

## REVIEW

# Leptospirosis and its Epidemiology: an update on

current knowledge and Public Health Challenges

Garoma Desa, Teferi Benti

**Keywords:** Animal, Epidemiology, Leptospirosis, Review

### ABSTRACT

Leptospirosis has been known to affect both man and numerous mammalian species resulting in morbidity and mortality. *Leptospira interrogans* is a pathogenic species that cause leptospirosis while *L. biflexa* is nonpathogenic. Currently, there is limited and fragmented information available regarding the present status and geographical distribution of leptospirosis. This lack of up-to-date data poses a significant challenge for understanding the true burden and spread of the disease. As a result, there is a pressing need to generate recent and reliable evidence to support the development of effective surveillance systems, targeted control strategies, and public health interventions aimed at minimizing the impact of the disease. Leptospirosis has a worldwide distribution due to the large spectrum of mammalian hosts that harbor and excrete the agent from their renal tubules. The central point on the epidemiology of leptospirosis is the state of the renal carrier, the animal that has its renal tubules colonized by leptospirae, which in turn are excreted in the urine infecting the environment. Leptospirosis is a serious zoonotic disease with significant public health implications due to its potential for severe complications and high mortality rates in both humans and animals. The disease can be directly transmitted through contact with secretions, blood or urine of infected animals, or indirectly through water contaminated mainly with urine of reservoir animals. Leptospirae penetrate intact mucous membrane of the mouth, nose or eyes or abraded, scratched or water softened skin and 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. In Ethiopia leptospirosis is a relatively unknown disease although already reported to occur in domestic animals. The disease is characterized by a broad range of clinical signs which can be presented as acute, sub-acute or chronic. Leptospirosis can be treated by antibiotics such as tetracycline, penicillin, doxycycline, streptomycin and erythromycin, while prevention is characterized by sanitary control and decrease in the risk of infection occurring due to contact with contaminated environments, infected wild animals as well as with synanthropic animals and rodents. Elimination of the carrier state, control of rodents in kennels, maintenance of environmental condition to discourage bacterial survival and isolation of infected animal need to be under taken in order to prevent the disease. Leptospirosis has been recognized as a re-emerging global public health problem due to the increased incidence in both developing and developed countries.

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**What do we already know about this topic?**

Leptospirosis has been known to affect both man and numerous mammalian species resulting in morbidity and mortality. *Leptospira interrogans* is a pathogenic species that cause leptospirosis while *L. biflexa* is nonpathogenic. Currently, there is limited and fragmented information available regarding the present status and geographical distribution of leptospirosis.

**What is the main contribution to Evidence-Based Practice from this article?**

This review clarifies evidence on the available knowledge on the elimination of the carrier state, control of rodents in kennels, maintenance of environmental condition to discourage bacterial survival and isolation of infected animal need to be under taken in order to prevent the disease. Leptospirosis has been recognized as a re-emerging global public health problem due to the increased incidence in both developing and developed countries.

**What are this research's implications towards health policy?**

The article provides a contribution to improve public health actions and prevention measures on this disease that is characterized by a broad range of clinical signs which can be presented as acute, sub-acute or chronic. Leptospirosis can be treated by antibiotics such as tetracycline, penicillin, doxycycline, streptomycin and erythromycin, while prevention is characterized by sanitary control and decrease in the risk of infection occurring due to contact with contaminated environments, infected wild animals as well as with synanthropic animals and rodents?

Authors' Contributions Statement:

Desa Conceptualized, undertook the review and wrote the Original manuscript; Benti reviewed the original manuscript and Validated the Methodology;

## INTRODUCTION

Leptospirosis is a widespread disease of animals and also a zoonosis of worldwide distribution. *Leptospira interrogans* is a pathogenic species that cause leptospirosis while *L. biflexa* is nonpathogenic. *Leptospira* have characteristic hooked ends and are tightly coiled with approximately 18 coils per cell (Doern, 2000). Leptospire have a typical double membrane structure in which the cytoplasmic membrane and peptidoglycan cell wall are closely associated and are overlaid by an outer membrane (Mohammed et al., 2011). Leptospirosis has worldwide distribution due to the large spectrum of mammalian hosts that harbor and excrete the agent from their renal tubules (Ko et al., 2009). The central point on the epidemiology of leptospirosis is the state of the renal carrier, the animal that has its renal tubules colonized by leptospirae, which in turn are excreted in the urine infecting the environment (Adler & Moctezuma, 2010). The source of infection in an area is determined by factors such as rodent density, population size of the farm and other domestic animals, sanitation of animal habitats, availability of

veterinary services for prompt detection and treatment of animal leptospirosis, control programs for animal leptospirosis, etc (Mathias and Levett, 2002).

All mammals appear to be susceptible to at least one species of *Leptospira*. Reservoir hosts among domestic animals includes cattle, dogs, sheep and pigs and they may act as carriers for several months (temporary carrier) while rodents usually remain carrier throughout their life (permanent carrier). Rodents are therefore considered as the major reservoir of infection (Yadeta et al., 2016).

The main sources of the disease are urine of infected or carrier animals, contaminated surface water, mud, feed, soil, aborted fetuses and uterine discharges (Levett et al., 2005). The disease can be directly transmitted through contact with secretions, blood or urine of infected animals, or indirectly through water contaminated mainly with urine of reservoir animals. The core determinants of transmission of leptospiral infection are the presence of carrier animals, suitability of the environment for the survival of leptospire and its one health aspect (Verma et al., 2013).

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 incubation period of leptospirosis depends on dose, infectious strain and host but is averagely between 7-14 days (Sykes et al., 2011).

In Ethiopia leptospirosis is a relatively unknown disease although already reported to occur in domestic animals. Leptospiral antibodies were detected four decades ago in domestic animals of the country with incidences of 91.2% in horses, 70.7% in cows, 57.1% in pigs, 47.3% in goats, 43.4% in sheep, 15.4% in camels and 8.3% in dogs using a microscopic agglutination test (Martin and Lilenbaum, 2014). However; there is little recent information about animal leptospirosis. According to Tsegaye et al. (2016), a total of 184 out of 418 horses had antibody titres of at least one of 16 serovars, demonstrating the presence of 16 serovars of *Leptospira* species in central and southern Ethiopian horses.

