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Leptospirosis and its Public Health Significance: A Review

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Abstract: Leptospirosis is a worldwide zoonosis of global importance. It occurs in both developing and developed countries and large outbreaks have been reported all over the world. Now leptospirosis is being recognized as emerging infectious disease. The disease is caused by spiral shaped bacteria called *Leptospira*, which has similar morphology. The disease is endemic to tropical and subtropical area where heavy rainfall and humanity is found. The disease is highly zoonotic through contact with urine from infected animal or though ingestion of contaminated feed and water by *Leptospira*. The clinical pictures of leptospirosis do not vary greatly with the species of animals. In human; individual working in agriculture and sewage, veterinarians and individuals in close contact with animals are risk groups. Direct examination, serology and molecular techniques are the mostly commonly used in the diagnosis of leptospirosis. Best results have been recorded with specific serum therapy and by administration of antibiotics like tetracycline, chloramphenicol and penicillin. Prevention and control of leptospirosis require elimination of the carrier state, control of rodents and maintenance of environmental condition and immunization of the animal.

Key words: Leptospirosis · Zoonosis · *Leptospira* · Public Health Hazard

INTRODUCTION

Leptospirosis is one of the world's most widely spread bacterial diseases caused by the genus *Leptospirae*, which is classified as a direct anthroponozonosis affecting human and a variety of animal species. Leptospirosis traditionally has to be considered as a rural based disease. However urban epidemics associated with severe form of the disease is also reported to occur annually resulting in significant mortalities [1].

Leptospirosis is a major cause of economic loss in farm animals. The majority of lepitospiral infections are of sub-clinical, associated with total infections causing abortions, still births and the birth for weak neonates with a higher death rate in cattle, horse, sheep, goat and pigs [2].

In human leptospirosis is characterized by a broad spectrum of clinical manifestations, varing from in apparent infection to total diseases. However, it's especially a greater problem in humid, tropical and sub tropical areas with heavy rainfall and neutral or alkaline soils, where most developing countries are found than in those with a temperate climate. The magnitude of the problem in this region can be largely attributed to climatic and environmental conditions but also to the great likelihood of contact with leptospiral contaminated environment [3, 4]. It is an emerging disease of world with wide distribution affecting large number of mammalian species including human being. Leptospirosis is potentially serious but treatable disease [3]. As a result, it is deserved by those involved in public health care and animal health service. Therefore, the objective of this paper was to review information regarding leptospirosis and its impact on public health significance.

General over View of Leptospira Organisms: Leptospirae are spirochetes that are morphologically and physiological uniform but serological and epidemiologically diverse [3]. They include both free living and parasitic species; *L. biflexa* and *L. interogans* respectively. The pathogenic leptospirae are divided in to 25 sero groups consisting of more than 200 serovars according to their pathogenic composition [5]. *L. biflexa* is free living saprophyte found in surface water and is seldom associated with infection in mammals [6].

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Morphology of the Organism: They are motile helical and also tightly coiled, flexible spirochetes 5-15 m long with very fine filament of spirals 0.1-0.5 μm wide one end of the organism often bent forming a hook [7]. Active rotational movement but not flagellar have been discovered electro micrography showing that a thin axial filament and a delicate membrane. In dark field microscopy it appears only as a chain of minute cocci [8]. The cell of *Leptospira* consists of outer sheet axial fibrils /endo flagella/ and cytoplasmic cylinder. The outer sheath combines features of a capsule outer membrane and peptidoglycan layer of cell wall the outer cell envelope surrounds completely the protoplasmic cylinder which consists of cytoplasm and nuclear region enclosed by cytoplasmic membrane cell wall complex [3, 9].

Cultural Characteristics: *Leptospirae* grow at 30°C in peptone broth containing 10% rabbit serum and on semi solid meat extract media containing 10% rabbit serum with-in 6-10 days round colonies 1-3 mm in diameter develop. *Leptospira* can also grow on corioalantoic membrane of embryonated egg [10]. However no growth occurs on blood agar and other routine media. *Leptospirae* are oxidase and catalase positive, many have lipase activity and some produced urease. They are obligate aerobes and drive energy from oxidation of long chain fatty acids and carbohydrate as major energy source Traditional media for *Leptospira* growth are essentially rabbit serum in solution ranging from normal saline to mixture of peptone, vitamin, electrolyte and buffers [8].

