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Global Epidemiological Overview of Leptospirosis

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Abstract: Leptospirosis is an infectious disease caused by *leptospira* species, which has over 20 serogroups and more than 250 serovars and distributed worldwide. wild mammals particularly, rodents are the primary reservoir of the infection where as domestic animals such as cattle, dogs and pigs 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. Leptospirae are excreted in the urine of the animals and they affect man when he comes into contact with urine of infected animals, directly or indirectly, when he is exposed to an environment contaminated by the urine of the infected animals such as soil and surface water. It has a considerable public health and economic impact. Primarily, leptospirosis is an occupational disease affecting many labourers (like: Veterinarians, rice field workers, farmers, sugarcane cutters, fishermen, meat-and sewer workers) in their productive age. Apart from the costs of treatment, this generates economic losses by a decreased income both at the personal and national level. There is an enormous economic impact on the international trade of animals and semen. Economic losses are also caused by cost for treatment and control and by reduced milk yields and reproductive failures. The diagnosis of this disease in man and animals is investigated by direct and indirect laboratory methods. Direct methods includes immunofluorescence staining, immunoperoxidase staining, silver staining and various methods of Polymerase Chain Reaction; while the indirect methods includes various types of ELISA tests, the spot agglutination test or methods reliably identifying the infecting serovars, such as the microscopic agglutination test. Human leptospirosis can be controlled by reducing its prevalence in wild and domestic animals. Leptospirosis in domestic animals can be controlled through vaccination with inactivated whole cells. Sanitation and control of rodents are also important for prevention and control. The reported prevalence values of animal infection across the world are between 2 and 46% depending on the animal species.

Key words: Epidemiology · Leptospirosis · Rodents · Urine of infected animals Zoonoses

INTRODUCTION

Leptospirosis is an important zoonotic disease caused by the infection with spiral-shaped bacteria known as *Leptospira* species. The disease occurs worldwide, but it is most common in temperate regions in the late summer and early fall and in tropical regions during rainy seasons [1]. The global burden of disease is unknown because of the paucity of data, but incidence estimates range from 0.1 to 1/100,000/year in temperate areas, to over 100/100,000/ year during epidemics in the tropics. An estimated 300,000 to 500,000 severe cases occur each year, with case fatality reports of up to 30% [2, 3]. Although the incidence of the disease seems to have decreased in developed countries, it is apparently emerging rapidly as a significant public health problem in developing countries. Some of the countries where leptospirosis is under surveillance have recorded this increase in incidence [4]. Most of the countries in South East Asia are endemic to leptospirosis. A number of outbreaks have occurred during the past few years in various places such as Nicaragua, Salvador and Rio de Janeiro in Brazil and Orissa, Mumbai and Andaman Islands in India and in the United States [5, 6].

Leptospirosis has been known to affect both man and animal 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

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through contact with secretions, blood or urine of infected animals, or indirectly through water contaminated mainly with urine of reservoir animals [7]. Several domestic and wild animals get infected, thus becoming renal carriers and shedding the pathogen through their urine [8]. Evidence of *Leptospira* species reservoir state has been demonstrated in all researched mammals and this fact is a central component on the persistence and epidemiology of leptospirosis [9].

Leptospirosis can occur in both urban and rural areas. In urban areas of developing countries, a contaminated environment due to various factors such as overcrowded slums, inadequate drainage and sanitation facilities for man and animals, presence of stray dogs, cattle, pigs, domestic rats and bandicoots, poor condition of slaughter houses and people walking bare foot contribute to the spread of the illness. In rural areas, high-risk groups are workers in rice fields, cane fields and other agricultural crops and animal husbandry staff. History of animal contact is not essential for diagnosis for leptospirosis in developing countries. It is impossible to trace the source of infection and any person can be infected, irrespective of direct contact with animals, due to contaminated environment [1]. Rural habitants are always under higher risk, especially in tropical climates where they are in close contact with potentially infected domestic and wild rodents in humid conditions [10].

In a highly globalized world, where boundaries are continually crossed due to different international activities, tropical diseases including leptospirosis have emerged as significant causes of morbidity and mortality. Concerning a disease that still requires further research, it is necessary to emphasize that study on the epidemiology and patterns of its global incidence may improve prevention practices. Hence the objective of this seminar paper was to highlight the current knowledge and give an overview on the epidemiology of leptospirosis.

