SYSTEMATIC REVIEW

Leptospirosis in Children: A Systematic Review of Clinical and Laboratory Manifestations

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Abstract

Background: Leptospirosis is a bacterial infection causing health risks in tropical and subtropical regions. It presents in children with varying clinical symptoms, from flu-like to severe multi-organ involvement. Early diagnosis is crucial for effective management, but is challenging due to non-specific symptoms and laboratory findings. **Methods:** An effective literature search was conducted across various electronic databases (e.g., PubMed, Scopus, ScienceDirect) for studies published up to 2024. Studies were selected based on predefined inclusion criteria focusing on pediatric cases of leptospirosis and their clinical and laboratory features. **Results:** A total of 9 studies met the inclusion criteria. Across studies, males were predominantly affected, particularly from rural or peri-urban areas with significant environmental exposure, such as contact with contaminated water or infected animals. The most common clinical features included fever, fatigue, myalgia, and gastrointestinal symptoms (nausea, vomiting, abdominal pain), with conjunctival suffusion being a hallmark in specific cases. Laboratory abnormalities often included elevated C-reactive protein (CRP), leukocytosis, thrombocytopenia, and markers of kidney injury such as increased BUN and creatinine. **Conclusion:** Leptospirosis remains an important pediatric health issue. The disease presents with nonspecific symptoms, making early diagnosis challenging. Renal involvement is common complication Severe cases with neurological or hematological manifestations require urgent attention.

Keywords

Leptospirosis, Child, Signs and Symptoms, Clinical Laboratory Techniques

Introduction

Leptospirosis is a globally important zoonotic infection caused by pathogenic spirochetes of the genus *Leptospira* and is associated with significant morbidity and mortality, particularly in tropical and subtropical regions (1). The disease was first described by Adolph Weil in 1886, who reported a severe febrile illness characterized by jaundice, renal involvement, and hemorrhagic manifestations, later termed Weil's disease (2). The disease is endemic in regions such as South and

Southeast Asia, sub-Saharan Africa, and Latin America, with increased transmission associated with occupational exposure, poor sanitation, and contact with contaminated water (3).

Clinically, leptospirosis presents a broad spectrum ranging from asymptomatic infection to severe multi-organ dysfunction. The disease is typically described in two clinical forms: anicteric and icteric, both progressing through an initial septicemic phase followed by an immune phase. Mild cases often resemble influenza-like illness with fever, headache, and myalgia, whereas severe disease (Weil's syndrome) is characterized by jaundice, acute kidney injury, and hemorrhagic complications (4).

In India, leptospirosis was first reported in 1929 from the Andaman and Nicobar Islands, and since then, cases have been documented in both sporadic and epidemic forms across multiple states.

Diagnosis remains challenging due to non-specific clinical presentation and overlap with other febrile illnesses.

Objective: The present study aims to provide a structured synthesis of existing evidence on pediatric leptospirosis, focusing on epidemiology, clinical features, laboratory parameters, diagnostic approaches, treatment, and outcomes. The review also acknowledges inherent limitations, including heterogeneity, small sample sizes, and retrospective study designs, while attempting quantitative synthesis where feasible.

Material & Methods

A systematic review of the literature was performed in databases (PubMed, Scopus, and ScienceDirect) to identify studies on leptospirosis published up to December 2024. Studies including randomized controlled trials, cohort studies, case–control studies, cross-sectional studies, and case series reporting clinical, laboratory, and treatment details of diagnosed pediatric leptospirosis cases were included. In vitro studies, case reports, non-human studies, and studies lacking sufficient clinical data were excluded.

The inclusion criteria focused on patients aged <18 years diagnosed with leptospirosis and reported between January 1, 2016, and December 31, 2024. Studies were selected based on the availability of comprehensive clinical presentation, laboratory findings, and treatment outcomes.

The following search string was used: (leptospirosis OR leptospira OR "Weil's disease") AND (clinical OR epidemiology OR symptoms OR signs OR haemorrhagic OR neurological OR laboratory OR treatment OR penicillin OR doxycycline OR azithromycin) AND (children OR pediatric).

All retrieved records were imported into a reference management system, and duplicates were removed prior to screening. Title–abstract screening and full-text review were independently conducted by two authors. Inter-rater agreement between reviewers was assessed using Cohen's kappa coefficient to ensure consistency in study selection. Discrepancies were resolved through discussion and consensus.