Epidemiology of Leptospirosis

Distribution and Usual Habitat: Leptospirosis as zoonosis has a worldwide distribution but most common in developing countries and warm climate where contact with infected animal or water contaminated with their urine is likely to occur [3]. *Leptospira* can survive in ponds, rivers, surface water, moist soil and mud when enviromental temperature is warm. As these enviromental temperatures are favourable and the pH is alkaline these fragile organisms can survive for a week and are transmitted mostly by direct contact [7]. Serovars of *L. interohaemorrhagiae, L. canicola*, *L. pomonai*, *L. hardijo* and *L. gripotyphosa* occur in all continents and outbreaks have been reported following natural disaster such as flooding and hurricane [4].

Table 1: Maintenance and incidental hosts for important serovars of *L. interogans* [7].

Serovar	Maintenance host	Incidental host
L. bratislava	pig	horse, dog
L. canicolla	dog	pig, cattle
L. grapityphosa	rodent	cattle, pig, horse, dog
L. hardiso	cattle	human
L. interohemorrhafiae	brown cat	domestic animals and human
L. pomona	pig, cattle	sheep, horse, dogs

Survival of the organism in the environment depends on variations in soil and water conditions in contaminated area. The organism is susceptible to drying and pH lower than 6 or greater than 8; ambient temperatures also lower than 7.1 °C or higher than 34 °C are detrimental to survival of the organism [2].

Source of Infection and Reservoir Hosts : A wide variety of animal species primarily mammals may serve as a source of human infection; those that can be considered the most important in this context includes small mammalian species notably pre-domestic rodents and insectivores, domestic animals [11]. In addition to these maintenance hosts any infected animal can be a source of infection to others of own kind or to other species including human. Each leptospira to be associated with particular serovar species of natural maintainance host, how ever there are many exceptions to this rule as one may to be carried by different hosts and one animal may act as host for different serovars (Table 1). In addition serovar may adapt to new host specie which may then become a natural reservoir for this infection [2].

Infection with leptospirae is maintained within a population of natural maintenance hosts by vertical and horizontal transmission, such population of natural animal host form the infection reservoir. The natural maintainace host ensures the continues circulation of a particular leptospiral serovar in a geographical area with out the need for others, while incidental hosts to be involved maintenance hosts may carry a particular certain leptospira in their kidney and shed with their urine for long period of time and sometimes for animal life [12].

Modes of Transmission

Animal to Animal: Leptospirosis can be transmitted from one carrier animal to another healthy animal through direct or indirect contact with urine or other body fluids that contain viable *Leptospira*. There is also other means

of transmission of infection between farm animals via congenital or neonatal infection. A viable infected neonate can harbour the infection for several weeks after birth and can act as a source of infection [2].

Sexual transmission of *Leptospira* by mating in rats, pigs and dogs has been reported [3]. Semen of an infected bull may contain leptospirae, so transmission by natural breeding or artificial insemination can occur but is uncommon [2].

Animal to Human: Human can acquire the infection of leptospirosis primarily from direct or indirect exposure to the urine or blood of infected animals other methods of transmission such as handling of infected animal tissues and ingestion of contaminated food and water are also possible [4, 13].

Human to Human: *Leptospirae* can also be transmitted from human to human by sexual intercourse, trans-placental from infected mother to the foetus and though breast milk, urine from patient suffering from leptospirosis should be considered infectious as *Leptospirae* cultured from blood. This should be virulent as infectious for sometimes before the onset of symptoms during the first 7-10 days of illness and by blood transfusion [14].

