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**Original Article**

# Prevalence of Leptospirosis among Cases of Undifferentiated Febrile Illness reported to a Tertiary Care Teaching Hospital of Kashmir Valley

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**Abstract**
**Background:** *Leptospirosis is a zoonosis that is globally being recorded as an epidemic threat in developing countries. The spectrum of disease ranges from sub clinical infection to a severe syndrome of multiorgan dysfunction. We conducted this study with an aim to estimate the prevalence of Leptospirosisin cases of undifferentiated febrile illness.*
**Material and Methods:** *All patients presenting with undifferentiated fever of >38$^{o}$ C of less than two weeks duration and who lacked localization or organ-specific clinical features were included in the study. IgM antibodies against leptospira antigen were detected by Elisa.*
**Results:** *The prevalence of Leptospirosis among the cases was estimated to be 6.4% [CI : 5.1-7.8].The highest prevalence of Leptospirosis was found in the age group of 20-39 years (9.4%) followed by age group 40-59 years (4.5%). Leptospirosis was found to be more prevalent among females (7.5%) than males (5.6%) and those living in rural areas (6.4%).The age of the cases ranged from 6 years to 65 years. Male:Female ratio was found to be 1.6:1. Most common presenting complaints were headache (77.3%), fatigue (32.84%), vomiting (31.97%), arthralgia (29.06%), severe myalgia (26.16%), cough (15.11%), nausea (14.53%), hypertension (4.65%), diarrhea (4.36%), and skin necrosis (3.19%). Age group >60 years (4.3%) and age group 0-19 years (2.7%).*
**Conclusion:** *Our analysis suggest that the prevalence of Leptospirosis in our study is far less than compared to other states of India.*
**Keywords**: *Leptospirosis, Undifferentiated febrile illness, Zoonosis.*

## Introduction

Acute undifferentiated febrile illness (AUFI) is a standout amongst the most overwhelming difficulties a doctor encounters. It is defined as a fever that ordinarily does not stretch out past a fortnight and lacks localization or organ-specific clinical features. It is a diagnostic and therapeutic challenge to health workers especially in constrained asset settings[(1)]. The previous five years have seen coordinated endeavors to comprehend the etiology of undifferentiated febrile illnesses[(2)]. These diseases can be

undefined clinically. Also, the decision of empiric antibiotics relies upon the etiologic profile which is variable and is area dependent. Leptospirosis, a zoonotic infection is predominant in regions with substantial rural and agrarian lifestyle is one of the emerging causes of AUFI[3]. Leptospirosis has been perceived as an imperative rising global public health issue as a result of its epidemic capabilities and expanding occurrence in both developing and developed nations[4]. The range of illness varies from sub clinical disease to a serious disorder of multiorgan dysfunction portrayed by headache, fever, myalgia, jaundice, hepatomegaly and seizures[5]. Limited studies have been done regarding the prevalence Leptospirosis in India and as far as state of Jammu and Kashmir is concerned only few case reports are available. The present study, was therefore, planned with an aim to estimate the prevalence of Leptospirosisin cases of undifferentiated febrile illness. Such surveillance data would promote awareness of Leptospirosis among local physicians and increase the probability that individual patients with Leptospirosis would be identified promptly and receive appropriate therapy early in the course of their illness.

## Materials and Methods

**Study Design:** Cross-sectional study

**Study Setting:** Department of Microbiology at Sher-i-Kashmir-Institute of Medical Sciences.

**Study Period:** 18 months from June 2016 to December 2018.

**Sample Size:** The prevalence of Leptospirosis ranges from 30-60% in India. Taking minimum prevalence into consideration, and absolute error of 6% at 95% CI, and 20% non response rate, the desired sample size for the study was 307.

**Inclusion Criteria:** All patients in the age group of 6-65 years presenting with undifferentiated fever of >38$^{o}$ C of less than 2 weeks duration and who lacked localization or organ-specific clinical features.

**Exclusion Criteria:** Patients who were unable to cooperate, unable to give consent, at extremes of age and had severe comorbidities.

