MEDWIN PUBLISHERS
Committed to Create Value for Researchers

Open Access Journal of Urology & Nephrology
ISSN: 2578-4676

# Leptospirosis One of the Risk Factor for Kidney Diseases

**Pati P[1]* and Rathore SK[2]**

[1]District Headquarter Hospital, India
[2]Khallikote University, India

***Corresponding author:** Pallabi Pati, District Headquarter Hospital, Berhampur, Ganjam, Odisha, India; Email: ricky_pati@yahoo.co.in

**Mini Review**
**Volume 8 Issue 1**
**Received Date:** January 04, 2023
**Published Date:** February 06, 2023
DOI: 10.23880/oajun-16000223

## Abstract

The disease leptospirosis is threatening both animals and humans. Leptospirosis can cause complications in multiple organs, including the kidneys early on, most often manifesting as tubulo-interstitial nephritis and tubular dysfunction. More than a million people are infected with leptospirosis every year, making it the most widespread zoonosis. Hotspots of leptospirosis and CKD are the agricultural intensive areas that are prone to flooding. Pallabi Pati Senior Research Fellow(SRF) Molecular Biology Division Regional Medical Research Centre(ICMR),Bhubaneswar. Lack of prompt treatment for acute leptospirosis can lead to chronic kidney damage and ultimately kidney failure. Because of the insidious nature for progression of CKD, the germs that cause it may be present in the kidney without causing any symptoms. Tubulointerstitial nephritis, interstitial fibrosis, and tubular atrophy are histologic findings of leptospirosis renal disease. Leptospirosis in adult male workers is associated with proximal tubule dysfunction, hypokalemia, and chronic kidney disease (CKD).

**Keywords:** Leptospirosis; Kidney Disease; Zoonosis

**Abbreviations:** CKD: Chronic Kidney Disease; ARDS: Acute Respiratory Distress Syndrome; MAT: Microscopic Agglutination Test; AKI: Acute Kidney Injury.

## Introduction

The zoonotic disease termed "Leptospirosis" is caused by the pathogenic bacterium *Leptospira interrogans* of the genus Leptospira. Leptospira interrogans (the pathogenic species) and Leptospira biflexa (a nonpathogenic species) are obligate aerobic spirochetes that can be found all over the world and are responsible for the zoonotic disease known as leptospirosis. There are approximately 210 serovariants within the L. interrogans complex, which consists of 23 serogroups. Leptospirosis is endemic in tropical regions, with epidemics breaking out every year around the time of the rainy season and in low-lying, flooded regions. It is a water-borne disease, and it can cause different kinds of clinical symptoms in humans. According to previous reports, this disease is generally found in poor and developing countries, but mostly in unhygienic environments. Rats are the major reservoir of this disease. This disease has a wide range of clinical symptoms such as headache, fever, diarrhea, vomiting, myalgia, rigors, nausea, and loss of appetite, and they appear suddenly after 2 to 26 days of incubation in 75% to 100% of patients. Jaundice and renal failure ("Weil's disease"), pulmonary hemorrhage, rhabdomyolysis, uveitis, acute respiratory distress syndrome (ARDS), optic neuritis, peripheral neuropathy, and myocarditis are major complications of leptospirosis. So the diagnostic process is a bit difficult due to the patient's unusual symptom constellation, and the disease must be treated systemically. It occurs everywhere. A systematic review and modelling study projected 1.03 million annual cases and 58,900 annual deaths. Leptospirosis infection spreads by contact with infected animal bodily fluids, such as blood, urine, tissues, and

organs, or by exposure of an open sore or mucosal surface to contaminated water. These are the two most common routes of transmission to humans [1].

The diagnosis can be made by microscopic agglutination test (MAT), immunochromatographic test, confirmatory test done by IgM ELISA, or polymerase chain reaction method. Leptospira can be extracted from blood samples at that time. After one to three days, symptoms may return in about 20% of patients, marking the beginning of the immune phase of the disease, which typically lasts anywhere from four days to a month. More serious symptoms, such as meningitis and uveitis, may appear in the later stages. The severity of leptospirosis is correlated with the magnitude of the host's humoral immune response, and IgM antibodies are frequently detected during this stage [2].

