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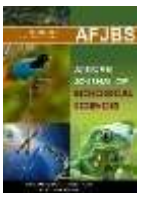

A Brief Review on Seroprevalence of Human Leptospirosis in India

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ABSTRACT

Human leptospirosis is an important health problem. It is mainly an occupational disease. Humans contract the disease mainly from consuming infected food, water and soil contaminated with infected animal's urine. *Leptospira* infection mainly affects the liver and kidney, and spread to other organs. ELISA can be a very helpful diagnostic technique especially in resource-poor settings. Our article provides classification, global burden, transmission, pathophysiology, diagnosis and management of leptospirosis caused by the bacteria *Leptospira*.

Keywords: Seroprevalence, Human leptospirosis, Global burden

Introduction

Leptospirosis is a disease that is transmissible from an animal to a human which is caused by the *Leptospira* spp. In India, Leptospirosis is emerging as an important health problem. It is predominantly an occupational disease, although a contaminated environment puts any individual susceptible to infection[1]. Leptospirosis is an emerging infectious illness that affects both humans and other vertebrates[2].

Leptospirosis is associated with wide distribution across the globe, covering torrid zone, semitropic, and mild temperature regions, and is considered as the infectious disease that is transmitted between species from animals to humans across the world[2]. Leptospires rely heavily on a moist atmosphere to survive. Leptospiral infections in humans are caused by either direct or

indirect ingestion of soil and water contaminated with the urine of diseased animals. Handling infected animals or animal tissue, eating or drinking infected food or water, and inhaling urine droplets are all feasible modes of transmission[3]. Other major characteristics that have been identified in the susceptibility towards this illness include raising animals, excessive rainfall, haphazard growth of cities, and agricultural lifestyle [4].

In several of the South East Asian countries, leptospirosis is endemic[2]. Leptospirosis was initially identified in India in 1931. *Leptospira* infection is known to be one of the main causes of acute fever sickness in Southern, Central, Eastern, and Western regions of India, where many cases have been reported[4]. Puerto Rico, Hawaii, Brazil, India, and Cuba all have outbreaks. Worldwide, it is estimated that there are over a million cases and almost 59,000 deaths per year[5,6].

Humans contract leptospirosis indirectly by contaminated food, water, or soil. *Leptospira* actively enters the bloodstream by wounds, skin abrasions, or mucous membranes and can live for extended periods of time in water or damp soil[7,8]. Leptospirosis mimics common life threatening infections such as dengue[9,10]. Leptospirosis is responsible for various clinical symptoms, from asymptomatic infections to icterohemorrhagic leptospirosis (Weil's Disease), which can result in lethal pulmonary bleeding.

A wide range of clinical signs, including fever, headache, rash, muscular rheumatism, conjunctival suffusion, enlarged liver, icterus, renal failure, inflammation of the linings of the brain (meninges), hyaline membrane disease, and massive hemoptysis, along with co-infections such as dengue, malaria, typhoid, and scrub typhus, make leptospirosis difficult to diagnose[11].

In humans, *Leptospira* infect the host by entering through the abraded skin from where they reach the bloodstream and is responsible for the bacteremia. After entering bloodstream, through circulation, bacteria reach organs and tissues of the host, where they proliferate and spread to the kidneys, liver, spleen, and lungs. On the fifth day after infection, the highest load of *Leptospira* can be detected in the blood[12].

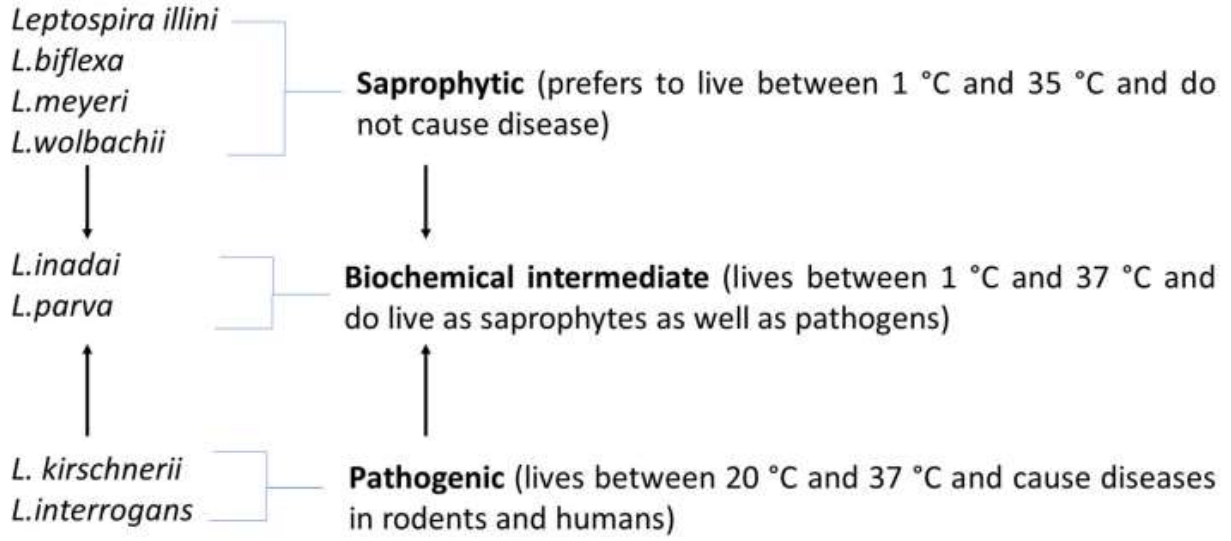
Leptospirosis takes 5-14 days, but it can take up to 30 days to incubate. There are two forms of *Leptospira* infection: icteric and anicteric. After that, there is immune phase, in which the bacteria cannot be found in the blood. Weil's Syndrome, the severe icteric form, involves bleeding disorder, jaundice, and acute renal failure[13,14].