The included studies' data (epidemiology, clinical features, laboratory parameters, treatment, and outcomes) were extracted into a pre-defined data extraction sheet. Data extraction was performed independently by two reviewers and cross-verified for accuracy.

Statistical analysis was conducted to calculate pooled proportions for the included variables using appropriate descriptive methods. All analyses were performed by MV, and results were verified for consistency.

The review protocol was not registered in PROSPERO; this has been acknowledged as a limitation.

Results & Discussion

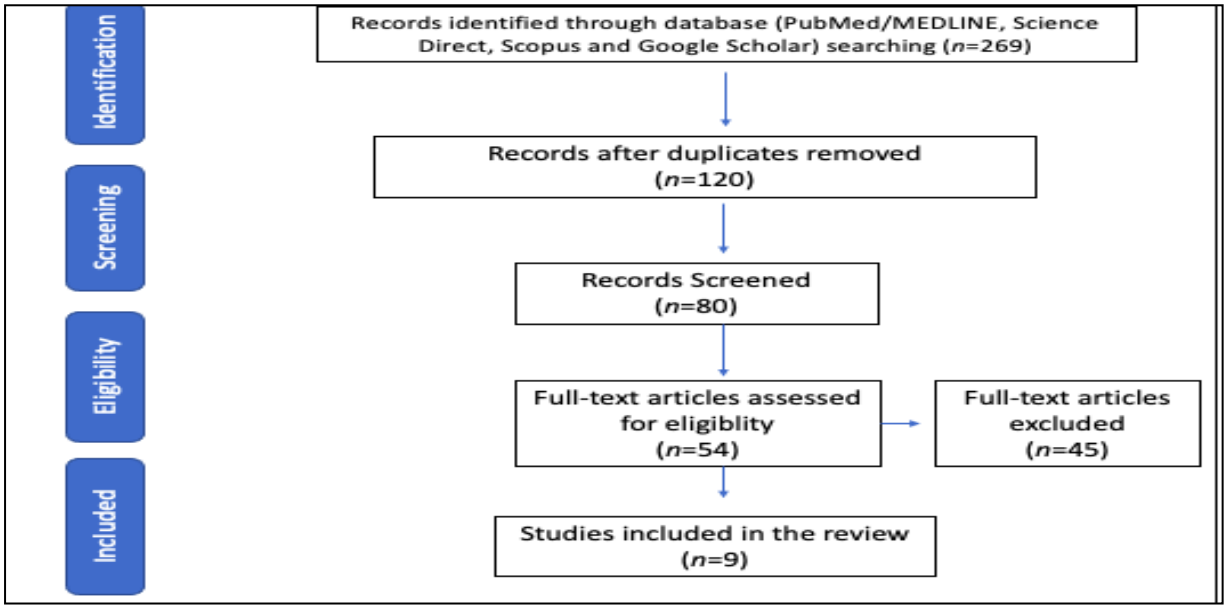
Included Studies: Our electronic search identified 269 records, of which duplicates were removed and 88 articles were screened through full-text evaluation. An additional six studies were identified through manual reference screening, resulting in a total of 94 studies assessed for eligibility. Finally, 9 studies met the predefined inclusion criteria and were included in the review (Figure 1).

Among the excluded studies, 28 were excluded due to lack of specific clinical or laboratory outcomes related to pediatric leptospirosis, 24 did not include pediatric patients or failed to

report age-specific data, and 8 involved mixed populations without separate analysis for pediatric cases. Additionally, 5 studies were excluded as they focused on non-leptospirosis febrile illnesses, 3 studies had insufficient sample size (<10 pediatric patients), and 3 studies did not clearly specify diagnostic criteria for leptospirosis.

These exclusions were applied to ensure methodological consistency and relevance to the pediatric population, although they may contribute to a reduced number of included studies, which has been acknowledged as a limitation.

Figure 1: PRISMA flow chart showing literature search process.



Characteristics of Involved Studies: The included studies collectively examine the epidemiological, clinical, and laboratory features of pediatric leptospirosis across diverse geographic regions, with notable variation in study design, sample size, and duration of data collection. The majority of studies were retrospective, while a smaller number employed prospective designs, reflecting methodological diversity in the available evidence.