Epidemiology

Etiology: Leptospirosis is caused by *Leptospira* species when 20 serogroups subdivided into at least 250 serovars (serologic varieties) [7]. The bacteria are highly motile, thin, flexible and filamentous, made up of fine spirals with hook-shaped ends. Motility is gained by writhing and flexing movements while rotating along the long axis. The bacterium is an obligate aerobic spirochete that share features of both Gram-negative and Gram-positive bacteria. Many classification methods have been used to divide up the pathogenic leptospirae into more workable groups and the pathogenic serovars are found in the species *Leptospira interrogans*, *L. noguchii*, *L. santarosai*, *L. meyeri*, *L. borgpetersenii*, *L. kirschneri*, *L. weilii*, *L. inadai*, *L. fainei* and *L. alexanderi* [11]. An antigenic classification scheme used in the past has divided them into distinct serogroups based on surface antigens, each containing one or more serovar. Newer classification schemes are based on genetic methodologies [9].

The leptospiral genome consists of two circular chromosomes [12] and the genome is large compared with the genomes of other spirochetes such as *Treponema* species [13] which indicates the ability of *Leptospira* species to live within diverse environments like in animal hosts and freely in the environment.

Occurrence: Leptospirosis is a global disease that may occur wherever the risk of direct or indirect exposure to urine or kidneys of infected animals is present [10]. 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 [9]. But spread is more in tropical regions than in temperate countries [14, 15]. This is attributed mainly to longer survival of leptospirae in warm and humid environments. Hence, China, Southeast Asia, Africa and South and Central America have immense areas where the disease is endemic. Leptospirosis occurs sporadically throughout the year in these areas, with a peak seasonal incidence in summer. Large epidemics are reported after monsoons and periods of unusually heavy rainfall. India, Kerala, Tamil Nadu and Andamans are endemic for leptospirosis. But now with better facilities to detect the disease, the disease is being reported from almost all parts of India [16-18]. Table 1 show the incidence of leptospirosis in humans in selected high-risk countries according to the data availability.

Hosts: All mammals appear to be susceptible to at least one species of *Leptospira.* The primary reservoir hosts for most *Leptospira* serovars are wild mammals, particularly rodents. 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 [32]. The specific reservoir hosts vary with the serovar and the geographic region. Disease in reservoir hosts is more likely to be asymptomatic, mild or chronic [11].

Table 1: Selected regions with reports on leptospirosis incidence in humans

Country or region	Incidence/100,000/year	References
Seychelles	101	Yersin *et al.* [19]
Andaman Islands	50	Pappas *et al.* [20]
Guadeloupe, French West Indies	41	Storck *et al*. [21]
Kerala, India	11.4	Mendhekar [22]
China	7.1	Victoriano *et al.* [23]
Thailand	4.1-40	Myint *et al.* [24]
Sri Lanka	11	Agampodi *et al.* [25]
French Polynesia	11	Pappas *et al*. [20]
Portugal, Azores Islands	11	Vieira *et al.* [26]
Cambodia	7.7	Seng *et al*. [27]
Costa Rica	6.7	Pappas *et al.* [20]
Hawaii	3.3	Ellis *et al*. [28]
Cuba	2.5	Pappas *et al.* [20]
Argentina	1.0	Pappas *et al.* [20]
Italy	0.13	Ciceroni *et al.* [29]
Germany	0.06	Jansen *et al.* [30]
Israel	0.05	Kariv *et al.* [31]

Risk Groups: Leptospirosis affects professionals that are constantly in contact with animals and their residues, especially reservoirs [33]. The epidemiology of the disease is dynamic. New risk groups can be formed as a result of alterations in agricultural and social practices or in the reservoir population [34]. The high risk groups for the disease are veterinarians, those working in animal husbandry or meat processing, wastewater treatment employees and military troops [35]. In recreational settings, leptospirosis is a hazard for those who come into direct contact with contaminated water such as travellers to tropical countries (e.g., ecotourism), campers, hikers, swimmers and hunters [1, 35]. Consequently, with the increased popularity of adventure racing, a growing population of susceptible individuals has emerged.

Sources of Infection and Transmission: Leptospirosis can be transmitted either directly between hosts or indirectly in the environment. *Leptospira* species can be ingested in contaminated food or water, spread in aerosolized urine or water, or transmitted by direct contact with the skin. The organisms usually enter the body through mucous membranes or abraded skin. They may also be able to penetrate intact skin that has been immersed for a long time in water. *Leptospira* species are excreted in the urine and can be found in aborted or stillborn fetuses, as well as in normal fetuses or vaginal discharges after calving. They can be isolated from the male reproductive organs. Human cases have also been transmitted during sexual intercourse, by breast feeding, from rodent bites and after laboratory accidents [36, 37].

Leptospira species do not multiply outside the host. In the environment, they require high humidity for survival and are killed by dehydration or temperatures greater than 50°C. They can remain viable for a few to many weeks or months in contaminated soil and for several weeks in cattle slurry. They can remain viable in water for several months under laboratory conditions, but do not survive as well in river water under natural conditions [38].

