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LEPTOSPIROSIS: A NEGLECTED DISEASE FROM NORTH INDIA

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ABSTRACT **Introduction:** Leptospirosis is a zoonotic disease caused by Leptospira interrogans and has been reported from various countries worldwide. As very few studies were conducted on leptospirosis from north India, this study was conducted to know the status of this disease in this region. **Material & Methods:** This retrospective hospital based study was conducted in the Department of Microbiology of a tertiary care super specialty teaching institute from north India for a period of two consecutive years. Blood specimens from acute febrile illness cases were tested for presence of IgM antibodies against Leptospira interrogans by rapid card (Leptocheck from TULIP) testing and ELISA (Leptospira IgM ELISA from PanBio). **Results:** Out of total 216 samples collected and included in this study, 40 were found to be positive for presence of IgM antibodies against Leptospira interrogans. Seropositivity for leptospirosis was observed to be 19%. Maximum number of patients were from economically productive age groups, 31-40 years of age group followed by 21-30 and 41-50 years of age groups. **CONCLUSION:** Leptospirosis was found to be a major cause of acute febrile illness from north India. It is neglected and under reported from most of the regions of India due to lack of clinician's suspicion. More studies with more samples are required on leptospirosis from this region to reach on final conclusion.

KEYWORDS : Leptospirosis, Acute Febrile Illness, Leptospira interrogans, Leptospira ELISA, MAT

INTRODUCTION:

Leptospirosis is a zoonotic disease caused by *Leptospira interrogans* and has been reported from various countries worldwide. The first report of a series of confirmed cases of leptospirosis that occurred in Andaman and Nicobar Island from India during 1929 was published in 1931 [1]. Cattle, buffaloes, horses, sheep, goat, pigs, dogs and rodents are common reservoirs of leptospires. Rodents were the first recognized carriers of leptospirosis. Prolonged carrier state is associated with rodents that can shed leptospires throughout their lifespan without clinical manifestations [2, 3]. Humans get infected through skin contact with water or soil containing urine from infected animals or consuming contaminated food or water [2].

It is widespread in southern, central, eastern and western India, where heavy monsoon, animal rearing practices and unplanned urbanization predispose to this infection [2, 3]. Though similar conditions exist in the north, reports of this disease from north India are few. Leptospirosis has been under-reported and under-diagnosed from India especially in north India due to lack of awareness of the disease and lack of appropriate laboratory diagnostic facilities. Combining clinical expertise and awareness with confirmatory laboratory back up dramatically increases the recognition of patients with leptospirosis [3]. According to a study conducted in Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow in 2001, the seroprevalence of leptospirosis was found to be 7% [4]. As very few studies were conducted on leptospirosis from north India, this study was conducted to know the seropositivity of leptospirosis from this region.

MATERIAL AND METHODS:

This prospective hospital based study was conducted in the Department of Microbiology of a tertiary care super specialty teaching institute from north India for a period of two years. Clinical samples from a total of 216 patients with acute febrile illness and clinically suspected leptospirosis were collected and processed.

Inclusion criteria:

Patients with fever of acute onset (less than 10 days) with one or more of the following signs/ symptoms:

(a) Cough with hemoptysis or unexplained breathlessness
(b) Bleeding tendency including subconjunctival hemorrhage
(c) Jaundice or laboratory evidence of liver dysfunction
(d) Signs of meningeal irritation

Exclusion criteria:

(a) Patients with chronic fever (more than 10 days)
(b) Patients who do not give consent

Personal data of patients along with detailed clinical history was obtained. Serum samples were tested by:

(c) Rapid card testing for *Leptospira* (Leptocheck by TULIP): Testing and interpretation for detection of IgM antibodies against *Leptospira* was performed according to manufacturer's instructions.

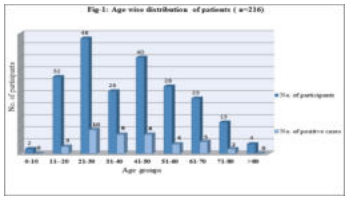
(d) ELISA Technique (*Leptospira* IgM ELISA by PanBio): ELISA testing and interpretation for detection of IgM antibodies against *Leptospira* was performed according to manufacturer's instructions.