**Procedure:** Three ml of blood was collected in a plain vial. Serum was pipetted out after blood was centrifuged at 2000 RPM for 10 minutes, separated and kept at - 80ºC until further use. IgM antibodies against Leptospira antigen were detected by ELISA, the kit for which was procured from Nova Tech Immunodiagnostics, Germany. 100 µl of standard/controls and diluted samples were poured into their respective wells. Well A1 was left for substrate blank. The wells were covered with foil supplied in the kit and incubated for 1 hour at 37 ℃. After the incubation the wells were aspirated and were washed 3 times with 300 µl of washing solution. At the end the remaining fluid was removed by tapping strips on tissue paper. 100 µl of Leptospira anti-IgM conjugate into all wells except substrate blank and cover with foil. Incubated for 30 min at room temperature without exposing to sunlight. It was again washed with 300 µl of substrate solution and dried. 100 µl of TMB substrate was added and incubated at 15 minutes in the dark.100 µl of stop solution was added to each well and absorbance was read at 450 nm.

**Statistical Analysis:** Data was entered in Microsoft Excel spreadsheet 2007. Variables were analyzed for frequency and percentage. Categorical variables were analyzed using chi-square test, p-value <0.05 was considered significant at 95% CI. All analysis were done using SPSS V.20.0.

**Ethical Issues:** Written Informed consent was obtained from each participant after explaining him the objectives of the study. The study had no ethical issue related to animal or human experimentation.

## Results

During the study period we received a total of 344 patients who fulfilled the inclusion criteria. All gave consent and were included in the study. The response rate among the cases was 100%. The

prevalence of Leptospirosis among the cases was estimated. Among 344 cases, 22 (6.4%) [CI: 5.1-7.8] cases were found to be positive.(Table 1) Age wise distribution of Leptospirosis positive patients among the study population is described in Table 2.

The age of the cases ranged from 6-65 years. Most of the cases in the study group 159 (46.22%) were young adults belonging to the age group of 20-39 years, among which 15 (9.43%) were found to be positive for Leptospirosis. Moreover, 88 (25.58%) study subjects were between 40-59 years among which 4 (4.55) had Leptospirosis infection. The association between positiveness rate and age group among the study subjects was found to be statistically insignificant (p-value 0.186). The average age of the patients was 32.5 years with a standard deviation of 0.774 years**.** The study population comprised of two hundred and twelve males (61.6%) and one hundred and thirty-two females (38.4%). The association was found to be statistically significant. The highest prevalence of Leptospirosis was found among female 8.19%. Furthermore, majority of the study participants were from rural areas 278 (80.8%) but there was no such major difference between the Leptospirosis prevalence. The association was found to be statistically insignificant.[Table 3]. Table 4 shows the common symptoms prevalent among the studied subjects. Headache was found to be the most common symptom found among 266 (77.32%) study subjects, followed by being fatigue and vomiting among 113 (32.84%) and 110 (31.97%)studied subjects respectively.

**Table 1:** Prevalence of Leptospirosis among the studied population

| Leptospirosis | Frequency (n) | Percentage (%) | CI (95%) |
|---|---|---|---|
| Positive | 22 | 6.4 | 5.1-7.8 |
| Negative | 322 | 93.6 | |
| Total | 344 | 100 | |

**Table 2:** Age wise distribution of Leptospirosis positive patients among the study population

| Age (years) | Leptospirosis Present | Leptospirosis Absent | Total n (%) | Prevalence (%) | P-value |
|---|---|---|---|---|---|
| **0-19** | 2 | 72 | 74 (21.51) | 2.7 | 0.186 |
| **20-39** | 15 | 144 | 159 (46.22) | 9.4 | |
| **40-59** | 4 | 84 | 88 (25.58) | 4.5 | |
| **≥ 60** | 1 | 22 | 23 (6.68) | 4.3 | |

P-value<0.05% Significant

**Table 3:** Distribution of gender and place of residence of the study population

| Variable | Leptospirosis Present | Leptospirosis Absent | Prevalence (%) | P-value |
|---|---|---|---|---|
| **Gender** | | | | 0.099 |
| Male | 12 | 200 | 6.00 | |
| Female | 10 | 122 | 8.19 | |
| **Residence** | | | | 0.336 |
| Rural | 18 | 260 | 6.92 | |
| Urban | 4 | 62 | 6.45 | |