Leptospirosis is characterized by a broad range of clinical symptoms in livestock with minor difference between species affected: acute, sub acute or chronic. Clinical signs of acute or sub-acute disease are observed in the leptospiremic phase and it is characterized by septicemia, high fever and anorexia, petechiation of mucosa, depression and acute hemolytic anemia with hemoglobinuria, jaundice and pallor of the mucosa (Pettrakovsky et al., 2014). Diagnosis of leptospirosis depends on the samples available and temporal stage of the illness. Laboratory tests used for the detection of leptospirae are microscopic evaluation, culture, molecular method, serology and animal inoculation (Ahmad et al., 2005).

Serology is the most frequently used diagnostic approach for leptospirosis (Toyokawa et al., 2011).

Leptospirosis can be treated by antibiotics such as tetracycline, penicillin, doxycycline, streptomycin and erythromycin (Katz et al., 2011), while prevention is characterized by sanitary control and decrease in the risk of infection occurring due to contact with contaminated environments, infected wild animals as well as with synanthropic animals and rodents (Tilahun et al., 2013).

Understanding the epidemiological features of leptospirosis is a critical step in designing interventions for reducing the risk of the disease transmission (Levett et al., 2005). Although little can be done in wild animals, leptospirosis in domestic animals can be controlled through vaccination, Prophylactic treatment of exposed animals with antibiotics, quarantine newly introduced animals of whatever the species for at least 4 weeks, rodent control, regular serological testing, improved environmental hygiene, separating young animals from adults and safe artificial insemination (Himani et al., 2013).

Leptospirosis has been recognized as a re-emerging global public health problem due to the increased incidence in both developing and developed countries (Vijayachari et al., 2008). Leptospirosis affects risk groups that are exposed to animal reservoirs or contaminated environments, such as abattoir and sewage workers, salver workers, coal mines, plumbers, farm workers, veterinarians, pet shop owners, meat handlers, military personnel, slaughter house workers and workers in fishing industry (Monahan et al., 2009).

The aim of this seminar paper is:

To review leptospirosis and its epidemiology

## Literature Review

### The Causative Agent

The genus *Leptospira* responsible for causing leptospirosis is classified under the order Spirochaetales, and is further sub-divided into three species namely saprophytic (such as the *Leptospira biflexa*), pathogenic (*Leptospira interrogans*) and host dependent (*Leptospira borgpetersenii*) (McBride et al., 2005; Lehmann et al., 2014). The disease is biphasic, with a septicemic phase followed by an immune

phase with antibody production and urinary excretion of the organism (Zavistanou and Babastikou, 2008). Morphologically leptospire are corkscrew-shaped bacteria, which differ from other spirochaetes by the presence of end hooks. Leptospire have a typical double membrane structure in which the cytoplasmic membrane and peptidoglycan cell wall are closely associated and are overlaid by an outer membrane (Mohammed et al., 2011).

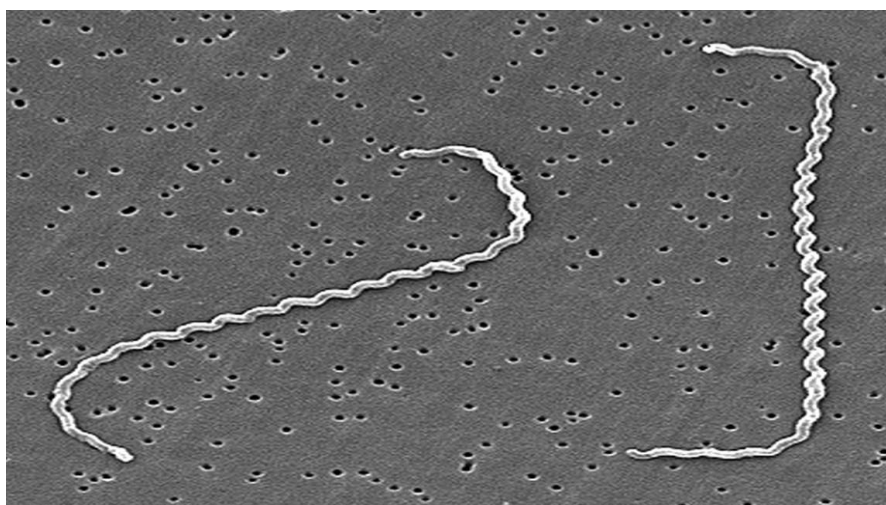


Figure 1: Causative agent of Leptospirosis  
Source: Levett et al., 2005

The genus *Leptospira* contains 22 species; 10 are regarded as pathogenic (*Leptospira interrogans*, *L. kirschneri*, *L. noguchii*, *L. alexanderi*, *L. weilii*, *L. alstonii*, *L. borgpetersenii*, *L. santarosai*, *L. kmetyi*, and *L. mayottensis*), 5 are of intermediate or unclear pathogenicity (*L.*

*inadai*, *L. fainei*, *L. broomii*, *L. licerasiae*, and *L. wolffii*), and the remaining 7 are nonpathogenic free-living saprophytic species that do not infect animal hosts (*L. biflexa*, *L. meyeri*, *L. wolbachii*, *L. vanthielii*, *L. terpstrae*, *L. yanagawae*, and *L. idonii*) (Marquez et al., 2017).

**Table 1:** Scientific Classification of *Leptospira*

Kingdom	Eubacteria
Phylum	Spirochaetes
Class	Spirochaetes
Order	Spirochaetales
Family	Leptospiraceae
Genus	<i>Leptospira</i>
Species	<i>L. interrogans</i>

Source: Sharma and Yadav, 2008.

