

# Decreasing trend of seroprevalence of leptospirosis at All India Institute of Medical Sciences New Delhi: 2014–2018

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## ABSTRACT

**Background:** Leptospirosis is an important emerging public health problem in India. There is limited information regarding the seroprevalence of leptospirosis in population from northern states of India. This study reports result of a 4-year-retrospective sero-epidemiological survey of leptospirosis conducted in a teaching tertiary care hospital in New Delhi, India. The aim of our study was to explore seroprevalence and clinical pattern of disease occurrence in suspected cases of leptospirosis and to search for any co-existing infections in northern areas such as New Delhi, India. **Methods:** The patients with clinically suspected leptospirosis who attended outpatient or admitted to the Departments of Medicine, Gastroenterology, Pediatrics and Neurology, etc. of our hospital were retrospectively analyzed. The qualitative determination of anti-leptospira-specific immunoglobulin (IgM) antibodies was carried out using commercially available enzyme-linked immunosorbent assay (ELISA) kit (Panbio Diagnostics, Brisbane, Australia). **Results:** Of these 1545 patients, 6.47% (100/1545) were seropositive for anti-leptospira-specific immunoglobulin (IgM) antibodies. Using modified Faine's criteria, a diagnosis of presumptive and possible leptospirosis was made in 79/100 (79%) and 21/100 (21%) patients. Significant declining trend of seroprevalence rate of leptospirosis from 26.90% in 2000–2010 and 20% in 2011–2014 to 6.47% in 2014–2018 ( $P$  value  $<0.05$ ) in our referral tertiary care center. Seventeen patients showed co-infection with other common pathogen prevailing locally. **Conclusion:** There is a need to increase awareness among public and clinicians, however, more region/province-wise studies on seroprevalence of leptospirosis are required to improve our understanding of the actual burden.

**Keywords:** Fever, leptospira, seroprevalence

## Introduction

Leptospirosis is an anthropozoonotic infection caused by the pathogenic *Leptospira* spp.<sup>[1]</sup> It is emerging as important public health problem in India.<sup>[2,3]</sup> Leptospirosis is primarily an occupational disease, but a contaminated environment makes any person vulnerable to infection.<sup>[4]</sup> The disease is responsible for a variety of clinical symptoms ranging from subclinical infections to fatal pulmonary hemorrhage and Weil's syndrome, therefore,

presents challenging scenarios to the clinicians.<sup>[5]</sup> Because of its wide spectrum of clinical symptoms such as fever, headache, myalgia, conjunctival suffusion, rash, hepatosplenomegaly, evidence of hemorrhage, renal failure, icterus, aseptic meningitis, acute respiratory distress syndrome (ARDS), and pulmonary hemorrhage and the co-infections like typhoid, malaria, scrub typhus, and dengue may present diagnostic dilemmas. It is imperative that a high index of suspicion for the diseases is required particularly in endemic areas. Therefore, the diagnosis is based on laboratory tests rather than on clinical symptoms alone. Leptospirosis has been underdiagnosed and underreported in the

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North India due to lack of awareness of the diseases, inadequate epidemiological data, and unavailability of appropriate diagnostic facility in this region. Diagnosis of leptospirosis is primarily based on microscopy and culture of clinical samples such as blood or urine; however, it is time-consuming and requires expertise. Molecular techniques can accurately differentiate the species, have greater sensitivity and specificity than microscopy.<sup>[6]</sup> However, considering their high cost and need for technical expertise these molecular techniques often limits its applications in the routine diagnostics in many resource-limited countries. Serological techniques such as microscopic agglutination test (MAT) and ELISA are helpful in the diagnosis; however, ELISA is the most preferred cost-effective serological method with both sensitivity and specificity of 95%.<sup>[6]</sup> The aim of the present study was to determine the seroprevalence, clinical pattern, and to look for any existing co-infections among suspected cases of leptospirosis attending the referral tertiary care hospital in North India.