Vasculitis is caused by the infectious disease leptospirosis. Due to dehydration and the direct effects of the toxins, which damage the vascular endothelium and increase permeability, patients with the severe form can develop hemodynamic alterations secondary to hypovolemia. Clinical evidence and epidemiological studies are used to make a diagnosis, which is then confirmed by laboratory testing. Clinical diagnosis can be challenging and may lead to the misdiagnosis of the following conditions: Viruses and bacteria can cause meningitis, malaria, and hepatitis, while mosquitoes and other insects can spread diseases like dengue and Hantavirus hemorrhagic fever. Early and distinctive hypokalemia from leptospirosis can help with the diagnosis. When antibody titres are four times higher than the reference value, the results are considered positive. The International Society for Leptospirosis conducted a study on its accuracy and found a false-negative rate of 13% [3,4].

## The Kidneys are Involved in Leptospirosis

Leptospirosis is a leading cause of AKI in tropical regions where the disease is endemic. This occurrence varies depending on disease severity, age, and the definition of AKI. The prevalence of AKI can be so high that more than 20% of acute kidney injury (AKI) cases are caused by leptospirosis in some countries. [5,6]. According to one previous report, only 60 cases of leptospirosis were detected out of 6,777 severe AKI cases, with a prevalence of 0.89%.This percentage is typical of hospitals of a similar type in industrialised nations [3].

## Clinical Presentations Observed in Leptospiral Kidney Issues

Kidneys are the basic organ for urine excretion, blood filtration and reabsorption [7]. Leptospirosis' impact on the kidneys can range from being subclinical, with only mild proteinuria and urinary sediment abnormalities, to being severe, with acute kidney injury. Urinary sediment contains both leukocytes and red blood cells. When proteinuria is present, it typically falls below 1 g per 24 hours. Casts of granules and biliary pigments are also visible [5,3].

Rapid increases in serum urea and creatinine, as well as jaundice, are symptoms of acute kidney injury. Hyperbilirubinemia is associated with a severe form of kidney injury, one that is often accompanied by oliguria and anuria in the affected patient. Previous research has linked leptospirosis to non-oliguric AKI and hypokalemia in 41% to 45% of patients [8]. According to another study conducted by Viriyakosol, et al. [9], leptospiral AKI associated with hemorrhagic diathesis was observed in 80% of the 58 patients, liver failure in 72%, respiratory failure in 38%, circulatory failure in 33%, pancreatitis in 25%, and rhabdomyolysis in 5%.In severe leptospiral AKI cases, the normal blood pressure in the arteries is too low, and the hemodynamic status and alterations are similar to those in sepsis patients. Elevated plasma concentrations of aldosterone and antidiuretic hormone result from systemic vasodilation. Altogether, these symptoms cause reduced dieresis followed by renal vasoconstriction [10-12].

## Renal Failure Caused by Leptospirosis

The most common triad of fever, jaundice, and acute renal failure [13] is observed in patients with severe acute infections. Reports from histological findings of primarily acute tubulointerstitial nephritis and acute tubular necrosis characterise acute renal failure, which is characterised by proximal tubule dysfunction, hypokalemia, and non-oliguria [14].

As per Yang et al., from 1997 In Taiwan, leptospirosis is one of the major causes of a wide variety of organ failures; at least 10% of patients suffer from leptospirosis organ failure. Penicillin and tetracycline, when given promptly, are highly effective and have the potential to dramatically rescue patients from multi-organ failure [14,15]. In severe condition of kidney issues or renal injury patients are treated with renal replacement therapy, artificial kidneys as one of the treatment alternatives [16]. The clinician should monitor the patient and as per the advice the proper treatment may be initiated.

According to Riefkohl, et al. [17] and Yang, et al. 2.3-52.7% of the population at risk develops chronic leptospirosis, and only if leptospira persists inside the tubular lumen and interstitium does it lead to either acute kidney injury or asymptomatic renal colonisation with subtle clinical

symptoms [17,18]. In animals, chronic leptospiral kidney infection is associated with interstitial fibrosis and chronic tubulointerstitial nephritis.