Jahan et al. (2021) conducted a prospective study over one year (January–December 2018) involving 70 pediatric patients in Uttar Pradesh, India (5). In contrast, Orhan and Elci (2024) performed a retrospective analysis in Southeast Turkey (2020–2022), including 36 cases of leptospirosis (6). De Souza et al. (2022) evaluated the epidemiological profile of 101 pediatric patients in Brazil (7), whereas Tomari et al. (2018) analyzed national surveillance data from Japan (2003–2015) (8), comprising 44 pediatric cases. Aygün et al. (2016) reported five cases associated with rodent exposure in Turkey (9), while De Thomasis et al. (2022) examined 21 cases from France and Reunion Island between 2008 and 2020 (10).

Across the included studies, male predominance was consistently observed (7,5,8), with most cases originating from rural or peri-urban settings. The majority of patients had environmental or occupational exposure, particularly involving contact with contaminated water or infected animals. The pediatric population ranged from 0 to 18 years, with some studies focusing specifically on younger children (0–12 years), while others included adolescents.

The duration of studies varied considerably, with some spanning multiple years and the longest extending up to 12 years (11). Commonly reported risk factors included exposure to contaminated water, animal reservoirs, and rural environmental conditions.

Table 1: Characterstics of involved studies.

Author/Year	Gender		Location		Mean Age	Age wise		
	M	F	Urban	Rural		0-6	7-12	13-18
Jahan et al. (2021) (9)	54 (77.1%)	16 (22.9)	42.9	57.1	-	48.6	51.4	-
Orhan & Elci, (2024) (3)	36 (100%)	0	8	92	15	-	-	-
Aygün et al. (2016) (20)	3 (60%)	2 (40%)						
de Souza et al. (2022) (4)	12 (92.3%)	1 (7.7%)	100%	0%				
Doneray et al. (2023) (10)	1 (100%)	-	-	100%	7	-	100%	-
Kay-ann, (2021) (12)	72 (84.7%)	13 (15.3%)	-	-	-	7.1	38.8	54.1
Singh et al. (2024) (13)	-	1 (100%)	-	-	8	-	1 (100%)	-
Tomari et al. (2018) (18)	40 (91%)	4 (9%)			14			
De Thomasis et al. (2022) (19)	18 (85.7%)	3 (14.3%)	-	-	13.4±3.4	-	-	-

Table 2: Clinical features in paediatric patients diagnosed with leptospirosis.

Author/Year	N	Fever	Cough	Headache	Chills	Myalgia	Bleeding	Conjunctival suffusion	Jaundice	Abdominal Pain	Renal involvement	Vomiting	Rash	Diarrhea
De Thomasis et al. (2022) (19)	21	95%				71%								
Aygün et al. (2016) (20)	5	80%		20%		20%			20%			20%		
Jahan et al. (2021) (9)	70		28.6%	28.6%	28.6%	14.3%	--	1.4%	7.1%	14.3%		21.4%	1.4%	
Orhan & Elci, (2024) (3)	36	75%		53%		50%				28%		75%		11%
de Souza et al. (2022) (4)	101	100%		77%		61.5%		46.1%	23.1%		7.7%	77%		46.1%
Doneray et al. (2023) (10)		Yes		Yes		Yes		Yes	Yes			Yes	Yes	
Kay-ann, (2021) (12)	85	70.6%		1.2%	2.4%		77.6%	1.2%	1.2%	7.1%		4.7%		
Singh et al. (2024) (13)	1	Yes		Yes								Yes		
Tomari et al. (2018) (18)	44	96%		14%		52%		52%	14%		25%		2%	

Table 3: Laboratory parameters of pediatric patients with leptospirosis.

Author/Year	N	TLC ↓	TLC ↑	AST ↓	AST ↑	ALP↑	CRP↑	Bil↑	Plt	Cr↑
Orhan & Elci, (2024) (3)	36				47%		61%	44%		8%
Aygün et al. (2016) (20)					20%			20%		80%
Doneray et al. (2023) (10)	1		Yes			Yes	Yes	Yes		Yes

Author/Year	N	TLC ↓	TLC ↑	AST ↓	AST ↑	ALP↑	CRP↑	Bil↑	Plt	Cr↑
Kay-ann, (2021) (12)	85				32.6%			44.4%		60%
Singh et al. (2024) (13)	1									
De Thomasis et al. (2022) (19)										Yes

Table 4: Details of methods used for diagnosis of leptospirosis in the included studies.