Virulence Factor of Leptospira Organisms: Virulent *Leptospirae* resist the bactericidal action of complement and neutrophils in non-immune hosts but are rapidly killed by either mechanism in the presence of specific epithelial and endothelial antibody [15]. The ability of *Leptospira* to invade Vero cells and to reduce apoptosis in macrophages was correlated with virulence; nevertheless the organism must penetrate host epithelial and endothelial cell barriers of both haematogenous spread and localization in target organs, such as liver and kidney [16, 17]. A cytotoxic glycol lipoprotein fraction is shown to inhibit hosts ATP ase with the activity ascribed to the presence of long chain fatty acid [18]. *L. pomona* in cattle causes intravascular haemolysis due to haemolytic exotoxin [3].

Pathogenesis of Leptospirosis: Leptospirae penetrate intact mucous membrane of the mouth, nose or eyes or abraded, scratched or water softened skin. They multiply rapidly after entering the vascular system, spread and further replicate in many tissues including kidney, liver, spleen, central nervous system, eye and genital tract. The extend of internal organ damage is available depending on the virulence of the organism and host susceptibility [18]. Renal colonization occurs in most infected animals because the organism replicate and persists in renal tubular epithelial cells, even in the presence of serum neutralizing antibodies; the organism may be seen within the proximal tubular cells which coincides with the on-set of shedding [2].

The invasive capacity of leprospirae may be related to their pathogenicity because non pathogenic *leptospirae* do not penetrate cells as deadly as pathogenic leptospirae. Damage to the endothelium of small blood vessels may result in ischemic damage to the renal parenchyma [3, 18].

Kidney involvement in many animal special is chronic and results in elimination of a large number of *leptospirae* in the urine. This is the main source of contamination and infection of human and other mammals. Human urine also contains the organism in the second and third week of infection. During human infection agglutination, complement fixing and lytic antibodies develop. Serum from convalescent patient protects experiment animals other wise fatal infection occurs. Immunity resulting from *Leptospira* infection in human and animal appears to be specific [10].

Clinical Signs of Leptospirosis in Animals: The clinical findings in leptospirosis are similar in each animal species and do not vary greatly with the specie of leptospirae except that of infection with *L. interohaemorragiae* usually causes severe septicaemia [19]. The clinical finding in the acute form of leptospirosis is maintained by septicaemia, with high fever anorexia, petechiation of mucosa depression and acute haemolytic anaemia with haemoglobin urea, jaundice and pallor of the mucosa. Milk production is markedly decreased and the secretion is red coloured or contains blood clot and the udder is lop and soft. The sub acute form of lentospirosis differs from the acute form only in degree. Fever is mild and hemoglobinuria is common but jaundice may or may not be present. The clinical findings in the chronic form of leptospirosis are mild and may be restricted to abortion. Abortion usually occurs during the last trimester of pregnancy [2].

Infertility and milk drop occurs only in pregnant or lactating cows because *Leptospira* organisms require pregnant uterus and lactating mammary gland to proliferate. Sudden drop in milk production may affect up to 50% of cows at one time and precipitate fall in the herds milk yield, the decline may last for up to 8 weeks but individual cows milk production will return to normal with in 1-14 days [2].

Laboratory Diagnosis: Specimens of whole blood for serological tests, mid-stream urine for dark field examination and kidney tissue from dead animal-because *leptospirae* remain viable in unfrozen kidney for several days after the death of the animal. In addition to kidney aborted fetus is the most likely organ to harbour leptospirae [13].

Direct Examination: Dark field microscopy, immunofluorescent stain and silver impregnation of fixed tissues are methods of direct examination. Method of direct examination by using dark field microscopy is limited to urine because other body fluids contain artefacts similar to *Leptospira* organisms, therefore, low speed centrifugation clears the interring particles but will not sediment. Methods using formalinized urine have been described but they destroy motility, which aids in identification of leptospira. However, negative result of *Leptospira* under direct examination does not rule out Leptospirosis [20].

Animal Inoculation: A sensitive technique for the isolation of *Leptospira* consists of the intraperitoneal inoculation of young guinea pig with fresh plasma or urine, within few days spirochetes become demonstrated in the peritoneal cavity. On the death of the animal haemorrhagic lesions with spirochetes are found in many organs [2].

Serology: Macroscopic and microscopic agglutination tests, complement fixation test and ELISA technique are used for the detection of leptospirae in serum. The macroscopic agglutination examination is a screening test and uses dead Ag but suffers from specificity [21].