Toll-like receptor-dependent pathways are important in leptospiral kidney disease. Tubular injury and inflammation are induced by Leptospira outer membrane proteins through a toll-like receptor-dependent pathway, which is followed by the activation of nuclear transcription factor kappa B and mitogen-activated protein kinases and the differential induction of chemokines and cytokines relevant to tubular inflammation [19]. A protein from the outer membrane of Leptospira bacteria has been linked to triggering the TGF-beta/Smad-associated fibrosis pathway, which results in the accumulation of extracellular matrix [20]. As a result, tubulointerstitial nephritis and fibrosis caused by leptospirosis serve as a model for studying the consequences of pathogen infection [21-25]. Toll-like receptors, in particular, may play a pivotal role as intermediaries.

Leptospirosis is diagnosed using clinical and epidemiological information, with confirmation from serology tests. The most common method of serology (called MAT) requires two blood samples to be taken two weeks apart. Antibody titers 4 times higher than the reference value for diagnosing acute leptospirosis are considered positive on the MAT. Tubulointerstitial nephritis is a hallmark of leptospirosis renal disease. Detection of leptospira DNA in kidney tissue or urine confirms the presence of acute or chronic carrier leptospirosis in animals method of serology (called MAT) requires two blood samples to be taken two weeks apart. Antibody titers 4 times higher than the reference value for diagnosing acute leptospirosis are considered positive on the MAT. Tubulointerstitial nephritis is a hallmark of leptospirosis renal disease. Detection of leptospira DNA in kidney tissue or urine confirms the presence of acute or chronic carrier leptospirosis in animals. Leptospiral nephropathy can be treated with appropriate antibiotics like penicillin or tetracycline [24,26-28].

## Conclusion

Early diagnosis will help the patient's recovery rate be faster, which will prevent the rate of transmission as well as disease progression. Cleanliness and hygiene practices are the major key factors to avoid this disease. Now-a-days, health facilities have improved a lot, which can help people progress with proper treatment. Early detection of Leptospirosis and prompt treatment can prevent organ and kidney failure caused by this disease.

## Author's Declaration

There is No conflict of interest

## Funding

No funds are received for the conceptualisation of this article.

## References

1. Costa F, Hagan JE, Calcagno J, Kane M, Torgerson P, et al. (2015) Global Morbidity and Mortality of Leptospirosis: A Systematic Review. PLoS Negl Trop Dis 9(9): e0003898.

2. Bharti AR, Nally JE, Ricaldi JN, Matthias MA, Diaz MM, et al. (2003) Leptospirosis: a zoonotic disease of global importance. Lancet Infect Dis 3(12): 757-771.

3. Daher ELD, Abreu KLSD, da Silva GBD (2010) Leptospirosis-associated acute kidney injury. J Bras Nefrol 32(4): 400-407.

4. Daher E, Zanetta DM, Cavalcante M, Abdulkader RC (1999) Risk factors for death and changing patterns in acute renal failure of leptospirosis. Am J Trop Med Hyg 61(4): 630-634.

5. Sitprija V, Rastegara A, Rocha H (1997) Tropical nephrology. In: Schrier RW, et al. (Eds.), Diseases of the Kidney. 6th (Edn.), Little Brown and Company, New York, pp: 2221-2268.

6. Sitprija V, Losuwanrak K, Kanjanabuch T (2003) Leptospiral nephropathy. Semin Nephrol 23(1): 42-48.

7. Pallabi P (2018) Some Information about the Morphology and Anatomy of the Human Kidney. Journal of Morphology and Anatomy 2(1): 1000109.

8. Seguro AC, Lomar AV, Rocha AS (1990) Acute renal failure of leptospirosis: Nonoliguric and hypokalemic forms. Nephron 55(2): 146-151.

9. Viriyakosol S, Matthias MA, Swancutt MA, Kirkland TN, Vinetz JM (2006) Toll-like receptor 4 protects against lethal Leptospira interrogans serovar icterohaemorrhagiae infection and contributes to in vivo control of leptospiral burden. Infect Immun 74(2): 887-895.

10. Yang CW, Wu MS, Pan MJ, Hong JJ, Yu CC, et al. (2000) Leptospira outer membrane protein activates NF- kB and downstream genes expressed in medullary thick ascending limb cells. J Am Soc Nephrol 11(11): 2017-2026.