(e) MAT (Microscopic Agglutination Test): All serum samples detected positive by either of the tests (rapid/ ELISA) were tested by MAT as a WHO gold standard and reference test for different serotypes/ serovars of *Leptospira* at WHO reference center for *Leptospira,* RMRC, (ICMR) Port Blair, Andaman and Nicobar Islands.

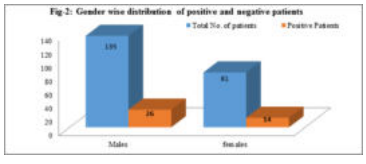
RESULTS:

In this study out of total 216 patients enrolled, 40 (19%) were observed positive by rapid card test, ELISA or MAT and 176 (81%) negative for leptospirosis.

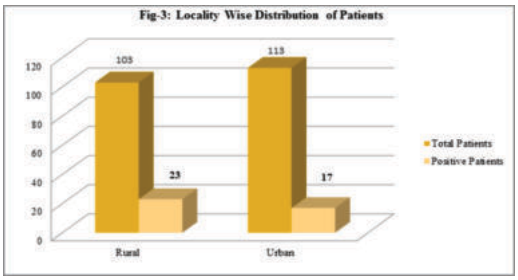
In this study maximum seropositivity (31.77%) was observed in the age group of 31-40 followed by almost equal seropositivity (20-22%) among age groups of 21-30, 41-50 and 61-70 years (Fig-1).



In this study 135 (62%) participants were males and 81 (38%) were females. Slightly more seropositivity was observed among males (19%), as compared to females (17%) (Fig-2).



In this study 48% participants were from rural and 52% were from urban locality. More seropositivity was observed in urban (20%) as compared to rural (17%) locality (Fig-3).



DISCUSSION:

Leptospirosis is an infectious disease caused by pathogenic leptospires. Leptospirosis is a common cause of acute febrile illness throughout the world. It is well documented as an endemic and epidemic zoonotic disease from all over the world including India. Humans get infected through cuts or abrasions of skin coming in contact with water or soil contaminated with urine from infected animals. Rarely transmission of leptospires can occur through indirect exposure of mucous membrane of nasal mucosa, oral cavity, and conjunctiva and after ingestion of contaminated food or water [2].

Leptospirosis remains one of the most common and most dreaded worldwide zoonotic infections [5, 6]. Related traditionally to certain socioeconomic or climatic conditions that favour endemicity in animal vectors and human exposure, it is generally confined to the developing parts of the world [6, 7]. It has been randomly reported from industrialized countries often as an imported disease following international travel to exotic destinations [7]. Mishima M et al in 2013 reported the first case in Japan of severe human leptospirosis imported from Vietnam [8]. In recent years, a new trend in human leptospirosis outbreaks has been observed related to recreational activities among the wildlife (a form of tourism that is becoming increasingly popular) and army expeditions, either for training or for combat-related purposes in similar environments [6, 9]. Awareness about the evolution of the global incidence of human disease is important for acknowledging the relative risks in international travel [6].

Leptospirosis is under-reported and under-estimated from all over the world especially from developing world including from north India, where factors for high incidence exist [6, 10]. The Seychelles islands possess the highest incidence of 432.1 per million population worldwide, with annually reported cases and incidence remaining more or less constant from 1988 onwards [10]. In India, leptospirosis is a major health problem related to the monsoons and poor sanitary conditions, with multiple epidemics reported. The Andaman and Nicobar Islands top the list of the most endemic areas of the world with incidence of 500 per million population as reported by Sharma S et al in 2006 from RMRC Port Blair [11].

Many studies revealed that leptospirosis is a major established cause of acute febrile illness from various parts of India especially south India. It was observed that prevalence of leptospirosis is higher in south Indian states as compared to north Indian. Prevalence in north Indian states was observed between 7% and 24% from very few studies as compared to prevalence of more than 50% from south Indian states. Rise in prevalence was also observed in recent past as compared to older studies from north India.