Author/Year	MFC	DGM	IgM ELISA	Rapid	MAT	PCR	Culture
Jahan et al. (2021) (9)	-	-	Yes	-	Yes	Yes	-
Orhan & Elci, (2024) (3)	-	-	-	-	Yes	Yes	-
de Souza et al. (2022) (4)	-	-	Yes	-	Yes	Yes	-
Kay-ann, (2021) (12)	-	-	-	-	Yes	-	-
Doneray et al. (2023) (10)	-	-	-	-	-	Yes	-
Singh et al. (2024) (13)	-	-	Yes	-	-	Yes	-
Tomari et al. (2018) (18)	-	-	Yes	-	Yes	Yes	Yes
Aygün et al. (2016) (20)	-	-	Yes	-	-	-	-

Table 5: Drugs used in different studies used in patients with leptospirosis.

Author/Year	Third-generation cephalosporins (ceftriaxone or cefotaxime) + doxycycline	Third-generation cephalosporins alone	Doxycycline	Amoxicillin-clavunate	doxycycline and ciprofloxacin	methyl prednisolone	Not using Antibiotics	Penicillin
Orhan & Elci, (2024) (3)	44%	25%	19%	3%	3%		6%	
Aygün et al. (2016) (20)								100%
Singh et al. (2024) (13)						Yes		
De Thomasis et al. (2022) (19)		Yes		Yes				

Table 6: Organ Involvement in pediatric patients with Leptospirosis.

Author/Year	Respirators alterations	Cardia alterations	Renal Failure	Meningism	Liver Dysfunction	Eye
de Souza et al. (2022) (4)	23.1%	15.4%	7.7%	7.7%		
De Thomasis et al. (2022) (19)	-	-	86%	-	-	
Doneray et al. (2023) (10)			Yes	Yes	Yes	
Singh et al. (2024) (13)						Yes
Tomari et al. (2018) (18)			Yes	Yes	Yes	
Kay-ann, (2021) (12)					Yes	

Clinical Features: Clinical manifestations reported across studies demonstrate considerable overlap and non-specific presentation. The most frequently observed symptoms include fever, fatigue, myalgia, and gastrointestinal disturbances such as nausea, vomiting, and abdominal pain.

Jahan et al. (2021) reported fever, chills, myalgia, headache, and abdominal pain as predominant clinical features (5). Similarly, Orhan and Elci (2024) identified fatigue, fever, and nausea/vomiting as the most common presenting symptoms (6). De Souza et al. (2022) described largely nonspecific and self-limiting clinical presentations among pediatric cases (7).

Tomari et al. (2018) documented fever (95%), myalgia (52%), and conjunctival suffusion (52%), highlighting conjunctival suffusion as a characteristic feature of pediatric leptospirosis (8). In addition, De Thomasis et al. (2022) reported fever (95%), myalgia (71%), and gastrointestinal symptoms (76%) as the most prevalent clinical manifestations in cases from France and Reunion Island (10).

Laboratory Parameters: Laboratory findings across studies indicate significant variability but consistent evidence of inflammatory and renal involvement in pediatric leptospirosis. Common abnormalities included elevated C-reactive protein (CRP), leukocytosis, neutrophilia, platelet alterations (thrombocytosis or thrombocytopenia), and impaired renal function markers such as elevated blood urea nitrogen (BUN) and creatinine levels.

Orhan and Elci (2024) reported marked elevation of CRP, with 61% of patients showing highly positive levels (>100 mg/L), indicating a strong inflammatory response (6). Jahan et al. (2021) demonstrated variable diagnostic positivity, with IgM ELISA (10%), MAT (5.7%), and PCR (4.3%), reflecting differences in diagnostic sensitivity and timing (5).

Tomari et al. (2018) identified leukocytosis, neutrophilia, thrombocytosis, and elevated renal parameters (BUN and creatinine) as common laboratory findings (8). In contrast, De Thomasis et al. (2022) reported thrombocytopenia in 81% of cases and a high prevalence of acute kidney injury (86%), including oligoanuria in 19% of patients, highlighting severe renal involvement (10).

Additional biochemical abnormalities reported by de Souza et al. (2022) (7) included hypophosphatemia, hypokalemia, and tubular proteinuria, further supporting the presence of renal dysfunction and electrolyte imbalance in affected children.

Details of Methods Used for Diagnosis: Leptospirosis is frequently underdiagnosed due to its non-specific clinical presentation, with the majority of cases presenting as undifferentiated febrile illness, while classical manifestations such as jaundice, renal failure, and pulmonary hemorrhage (Weil's disease) are less common. As a result, laboratory confirmation remains essential, as clinical features alone are often insufficient for diagnosis.