The higher percentage of seropositivity during time may be explained by the monsoon season, which is when the disease was discovered to be the most prevalent. Leptospirosis in humans has not been considered a severe public health concern, despite the fact that the pathogen has been discovered in agricultural animals in northern India. This is most likely because arid climates have low transmission risks. Given that India has seen unusually strong monsoon for 13 years running, environmental changes may be promoting the spread of this organism. Two or more northern Indian cities, Varanasi and Chandigarh, have lately reported rated of *Leptospira* of 8.8% and 21.4%, respectively[15,1]

Classification

Using a mosaic of their lipopolysaccharide (LPS) antigens, surface-exposed epitopes uniquely express themselves to classify leptospires into different serovars. At first, *Leptospira* was solely divided into two species: L. interrogans and L. biflexa, which distinguishes between infective

and non-infective species. Subsequently, the homologous antigens found in these two classifications allowed for further division into distinct serovars (about sixty serovars under L. biflexa and under two hundred & twenty-five serovars under L. interrogans). With over 200 distinct serovars under *Leptospira*, at least 21 more species have been recognized as time goes on. The taxonomy of *Leptospira* is actually much more extensive and sophisticated than it first appears to be. According to the capability of *Leptospira* to cause disease, there are three basic classification of *Leptospira*[16].



Flow Chart 1 - Relationship and the clear distinctions amongst saprophytic, intermediate, and pathogenic *Leptospira*

Global Burden and Epidemiology

Leptospirosis, most commonly occurs in tropical region, accounting for 73% of cases, particularly in South-East Asia, East Sub-Saharan Africa, the Carribean and Oceania[17]. People living in temperate and tropical climes, both in rural and urban regions, are primarily affected by leptospirosis. Numerous investigations have demonstrated that *Leptopsira* causes at least one million cases and almost 60,000 fatalities per year[18]. The global burden of leptospirosis is expected to increase with demographic changes as a result of a rise in the number of urban poor in tropical countries as storms and urban flooding worsen owing to climate change[19]. As the significance of the illness in tropical countries was acknowledged, protocols for the identification and management of leptospires were created. About 15 years ago, the first step to gather global data on the incidence of *Leptospira* infection were published. International Society Survey collects the global data and based on that estimation, the incidence of annual leptospirosis annually was about 350,000 to 500,000. The global burden of leptospirosis was seems to be underestimated due to numerous reasons, and to overcome these, WHO established the

Leptospirosis Burden epidemiology Reference Group (LERG). Five to fourteen instances of endemic and epidemic human *Leptospira* are estimated to occur annually worldwide per 100,000 people, according to the LERG report[19]. In northern India, true incidence of leptospirosis is not known due to lack of diagnostic methods and awareness. Human leptospirosis was reported in Delhi in 1966, a state in northern India[20]. Leptospirosis is an occupational disease primarily in developed countries. Since 1931, leptospirosis, a zoonosis with grave complications and deaths, has been known to exist in India[19,20]. There is not much information about leptospirosis from Delhi region. In India most cases are reported from four major states including Kerala, Gujarat, Tamil Nadu and Maharashtra[21].