Seroprevalence of 5% was observed in a study conducted in PGIMER, Chandigarh (Sethi S. et al. 2003). Seroprevalence of 7% was reported in a study conducted in SGPGIMS, Lucknow (Manocha H. et al. 2004) [4]. In a study conducted at PGIMER, Chandigarh, seroprevalence of 11.7% in 2005 and 20.5% in 2008 was reported (Sethi S. et al. 2010) [12]. A seroprevalence of 20.45% was also reported in a study conducted at AIIMS, New Delhi (Chaudhry R. et al. 2017) [13].

In this study 19% of seropositivity was observed which is almost same as observed in other studies from north India in recent past. Analysis of older studies and this study along with other studies in recent past revealed a sustained rise in the seropositivity of leptospirosis. This may be due to increased awareness for leptospirosis among clinicians in this region leading to early diagnosis and treatment. Previously leptospirosis was underestimated and underdiagnosed due to lack of suspicion and awareness among clinicians.

Majority of the patients of leptospirosis were observed in 26-40 years of age as observed by Sethi S et al in 2003 [14]. About 65% patients of leptospirosis were reported in 21-50 years of age in another study conducted at PGIMER, Chandigarh (Sethi S. et al. 2010) [12]. In this study we observed a higher prevalence in the age group of 31-40, 21-30, 31-40 and 41-50 years. In this study we observed majority of the patients of leptospirosis (65%) in 21-50 years of age which was also reported in previous studies. This is probably due to occupational exposure as well outdoor recreational activities in this age group, as occupational as well as other outdoor and recreational activities are common in this group [15]. Due to the same reason the prevalence was observed to be very less in the extremes of age groups (□20 and >70 years) as compared to other age groups.

According to previous studies on leptospirosis more seropositivity was reported in males as compared to females. Males were 66% and females were 34% among leptospirosis cases in a study conducted at AIIMS, New Delhi (Chaudhry R et al. 2017) [13]. Among seropositive patients 59% males as compared to 41% females were also reported in a study from Chennai (Jacob SM et al. 2018) [16]. In our study we observed 65% males as compared to 35% females among all leptospirosis patients which are almost similar to the male preponderance as reported in previous studies. This difference in the seroprevalence between males and females is due to more outdoor and occupational activities leading to contact with animals and contact with contaminated environment in males. The male preponderance may be due to the fact males are more outgoing and spend more time in extracurricular activities (sports) outside their homes [16]. They may also spend more time playing games in contaminated water. Males are more commonly associated with recreational and agricultural exposure to contaminated environment [13, 16].

In this study slightly more seropositivity from urban areas was observed as compared to the rural areas. In this study major difference in the prevalence of leptospirosis among rural and urban localities was not observed as compared to previous studies. This higher prevalence in urban areas may be due to water logging during heavy rain falls and floods. Domestic or small mammals such as dogs, cats or rodents are also prevalent in urban areas. Favourable conditions for transmission of leptospires such as direct contact with infected animals, indirect contact with urine of infected animals and contact with contaminated environment are also present in urban localities. Indirect contact with contaminated water during recreational exposure (during taking bath in lakes and rivers and outdoor games) are also more common in urban community. History of recreational and outdoor activities such as taking bath in ponds and lakes, camping and outdoor games is important to explore rural and urban distribution of leptospirosis. The possibility of any other factor responsible for this unexpected rise in prevalence in urban people in this geographical area could not be denied. More studies are needed to know about the changing trend of leptospirosis in rural and urban populations.

CONCLUSION:

Leptospirosis is one of the important cause of acute febrile illness all over the world. Clinicians do not usually suspect and investigate for Leptospira due to lack of research data available on this subject from a particular region. General trend among physicians is only to investigate for usual causes of acute febrile illness such as dengue, enteric fever and malaria followed by classifying as viral fever if reports come negative. Clinical suspicion is more important to investigate for other unusual causes of acute febrile illness such as scrub typhus, leptospirosis and chikungunya etc.

ETHICAL CLEARANCE: This study was approved by institutional ethical committee.

CONFLICTS OF INTEREST: No conflicts of interest to disclose.
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