Clinical Signs: In humans, the incubation period of leptospirosis ranges from 2 to 21 days with a mean of 10 days. *Leptospira* infections can be asymptomatic or symptomatic depending on host susceptibility and the serovar involved [39]. Of the symptomatic illnesses, 90% are self-limited, flu-like illnesses, but 5-10% of infections can result in multi-organ damage, including liver failure, renal failure and hemorrhagic pneumonitis. Men seem to be more likely to manifest severe disease than women [39]. The classic clinical syndrome has two phases: a septicemic and an immune phase [1]. It is in the immune phase that organ-specific damage and more severe illness is seen. The typical presenting signs of leptospirosis in humans are fever, headache, chills, conjunctival suffusion and myalgia [35]. Less common signs include a biphasic fever, meningitis, photosensitivity, rash and hepatic or renal failure.

In cattle, fever and anorexia occur with rapid decline in milk yield and atypical mastitis; Pregnant cows abort with retention of the placenta. Also, mild jaundice and severe anaemia occur with enlarged and friable liver and swollen kidneys. Hemoglobinuria, dyspnea, meningitis, rapid dehydration and death may also occur. Conjunctivitis and periodic ophthalmia (horse); in pigs subclinical infection is common, though it can cause abortion and birth of weak piglets. In dogs and cats, gastroenteritis, jaundice and nephritis may occur [11, 39].

Diagnosis: Leptospirosis of man and animals is investigated by direct and indirect laboratory methods. Direct methods are the isolation of the causative agent and the identification of *Leptospira* species antigens in tissue and body fluids using such methods like immunofluorescence staining, immunochemistry, immunoperoxidase staining, silver staining and various methods of Polymerase Chain Reaction (PCR) [40, 41]. Direct visualization of leptospirae in blood or urine by dark field microscopic examination has been used for diagnosis. But, artefacts are commonly mistaken for leptospirae and the method has both low sensitivity and

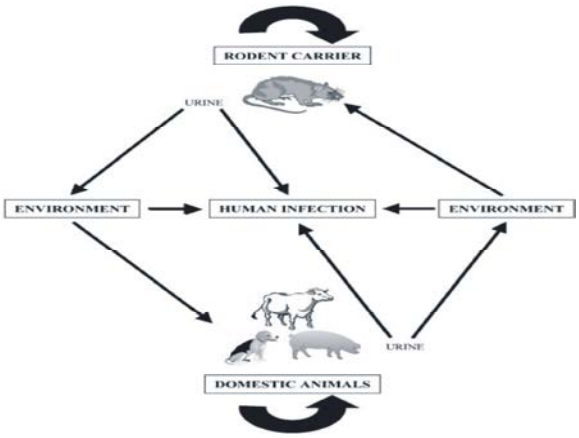

Fig. 1: Transmission cycle of leptospirosis
Source: Alder and Moctezuma [9]

specificity [42]. Several polymerase chain reaction (PCR) assays have been developed for the detection of leptospirae, but few have been evaluated in clinical studies and there have been no multicenter studies of multiple molecular diagnostic methods [43]. The chief advantage of PCR is the prospect of confirming the diagnosis during the early acute (leptospiremic) stage of the illness, before the appearance of immunoglobulin M (IgM) antibodies, when treatment is likely to have the greatest benefit. In fulminating cases, in which death occurs before seroconversion, PCR may be of great diagnostic value [43]. Leptospiral DNA has been amplified from serum, urine, aqueous humour and a number of tissues obtained at autopsy [44]. For early diagnosis, serum is the optimal specimen. Urine from severely ill patients is often highly concentrated and contains significant inhibitory activity.

Leptospirae can be isolated from blood, CSF and peritoneal dialysis fluids during the first 10 days of illness. Specimens should be collected while the patient is febrile and before antibiotic therapy is initiated. One or two drops of blood should be inoculated directly into culture medium at the bedside. Survival of leptospirae in commercial blood culture media for several days has been reported [45]. Urine can be cultured after the first week of illness. Specimens should be collected aseptically into sterile containers without preservatives and must be processed within a short time of collection; best results are obtained when the delay is less than 1 hour, because leptospirae do not survive well in acidic environments [46]. Cultures are performed in albumin-polysorbate media such as EMJH (Ellinghausen-McCullough-Johnson-Harris) medium [46], which is available commercially. Primary cultures are performed in semisolid medium, to which 5-fluorouracil is usually added as a selective agent. Cultures are incubated at 30°C for several weeks, because initial growth may be very slow. Isolated leptospirae are identified to serovar level by traditional serologic methods or by molecular methods, such as pulse field gel electrophoresis [47].