### 2.1.1. Physicochemical properties of leptospire

Moist environments with a neutral pH provide suitable conditions for survival of leptospire. Soil moisture, surface water temperature and humidity influence the survival of leptospire in the environment (Spickler and Leedom, 2013; Joshi et al., 2017). They optimally survive for weeks in the environment. These organisms do not survive in freezing conditions. They are killed by dehydration or temperature in excess of 50°C. For disinfection purposes, leptospire are inactivated by 70% ethanol, glutaraldehyde, formaldehyde, detergents and acid. They are also destroyed by moist heat, at 121°C for 15 minutes and by pasteurization (Prevention (US) and National Association, 2005). Leptospire are obligate aerobes with an optimum growth temperature of 28–30°C. They grow in simple media enriched with vitamins B1 and B12, long-chain fatty acids and ammonium salts. Long-chain fatty acids are utilized as the sole carbon source and are metabolized by  $\beta$ -oxidation (Adler & Moctezuma, 2010).

Leptospira has the general structural characteristics that distinguish spirochetes from other bacteria. The cell is encased in a three- to five-layer outer membrane. Beneath this outer membrane are the flexible, helical peptidoglycan layer and the cytoplasmic membrane; these encompass the cytoplasmic contents of the cell. The structures surrounded by the outer membrane are collectively called the protoplasmic cylinder. An unusual feature of the spirochetes is the location of the flagella, which lie between the outer membrane and the peptidoglycan layer. Leptospira spp share a number of general features with other spirochetes, yet they differ in many ways from other spirochetal pathogens, such as *Treponema pallidum* and *Borrelia burgdorferi*

(Ren, et al., 2003).

The basal bodies of *Leptospira* periplasmic flagella resemble those of Gram-negative bacteria, whereas those of other spirochetes are similar to the basal bodies of Gram-positive bacteria. *Leptospira* differs from other spirochetes in lacking glycolipids and having diaminopimelic acid rather than ornithine in its peptidoglycan. The periplasmic flagella are attached to the protoplasmic cylinder sub terminally at each end and extend toward the center of the cell, but do not overlap as they do in other spirochetes. The number of periplasmic flagella per cell varies among the spirochetes. In liquid media, one or both ends are usually hooked. They are too thin to be visible under the ordinary microscope. Dark-field microscope is most often used to observe leptospire (Narayan, 2009).

### 2.1.2. Classification of the causative agent

The spirochetal are an order of bacteria dividing itself into two families: Spirochaetaceae and Leptospiraceae. Within the family Spirochaetaceae, we can find *Treponema* types, *Serpulina* and *Borrelia*. The agent of leptospirosis, the genus *Leptospira*, belongs to the family of Leptospiraceae (Mohammed et al., 2011).

Leptospire are bacteria which can clinically be either pathogenic (i.e. having the potential to cause disease in animals and humans) or saprophytic (i.e. free living and generally considered not to cause disease) (Levett et al., 2005). Initially, two species of *Leptospira* were recognized, namely pathogenic *Leptospira interrogans* and saprophytic *Leptospira biflexa*. Recently, several species of *Leptospira* have been differentiated on the basis of their DNA-relatedness (Adler & Moctezuma, 2010).

*Leptospira* are also classified based on their serovar. About 250 pathogenic serovars of

Leptospira are recognized. The most prevalent serotypes in the United States are Canicola, Grippotyphosa, Hardjo, Icterohaemorrhagiae and Pomona. The diverse sugar composition of the lipopolysaccharide on the surface of the spirochete is responsible for the antigenic difference between serovars. Antigenically related serovars are grouped into 24 sero groups, which are identified using the microscopic agglutination test (MAT). A given sero group is often found in more than one species, suggesting that the lipopolysaccharide (LPS) genes that determine the serovar are exchanged between species (Devishree, 2015).

## 2.2. Epidemiology

Leptospirosis has a worldwide distribution. It occurs in both temperate and tropical regions; the incidence in the tropics is approximately 10 times higher than in temperate regions (Adler & Moctezuma, 2010). This is attributed mainly to longer survival of leptospires in warm and humid environments. Leptospirosis is not limited to developing countries. Retrospective reviews of the disease epidemiology have been reported from Ireland, Denmark and Italy (Zavistanou and Babastikou, 2008).

Feral and domestic mammals (cattle, pigs and dogs) as well as reptiles and amphibians serve as a source of permanent maintenance hosts or reservoirs for over 250 known serovars of the genus *Leptospira*. The organism infects a variety of both wild and domestic mammals, especially rodents, cattle, swine, dogs, horses, sheep, and goats. The disease rarely occurs in cats. Animals can be asymptomatic or develop clinical infection, which can be fatal. Infection in small rodents usually occurs during infancy, and, once infected, animals may shed the organism in their urine intermittently or continuously throughout life, resulting in contamination of the environment, particularly water (Zavistanou and Babastikou, 2008).

Leptospires are ubiquitous spirochetes. The pathogenic leptospires shed in the urine of the carrier animals, contaminate the environment and cause human and animal infection. A pattern of disease seasonality has been described with a peak incidence occurring in summer or fall in temperate regions and during rainy seasons in warm climate regions (Levett et al., 2005). While the saprophytic species is a usual contaminant of surface waters, pathogenic leptospires mainly colonize the proximal tubules of nephrons of their natural host animals (mainly in rodents and domestic mammals) and are excreted in urine (Lau et al., 2010; Mwachui et al., 2015). Pathogenic leptospires do not multiply outside the host animals (in the environment) (Spickler and Leedom, 2013).

