while pomona and grippotyphosa being the most prevalent serovars among them. However, among cattle, serovar Hardjo is the most important in causation of

disease. Among the Asian countries, the highest prevalence of leptospirosis was found in India. Leptospirosis is mainly transmitted by direct contact with infected urine, and bacteria are mainly entered through ruptured skin. In house IgM ELISA is highly specific technique for *Leptospira* diagnosis. However, among the serological test, ELISA is more sensitive test for *Leptospira* diagnosis. Most effective treatment for *Leptospira* is doxycycline or azithromycin; however, former is not recommended in pregnancy. However, in severe cases, blood transfusion is also a best choice to save the life of animal. At last, the most effective way to control the disease is vaccination at early age of life following booster doses to avoid from more severe economic losses.

Author details

Amjad Islam Aqib^{1*}, Muhammad Ijaz², Shahid Hussain Farooqi³,
Muhammad Shoaib⁴, Muhammad Fakhar-e-Alam Kulyar⁵ and Khadija Yasmeen⁵

1 Department of Medicine, Cholistan University of Veterinary and Animal Sciences, Bahawalpur, Pakistan

2 Department of Clinical Medicine and Surgery, University of Veterinary and Animal Sciences, Lahore, Pakistan

3 Department of Clinical Sciences, KBCMA College of Veterinary and Animal Sciences, Narowal, Pakistan

4 Institute of Microbiology, University of Agriculture, Faisalabad, Pakistan

5 Department of Clinical Medicine and Surgery, Faculty of Veterinary Sciences, University of Agriculture, Faisalabad, Pakistan

*Address all correspondence to: amjadwaseer@gmail.com

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