The Indirect methods of investigating leptospirosis are based on the detection of specific serum antibodies. These methods are either methods detecting serum antibodies without discriminating on serovars, such as various ELISA tests, indirect immunofluorescence, the spot agglutination test or methods reliably identifying the infecting serovars, such as the microscopic agglutination test (MAT). Microscopic agglutination test (MAT) is used as the 'gold standard' serological test even though the test is very tedious and requires the maintenance of several leptospiral serovars in the laboratory. Also the test requires the expertise personnel to read the results [48]. IgM ELISA test is, rapid and easy to perform which is popularly done for the diagnosis of acute leptospirosis. However, with the exception of isolation, none of the currently available diagnostic methods are suitable for studying microbial pathogenicity (structure, products and biochemical characteristics). Isolation is also required for accurately placing the agent into serogroups [49, 50].

Treatment: Antibiotic treatment early in the illness may shorten the duration of fever and hospitalization. Antibiotics used to treat leptospirosis include tetracycline, penicillin/ampicillin, doxycycline, streptomycin and the erythromycin [35]. The efficacy of treatment may depend on the serovar. Fluid therapy, blood transfusions and other supportive care may also be necessary. In beef herds, further abortions may be prevented by vaccination and treatment of all animals with antibiotics, if leptospirosis is diagnosed early during an outbreak. In dairy cattle, only infected animals are usually treated, due to the potential loss of milk sales [51, 52, 35].

Prevention and Control: Human leptospirosis can be controlled by reducing its prevalence in wild and domestic animals. Although little can be done in wild animals, leptospirosis in domestic animals can be controlled through vaccination with inactivated whole cells or an outer membrane preparation [53].

Leptospirosis vaccines are available for pigs, cattle and dogs. Although the vaccines prevent disease, they do not completely prevent infection or the shedding of the organisms. Immunity is largely serovar specific: vaccines are protective only against the included serovars

or closely related serovars. Prophylactic treatment of exposed animals with antibiotics can also prevent disease [11]. Sanitation and the prevention of contact with contaminated environments or infected wildlife, particularly rodents, can decrease the risk of infection or rodent-vector control preferably through the use of slow acting rodenticides and improved hygiene may be some of the measures for diminishing the risk of leptospirosis transmission. Occupational hygiene (in sewers, farmers and other high risk groups) that includes the use of water proof shoes and gloves is fundamental for preventing human leptospirosis [54]. Animals should not be allowed to drink from or enter contaminated bodies of water or since some outbreaks have been associated with drinking of contaminated water, water purification should be implemented. Good sanitation can reduce the risk of infection in kennels and in areas where livestock give birth. Replacement stock should be selected from herds negative for leptospirosis. Animals not known to be *Leptospira*-free should be quarantined for 4 weeks and tested before being added to the herd [11].

Status of Leptospirosis in Ethiopia: Although there is no documented information so far concerning the occurrence of leptospirosis in animals in Ethiopia, climatologic, socioeconomic and other factors are highly favourable for the occurrence and spread of the disease in the country. In the case of human leptospirosis, there is a pilot study in Wonji Hospital. According to Eshetu *et al.* [55], from a total of 59 febrile patients attending the outpatient department of Wonji Hospital, 47.46% of the patients were positive for leptospirosis and the occurrence of the disease was more common in males than females.

Economic Importance: The reported prevalence values of animal infection across the world are between 2 and 46% depending on the animal species [56-58]. Given this wide variation in reported prevalence values and the contributions to the factors such as climate, animal species, time of the year, method of investigation (serovar inclusion in testing), there is not a safe way to calculate the economic impact of the infection among animals.

However, it appears that the disease is of major economic concern when it is involved in the reproductive failure of food producing animals [59]. Infection of the reproductive system could result in a “storm of abortions” causing considerable economic losses from meat and milk reductions [60]. Furthermore, these losses appear as more significant among cattle and pigs, because these animal species are considered less resistant than small ruminants [49].

CONCLUSION AND RECOMMENDATIONS

Leptospirosis is probably the world’s most widespread zoonosis of global importance caused by different *leptospirae* species. It occurs in both developed and developing countries and affects both human and animals. Leptospirae are excreted in the urine of the animals and they affect man when he comes into contact with urine of infected animals, directly or indirectly. Therefore, understanding the epidemiology of this infectious disease is a critical step for designing interventions and consequently diminishing the risk of leptospirosis transmission. Leptospirosis in animals is less well documented, so further study is needed since animal infection is the source of human infections. There is scarce of information regarding to leptospirosis in African countries including Ethiopia, therefore study should be conducted to estimate the prevalence of the disease. Contaminated urine is highly infectious for people and for susceptible animal species; therefore, contact with urine on mucous membranes or skin abrasions should be avoided. When handling infected animals or dealing with areas of contamination, protective gear should be worn such as gloves, eye protection and face masks.

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