The source of infection in an area is determined by factors such as rodent density, population size of the farm and other domestic animals, sanitation of animal habitats, availability of veterinary services for prompt detection and treatment of animal leptospirosis, control programs for animal leptospirosis etc. Several rodent species were associated with the disease including *Rattus rattus*, *R. norvegicus*, *Mus musculus*, *Bandicota bengalensis*, *Bandicota indica*, and others (Mathias and Levett, 2002; Tilahun et al., 2013). Other animals such as dogs although vaccinated against *Leptospira* can shed the organism in their urine and this may result in domestic transmission in humans. In general, an infected animal can remain symptom-free and shed infectious organisms in the urine for its entire life time (Freitas et al., 2004). Infected animals transfer the leptospirosis infectious agent to their offspring either in-utero or during neonatal period. Leptospirosis should be considered as a disease of the environment. In this regard, a number of outbreaks have been related to heavy rain falls

in various rural locations including India, Salvador, Nicaraguan, Philippines, Peru and Argentina (Ma, 2004; Vanasco et al., 2008). Additionally, leptospirosis was documented after the hurricane in Puerto Rico in 1996 (Zavistanou and Babastikou, 2008). In livestock, leptospire have been evidenced not only in the urine but also in semen and vaginal discharges, characterizing a reproductive disorder among animals (Lilenbaum et al., 2008).

Leptospire require special conditions for their development. They are able to survive in alkaline soil, mud, swamps, streams, rivers, organs and tissues of live or dead animals and diluted milk. Survival of pathogenic leptospire in the environment is dependent on several factors including pH, temperature and the presence of inhibitory compound. The microorganism survives in the environment if mean temperature remains at about 22°C year round and the fluctuations are not more than 5°C (Melo et al., 2010). In general, they are sensitive to dryness, heat, acids and basic disinfectants (Adler & Moctezuma, 2010). Natural hosts are disseminating the agent in nature through their urine (Lucheis and Ferreira, 2011), because leptospire remain and multiply in the kidney tissue for long time and in some instances for the life of the host (Zayitsanou and Babatsikou, 2008).

### 2.2.1. Host

#### Maintenance hosts

An animal infected with a host-adapted serovar of the organism is a maintenance or reservoir host. Each serovar is adapted to a particular maintenance host, although they may cause disease in any mammalian species. A serovar behaves

differently within its maintenance host species and incidental or accidental hosts (Radostits et al., 2006). The disease is maintained in nature by chronic infection of the renal tubules of these maintenance hosts (Levett et al., 2005). Maintenance host is characterized by high susceptibility to infection, endemic transmission within the host species, relatively low pathogenicity for its host, tendency to cause chronic rather than acute disease, producing insidious economic loss through reproductive losses, persistence of the serovar in the kidney and sometimes the genital tract, low antibody response to infection and low efficacy of vaccination in prevention of infection. Examples of this relationship are serovar Bratislava in swine and serovar hardjo bovis in cattle (Radostits et al., 2006).

The primary reservoir hosts for most *Leptospira* serovars are wild mammals, particularly rodents and Reservoir hosts among domestic animals includes cattle, dogs, sheep and pigs and they may act as carriers for several months (temporary carrier) while rodents usually remain carrier throughout their life (permanent carrier). Rodents are therefore considered as the major reservoir of infection (Tilahun et al., 2013).

#### Accidental (incidental) hosts

Exposure of susceptible animals to non-host-adapted serovars results in accidental or incidental disease. Incidental host is characterized by relatively low susceptibility to infection but high pathogenicity for the host, a tendency to cause acute and severe rather than chronic disease. An example of this relationship is infection by serovar Pomona in cattle which is pig adapted serovar (Radostits et al., 2006). Humans are incidental hosts for *Leptospira* species (Ko et al., 2009).

**Table 2:** Maintenance and incidental hosts for important serovars of *L. interrogans*

Serovar	Maintenance host	Incidental host
<i>L. bratislava</i>	Pig	Horse, dog
<i>L. canicola</i>	Dog	Pig, cattle
<i>L. graphityphosa</i>	Rodent	Cattle, pig, horse, dog
<i>L. hardjo</i>	Cattle	Human
<i>L. interohemorrhagie</i>	Brown cat	Domestic animals and human
<i>L. pomona</i>	Pig, cattle	Sheep, horse, dogs

Source: Fentahun and Alemayehu, 2012.

### 2.2.2. Risk factors

#### Host and management risk factors

Animals of all age groups can be affected by leptospirosis, but young animals are affected more often and with higher morbidity (Radostits et al., 2006). Although leptospirosis virtually occur in all mammalian species, it occur commonly in cattle, sheep, goats, dogs, horses and pigs, but illness seems to be rare in

cats (Levett et al., 2005). Certain management factors that pose risks of infection are infected animal introduced into herds, co-grazing or common grazing with infected ones, access to contaminated water supplies such as streams, rivers, flood or drainage water and purchasing or loan of infected male animals for natural insemination (Radostits et al., 2006).



Figure 2: Reservoir host contaminating the environment Source: Cárdenas et al., 2018;  
Source: Miller et al., 2011 Pathogen risk factors

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 (Fentahun and Alemayehu, 2012). 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 for both hematogenous spread and localization in target organs, such as liver and kidney (Meites et al., 2004). A cytotoxic glycolipoprotein fraction is shown to inhibit

hosts ATPase with the activity ascribed to the presence of long chain fatty acid L. pomona in cattle causes intravascular haemolysis due to hemolytic exotoxin (Craig et al., 2006).

### 2.3. Modes of Transmission

The core determinants of transmission of leptospiral infection are the presence of carrier animals, suitability of the environment for the survival of leptospirae and interaction between man, animals and environment. Various environmental factors such as poor sanitation, water stagnation, climatic conditions, reservoir and carrier animal population like rodents in a particular region influence the survivability of leptospirae in soil and favour transmission of the disease (Nally et al., 2016; Barragan et al., 2017). The infecting agent is transmitted from one animal carrier to another via direct or indirect contact with urine or other body fluids that contain viable leptospirae (Bryan et al., 2011).