## Methods

### Study area, population, and period

The present study was carried out in the Department of Microbiology, All India Institute of Medical Sciences, New Delhi, India. Between the year July 2014 and May 2018, the patients with clinically suspected leptospirosis who attended outpatient or admitted to the Departments of Medicine, Gastroenterology, Pediatrics and Neurology, etc. of our hospital were retrospectively analyzed. Inclusion criteria as laid down in the International Leptospirosis Society (ILS) guidelines were followed.<sup>[7]</sup> Patients who were suspected clinically of leptospirosis and presented with a history of fever for >7 days accompanied with any of the following manifestations i.e., severe headache, severe myalgia, conjunctival suffusion, uveitis, arthralgia, rash, hepatosplenomegaly, evidence of hemorrhage, renal failure, icterus, aseptic meningitis, ARDS, and pulmonary hemorrhage were included in this study. The details of these patients were analyzed as per a well-structured proforma that included the detailed clinical history and laboratory data from the hospital records. Modified Faine's criteria was used for diagnosis of presumptive and possible leptospirosis.<sup>[8]</sup>

### Collection and processing of samples

About 5 ml of venous blood without anticoagulant was collected during the acute phase from all patients taking aseptic measures. Serum was separated as per standard protocol.

### Serological evaluation

The qualitative determination of anti-leptospira-specific immunoglobulin (IgM) antibodies was carried out using commercially available ELISA kit (Panbio Diagnostics, Brisbane, Australia). The ELISA test was performed as per manufacturer's instructions. Serum samples obtained from 25 healthy participants who served as controls, were also analyzed.

In this study, we also looked for co-infections which share some clinical manifestations with leptospirosis were also

investigated. Those specifically looked for are typhoid, malaria, dengue/dengue hemorrhagic fever (DHF), and scrub typhus. Malaria screening included examination of peripheral blood smear with Giemsa staining, Acridine Orange staining under UV light, immunochromatographic test, and the Quantitative Buffy Coat (QBC) assay (QBC Diagnostic Inc., Philipsburg, USA). The Widal test is for typhoid detection. Dengue virus and scrub typhus were diagnosed serologically using commercial ELISA kits (Dengue Duo Cassette, PanBio, France).

### Statistical analysis

The data collected were analyzed using the STATA/SE version 14.0 statistical software (Stata Corp, Texas, USA). Categorical data were described using numbers and percentages. Data generated from the present study have been presented in the form of tables and all descriptive analyses have been shown in percentages. *P* value has been calculated to analyze statistically significance.

## Results

A total of 1545 patients were included in the present study. Of these 1545 patients, 6.47% (100/1545) were seropositive for anti-leptospira-specific immunoglobulin (IgM) antibodies. None of the healthy controls were positive. Among these 100 patients, 80.31% were males and 19.68% were females and the male-to-female ratio was 4.08:1. The results showed that males are at higher risk of being seroreactive than females ( $\chi^2 = 16.5$ ,  $P = 0.00$ ). The age ranged from 2 to 98 years with a mean age of  $40.5 \pm 16.11$  years and median value of 40 years. Of the total 100, 94 (94%) were adults and 6 (6%) were children  $\leq 15$  years of age. Most of the patients were adults followed by children  $\leq 15$  years ( $\chi^2 = 146.1$ ,  $P = 0.00$ ). According to modified Faine's criteria a diagnosis of presumptive and possible leptospirosis was made in 79/100 (79%) and 21/100 (21%) patients. Seasonal variation was noted and seroprevalence rate was highest during the monsoon 52/1545 (52%) (June–September) season, followed by 27/1545 (27%) pre-monsoon (February–May), and 21/1545 (21%) post-monsoon (October–January) season. Results showed that area of residence was statistically associated ( $P < 0.05$ ) with leptospiral seroprevalence, revealing that people living and working in rural areas are at higher risk [odds ratio (OR) = 4.52; confidence interval (CI) = 2.8–6.9] for leptospiral exposure than people living and working in the urban areas. The seroprevalence varied from 2.20 to 0.45% between 2014 and 2018, with a mean of 6.47%. The decreasing trend of seroprevalence was noted from the year 2014 to 2018. The common presenting features were fever in 100 (100%) followed by jaundice in 49 (49%). The commonest complication noted was renal involvement in 30 (30%) followed by neurological (behavioral changes, altered sensorium, and meningitis) in 16 (16%), pulmonary involvement in 11 (11%), and cardiovascular involvement in 2 (2%) [Table 1]. There was clustering of cases in the monsoon season, which further increases the likelihood of co-infections that circulate during these months. The maximum number of co-infections

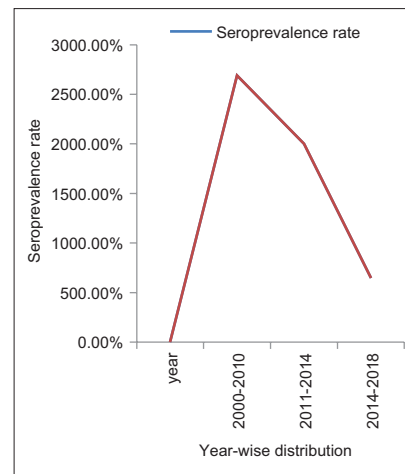
**Table 1: Clinical features of leptospirosis patients**