P-value<0.05% Significant

**Table 4:** Symptomology among the studied patients

| Symptom | Frequency (n) | Percentage (%) |
|---|---|---|
| Headache | 266 | 77.32 |
| Fatigue | 113 | 32.84 |
| Vomiting | 110 | 31.97 |
| Arthralgia | 100 | 29.06 |
| Severe Myalgia | 90 | 26.16 |
| Cough | 52 | 15.11 |
| Nausea | 50 | 14.53 |
| Hypertension | 16 | 4.65 |
| Diarrhea | 15 | 4.36 |
| Skin Necrosis | 11 | 3.19 |
| Renal Failure | 8 | 2.32 |
| Hemorrhage | 7 | 2.03 |
| Pneumonia | 6 | 1.74 |
| Hepatitis | 4 | 1.16 |
| Renal Failure | 2 | 0.58 |

## Discussion

The present study was thus undertaken to determine the prevalence of Leptospirosis in patients of undifferentiated febrile illness (UFI) in our hospital (Sher-i-Kashmir Institute of Medical Sciences). Patients were recruited from OPD, Medicine and Pediatrics ward. Our study population comprised of 80.8% (278) rural dwellers whereas 19.2% (66) patients were urban dwellers. The rural predominance of our study population maybe due to the agrarian lifestyle, poor hygiene practices, greater exposure to contaminated water of people living in villages. IgM ELISA was carried out to determine the prevalence of Leptospirosis in our study population which revealed that out of a total of three hundred and forty-four patients, 6.4 % (22) were positive 93.6% (322) tested negative. In a study conducted by Salim *et al*.(2017), in Columbia, it was found that out of a total of 69 patients of undifferentiated febrile illness, 39% (27) were found to have Leptospirosis.[6]Another study by H. Sahira *et al*. (2014), in Kerala revealed that, out of a total of 1924 patients presenting with undifferentiated febrile illness, 11.2% (220) tested positive for Leptospirosis by IgM- ELISA.[7] Manock (2009) in his study done in Ecuador (2009) found that, Leptospirosis comprised 13.2% of patients of undifferentiated febrile illness.[8]In contrast to this a study by Gowri Veligandla *et al* (2016) found that out of a total of 116 patients of AUFI there were no detected cases of Leptospirosis.[9] The highest prevalence of Leptospirosis amongst our study population was found in the age group of 20-39 years (21.4) followed by age group 40-59 years (12.1), age group >60 years (7.7) and lastly age group 0-19 years (6.5). The p-value was found to be statistically insignificant at 0.186, The prevalence of Leptospirosis as per gender in the study population demonstrated that higher prevalence of Leptospirosis was found in the female gender 7.5% as compared to the female gender 5.6%. The p-value was found to be statistically insignificant at 0.099. The female predominance of Leptospirosis in our study may be attributed to women here working in paddy fields during the rice harvesting season. In a study by Antony J. *et al.* (2007) 1,523 confirmed cases of Leptospirosis in a tertiary hospital in Kerela, comprised of 993 (65.20%) males and 530 (33.02%) females. The case fatality of Leptospirosis was 4.13%, and it was high in the age group 40-60 years in both sexes.[10] In our hospital, Rubeena Shaheen *et al.* (2006) carried out a study in which a total of 72 cases of PUO were included. Serum samples were sent to RMRC, Port Blair, for microscopic agglutination test (MAT) while the remaining portion of the samples were subjected to Lepto-Dipstick assay. Of the 72 studied cases, 43 were males and 29 females, predominantly in the age group of 21-40

yrs. Laboratory tests showed 23.35% (10/43) males and 10.34% (3/29) females to be positive for Leptospirosis. Results showed that 1 of the 15 urban (6.66%) and 14 of the 57 rural (24.56%) patients were positive for Leptospira antibodies respectively.[11]

**Conclusion**

Acute undifferentiated febrile illness (AUFI) though an entity relatively new as compared to pyrexia of unknown origin (PUO) is a clinical and microbiological predicament. So, it was not surprising that the majority of the cases in our study remained undiagnosed and would thus classify and true AUFI.Not only is our study is the first of its kind in the valley providing an insight in the etiology of AUFI, it will also raise awareness to disease which is not usually considered as differential diagnosis of AUFI. Leptospirosis has for long been overlooked in Kashmir valley and the results of this study provide substantial information to overturn this trend and commands clinicians to work hand in hand with microbiologists to unravel this diagnostic mystery.

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