Direct transmission occurs via oronasal exposure with infected urine, venereal or

placental transfer, bite wounds, or ingestion of infected tissues. Leptospire contact with mucous membranes and abraded skin can also be a method of transmission (Thayaparan et al., 2013). Indirect transmission, a very common form of transmission, occurs via handling infected animal tissues, exposure to contaminated sources of water, for example ponds, rivers and water catchment tanks, as well as soil, food (Colegrove et al., 2005). The usual method of transmission of the leptospirae is via the urine. They can survive up to six hours in urine. Moist soil, ponds or slow moving streams with a temperature of 22°C can keep them viable for several weeks. Infected milk and semen of an infected bull may contain leptospirae, so transmission through milk and natural breeding or artificial insemination can occur but it is uncommon. Aborted fetuses from a known infected animal can be a source of infection although most attempts at isolation of the leptospirae fail in such cases (Fentahun & Alemayehu, 2012).

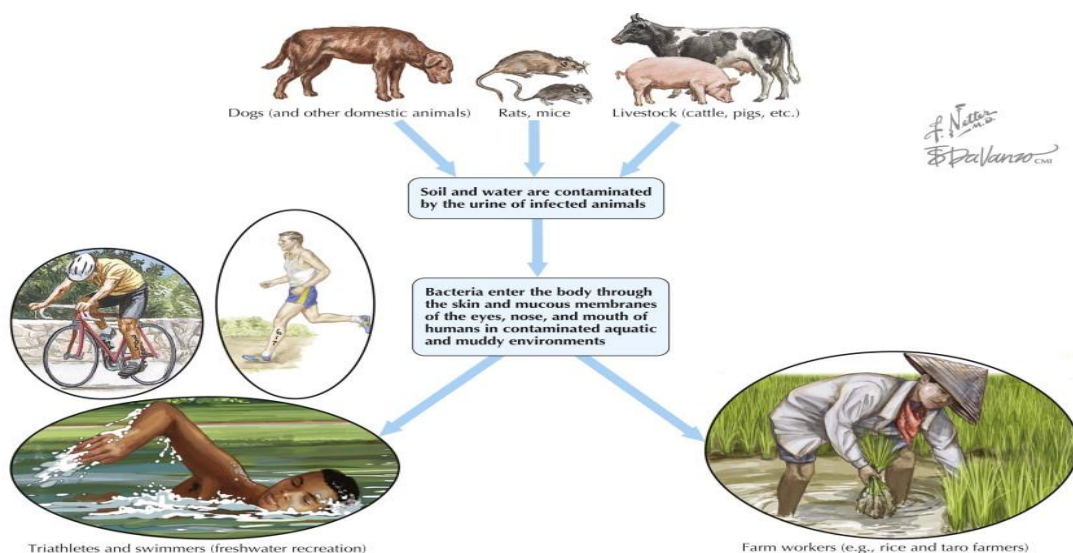


Figure 3: Ways of transmission of Leptospirosis

Source: Keystone et al., 2012

### 2.4. Pathogenesis

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 extent of internal organ damage is available depending on the virulence of the organism and host susceptibility (Craig et al., 2006).

There are three possible pathways after the systemic circulation. If the animal has a high and adequate antibody titer the body will be cleared from leptospirae and no clinical signs can be seen. Animal with a moderate antibody can present with a mild or short leptospiremia followed by mild clinical signs. Leptospirae are then eliminated through the kidneys and after the elimination the animal will not continue to shed leptospirae. If the animal has a low or absent antibody titer there will be a multiplication of leptospirae in the bloodstream (Goldstein, 2010).

The endothelium will be damaged which can cause ischemia in different organs such as the kidneys (renal tubular necrosis), liver (hepatocellular damage) or lungs. Neutrophils and thrombocytes are stimulated by lipopolysaccharides (LPS) in the outer membrane of the leptospirae and this contributes to inflammation and coagulatory abnormalities. The LPS can contribute to the renal and hepatic damage. Meningitis can develop if the leptospirae enter the nervous

system or cerebral spinal fluid in the acute phase of the disease. If bacteria persist despite the antibody response, then immune-complex-mediated meningitis can occur. When this phenomenon occurs in the eyes it causes uveitis (Adler & Moctezuma, 2010).

The incubation period of leptospirosis depends on dose, infectious strain and host but is averagedly between 7-14 days (Sykes et al., 2011). According to (Levett et al., 2005) antibodies become detectable 5-7 days after infection. It takes about two weeks for the leptospirae to reach the proximal tubular cells and the tubular lumen in the kidneys. In the best case scenario, the antibodies will clear the blood and tissues from leptospirae. The bacteria can also become eliminated from the kidneys and no leptospirae will thus be shed in the urine. In some animals, despite an increased antibody titer, the bacteria can replicate and persist in the renal tubular cells. This may result in chronic shedding of leptospirae in the urine for days to months, even years (Azocar et al., 2014).

The invasive capacity of leptospirae may be related to their pathogenicity because non pathogenic leptospirae do not penetrate cells as deadly as pathogenic leptospirae (Craig et al., 2006).