Symptoms	Patients (%)
Anicteric presentation	
Fever	100
Myalgia	46
Headache	48
Rash	19
Arthritis/arthritis	6
Icteric presentation	
Jaundice	49
Hepatomegaly	36
Splenomegaly	21
Hemorrhage of any kind	27
Others	
Renal involvement	30
Pulmonary involvement	11
Neurological involvement	16
Cardiovascular involvement	2

of leptospirosis was observed with typhoid ( $n = 7$ ) followed by dengue ( $n = 5$ ), scrub typhus ( $n = 4$ ), and malaria ( $n = 1$ ).

## Discussion

There is limited information regarding the seroprevalence of leptospirosis in population from Delhi. Most cases reported from India are from the four major states i.e., Kerala, Gujarat, Tamil Nadu, and Maharashtra.<sup>[9,10]</sup> Leptospirosis is often not recognized or is erroneously mistaken for other diseases with similar symptoms. This study can help primary care physicians and other clinicians in better patient management and reducing their further transmission. In this study we have included patients with clinical criteria for leptospirosis, 6.47% of cases were seropositive for leptospirosis. The seropositivity rate observed in our study was much lower than studies from other parts of the country 17.8–40.5%.<sup>[11]</sup> Furthermore, another interesting observation that was noted is a significant declining trend of seroprevalence rate of leptospirosis from 26.90% in 2000–2010 and 20% in 2011–2014 to 6.47% in 2014–2018 ( $P$  value  $< 0.05$ ) in our referral tertiary care center which receives a significant number of patients with such illnesses [Figure 1].<sup>[8,12]</sup> This decrease may be attributed to several factors such as increase in awareness, improved hygienic practices, use of safe drinking water, and better socioeconomic condition. Gender variation in seroprevalence i.e., with higher antibody prevalence observed in males (80.13%,  $P < 0.05$ ) is in consistent with other studies.<sup>[13,14]</sup> The higher prevalence in young males is generally attributed to their more frequent outdoor activities. The seasonal variation was observed in this study, we observed higher seroprevalence rate of leptospirosis during monsoon season, which is in consistent with some of the earlier studies and higher rate of contamination may be implicated during monsoon season.<sup>[14]</sup> Furthermore, flooding, unprotected entry into water sports areas, contact with rodents and wild lives, and low educational status are the risk factors most commonly encountered for survival and transmission



**Figure 1: Decreasing trend of seroprevalence of leptospirosis infection**

of *Leptospira*. Seroprevalence rate was higher in people living and working in rural areas than urban areas in our study. This might be due to the rural population being more involved in agriculture activities and are more exposed to rodents as agriculture and animal-related activities are the main occupation in rural areas of India.<sup>[15,16]</sup> Our results are in line with previous published studies.<sup>[17,18]</sup> In our study, the commonest presentation was fever with or without rigors followed by jaundice in 80% of patients which was in concordance to the rate reported from South India.<sup>[19]</sup> However a study from Northern-eastern states reported headache as predominant symptoms (84.21%) followed by fever (73%).<sup>[20]</sup> The severe and unusual manifestation (neurological, cardiac, and pulmonary leptospirosis) are often missed which lead to delay in initiation of appropriate therapy and further progressed into complications. There is need to investigate cases in laboratory to confirm clinically suspected patients in order to initiate early treatment effectively. In our study, the patients were also looked for co-infections like typhoid, malaria, scrub typhus, and dengue. These co-existing infections may present diagnostic dilemmas. It is imperative that a high index of suspicion for the diseases is required particularly in endemic areas.

## Conclusion

We conclude that serological test like ELISA is useful for seroprevalence study to determine the problem load particularly in resource-limited countries. This can help in better patient management, reducing the transmission improving socioeconomic condition, and better hygienic practices. The seroprevalence rate has shown a significant fall over the years; however, leptospirosis still remains an important public health problem, which needs to be diagnosed to allow specific treatment. Considering the scarcity of information available in our country, more region/province-wise studies on seroprevalence of leptospirosis are required to improve our understanding of the actual burden. Further, more training and education of primary care physicians are required in primary care setting in this regard to understanding of this problem and its prevention.

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## Conflicts of interest

There are no conflicts of interest.

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