Transmission

Leptospire survival is significantly influenced by a moist environment. Leptospiral infections in people are brought on by direct or indirect contact with water or soil tainted by an infected animal's urine. Additional methods of transmission include handling diseased animals or animal tissue, consuming tainted food or drink, and perhaps inhaling urine droplets. Heavy rainfall, animal rearing practices, unplanned urbanization, and an agricultural lifestyle are some significant characteristics that have been linked to an increased risk of contracting this disease[2]. Human leptospirosis presents in a variety of clinical presentations. A modest, self-limiting acute fever disease to a severe, potentially fatal disorder with multiple organ dysfunction can be the range of clinical presentations in humans. There can be varying degrees of impact on various organ system, and a wide range of aberrant symptoms have also been documented. Leptospirosis mimics common life threatening infections such as dengue. Incubation period of leptospirosis ranges from 2-21 days. *Leptospira* disease patterns are biphasic, with an acute or septicemic phase lvsting one week and an immunological phase lasting an additional one week. Infection can be symptomatic and asymptomatic, 90% of the infections are self-limited or flu-like illness and 5-10% infections are results in multi-organ damage[17].

Pathophysiology

In humans, *Leptospira* infect the host by entering through the abraded skin from where they reach the bloodstream and is responsible for the bacteremia. After entering bloodstream, through circulation, bacteria enter the host's organs and tissues, multiplying and spreading throughout the kidneys, liver, spleen, and lungs. On the fifth day after infection, the highest load of *Leptospira* can be detected in the blood[12].

Leptospira causing bleeding disorder by hemolytic and cytotoxic action of hemolysin SphH, protein of *Leptospira* are able to penetrate several mammalian cells to generate, by rupturing the cell wall and resulting in the formation of hemorrhages [22]. Leptospirosis in the liver leads to hepatocyte disarray and disruption of intercellular associations, which culminates in mild increase in SGOT, SGPT, and bilirubinostasis, which generates jaundice.

Bacterium invades the renal tubules in the kidneys, and encourages infiltration of lymphocytes. Acute renal injuries and electrolyte abnormalities, such as hypopotassaemia, excessive loss of sodium in the urine, magnesium deficiency, and sudden reduction in creatinine clearance, are clinical manifestations of kidney damage. The identification of Glucagon like peptide in tissues

demonstrates the significance of this endotoxin in *Leptospira* pathogenesis and pathogenicity.[23,24,25,26,27].

Through clinical trials, the hypokalemia associated with leptospirosis was examined to see whether the patient's inadequate levels of potassium in the blood were caused by potassium recirculating into their cells. Both outside the cell and inside the cell had low amounts based on serum and intraerythrocytic potassium levels[28]. Additionally, it has been observed that individuals suffering with acute renal failure had lower intraerythrocytic potassium levels compared with patients without ARF, which may be correlated with the seriousness of the illness[39].

Diagnosis

There are various methods available for the diagnosis of leptospirosis which includes General clinical laboratory findings, Microscopy, Culture, Molecular methods and, Serological methods. Serological methods can detect this disease after 6th day of disease onset. It can detect serum antibodies by using Microscopic agglutination assay which is a gold standard test for *Leptospira.* Other tests include Lepto dipstick assay and Enzyme-linked immunosorbent assay (ELISA), they both are most commonly used techniques. In leptospiral diagnosis excepting MAT, ELISA and IHA (Indirect hemagglutination assay) have gained popularity over time. ELISA detects IgM antibodies in the patient's serum, MAT is used as a reference test. The advantage of ELISA over MAT is that it does not required the use of live antigens for diagnosis[30]. ELISA can prove to be a very useful diagnostic method especially in resource-limited settings[31].

Management

Understanding the epidemiological features of leptospirosis is crucial to developing treatments that reduce the disease's spread. It can be tough not to come into contact with free-ranging wildlife and domestic animals, which are potential hosts for the *Leptospira* infection, and rodents, raccoons, shunks that are abundant in both rural and urban areas. Therefore, improving the cleanliness of the environment to reduce the possibility of food, water and soil contaminated by the urine of infected animals is necessary. Management of rodents is one therapy strategy to lower the likelihood of leptospirosis transmission. Although, there is little that can be done with wild animals, vaccination can control leptrospirosis in domestic animals with inactivated whole cells or an outer membrane preparation. In order to prevent human leptospirosis, occupational hygiene is pivotal, including protection from contaminated water and soil by wearing waterproof shoes and gloves in sewers and while handling animals, farmers, and other high-risk population. Awareness progrmmes and public education also works[32].

Leptospirosis is prevented by avoiding potential infection and administering pharmacological prophylaxis to high-risk people. Antibiotic treatment early in the disease may reduce the duration of fever and hospitalization. List of antibiotics which can be used in the treatment of *Leptospira* infection are tetracycline, penicillin/ampicillin, doxycycline, streptomycin, and the erythromycin[33]. Sometimes in the artificial insemination centres, Streptomycin is added to the semen of bulls as a preventive measure[32]. It is recommended to start taking 200 mg of Doxycyline once a week before exposure and to keep taking it for the whole period of exposure. There isn't a human vaccine available right now[17].

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