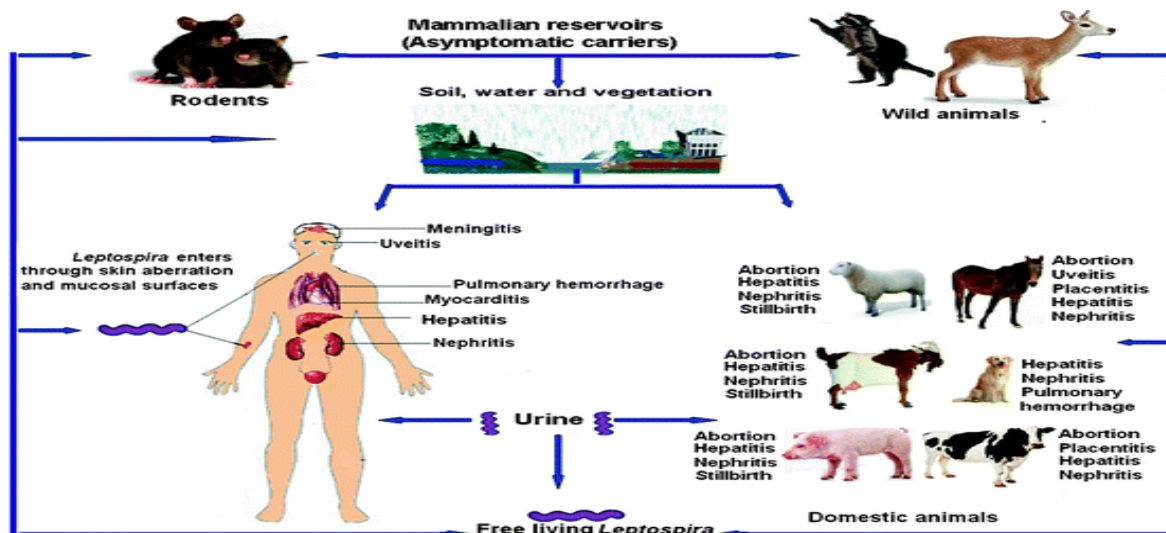


Figure 4: *Leptospira* invasion, pathogenesis and persistence

Source: Yan et al., 2009

## 2.5. Status of Leptospirosis in Ethiopia

In Ethiopia leptospirosis is a relatively unknown disease although already reported to occur in domestic animals. However, climatologic, socio-economic and cultural factors, playing an important role in the prevalence and spread of leptospirosis, are highly prevalent in Ethiopia. Leptospirosis in Ethiopia is currently underreported due to unawareness and the actual prevalence is expected to be high. It is a disease of tropical countries and often is endemic, although in Ethiopia its prevalence in humans is totally unknown and there is no documented evidence on its occurrence (Martin and Lilenbaum, 2014).

High prevalence of leptospirosis was observed in Wonji which could be due to the tropical climate, repeated contact of the population with stagnant water and mud especially with the water that is being used for irrigating the sugarcane plantation, lack of hygiene and poor living conditions (Annual Report, 2002/2003). According to Eshetu et al. (2004), from a total of 59 febrile patients attending the outpatient department of Wonji Hospital, 47.46% of them were positive for leptospirosis and the occurrence of the disease was more common in males than females.

In Ethiopia, leptospiral antibodies were detected four decades ago in domestic animals with incidences of 91.2% in horses, 70.7% in cows, 57.1% in pigs, 47.3% in goats, 43.4% in sheep, 15.4% in camels and 8.3% in dogs using a microscopic agglutination test (Martin and Lilenbaum, 2014). However; there is little recent information about animal leptospirosis.

According to Tsegaye et al. (2016), a total of 184 out of 418 horses had antibody titres of at least one of 16 serovars, demonstrating the presence of 16 serovars of *Leptospira* species in central and southern Ethiopian horses. This means, 44% of the sampled horses were seropositive to at least one serovar. The first human leptospirosis in Ethiopia was reported from Wonji hospital, central Ethiopia, where 47.5% of febrile patients ( $n = 59$ ) were positive for leptospiral infection (Yimer et al., 2004).

## 2.6. Clinical Signs of Leptospirosis in Animals

The clinical findings in leptospirosis are similar in each animal species and do not vary greatly with the species of leptospirae except that of infection with *L. interrogans* usually causes severe septicemia (Colagross et al., 2002).

In animals, the clinical signs of leptospirosis are often related to kidney disease, liver disease or

reproductive dysfunction. Leptospirosis is characterized by a broad range of clinical symptoms in livestock with minor difference between species affected: acute, subacute or chronic. Clinical signs of acute or sub-acute disease are observed in the leptospiremic phase and it is characterized by septicemia, high fever and anorexia, petechiation of mucosa, depression and acute hemolytic anemia with hemoglobinuria, jaundice and pallor of the mucosa. The sub acute form of leptospirosis differs from the acute form only in degree. Fever is mild and hemoglobinuria is common but jaundice may or may not be present (Radostits et al., 2007; Adler and Moctezuma, 2010).

Clinical signs related to chronic infections in livestock are usually associated with reproductive losses through abortion, stillbirth, infertility and mastitis and milk drop syndrome. Abortion usually occurs during the last trimester of pregnancy. Infertility and milk drop occurs only in pregnant or lactating cows because *Leptospira* organisms prefer pregnant uterus and lactating mammary gland to proliferate (Radostits, 2006). 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 cow's milk production will return to normal within 1-14 days (Fentahun & Alemayehu, 2012).

Infections in goats and sheep can be severe or subclinical and may manifest as reproductive problems such as infertility, abortion and stillbirth (Zacarias et al., 2008). In various studies anorexia, lethargy and vomiting were the three most common clinical signs in dogs with leptospirosis. Weight loss, polyuria, diarrhea, abdominal or lumbar pain, musculoskeletal pain and dehydration were also common (Greenlee et al., 2004).

The clinical features of equine leptospirosis are essentially similar to those observed in other animals, such as cattle, with low-grade fever, listlessness and anorexia the most common presentation in milder disease. In more severe forms of disease, a range of typical signs may occur, including conjunctival suffusion, jaundice, anemia, petechial hemorrhages on the mucosa and general depression. Renal failure may also occur, especially in foals. Infection of pregnant mares can result in placentitis, abortion and stillbirths (Verma et al., 2013).



Figure 5: Abortion in dairy cow due to *Leptospira*  
Source: Anwar et al., 2013

## 2.7. Necropsy Findings

Leptospirosis is characterized by the development of vasculitis, endothelial damage and inflammatory infiltrates composed of monocytes, plasma cells, histiocytes and neutrophils. On gross examination, petechial hemorrhages are common and organs are often discolored due to the degree of icterus (Levett et al., 2005). The histopathology is most marked in the liver, kidneys, heart and lungs but other organs may also be affected according to the severity of the individual infection. The overall structure of the liver is not significantly disrupted, but intra hepatic cholestasis, Hypertrophy and hyperplasia of Kupffer cells is evident while in the kidneys, interstitial nephritis is the major finding accompanied by an intense cellular infiltration composed of neutrophils and monocytes. Leptospire can be seen within the renal tubules (Radostits et al., 2006).