11. Yang CW, WU MS, Pan MJ, Hsleh WJ, Vandewalle A, et al. (2002) The leptospira outer membrane protein LipL32 induces tubulointerstitial nephritis-mediated gene expression in mouse proximal tubule cells. J Am Soc

Nephrol 13(8): 2037-2045.

12. Siriwanij T, Suttinont C, Tantawichien T, Chusil S, Kanjanabuch T, et al. (2005) Haemodynamics in leptospirosis: effects of plasmapheresis and continuous venovenous haemofiltration. Nephrology (Carlton) 10(1): 1-6.

13. Yang CW (2007) Leptospirosis renal disease: understanding the initiation by Toll-like receptors. Kidney Int 72(8): 918-925.

14. Yang CW, Wu MS, Pan MJ (2001) Leptospirosis renal disease. Nephrol Dial Transplant 16(Suppl 5): 73-77.

15. Yang HY, Yen TH, Lin CY, Chen YC, Pan MJ, et al. (2012) Early identification of leptospirosis as an ignored cause of multiple organ dysfunction syndrome. Shock 38(1): 24-29.

16. Pati P, Rathore SK (2018) The Necessity of Human Kidney and Artificial Kidneys for the Human Health. Journal of Kidney 4(2): 1000166.

17. Riefkohl A, Rubio OR, Laws RL, McClean MD, Weiner DE, et al. (2017) Leptospira seropositivity as a risk factor for Mesoamerican Nephropathy. Int J Occup Environ Health 23(1): 1-10.

18. Yang HY, Hung CC, Liu SH, Guo YG, Chen YC, et al. (2015) Overlooked risk for chronic kidney disease after leptospiral infection: a population-based survey and epidemiological cohort evidence. PLoS Negl Trop Dis 9(10): e0004105.

19. Tian YC, Hung CC, Li YJ, Chen YC, Chang MY, et al. (2011) Leptospira santorosai Serovar Shermani detergent extract induces an increase in fibronectin production through a Toll-like receptor 2-mediated pathway. Infect Immun 79(2): 1134-1142.

20. Tian YC, Chen YC, Hung CC, Chang CT, Wu MS, et al. (2006) Leptospiral outer membrane protein induces extracellular matrix accumulation through a TGF-beta1/Smad-dependent pathway. J Am Soc Nephrol 17(10): 2792-2798.

21. Chang MY, Cheng YC, Hsu SH, Ma TL, Chou LF, et al. (2016) Leptospiral outer membrane protein LipL32 induces inflammation and kidney injury in zebrafish larvae. Sci Rep 6: 27838.

22. Hsu SH, Lo YY, Tung JY, Ko YC, Sun YJ, et al. (2010) Leptospiral outer membrane lipoprotein LipL32 binding on toll-like receptor 2 of renal cells as determined with an atomic force microscope. Biochemistry 49(26): 5408-5417.

23. Yang CW (2007) Leptospirosis in Taiwan – an underestimated infectious disease. Chang Gung Med J 30(2): 109-115.

24. Andrade L, Daher EDF, Seguro AC (2008) Leptospiral nephropathy. Semin Nephrol 28(4): 383-394.

25. Fanton DM, Quellard N, Fernandez B, Ratet G, Lamande SL, et al. (2014) Leptospira Interrogans induces fibrosis in the mouse kidney through Inos-dependent, TLR- and NLR-independent signaling pathways. PLoS Negl Trop Dis 8(1): e2664.

26. Day N (2022) Leptospirosis: Epidemiology, Microbiology, Clinical Manifestations, and Diagnosis. UpToDate. In: Post TW (Ed.), Up-to-date, Waltham, MA.

27. Victoriano AFB, Smythe LD, Gloriani-Barzaga N, Cavinta LL, Kasai T, et al. (2009) Leptospirosis in the Asia Pacific region. BMC Infectious Diseases 9: 147.

28. Yang CW (2018) Leptospirosis Renal Disease: Emerging Culprit of Chronic Kidney Disease Unknown Etiology. Nephron 138(2): 129-136.