Diagnostic approaches across the included studies demonstrated considerable variability, encompassing serological, molecular, and surveillance-based methods. Jahan et al. (2021) utilized IgM ELISA, Microscopic Agglutination Test (MAT), and PCR, with MAT and PCR providing higher specificity for confirmation (5). Orhan and Elci (2024) incorporated laboratory indicators such as elevated C-reactive protein (CRP) as supportive diagnostic evidence (6).

De Souza et al. (2022) identified cases based on World Health Organization (WHO) diagnostic criteria using notification data (7), whereas De Thomasis et al. (2022) confirmed cases through laboratory-based diagnosis in a multicenter retrospective analysis (10). Tomari et al. (2018) relied on national surveillance data comprising laboratory-confirmed cases (8).

Diagnostic strategies varied according to regional resource availability, with molecular techniques such as PCR used in certain settings, while others relied primarily on serological testing or clinical criteria. Additionally, Singh et al. (2024) employed advanced diagnostic modalities including MRI, visual evoked potential testing, and ophthalmological evaluation to identify leptospirosis-associated complications such as optic neuritis (12).

Drugs Used in Different Studies: Antibiotic therapy constituted the primary treatment modality across the included studies, with most patients demonstrating a favorable clinical response. De Thomasis et al. (2022) reported the use of amoxicillin and third-generation cephalosporins in accordance with established treatment guidelines (10). Aygün et al. (2016) administered high-dose penicillin, resulting in complete recovery within 10 days among all reported cases (9).

Although Jahan et al. (2021) did not specify detailed treatment regimens, the study emphasized the importance of early diagnosis and timely initiation of therapy in improving clinical outcomes (5). Across studies, no evidence of antimicrobial resistance or treatment failure was reported.

In addition to antimicrobial therapy, supportive management played a crucial role, particularly in patients with systemic involvement. This included fluid resuscitation, electrolyte correction (e.g., hypokalemia), and management of hematological abnormalities such as thrombocytopenia, reflecting the need for a multidisciplinary approach in moderate to severe cases.

Organ Involvement: Organ involvement in pediatric leptospirosis demonstrates a predominant multisystem pattern, with renal complications being the most frequently reported. De Thomasis et al. (2022) observed acute kidney injury in 86% of patients, with 19% developing oligoanuria, although none required dialysis and overall renal outcomes were favorable (10). Similar trends of renal involvement were reported by Jahan et al. (2021), although specific prevalence rates were not detailed (5). Tomari et al. (2018) further supported these findings, identifying elevated creatinine and blood urea nitrogen (BUN) as key indicators of renal dysfunction (8).

Beyond renal involvement, leptospirosis also demonstrated neurological and systemic complications. Singh et al. (2024) reported a rare case of bilateral optic neuritis, highlighting potential central nervous system involvement, including complications such as aseptic meningitis and visual impairment (12).

The multisystem nature of the disease was further emphasized by Aygün et al. (2016), who described a case of secondary hemophagocytic syndrome following rodent exposure, indicating severe immune-mediated complications (9).

Conclusion

Leptospirosis represents a significant yet under-recognized pediatric infection with diverse clinical manifestations and substantial diagnostic challenges. The disease commonly presents with non-specific symptoms such as fever, myalgia, and gastrointestinal disturbances, often mimicking other febrile illnesses and contributing to underdiagnosis.

Laboratory findings consistently indicate inflammatory response and renal involvement, with abnormalities such as elevated CRP, leukocytosis, thrombocytopenia, and acute kidney injury being frequently observed. Diagnosis relies primarily on serological and molecular methods, although variability in diagnostic approaches across regions contributes to heterogeneity in reported outcomes.

Renal involvement emerges as the most common complication, while neurological and multisystem manifestations highlight the severity of the disease in certain cases. Early diagnosis and timely initiation of appropriate antibiotic therapy, along with supportive care, are critical for improving clinical outcomes.

However, the available evidence is limited by heterogeneity, small sample sizes, and predominance of retrospective studies, underscoring the need for well-designed prospective studies and standardized diagnostic approaches to better understand pediatric leptospirosis and improve patient management.

Authors Contribution

MV: Conception and design of the work, Drafting the work, Supervision, Accountability of the work. **RV:** Conception and design of the work, Drafting the work, Supervision, Accountability of the work

Financial Support and Sponsorship

Nil

Conflict of Interest

There are no conflicts of interest.

Declaration Of Generative AI And AI Assisted Technologies In The Writing Process

The author has not used any generative AI/AI assisted technologies in the writing process.

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