By electron microscopy, the tubular cell brush borders are denuded, the tubular basement membrane is thickened and tubular cells exhibit mitochondrial depletion (In addition, minor changes are seen in the glomeruli), suggesting an anatomical basis for proteinuria in leptospirosis. Pathological findings in the heart include interstitial myocarditis with infiltration of predominantly lymphocytes and plasma cells, petechial hemorrhages (particularly in the epicardium), mononuclear infiltration in the epicardium, pericardial effusions and coronary arteritis. In the lungs, pulmonary congestion and hemorrhage are common while perivascular cuffing and vascular lesions in the meninges are observed in the brain (Levett et al., 2005).

## 2.8. Diagnosis

The diagnosis of leptospirosis is made using a combination of epidemiologic information, clinical findings, serology and cultures (Ahmad et al., 2005). Serologic tests include the

macroscopic slide test, complement fixation test (CFT), micro agglutination test (MAT) and enzyme linked immune sorbent assay (ELISA). The CFT, macroscopic slide test and ELISA are genus specific and are useful for screening sera and detecting IgM levels. It can be complex and involves direct and indirect diagnostic tests. Indirect tests detect anti-leptospiral antibodies while direct ones investigate antigens or nucleic acids of leptospirae in animal tissues or body fluid. The choice of the test depends on the animal species (herd or individual test) and the method available in the region (Lucheis and Ferreira, 2011).

In the acute phase, during the febrile period, leptospirae can be found in blood, lymph, urine, semen, milk and cerebrospinal, thoracic and peritoneal fluid, as well as in fragments of organs collected during necropsy (liver, kidney and lung) and in miscarriage products, such as the fetus and placenta (Segura et al., 2005; Aguiar et al., 2006).

### 2.8.1. 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 artifacts similar to *Leptospira* organisms, therefore, low speed centrifugation clears the entering 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 (Regmi et al., 2017).

### 2.8.2. Animal inoculation

A sensitive technique for the isolation of *Leptospira* consists of the intra peritoneal inoculation of young guinea pig with fresh plasma or urine, within few days spirochetes

become demonstrated in the peritoneal cavity. The animals should be examined twice daily and a drop of peritoneal fluid can be examined with dark field microscopy for active leprospirae from the third to the seventh day (Sharma and Yadav, 2008). On the death of the animal haemorrhagic lesions with spirochetes are found in many organs (Fentahun and Alemayehu, 2012).

### 2.8.3. Serology

Macroscopic and microscopic agglutination tests, complement fixation test and ELISA technique are used for the detection of leprospirae in serum. The macroscopic agglutination examination is a screening test and uses dead Ag but suffers from specificity. The microscopic agglutination test (MAT) is the most commonly used serological test for the diagnosis of leptospirosis. In animals which survive infection, *Leptospira* can be readily diagnosed on the bases of demonstrating rising antibody titer in acute or convalescent sera (Subharat et al., 2011).

MAT is particularly useful 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 (Radostits et al., 2007). The ELISA test is much more accurate than other tests and has much advantage from point of view of laboratory practices. 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 (Hirsh et al., 2004).

### 2.8.4. 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 at ante

or post mortem. Several primary pairs for PCR detection of *Leptospira* have been described; some are based on specific gene targets such as 16s to 23s ribosomal genes or repetitive elements while others have been constructed from genomic libraries (Bharti et al., 2003).

### 2.8.5. Culture

*Leptospira* organisms could be isolated from body fluids, mainly urine. Nevertheless, tissue from dead animals is giving a greater opportunity of a successful isolation, if target tissue is not autolyzed. Such target tissue is kidney, liver, lungs and brain. If the agent is suspect for abortions, isolation could be attempted from non-autolyzed abortion materials or tissue samples from a freshly aborted fetus. Isolation of the microorganism from fetal tissue (kidney, liver, lungs) confirms maternal infection (Adler & Moctezuma, 2010). Isolation requires expensive and properly prepared and kept culture media. Inoculated media are incubated at 28-30 °C for several weeks or months. Cultures are incubated in dark and quite environment. Time of incubation depends on the serovar. Serovars such as Pomona and Grippotyphosa require the least time incubation up to 10 days. Regardless of time required for isolation, the inoculated culture media must be protected from contamination, thus require the addition of antimicrobial agents selected to inhibit growth of contaminants (Ko et al., 2009).

### 2.9. Treatment

Treatment with effective antibiotics should be initiated as soon as the diagnosis of leptospirosis is suspected and preferably before the fifth day after the onset of illness. Clinicians should never wait for the results of laboratory tests before starting treatment with antibiotics because serological tests do not become positive until about a week after the onset of illness. Antibiotics to treat leptospirosis include penicillin G and

Doxycycline. In more severe cases cefotaxime or ceftriaxone should be preferred (Ressner et al., 2008).

Antibiotics are used to reduce fever & bacteria within the bloodstream thus rapidly reduce fatal complications of infection such as liver or kidney failure. Glucose and salt solution infusions may be administered (Devishree, 2015).

#### 2.10. Control and Prevention

Important control measures include control of livestock infection with good sanitation, immunization and proper veterinary care. Prevention of leptospirosis involves elimination of the carrier state, control of rodents in kennels, maintenance of environmental condition to discourage bacterial survival and isolation of infected animal and is characterized by sanitary control and decrease in the risk of infection occurring due to contact with contaminated environments, infected wild animals as well as with synanthropic animals and rodents (Tilahun et al., 2013).

Draining or fencing of stagnant water may reduce 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. 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 (Vijayachari et al., 2008).

Vaccines are available for use in cattle, dogs, and pigs. These vaccines offer serovar-specific protection from leptospirosis on a short-term basis, approximately 1 year (Hartskeerl et al., 2011). For livestock, multiple vaccines exist against various serovars and are available for those most commonly found in each country. For example, a pentavalent vaccine is available

for the serovars Pomona, Grippotyphosa, Canicola, Icterohaemorrhagiae, and Hardjo in Canada and the United States (Divers, 2016). There are currently two vaccines available for dogs, one containing the serovars Icterohaemorrhagiae and Canicola, and the other, Icterohaemorrhagiae, Canicola, Grippotyphosa, and Pomona (Sykes et al., 2011).