The microscopic agglutination test (MAT) is the most commonly used serological test for the diagnosis of lepsopirosis. In animals which survive infection, leptospira can be readily diagnosed on the bases of demonstrating rising antibody titre in acute or convalescent sera. The MAT is particularly usefully in diagnosis of disease associated with incidental host adapted serovars, or acute disease associated with host adapted serovars. It's less useful in the diagnosis of chronic infection or may persist from sub-clinical infection [2].

The ELISA test is much more accurate than other tests and has much advantage from point of view of laboratory practises. It has excellent diagnostic specificity and sensitivity, convenient technical feature including automation and can be used efficiently as serenity test for large number of serum samples [22].

Molecular Method of Diagnosis: DNA amplification using PCR and DNA primers have become an excellent diagnostic tool for detecting the presence of *Leptospira* in animal tissues and fluids and it can be applied to blood, urine, CSF and tissue samples anti or post mortem [23]. Several primary pairs for PCR detection of *Leptospira* have been described; some are based on specific gene targets such as 165 to 235 ribosomal genes or repetitive elements while others have been constructed from genomic libraries [24].

Differential Diagnosis

Bovine*:* Diseases that cause abortion especially in second and third trimesters like-brucellosis, bovine genital campylobacteriosis, trichomoniasis, bacillary hemoglobinuria and other diseases [3].

Canine: Canine hepatitis, distemper, ehrlichiosis, babesiosis and sporadic febrile diseases caused by various bacteria and viruses [6, 8].

Equine: Other febrile diseases can cause abortion such as equine viral abortion, equine viral arthritis and various bacteria [2].

Treatment: Treatment must be early to be effective. A large single intra muscular dose of dihydro streptomycin (25mg/kg) will cure the carrier state in bovine severe leptospirosis can be treated with antibiotics such as doxycycline, ampicillin, amoxicillin, penicillin and erythromycin [25]. Supportive treatments and management of complications such as renal failure and hepatic complications, haemorrhage and CNS diseases may also important.

Specific serum therapy formerly applied especially in dogs has been replaced by treatment with antibiotics [3]. In serious acute cases antibiotics can be supplemented with glucose and vitamin C and deoxycorticosterones which have been recommended to spread up to elimination of urea. Further individual treatment will depend on the clinical condition of the animal and special attention must be given to function of Kidneys [26].

Blood transfusion is indicated as treatment for haemolytic anaemia. In acute lepsopirosis of cattle the clinical indication for blood transfusion includes obvious pallor of the mucus membrane, weakness and tachycardia [2].

Control and Prevention: Prevention of leptospirosis involves elimination of the carrier state, control of

rodents in kennels, maintenance of environmental condition to discourage bacteria survival and isolation of infected animal. Draining or fencing of stagnant water may reduces transmission, limiting rodents and wild life contact with cattle and their feed and water is often difficult to accomplish but it reduces the potential for transmission of leptospirosis [27].

The major risk for control is introduction of carrier animals of any species or reintroduction by rodents, or by other wild life. It is because of this risk that most programs aim at containment rather than eradication. The first step in control is to identify the source of original infection [28]. Therefore, leptospirosis can be controlled by vaccination in individual form [29]. Vaccination against leptospirosis in cattle and swine is generally used as an effective method for control of the disease. Most of the vaccines are formation inactivated bacterins containing one or more serotypes. The immune response is serotype specific; therefore protection is dependent on the use of bacterins containing serotype prevalent in the area. Regular serological testing in herds vaccinated annually can be used to monitor new infection [30].

Public Health Significance of Leptospirosis

Risk Factors: Leptospirosis is seasonal with most cases seen during summer and fall in temperate region. In tropical climate the peak incidence occurs during the rain season. Large outbreaks have been seen after floods. Occupational exposure thought to be responsible for 30-50% of cases. Occupations with high risk of infection include salver workers, coal mines, plumbers, farm workers, veterinarians, pet shop owners, abattoir workers, meat handlers, slaughter house workers and workers in fishing industry. About 8-29% of workers who deal with live-stock have antibodies to leptospira. Recreational activities that increase the risk of lepsopirosis include gardening and water sports such as canoeing, swimming and white water rafting residents of some urban areas are exposed via rat urine [2].

