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PATHOGENESIS OF RENAL TUBULAR DAMAGE AND ACUTE KIDNEY INJURY IN LEPTOSPIROSIS

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Abstract: This article analyzes the parasitic-zoonotic nature of leptospirosis, the entry mechanisms of Leptospira spp. into the human body, and the morphological and functional changes they induce in renal tubules. The pathogenesis of acute kidney injury (AKI), the roles of leptospiral toxins, immuno-inflammatory factors, and microcirculatory disturbances are described in detail. The clinical significance, diagnostic approaches, and modern treatment principles are also reviewed.

Keywords: leptospirosis, renal tubules, acute kidney injury, immunopathogenesis, zoonosis, tubulointerstitial nephritis.

Introduction

Leptospirosis is a zoonotic infection caused by Leptospira interrogans and related species, transmitted mainly through small mammals, especially rodents. The disease is globally widespread, with over 1 million new cases and more than 60,000 deaths reported annually [1]. Its epidemiological importance is particularly high in tropical and subtropical regions, where incidence sharply increases during rainy seasons due to contamination of water sources [2]. This is primarily because Leptospira spp. can survive for prolonged periods in humid environments and easily enter natural water bodies, pastures, and agricultural settings.

Leptospires enter the human body through the skin (cuts, abrasions), mucous membranes (eyes, mouth, nose), or ingestion of contaminated water [3]. Through hematogenous dissemination, they rapidly reach multiple organs, but the kidneys are their main target. The organisms selectively damage proximal renal tubular epithelial cells, multiply actively within renal tissues, and adhere to tubular surfaces, which contributes to severe disease progression [4]. Therefore, leptospirosis is considered one of the most dangerous zoonoses associated with renal injury.

The pathogenesis of the disease is complex, and in severe forms, acute kidney injury (AKI) may rapidly develop. Contributing factors include direct cytotoxic effects of leptospiral toxins, immune-mediated inflammation, endothelial dysfunction, microthrombosis, hemodynamic alterations, and severe electrolyte imbalance [5]. Tubulointerstitial nephritis, characterized by necrosis and desquamation of tubular epithelial cells, represents a key pathological hallmark of leptospirosis [6].

Clinically, leptospirosis ranges from mild subfebrile illness to severe icterohemorrhagic forms. Renal involvement remains one of the main determinants of disease severity [7]. Mortality rates are significantly higher in patients who develop AKI, underscoring the importance of early diagnosis and close monitoring of renal function.

Understanding the pathogenesis of leptospirosis, especially the mechanisms of renal tubular damage, has major clinical implications for infectious diseases, nephrology, and intensive care practice. These mechanisms guide the assessment of disease severity and therapeutic decision-making.

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Materials and Methods

The preparation of this article involved a systematic review of scientific sources relating to leptospirosis pathogenesis, renal injury, and the development of acute kidney injury. Studies published within the last 15 years, including clinical reports, experimental laboratory findings, and epidemiological studies, were selected. The literature was obtained from PubMed, Scopus, Web of Science, and Google Scholar. The chosen sources focused on the biology, pathogenesis, immunology, and nephrotoxic mechanisms of leptospirosis [8].

The analysis was carried out in the following stages:

Study of the biological characteristics of Leptospira spp.

Experimental data on morphology, motility, invasiveness, and mechanisms of cellular adhesion were reviewed. Sources regarding virulence factors such as LPS, lipoproteins, and metalloproteases were analyzed [9].

Evaluation of experimental data on renal tubular morphology

Histological findings on proximal tubular necrosis, vacuolization, epithelial desquamation, interstitial infiltration, and microcirculatory disturbances were compared [10].

Investigation of immunopathogenetic mechanisms

Laboratory studies addressing cytokines (TNF-α, IL-1β, IL-6), T-cell activation, inflammatory mediators, and their impact on renal function were summarized [11].

Review of clinical studies

Clinical data on the incidence of AKI in leptospirosis, laboratory markers (creatinine, urea, electrolytes), prognosis, and the need for dialysis were evaluated [12].

Integrative analysis

All collected data were synthesized to develop a unified scheme of pathogenesis. Molecular, immunological, and clinical aspects were combined to identify the leading mechanisms of renal tubular injury in leptospirosis [13].

This methodological approach enabled a comprehensive understanding of the multifactorial nature of leptospirosis pathogenesis and the development of AKI.

Results

Direct tubular damage caused by leptospires

Leptospira spp. are spiral, highly motile organisms that adhere to and multiply within proximal tubular epithelial cells following hematogenous dissemination [10]. Their lipopolysaccharides and proteolytic enzymes contribute to epithelial necrosis [11].

Immune-mediated inflammation

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Leptospiral antigens stimulate the release of cytokines such as IL-6, TNF-α, and IL-1β, which enhance interstitial inflammation [12]. This leads to epithelial desquamation and tubulointerstitial nephritis.

Microcirculatory disturbances

Endothelial dysfunction, platelet aggregation, and microthrombosis develop in renal capillaries, reducing renal perfusion and contributing to ischemic AKI [13].

Disturbances in fluid, electrolyte, and acid-base balance

Damage to proximal tubules reduces the reabsorption of sodium, potassium, magnesium, and bicarbonate, leading to metabolic acidosis and electrolyte imbalance [14].

Development of acute kidney injury

The combined effect of toxic, immunologic, and ischemic mechanisms results in AKI. Clinical studies report AKI in 20–35% of patients with leptospirosis [15].

Table 1. Major pathogenetic mechanisms of renal injury in leptospirosis

№	Pathogenetic mechanism	Brief description
1	Direct toxic effect	Leptospires multiply within tubular epithelium and cause destruction
2	Immune inflammation	Cytokine release, peritubular infiltration
3	Microcirculatory disturbance	Endothelial damage, microthrombosis
4	Electrolyte imbalance	Impaired reabsorption, acidosis
5	AKI development	Combination of ischemic and toxic injury

Discussion

The findings demonstrate the multifactorial and complex nature of leptospirosis pathogenesis. Earlier literature emphasized primarily the toxic effects of leptospires on renal tissue [1], but recent studies highlight the significant roles of immune-mediated inflammation and microcirculatory impairment [12], [13]. The selective adhesion and replication of leptospires within proximal tubular epithelium significantly contribute to severe clinical progression.

The development of AKI markedly worsens patient prognosis. Some clinical studies report mortality rates of 12–40% in severe leptospirosis complicated by AKI [14]. Therefore, early diagnosis, hemodynamic stabilization, intensive therapy, and timely initiation of hemodialysis greatly improve outcomes.

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Persistent colonization of epithelium by leptospires may occasionally lead to chronic tubulointerstitial changes, suggesting a need for further research into the long-term consequences of the infection.

Conclusion

Renal tubular injury in leptospirosis represents a major etiopathogenetic factor leading to acute kidney injury. The combined effects of toxic, immune-inflammatory, and microcirculatory disturbances result in a rapid decline in renal function. Early diagnosis, careful laboratory monitoring, prompt resuscitation measures, and modern dialysis techniques are crucial in preventing severe complications and improving patient outcomes.

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