To date various types of vaccines have been experimentally considered as good candidates for effectively preventing infection, or at least clinical disease (Wang and Wegrzyn, 2007). Recombinant, lipopolysaccharide, DNA and inactivated - attenuated vaccines have been experimentally tested with various results on effectiveness and safety among animals. Those widely investigated for use in animals are attenuated and inactivated vaccines, but the protection conferred by them is partial, due to lack of cross immunity among serovars (Eslabao et al., 2010). Leptospirosis in domestic animals can be controlled through vaccination with inactivated whole cells or an outer membrane preparation (Palaniappan et al., 2007).

#### 2.11. Public Health Significance of Leptospirosis

Leptospirosis continues to be an important health hazard with concomitant economic burden, especially among rural dwellers in tropical regions of the world (Wasiński and Dutkiewicz, 2013; De Vries et al., 2014).

Leptospirosis is a serious zoonotic disease with significant public health implications due to its potential for severe complications and high mortality rates in both humans and animals. The disease affects risk groups that are exposed to animal reservoirs or contaminated environments, such as abattoir and sewage workers, salver workers, coal mines, plumbers, farm workers, veterinarians, pet shop owners, meat handlers, military personnel, slaughter house workers and workers in fishing

industry (Monohan et al., 2009).

The majority of the important reservoirs of leptospirosis are small mammals such as rodents; however, large herbivores are also seen as important sources of infection (Ellis, 2015). The majority of the reservoir hosts do not exhibit any clinical sign of the disease. These reservoirs can act as a source of infection to humans and other domestic animals that may in turn transmit the infection to humans and other susceptible animals (Agampodi et al., 2013).

Rodents are widely considered the most important transmission sources of leptospirosis (Adler & Moctezuma, 2010). Two of the rat species that predominate dwelling in close proximity to humans are the *Rattus* and *Rattus norvegicus*. Both of them have been described as the main reservoir of pathogenic *Leptospira* species (Loan et al., 2015). In addition, other mammals like dogs, cattle and pigs have all been incriminated as maintenance hosts of the bacteria, whereby they become infected, recover from the disease, but the bacteria

persist in their kidneys and are shed continuously (Goarant, 2016).

Contact with various species of animals, animal tissue, animal urine and wet environment and occupational and recreational exposure to contaminated water bodies have been implicated as risk factors (Radostits, 2006). Leptospirosis has been recognized as a re-emerging global public health problem due to the increased incidence in both developing and developed countries (Vijayachari et al., 2008). In the developed world, the incidence of the disease has come down substantially and most cases that occur now are associated with recreational exposure to the contaminated water. Contrastingly, the incidence appears to be increasing in developing countries (Tangkanakul et al., 2005). According to Pavli and Maltezou, 2008, Men are more frequently diagnosed with leptospirosis compared with women and this has been traditionally attributed to the over representation of men in high-risk occupations.

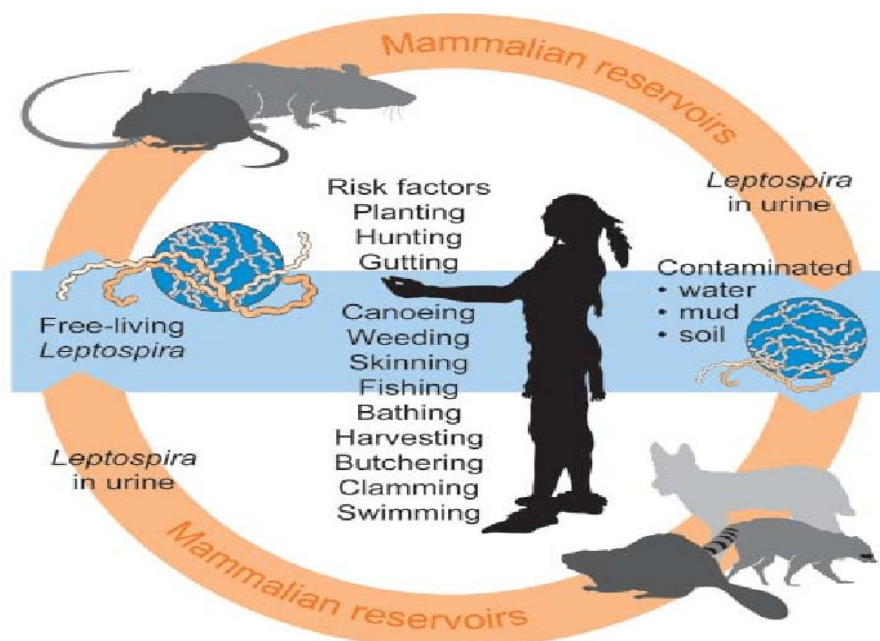


Figure 6: Risk factors for human  
Source: Van et al., 2017

### 3. CONCLUSION AND RECOMMENDATIONS

Leptospirosis has been known to affect both man and numerous mammalian species worldwide resulting in morbidity and mortality. Infection in domestic animals and wildlife can lead to economic loss and pose a potential spread to the communities. The disease can be directly transmitted through contact with secretions, blood or urine of infected animals, or indirectly through water contaminated mainly with urine of reservoir animals. In tropical areas where people and animals live in close contact, and warm and humid conditions favor environmental survival and transmission of the pathogen.

Based on the above conclusion the following recommendations were forwarded;

- Public education on the transmission and

source of infection of the disease need to be under taken.

- Strict movement control of animal from one area to another in order to prevent the spread and transmission of the disease from infected cattle to the non-infected ones.
- Important control measures including control of livestock infection with good sanitation, immunization, and proper veterinary care should be taken.
- Elimination of the carrier state, control of rodents in kennels, maintenance of environmental condition to discourage bacterial survival and isolation of infected animal need to be under taken in order to prevent the disease.

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