Morbidity and Mortality: Most cases of leptospirosis are asymptomatic or mild. The overall case fatality rate is 1-5%. The mortality varies with the form and is higher in the elderly. The icteric form is rarely fatal. The icteric form, which occurs in 5-10% of all patients, has an overall mortality rate of 5-15% and a 54% case fatality rate in severe cases with myocardial involvement. Most patients with kidney failure, hepatic disease or anterior uveitis eventually recover with full kidney or liver functions and vision [15].

Leptospirosis in Human: Human infection varies from asymptomatic to severe; some serovars are associated with some syndromes. Usually human lepsopirosis is biphasic illness. The first phase is called the acute or septicemic phase, usually begins abruptly and lasts approximately a week. This phase is characterized by non specific signs including fever, chills, headache and conjunctival suffusion [31]. Other symptoms may include photophobia, lymphadenopathy abdominal pain, nausea, vomiting, a sore throat, cough and jaundice may be also seen in more severe infection [32].

The second phase of leptospirosis, is called the immune phase, characterized by the development of anti leptospiral antibodies and excretion of leptospiral organisms with urine and also two forms of the disease are seen in this phase; Icteric and an-icteric forms [33].

Most infections are anicteric form. The most important symptoms in this form are associated with aseptic meningitis. Severe headache stiffness and other meningial symptoms occur in approximately half of all patients and usually last a few days. Less common symptoms include cranial nerve palsies, encephalitis, confusion and change in consciousness. Death is rare in the typical anicteric form, however, a syndrome of fatal pulmonary haemorrhage, without jaundice has recently reported [3, 12].

The icteric form is more severe and it occurs in 5-10% of all patients, often rapidly progressive and may be associated with multiorgans failure. The most commonly involved organ systems are kidney, liver and central nervous system [31]. In the icteric form, there may be no period of improvement between the septicemic and immune phases. Jaundice can be seller and may give the sin and orange tone, but it is not associated with severe hepatic necrosis, acute renal failure occurs in 16-40% cases [33].

Some patients may have pulmonary symptoms with clinical signs ranging from cough, dyspnoea, chest pain and mild to sever haemoptysis. Cardiac involvement can result in congestive heart failure, myocarditis and pericarditis [34]. Haemorrhage may also be seen as epitasis, purpura and echymoses [33]. Severe gastrointestinal bleeding, adrenal or subarachnoid haemorrhage and pulmonary haemorrhages can occur. Death can occur from kidney failure, cardiac involvement, pulmonary haemorrhage or other serious organ dysfunction [35]. Anterior Uveitis occurs up to a year after re-covering in 2-10% of cases. Iridocyclitis and chorio retinitis can also be complications and may persist for years. Abortion, fetal death and rare congenital infections in new born have been reported. Abortion can occur at any time including the convalescent period [2].

CONCLUSIONS AND RECOMMENDATIONS

Leptospirosis is among the widest spread hazards to animal health as will as important and occupation hazard to butchers, farmers and veterinarians. Infections with *Leptospira* are maintained within a population of natural maintenance hosts by vertical and horizontal transmission and rodents have been recognized to be the most important and widely distributed reservoirs of leptospiral infection. Human leptospiral infections result primarily from direct or indirect exposure to urine of infected animals. Handling of infected animals and their tissues, ingestion of contaminated land water, sexual intercourse and trans-placental transmission are other modes of infection. Mortality in human with leptospirosis remains significant because of delay in diagnosis due to lack of diagnostic infrastructure. Therefore the following points are forwarded as recommendations:

Strict hygiene and prevention of contamination from urine and body fluids of infected animals should be made, therefore, individuals which have close contact with animals; agricultural and sewage workers as well as who have close contact with contaminated water should be informed about the risk. Treating infected animals and increasing awareness of the risk population should be made. As an emerging disease, it needs attention; therefore, researchers should be concerned regarding to the status of leptospirosis in Ethiopia.

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